COMPLEX ADAPTIVE INTELLECTUAL PROPERTY AND BIOMEDICAL INNOVATION SYSTEMS

Bridging the Gap between Law and Science and Understanding the Role of Agents and Openness in Systems' Reform

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ABSTRACT

This dissertation applies complex adaptive systems (CAS) theory to study the interaction and coevolution of intellectual property (IP) and biomedical innovation systems and focuses on agents building these systems, especially in developing countries. It combines legal and policy analysis and insights from behavioural science to investigate the challenges and opportunities to understand and reform these systems to promote access to knowledge and follow-on innovation through bottom-up approaches.

Multiple niches' combination results in a complex biomedical innovation ecosystem that relies on the diversity of agents and their behaviours to thrive. This dissertation studies the hypothesis that clarifying how and why IP and biomedical innovation systems (law and science) interact and coevolve enables tailored co-design and reform to promote access to knowledge and innovation in these systems. Identifying commonalities—shared features and principles—between these systems and improving agents' comprehension about them may uncover new pathways for joint reform and harness the complexity within these systems.

In the coevolutionary story of complex adaptive IP and biomedical innovation systems, openness emerges as a critical element to success. The study of interactions and agents' emergent behaviours (academics, researchers, and legal experts) at the bottom layers of these CAS organizational frameworks guides the evaluation of openness. This research aims to inform law and policy-making processes, lead to experimentation of new biomedical research and development (R&D) models and legal innovation to regulate them, promote agent-centred evaluations and bottom-up reforms in these systems, especially in Brazil and other developing countries.

RÉSUMÉ

Cette thèse applique la théorie de systèmes complexes adaptatifs (SCA) afin d'analyser la coévolution et l'interaction entre la propriété intellectuelle (PI) et les systèmes d'innovation biomédicale à partir de la perspective d'agents qui prennent part ou travaillent dans de tels systèmes, en particulier dans les pays en développement. Elle combine les sciences comportementales et l'analyse juridique pour évaluer les défis et les opportunités pour comprendre et réforme ces systèmes dans l'objectif de promouvoir l'accès au savoir et le suivi des innovations dans ces pays.

La combinaison de plusieurs niches aboutit à la création d'un écosystème d'innovations biomédicales complexe qui dépend, pour prospérer, de la diversité d'agents et des comportements de ces derniers. Cette thèse teste l'hypothèse selon laquelle clarifier comment et pourquoi le droit et la science interagissent et co-évoluent permet la co-conception de PI et de systèmes d'innovation biomédicale (droit et science) qui promouvraient de manière plus efficace l'accès au savoir et l'innovation. Identifier les traits communs—caractéristiques et objectifs partagés—entre ces systèmes et améliorer la compréhension que les agents en ont pourraient révéler de nouvelles voies de reformes communes et exploiter maîtriser la complexité qui existe à l'intérieur de ces systèmes.

Dans l'histoire co-évolutive de la PI complexe adaptative et des systèmes d'innovation biomédicale, l'ouverture apparaît comme un élément essentiel du succès de ces systèmes. L'évaluation de l'ouverture et cette thèse en général sont guidée par l'étude des interactions et des comportements des agents (académiques, chercheurs et experts légaux) situés à l'échelon le plus bas des structures organisationnelles de ces systèmes. Cette recherche vise à informer les processus d'élaboration de lois et politiques, à mener de nouvelles recherches afin de développer de nouveaux modèles biomédicaux de recherche et développement (R&D) et favoriser l'innovation juridique em ce qui a trait à leur régulation, ainsi qu'à promouvoir, dans ces systèmes, des évaluations centrées sur les agents et des reformes conçues à partir de la base, particulièrement au Brésil et dans les pays en développement.

RESUMO

Esta dissertação aplica a teoria dos sistemas adaptativos complexos (SAC) para estudar a interação e coevolução dos sistemas de propriedade intelectual (PI) e inovação biomédica e foca a análise nos agentes que constroem esses sistemas, especialmente em países em desenvolvimento. Combina análises jurídicas e de políticas e percepções da ciência comportamental para investigar os desafios e oportunidades para compreender e reformar esses sistemas para promover acesso ao conhecimento e à inovação por meio de abordagens 'bottom-up.'

A combinação de vários nichos resulta em um complexo ecossistema de inovação biomédica que depende da diversidade de agentes e seus comportamentos para prosperar. Esta dissertação estuda a hipótese de que esclarecer como e por que os sistemas de PI e inovação biomédica (direito e ciência) interagem e coevoluem permite co-projetá-los e reformá-los para promover o acesso ao conhecimento e à inovação. Identificar semelhanças—características e princípios comuns—entre esses sistemas e melhorar a compreensão dos agentes sobre eles pode indicar novos caminhos para reformas conjuntas e meios de se beneficiarem da complexidade desses sistemas.

Na história coevolucionária de sistemas adaptativos complexos de PI e inovação biomédica, a abertura ('openness') aparece como um elemento crítico para o sucesso desses sistemas. O estudo das interações e comportamentos emergentes dos agentes (acadêmicos, pesquisadores e juristas) nas camadas inferiores das estruturas organizacionais nesses SAC orienta o estudo da abertura. Esta pesquisa visa informar processos legislativos e de formulação de políticas, conduzir à experimentação de novos modelos biomédicos de pesquisa e desenvolvimento (P&D) e inovação jurídica para regulá-los e, promover avaliações centradas em agentes e abordagens 'bottom-up' para reformas nesses sistemas, especialmente no Brasil e outros países em desenvolvimento.

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To my parents. To Sebastião, who is deeply missed and loved and is always in my thoughts and heart. To Terezinha, for her unconditional love and support.

LIST OF ACRONYMS[1]

ABM	Agent-Based Model
ABPI	Association of the British Pharmaceutical Industry
AI	Artificial Intelligence
Anvisa	Agência Nacional de Vigilância Sanitária / National Health Surveillance Agency (Brazil)
AMR	Antimicrobial Resistance
APPMS	Agenda de Prioridades de Pesquisa do Ministério da Saúde / Ministry of Health Research Priority Agenda (Brazil)
ARV	Antiretroviral
AUTM	Association of University Technology Managers
BITs	Bilateral Investment Treaties
BoP	Bottom or Base of the Pyramid[2]
BRICS	Brazil, Russia, India, China, and South Africa
CAS	Complex Adaptive System / Complex Adaptive Systems
CAPES	Coordenação de Aperfeiçoamento de Pessoal de Nível Superior / Coordination of the Improvement of Higher Level Personnel (Brazil)
CDB	Convention on Biological Diversity
CEWG / WHO	Consultative Expert Working Group on Research and Development: Financing and Coordination / World Health Organization
CIS	Complexo Industrial da Saúde / Industrial Complex of Health (Brazil)

[1] For terms that are translated from Portuguese, I opted to keep the acronym as it is in Portuguese. Those institutions and regulations that originate in Brazil have a reference in brackets indicating this is the case.

[2] See: Gillian Hadfield, *Rules for a Flat World: Why Humans Invented Law and How to Reinvent It for a Complex Global Economy*, 1 edition ed (New York, NY: Oxford University Press, 2016) c 12.

CNPq	Conselho Nacional de Desenvolvimento Científico e Tecnológico / National Council of Scientific and Technological Development (Brazil)
DECIIS/SCTIE/MS	Secretaria de Ciência, Tecnologia e Insumos Estratégico Science, do Ministério da Saúde / Technology and Strategic Inputs Secretary of the Ministry of Health (Brazil)
DNA	Deoxyribonucleic Acid
DND*i*	Drugs for Neglected Diseases
Embrapii	Empresa Brasileira de Pesquisa e Inovação Industrial / Brazilian Agency for Industrial Research and Innovation (Brazil)
ENPI	Estratégia Nacional de Propriedade Intelectual / National Intellectual Property Strategy (Brazil)
ENCTI	Estratégia Nacional de Ciência, Tecnologia e Inovação (ENCTI
EU	European Union
FAIR Data Principles	Findable, Accessible, Interoperable, and Reusable Data Principles
FAPESP	Fundação de Amparo à Pesquisa do Estado de São Paulo / São Paulo Research Foundation (Brazil)
FDA	Food and Drug Administration
FORMICT	Formulário para Informações sobre a Política de Propriedade Intelectual das Instituições Científicas, Tecnológicas e de Inovação do Brasil / Form for Information on the Intellectual Property Policy of Scientific, Technological and Innovation Institutions in Brazil (Brazil)
Fiocruz	Fundação Oswaldo Cruz / Oswaldo Cruz Foundation (Brazil)
FORTEC	Fórum Nacional de Gestores de Inovação e Transferência de Tecnologia / National Forum of Innovation and Technology Transfer Managers (Brazil)
FTAs	Free Trade Agreements
GALF	Global Access License Framework
GDP	Gross domestic product

GII	Global Innovation Index
GTCA	Grupo de Trabalho em Ciência Aberta da Fiocruz / Fiocruz Working Group on Open Science (Brazil)
HGP	Human Genome Project
HIV/AIDS	Human Immunodeficiency Virus / Acquired Immune Deficiency Syndrome
IBICT	Instituto Brasileiro de Informação em Ciencia e Tecnologia / Brazilian Institute of Information in Science and Technology (Brazil)
IBGE	Instituto Brasileiro de Geografia e Estatística / Institute of Geography and Statistics (Brazil)
ICTs	Information and Communication Technologies
ICTs	Instituições Científicas e Tecnológicas / Science and Technological Institutions
ICTSD	International Centre for Trade and Sustainable Development
INCTs	Institutos Nacionais de Ciência e Tecnologia / National Science and Technologies Institutes (Brazil)
INN	International Non-Proprietary Name
INPI	Instituto Nacional de Propriedade Industrial / National Institute of Industrial Property (Brazil)
IP	Intellectual Property
IPEA	Instituto de Pesquisa Econômica Aplicada / Institute for Applied Economic Research (Brazil)
IPRs	Intellectual Property Rights
IT	Information Technology
LGPD	Lei Geral de Proteção de Dados / General Law for Data Protection (Brazil)
LPI	Lei de Propriedade Industrial / Brazilian Industrial Property Law (Brazil)

MCTI	Ministério da Ciência, Tecnologia e Inovações / Ministry of Science, Technology, and Innovations (Brazil)
MEC	Ministério da Educação / Ministry of Education (Brazil)
Mercosul	Mercado Comum do Sul / Southern Common Market
MICS	Ministério da Indústria, Comércio Exterior e Serviços / Ministry of Industry, Foreign Trade and Services (Brazil)
MMA	Ministério do Meio Ambiente / Environment Ministry (Brazil)
MNI	Montreal Neurological Institute-Hospital, McGill University / The Neuro
MPP	Medicines Patent Pool
MS	Ministério da Saúde / Ministry of Health (Brazil)
MSF	Médecins Sans Frontières
MTA	Material Transfer Agreement
NCD	Non-Communicable Disease
NGOs	Non-Governmental Organizations
NDS	New Development State
NITs	Núcleos de Inovação Tecnológica / Clusters of Technological Innovation (Brazil)
OECD	Organisation for Economic Co-operation and Development
OER	Open Educational Resources
PAHO	Pan-American Health Organization
PCT	Patent Cooperation Treaty
PDP	Product Development Partnership
PPP	Public-Private Partnership
R&D	Research and Development
RD&I	Research, Development, and Innovation

SciELO	Scientific Electronic Library Online (Brazil)
SGC	Structural Genomics Consortium
SDGs	Sustainable Development Goals
S&T	Science and Technology
STIs	Sexually Transmitted Infections
ST&I	Science, Technology, and Innovation
SUS	Sistema Único de Saúde / Unified Health System (Brazil)
TK	Traditional Knowledge
TRIPS agreement	Agreement on Trade-Related Aspects of Intellectual Property Rights
TTO	Technology Transfer Office
UAEM	Universities Allied for Essential Medicines
UN	United Nations
UNCTAD	United Nations Conference on Trade and Development
UNESCO	United Nations Educational, Scientific, and Cultural Organization
UNICAMP	Universidade de Campinas / University of Campinas (Brazil)
UPOV	International Union for the Protection of New Varieties of Plants
USP	Universidade de São Paulo / University of Sao Paulo (Brazil)
WHA	World Health Assembly
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

INTRODUCTION

Overview

The failures of intellectual property (IP) systems[3] to promote access to knowledge and health technologies and to foster innovation in the biomedical field have been widely reported by IP scholars. These include issues with accessing health technologies and generating and sharing the data, information, and knowledge that are necessary to create them. Scholars also point to a critical imbalance between the protection of intangible assets and the potential benefits, such as innovation and the advancement of science. They argue that problems such as weak patents, patent trolls, over-prosecution of intellectual property rights (IPRs), excessive protection of intangible assets, anti-competitive practices and rule manipulation call for an urgent rethink and reform of the IP system.[4]

The impact of such failures is felt more drastically in developing and least-developed countries where other developmental issues such as corruption, social and economic inequalities, and deficiencies in education and infrastructure aggravate access to health technologies.[5] In Brazil, the federal

[3] IP systems regulate, by the means of law and policy, intellectual assets generated by the activities of agents comprising biomedical innovation systems through different categories of IPRs (patents, copyrights, trademarks, trade secrets, etc.). These intangible assets are translated into different products and processes, such as inventions (medicines, vaccines, diagnostic kits, research materials and tools), academic papers, and databases.

[4] For initial thoughts on these issues, see: John H Barton et al, *Views on the Future of the Intellectual Property System*, 1 (International Centre for Trade and Sustainable Development, 2007); E Richard Gold et al, "The unexamined assumptions of intellectual property: adopting an evaluative approach to patenting biotechnological innovation" (2004) 18:4 Public Aff Q 299–344; Peter Drahos & John Braithwaite, *Information Feudalism: Who Owns the Knowledge Economy?* (New York: The New Press, 2007); Joseph E Stiglitz, "How Intellectual Property Reinforces Inequality", online: *Opinionator* <http://opinionator.blogs.nytimes.com/2013/07/14/how-intellectual-property-reinforces-inequality/>; Jerome Reichman & Keith Maskus, "The Globalization of Private Knowledge Goods and the Privatization of Global Public Goods" (2005) J Int Econ Law 279–320; James Bessen & Michael J Meurer, *Patent Failure: How Judges, Bureaucrats, and Lawyers Put Innovators at Risk* (Princeton: Princeton University Press, 2009); Michael Heller, *The Gridlock Economy: How Too Much Ownership Wrecks Markets, Stops Innovation, and Costs Lives*, first trade paper edition ed (New York: Basic Books, 2010); Fiona Murray & Scott Stern, "When Ideas Are Not Free: The Impact of Patents on Scientific Research" (2006) 7 Innov Policy Econ 33–69.

[5] For initial considerations on the failures of IP systems, especially from the perspective of developing countries, see: Joseph Stiglitz et al, "The Role of Intellectual Property Rights in Developing Countries: Some Conclusions" in *Intellect Prop Rights Leg Econ Chall Dev* (Oxford, UK and New York: Oxford University Press, 2014) 503; Keith E Maskus, Mohamed Lahouel, & others, "Competition policy and intellectual property rights in developing countries" (2000) 23:4 World Econ 595–611; Frederick M Abbott, Carlos M Correa & Peter Drahos, *Emerging Markets and the World Patent Order* (Cheltenham: Edward Elgar Pub, 2015); Barton et al, *supra* note 4.

government's response to the pandemic has been so chaotic that it is disastrous for the Brazilian population.[6] For example, current discussions about IP waivers—the temporary suspension of IPRs related to health technologies to facilitate their production, accessibility, and affordability—in the context of the COVID-19 pandemic have taken a long road to reach a solution. After decades of historical international leadership in access to medicines and IPRs—especially concerning the HIV/Aids pandemic and the creation of a worldwide renowned universal treatment program[7]—the present administration has refused to support partners like India and South Africa in their IP waiver proposal to the World Trade Organization (WTO).[8] This situation led other agents (NGOs, research and academic communities, and politicians) to

[6] See: *An unprecedented attack on human rights in Brazil: the timeline of the federal government's strategy to spread Covid-19*, by Deisy Ventura & Rossana Reis, Bulletin Rights in the Pandemic 10 (Sao Paulo, Brazil: EPEDISA/USP and Conectas Human Rights, 2021); Deisy Ventura, Fernando Mussa Abujamra Aith & Rossana Reis, "Covid-19 in Brazil: the government has failed to prevent the spread of the virus" *BMJ Opin* (5 March 2021), online: <https://blogs.bmj.com/bmj/2021/03/05/covid-19-in-brazil-the-government-has-failed-to-prevent-the-spread-of-covid-19/>; Deisy Ventura, Fernando Mussa Abujamra Aith & Rossana Reis, "The catastrophic Brazilian response to covid-19 may amount to a crime against humanity" *BMJ Opin* (5 April 2021), online: <https://blogs.bmj.com/bmj/2021/04/05/the-catastrophic-brazilian-response-to-covid-19-may-amount-to-a-crime-against-humanity/>; Conectas Human Rights, "New study: Brazilian federal government blocked measures against Covid-19", (21 January 2021), online: *Conectas* <https://www.conectas.org/en/noticias/new-study-exposes-federal-government-strategy-to-spread-covid-19/>.

[7] Access to medicines IPRs and the use of the WTO-TRIPS Agreement flexibilities (mainly, compulsory license) have been a constant topic in Brazilian IPRs history, considering its National Program on HIV/Aids, Sexual Transmitted Diseases (STDs) and Hepatitis. For more information about it, see: Maria Auxiliadora Oliveira et al, "Has the implementation of the TRIPS Agreement in Latin America and the Caribbean produced intellectual property legislation that favours public health?" (2004) 82:11 Bull World Health Organ 815–821; Gabriela Costa Chaves, Marcela Fogaça Vieira & Renata Reis, "Access to medicines and intelectual property in Brazil: reflections and strategies of civil society" (2008) 5:8 Sur Rev Int Direitos Hum 170–198; Gabriela Costa Chaves et al, "Strategies for price reduction of HIV medicines under a monopoly situation in Brazil" (2015) 49 Rev Saúde Pública, online: <http://www.scielo.br/scielo.php?script=sci_abstract&pid=S0034-89102015000100309&lng=en&nrm=iso&tlng=pt>; Priscilla M D G César et al, *Direitos de Propriedade Intelectual e Saúde Pública: O Acesso Universal aos Medicamentos Anti-Retrovirais no Brasil* (Sao Paulo: IDCID, 2007); Bernardo Galvão-Castro et al, "HIV/Aids and COVID-19 in Brazil: in four decades, two antithetical approaches to face serious pandemics" (2021) 116 Mem Inst Oswaldo Cruz e210071.

[8] See: Council for Trade-Related Aspects of Intellectual Property Rights, *IP/C/W/669/Rev.1. Waiver from certain Provisions of TRIPS Agreement for the Prevention, Containment and Treatment of Covid-19. Revised Decision Text. Communication from the African group, the Plurinational State of Bolivia, Egypt, Eswatini, Fiji, India, Indonesia, Kenya, the LDC Group, Maldives, Mozambique, Namibia, Pakistan, South Africa, Vanuatu, the Bolivarian Republic of Venezuela and Zimbabwe* (World Trade Organization (WTO), 2021); Candice Sehoma, "In landmark move, India and South Africa propose no patents on COVID-19 medicines, tools during pandemic", (7 October 2020), online: *Médecins Front Access Campaign* <https://msfaccess.org/landmark-move-india-and-south-africa-propose-no-patents-covid-19-medicines-tools-during-pandemic>; Luisa Enria et al, "A TRIPS waiver is urgently needed to make progress on COVID-19 vaccine equity", (15 July 2021), online: *COVID-19 Clin Res Coalit* <https://covid19crc.org/viewpoints/2021/a-trips-waiver-is-urgently-needed-to-make-progress-on-covid-19-vaccine-equity/>.

propose a bill on this matter approved by Congress[9] but sanctioned by President Jair Bolsonaro with changes. Specifically, the veto on provisions that required the patent owner to transfer knowledge and provide active pharmaceutical ingredients to produce medicines and vaccines is concerning and might harm effective pandemic response and preparedness in Brazil.[10]

Standing against the political disarticulation at the federal level, several stakeholders—especially researchers and academics—joined forces in the pandemic response. For instance, University of Sao Paulo (USP) Polytechnic School researchers have developed an emergency respiratory support device (INSPIRE) in collaboration with various partners, including USP Law School. INSPIRE addresses the demands of hospitals and remote regions caused by the COVID-19 pandemic. As a low-cost, fast production, and portable equipment, INSPIRE uses Brazilian technology and materials that are easier to find nationally.[11] Also, the Federal University of Pelotas (UFPel) issued an ordinance to facilitate licensing (via a royalty-free process) and technology transfer that may be useful to the pandemic response.[12] This was a bold move by UFPel at the beginning of the pandemic when stakeholders were still starting to

[9] Felipe Carvalho, "Vacinas e medicamentos: bens comuns ou artigos de luxo?", (30 August 2021), online: *Congr Em Foco* <https://congressoemfoco.uol.com.br/opiniao/forum/vacinas-e-medicamentos-bens-comuns-ou-artigos-de-luxo/>; Câmara dos Deputados, *Projeto de Lei (PL 12/2021)*, (6 May 2021).

[10] Pedro Ivo de Oliveira, "Lei que quebra patentes de vacinas é sancionada com vetos", *Agência Bras* (3 September 2021), online: <https://agenciabrasil.ebc.com.br/politica/noticia/2021-09/lei-que-quebra-patentes-de-vacinas-e-sancionada-com-vetos>; Sandra Manfrini, "Bolsonaro sanciona com vetos lei que permite quebra temporária de patentes", *CNN Bras* (3 September 2021), online: <https://www.cnnbrasil.com.br/saude/sancionada-com-vetos-lei-que-permite-quebra-temporaria-de-patentes/>.

[11] Escola Politécnica da USP, *O que é o Projeto Inspire?* (Sao Paulo, Brazil, 2020); Escola Politécnica da USP, "Inspire – Ventilador Pulmonar Aberto de Baixo Custo", online: <https://www.poli.usp.br/inspire>; Jornal da USP no Ar 1ª edição / Rádio USP, "Ventilador pulmonar Inspire é exemplo de sucesso da parceria entre USP e Marinha", *J USP* (31 May 2021), online: <https://jornal.usp.br/atualidades/ventilador-pulmonar-inspire-e-exemplo-de-sucesso-da-parceria-entre-usp-e-marinha/>; Jornal da USP no Ar 1ª edição / Rádio USP, "Projeto Inspire é o conhecimento da universidade que chega à sociedade", *J USP* (13 October 2020), online: <https://jornal.usp.br/atualidades/projeto-inspire-e-conhecimento-da-universidade-que-chega-a-sociedade/>.

[12] Pró-Reitoria de Gestão da Informação e Comunicação & Coordenação de Comunicação Social-UFPel, "UFPel irá licenciar patentes e transferir tecnologias relacionadas à COVID-19 de forma gratuita", (15 April 2020), online: *Coord Comun Soc* <http://ccs2.ufpel.edu.br/wp/2020/04/15/ufpel-ira-licenciar-patentes-e-transferir-tecnologias-relacionadas-a-covid-19-de-forma-gratuita/>; Conselho Coordenador do Ensino, da Pesquisa e da Extensão (COCEPE), *Portaria 732/2020* (Universidade Federal de Pelotas (UFPel), 2020).

discuss the use of TRIPS flexibilities and IP waivers[13] to minimize the impact of IPRs in access to health technologies and innovation in that context. Such actions were critical in providing a better response to the pandemic due to their decentralized nature. Furthermore, these examples assert the importance of different stakeholders in rethinking the relationship between law and science[14] and their interaction and coevolution.

The insufficient number of innovative approaches toward the regulation of IP and biomedical innovation systems prevents developing and least-developed countries from fully realizing their research, development, and innovation (RD&I) capacities, inhibiting the performance of their academic and research communities. Yet, strengthening research and development (R&D) capacity, promoting access to educational resources, data, and information under an enabling infrastructure, as well as improving technical assistance and technology transfer remain significant challenges.[15] Such challenges manifest in

[13] TRIPS flexibilities are exceptions and limitations adopted by different countries in implementing IPRs nationally while still respecting the requirements of the WTO-TRIPS Agreement. They aim to protect the public interest, public order, health, and environment. IP waivers refer to the temporary suspension of IPRs, especially in critical situations as the COVID-19 pandemic and intend to facilitate the production, accessibility, and affordability of technologies protected by IPRs. Chapter Three provides further discussions on these topics. For initial thoughts, see: Carlos M Correa, "Flexibilities provided by the Agreement on Trade-Related Aspects of Intellectual Property Rights" (2018) 96:3 Bull World Health Organ 148; Enria et al, *supra* note 8; "India and South Africa proposal for WTO waiver from IP protections for COVID-19-related medical technologies", online: *Médecins Front Access Campaign* <https://msfaccess.org/india-and-south-africa-proposal-wto-waiver-ip-protections-covid-19-related-medical-technologies>.

[14] This dissertation uses the term law as synonym for legal system and its legal infrastructure comprised by diverse types of regulation and subsystems (IP system) and science as synonym for innovation system (and its subsystems like the biomedical innovation system), or to generally describe the scientific endeavour.

[15] See: Dean Baker Stiglitz Arjun Jayadev and Joseph, "Innovation, Intellectual Property, and Development: A Better Set of Approaches for the 21st Century", online: <http://cepr.net/publications/reports/innovation-intellectual-property-and-development-a-better-set-of-approaches-for-the-21st-century> at 54–58; *Research and Development to Meet Health Needs in Developing Countries: Strengthening Global Financing and Coordination.Report of the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG)*, by John-Arne Røttingen et al, Report of the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG) (Geneva: World Health Organization (WHO), 2012).

how to coherently design and reform legal and policy instruments and set coordinated strategies to address local problems while considering the global scene for biomedical RD&I.[16]

In 2016, the United Nations High-Level Panel on Access to Medicines restated that "[p]ublic-health sensitive intellectual property rules and mechanisms can help address the misalignment between profit-driven innovation models and public health priorities."[17] Finding a balance in the co-design and reform of IP and biomedical innovation systems presents both a challenge and an opportunity. Innovating in these systems' evaluation and understanding and implementing strategies that inform their co-design and reform may assist in balancing multiple agents' interests, addressing different countries' social and economic developmental needs, and achieving access to knowledge and innovation goals.

Access to Knowledge and Innovation in the Spotlight

The IP and biomedical innovation systems are known for being complex. As complex as they are in isolation, their interaction and coevolution over time can be described as 'wickedly complex.'[18] This makes the regulation of biomedical RD&I through the medium of IPRs a significant challenge. This challenge arises from the competing and often contrasting needs of regulators, those subject to regulation

[16] As Anatole F. Krattiger states: "The issues of innovation and access are inevitably intertwined, cutting across distinct policy areas, in particular, public health, intellectual property (IP) and international trade. Finding the right balance between health, trade and IP policies to sustain innovation and ensure widespread access to life-saving technologies is one of the primary public policy challenges of our time." Anatole F Krattiger, "Promoting access to medical innovation" *WIPO Mag* (September 2013) 5 at 5.

[17] They further highlighted the importance of flexibilities in the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) in this response, the role of policies and public funding in health technologies' access and innovation, and open innovation models to accelerate innovation while guaranteeing access. In this sense, see: World Health Organization, World Intellectual Property Organization & World Trade Organization, *Promoting Access to Medical Technologies and Innovation: Intersections between public health, intellectual property and trade*, 2nd ed (Geneva, Switzerland: Trilateral study by the World Health Organization (WHO), World Intellectual Property Organization (WIPO) and World Trade Organization (WTO), 2020) at 8.

[18] As explained later, this dissertation applies Complex Adaptive Systems (CAS) theory to analyze the interaction and coevolution of IP and biomedical innovation systems. While the conceptualization of complex problems bears similarities across theories, complexity itself is tackled differently in each theory. It should be noted that there are other possible approaches that are not explored in this dissertation, such as the study of wicked problems, that is, "a problem that is complex, difficult to define, with no immediate solution, and one in where every wicked problem can be considered to be a symptom of another problem." Tania Bubela, E Richard Gold & Jean-Frédéric Morin, "Wicked Issues for Canada at the Intersection of Intellectual Property and Public Health: Mechanisms for Policy Coherence" (2010) 4 McGill JL Health 3 at 5; Horst W J Rittel & Melvin M Webber, "Dilemmas in a general theory of planning" (1973) 4:2 Policy Sci 155–169.

and those who benefit (or hope to benefit) from the results of biomedical RD&I, such as patients, hospitals, pharmaceutical companies, small biotechnology companies, and insurers. The desire to open a dialogue between two highly specialized technical fields often pulls the regulatory system in different (albeit not necessarily incompatible) directions. Agents also wish to foster follow-on innovation that effectively balances the diverse interests of other agents working within and for them.

There have been advances worldwide regarding access to health technologies.[19] However, there is still a long road ahead before society reaches the goal of complete, fair, and equal access to biomedical solutions across different countries.[20] As stated by the Access to Medicines Foundation:

> All people share the right to the highest attainable standard of health, as noted in the WHO Constitution. Yet access to medicine continues to be out of reach for an estimated two billion people worldwide. Huge advances are being made toward internationally agreed global health targets. Nevertheless, new and complex health challenges continue to emerge, demanding sustained commitment and deeper cooperation from many different sides, as well as wider adoption of proven solutions. Providing access depends on a complex range of factors and stakeholders.[21]

Alongside the need to guarantee and expand access to health technologies—and related information, data, and knowledge—is the need to promote innovation in the biomedical field. To do so, it is essential to understand how, and under which rules, biomedical RD&I is organized and conducted. Biomedical innovation faces problems in productivity and efficiency that require advances in basic and applied knowledge. These advances would engender better results from scientific activities, improvements

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[19] Accordingly to the World Health Organization (WHO): "A health technology is the application of organized knowledge and skills in the form of devices, medicines, vaccines, procedures and systems developed to solve a health problem and improve quality of lives." World Health Assembly (WHA), *Resolution WHA60.29: Health technologies* (Sixtieth World Health Assembly (WHA), 2007).

[20] Even though the herein citation refers to access to medicines, there is a broader range of health technologies that are out of reach to most of the world's population because they are unaffordable. These technologies include vaccines, diagnostics tests, gene therapy and personalized medicine techniques, etc. For more information on these issues, see generally: Access to Medicine Foundation, *Access to Medicine Index 2018* (2018); *The Access to Vaccines Index*, by Access to Medicines Foundation (The Netherlands: Access to Medicines Foundation, 2017); Christine Årdal et al, "International cooperation to improve access to and sustain effectiveness of antimicrobials" (2016) 387:10015 The Lancet 296–307; "WHO | Antimicrobial resistance", online: *World Health Organ WHO* <http://www.who.int/antimicrobial-resistance/en/>; *G-FINDER: Global Funding of Innovation for Neglected Diseases*, G-FINDER: Global Funding of Innovation for Neglected Diseases, by Policy Cures Research, G-FINDER: Global Funding of Innovation for Neglected Diseases Summary (Australia: Policy Cures Research, 2019); Policy Cures Research, "R&D pipeline tracker", online: *RD Pipeline Tracker* <https://www.pipeline.policycuresresearch.org>.

[21] Access to Medicines Foundation, *supra* note 20 at 10.

of current treatments, the invention of new treatments and, eventually, the fulfilment of the highest health standards.[22]

Several factors interfere with promoting access and innovation, such as the specificities of particular diseases, local needs and problems of diverse populations, and clashes between market-driven and health-driven approaches to health. For example, there is a need to correct market failures and address health problems, mainly affecting developing and least-developed countries, such as neglected diseases.[23] Yet, there are also problems related to rare or orphan diseases, non-communicable diseases (NCD), mental

[22] For initial thoughts on these questions, see: *A New Pharmaceutical Commons: Transforming Drug Discovery*, Policy Paper, by Chas Bountra, Wen Hwa Lee & Javier Lezaun, Oxford Martin Policy Paper Policy Paper (Oxford: Oxford Martin School, 2017); World Health Organization, World Intellectual Property Organization & World Trade Organization, *supra* note 17; World Health Organization, World Trade Organization & World Intellectual Property Organization, *Promoting Access to Medical Technologies and Innovation: Intersections between public health, intellectual property and trade*, 1st ed (Geneva: Trilateral study by the World Health Organization (WHO), World Intellectual Property Organization (WIPO) and World Trade Organization (WTO), 2013); Krattiger, *supra* note 16.

[23] The WHO defines: "Neglected tropical diseases (NTDs)–a diverse group of communicable diseases that prevail in tropical and subtropical conditions in 149 countries–affect more than one billion people and cost developing economies billions of dollars every year. Populations living in poverty, without adequate sanitation and in close contact with infectious vectors and domestic animals and livestock are those worst affected." The list of neglected diseases varies among institutions, but some of these diseases are dengue, rabies, trachoma, Buruli ulcer, yaws, leprosy, Chagas disease, Human African trypanosomiasis (sleeping sickness), Leishmaniases, malaria, etc. For further definitions and thoughts about neglected diseases and biomedical RD&I in this area, see: World Health Organization (WHO), "Neglected tropical diseases", online: *WHO* <http://www.who.int/neglected_diseases/diseases/en/>; Drugs for Neglected Diseases (DNDi), "About Us – DNDi", online: *Drugs Neglected Dis DNDi* <https://www.dndi.org/about-dndi/>; Carlos M Morel et al, "Health Innovation Networks to Help Developing Countries Address Neglected Diseases" (2005) 309:5733 Science 401–404; *Research and Development to Meet Health Needs in Developing Countries: Strengthening Global Financing and Coordination: Report of the Consultative Expert Working Group on Research and Development: Financing and Coordination*, by World Health Organization (Geneva: World Health Organization, 2012); Suerie Moon, Jorge Bermudez & Ellen't Hoen, "Innovation and Access to Medicines for Neglected Populations: Could a Treaty Address a Broken Pharmaceutical R&D System?" (2012) 9:5 PLOS Med, online: <http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001218>; Policy Cures Research, *supra* note 20; World Health Organization, "TDR | World Health Organization", online: *WHO* <http://www.who.int/tdr/en/>; Sophie Edwards, "R&D for neglected diseases reliant on just two donors, G-FINDER report warns", *Devex* (14 December 2017), online: <https://www.devex.com/news/sponsored/r-d-for-neglected-diseases-reliant-on-just-two-donors-g-finder-report-warns-91754>.

health, pandemics and epidemic diseases, antimicrobial resistance (AMR), and maternal and child health.[24]

Adding tension to the problem of balancing access and incentive is the lack of transparency and trust among the different agents participating in the biomedical innovation ecosystem and the pharmaceutical industry's business model. This is because the assessment of productivity and efficiency of the biomedical innovation system is deeply tied to the costs and risks of developing health technologies. This tension increases when market-needs and health-needs approaches to regulate the biomedical innovation system surface alongside multiple agents' interest in this system.[25]

Major factors underpin conflicts between access to knowledge and promoting innovation. These include establishing research priorities, increases in revenue and profits, innovation costs, and the distribution of diseases worldwide.[26] Because biomedical RD&I models have traditionally been designed to respond to the needs of developed countries' populations, many diseases that affect developing and least-developed countries are not high on R&D priority lists, even though they account for most of the

[24] For more information about these issues, see: Årdal et al, *supra* note 20; Bibhav Acharya et al, "Partnerships in mental healthcare service delivery in low-resource settings: developing an innovative network in rural Nepal" (2017) 13:1 Glob Health 2; Nicole Lurie, Gerald T Keusch & Victor J Dzau, "Urgent lessons from COVID-19: why the world needs a standing, coordinated system and sustainable financing for global research and development" (2021) 397:10280 The Lancet 1229–1236; Zulfiqar A Bhutta et al, "Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost?" (2013) 382:9890 The Lancet 452–477; Christine M Cutillo, Christopher P Austin & Stephen C Groft, "A Global Approach to Rare Diseases Research and Orphan Products Development: The International Rare Diseases Research Consortium (IRDiRC)" in *Rare Dis Epidemiol Update Overv* Advances in Experimental Medicine and Biology (Springer, Cham, 2017) 349.

[25] Ellen 't Hoen, *Private Patents and Public Health* (The Netherlands: Health Action International, 2016); Joseph A DiMasi, Henry G Grabowski & Ronald W Hansen, "Innovation in the pharmaceutical industry: New estimates of R&D costs" (2016) 47 J Health Econ 20–33; James Love, "The 2016 Tufts estimates of the risk adjusted out-of-pocket costs to develop a new drug", (12 April 2016), online: *Knowl Ecol Int - James Loves Blog* <http://www.keionline.org/node/2464>; Mariana Mazzucato, "High cost of new drugs" (2016) 354 BMJ i4136; Mariana Mazzucato & Victor Roy, "Rethinking value in health innovation: from mystifications towards prescriptions" (2019) 22:2 J Econ Policy Reform 101–119.

[26] World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22; World Health Organization, World Intellectual Property Organization & World Trade Organization, *supra* note 17; Jorge Bermudez & Jorge Bermudez, "Contemporary challenges on access to medicines: beyond the UNSG High-Level Panel" (2017) 22:8 Ciênc Amp Saúde Coletiva 2435–2439; Krattiger, *supra* note 16.

global population.[27] In contrast, research on NCDs (for instance, cancer, diabetes, and obesity) is more profitable and thus more attractive to firms and researchers. Developed country diseases create long-lasting markets for chronic treatments (which generally require life-long medical treatment), as opposed to research into malaria, tuberculosis, and Chagas disease. The latter group consists of potentially curable diseases that affect large populations without market power.[28]

The global epidemiological profile has changed over time, with NCDs also affecting populations in both developed and developing and least-developed countries. However, policy responses have not succeeded in generating biomedical innovation at the desired level, even for priority diseases. Concurrently, there is a growing concern about the global spread of major epidemics, such as that caused by Ebola, the Zika virus or SARS-CoV-2, and looming health problems such as AMR. Similarly, diseases caused by poverty are no longer locally contained. Our networked society challenged the virtual barriers of knowledge dissemination and diminished physical barriers by intensifying the movement of people across the world.[29]

The biomedical innovation system is multifaceted and organizationally complex. Members of the Oxford Martin School explain this situation:

> (…) Despite significant advances in our understanding of the biological basis of disease, pharmaceutical R&D is struggling to sustain the levels of productivity and efficiency it reached in the second half of the 20th century.

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[27] *15 Years of Needs-Driven Innovation for Access: Key lessons, challenges, and opportunities for the future*, by Drugs for Neglected Diseases (DNDi), dndi.org (Geneva, Switzerland: Drugs for Neglected Diseases (DNDi), 2019) at 15; *Executive Summary: 15 Years of Needs-Driven Innovation for Access: Key lessons, challenges, and opportunities for the future*, by Drugs for Neglected Diseases (DNDi), dndi.org (Geneva, Switzerland: Drugs for Neglected Diseases (DNDi), 2019); Policy Cures Research, *supra* note 20.

[28] Gavin Yamey & Carlos Morel, "Investing in Health Innovation: A Cornerstone to Achieving Global Health Convergence" (2016) 14:3 PLOS Biol e1002389; Gavin Yamey, "The world's most neglected diseases" (2002) 325:7357 BMJ 176–177.

[29] "Currently, 4800 million people live in developing countries, representing 80% of the world population. Of this number, 2700 million, representing 43% of the world population, live on less than US$ 2 a day. Communicable diseases account for 50% of the developing countries' burden of disease. Furthermore, poverty, among other factors, directly affects the acquisition of health products and medical devices, especially in developing countries". World Health Assembly (WHA), *WHA62.16 - Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property. WHA resolution; Sixty-second World Health Assembly, 22 May 2009* (World Health Organization (WHO), 2009); "WHO | Global strategy and plan of action on public health, innovation and intellectual property", online: *WHO* <http://www.who.int/phi/publications/gspa-phi/en/> at 3.

> (…) There is no magic bullet that will solve the structural difficulties of drug discovery, and new ideas will always need to be tailored to the specific scientific and organisational challenges of each therapeutic area. Yet strengthening the open component of the ecosystem has the potential to radically transform how we tackle the medical challenges of our century in a way that is beneficial to patients and producers alike.
> (…) These systemic weaknesses in the pharmaceutical R&D ecosystem will not be solved by simply doubling down on traditional economic incentives. The history of drug discovery over the last two decades indicates that increasing the volume of research funding or extending IP protections fails to enhance the overall efficiency of pharmaceutical R&D. This is an inelastic system, unable to extract the full benefit from new economic or scientific inputs, and a system that cannot be re-energised simply by intensifying conventional financial or proprietary incentives.[30]

Each of these systemic issues requires tailored and coordinated actions and strategies to address them. Further, they intersect deeply with one another with the result that we can only solve one by solving all. The solution rests on acknowledging that each sub-problem combines into a multi-systemic problem that calls for multi-systemic thinking and approaches. No matter how well-organized societies may be, new problems with unintended and unpredictable consequences will arise. This uncertainty brings even more complexity to the global health scene.

In a connected and information-reliant world, there is a fluid and unpredictable zone in which multiple global health problems arise and require answers from diverse Complex Adaptive Systems (CAS)[31] and agents that form society. Some of these problems become health crises, such as the COVID-19 pandemic or the 2014 Ebola outbreak, while others are relatively less urgent and remain manageable depending on the countries affected by them. However, even this second category of crisis is no less important for human rights and social and economic development.[32] In this diversity of health problems, the ability or inability of various local populations to quickly respond and their views on how to tackle

[30] Bountra, Lee & Lezaun, *supra* note 22 at 6, 9.
[31] The acronym CAS stands for complex adaptive systems (plural) or complex adaptive system (singular) depending on the context and the need to evaluate a specific system.
[32] See: Røttingen et al, *supra* note 15; Paulo Marchiori Buss et al, "Development, health, and international policy: the research and innovation dimension" (2016) 32 Cad Saúde Pública, online: <http://www.scielo.br/scielo.php?script=sci_abstract&pid=S0102-311X2016001402001&lng=en&nrm=iso&tlng=en>; Mario Viola de Azevedo Cunha et al, *New technologies and human rights: challenges to regulation* (2013); Laurence R Helfer & Graeme W Austin, *Human rights and intellectual property: mapping the global interface* (Cambridge University Press, 2011).

these issues also vary. Multiple connections and different layers of agents' interactions and systems characterize all these problems.

Access to knowledge and innovation crises are embedded in global health crises. Therefore, they need to be jointly tackled in the context of the systems they occur. This dissertation considers these health problems as being 'global' because their effects are extensively felt and quickly spread. In practice, this means that solving a health crisis in one location should become a concern of multiple agents around the globe.[33] Even though more data and empirical analysis are needed to better clarify these connections and point out hidden factors that aggravate problems and interfere with their potential solutions, multiple agents have already called attention to these crises and linked them with IPRs protection.[34]

Access to health technologies is a global need, yet many lack this access because technologies are unaffordable, inaccessible, or unavailable. This problem affects not only developing and least-developed countries' populations but also developed countries where part of the population cannot afford private insurance and/or count on well-established public health systems to provide them, such as in the USA. Even in countries with public health systems with universal coverage, such as Brazil, escalating prices of health technologies, changes in the epidemiologic profile, and an ageing population create a scenario in which paying the cost of public healthcare compromises a significant amount of public resources.[35]

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[33] Bandy X Lee et al, "Transforming Our World: Implementing the 2030 Agenda Through Sustainable Development Goal Indicators" (2016) 37:1 J Public Health Pol J Public Health Policy 13–31; Buss et al, "Development, health, and international policy", *supra* note 32; Årdal et al, *supra* note 20; Buss et al, "Development, health, and international policy", *supra* note 32; Lurie, Keusch & Dzau, "Urgent lessons from COVID 19", *supra* note 24; *The R&D Preparedness Ecosystem: Preparedness for Health Emergencies Report to the Global Preparedness Monitoring Board*, by Gerald Keusch & Nicole Lurie (US National Academy of Medicine, 2020).

[34] See, initially: Gold et al, "The unexamined assumptions of intellectual property", *supra* note 4; "PACEOMICS-POLICY BRIEF: Intellectual asset management in personalized medicine innovation: public policy issues" PACEOMICS, Montreal, Canada (June 2016); Barton et al, *supra* note 4; Røttingen et al, *supra* note 15; Krattiger, *supra* note 16.

[35] Chaves et al, *supra* note 7; César et al, *supra* note 7; Fabrício Pasquot Polido, Calixto Salomão Filho & Maristela Basso, "Propriedade intelectual e preços diferenciados de medicamentos essenciais : políticas de saúde pública para países em desenvolvimento" (2005), online: <https://bdjur.stj.jus.br/jspui/handle/2011/29101>; *The Brazilian Innovation System: A Mission-Oriented Policy Proposal*, by Mariana Mazzucato & Caetano Penna, Avaliação de Programas em CT&I Apoio ao Programa Nacional de Ciência (Plataformas de conhecimento) 1 (Brasilia: Centro de Gestão e Estudos Estratégicos (CGEE), 2016); Chaves, Vieira & Reis, "Access to medicines and intelectual property in Brazil", *supra* note 7.

These access to knowledge and innovation crises challenge law and policymakers to appropriately and fairly regulate biomedical R&D, which involves prioritizing services and resources. States must balance divergent interests put by private and public agents that alternatively claim the benefit of market-based solutions to health crises versus the value of regulatory interventions to promote access to health technologies.[36] In undertaking this task, the importance of an ongoing, consistent dialogue between law and policymakers and those performing science is crucial to improving the outcomes of complex adaptive IP and biomedical innovation systems. Equally important is the dialogue between those performing science (academic and research communities) and legal agents who provide institutional-level advice on IP practices, policies, and strategies. Therefore, there is a need to clarify the relationship between law and science to sustain agents' evidence-based decision-making and promote diversity in sources generating legal and regulatory innovation.

Several examples illustrate how this complex relationship is affected by how agents interact within IP and biomedical innovation systems and see their roles in these systems. Law and policy's effectiveness in addressing problems also depends on how agents answer to the uncertainty arising within these systems

[36] See: Drahos & Braithwaite, *supra* note 4; Susan Sell, *Power and Ideas: North-South Politics of Intellectual Property and Antitrust* (Albany: State University of New York Press, 1997); Susan Sell, *Private Power, Public Law: The Globalization of Intellectual Property Rights* (Cambridge, U.K. ; New York: Cambridge University Press, 2003); Moon, Bermudez & Hoen, "Innovation and Access to Medicines for Neglected Populations", *supra* note 23; Peter K Yu, "International enclosure, the regime complex, and intellectual property schizophrenia" (2007) Mich State Law Rev 1–33; *Pharmaceutical Innovation and Access to Medicines*, Text, by Organisation for Economic Cooperation and Development (OECD), OECD Health Policy Studies Text (Paris: Organisation for Economic Cooperation and Development (OECD), 2018) ISBN 978-92-64-30739-1 (pdf); World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22; World Health Organization, World Intellectual Property Organization & World Trade Organization, *supra* note 17; Røttingen et al, *supra* note 15.

and manage their imperfect understanding of them.[37] By highlighting uncertainty, it is possible to reveal the larger role of less visible factors in addressing problems within systems. The invisibility of these factors stems from a gap in agents' understanding of what the system is, what they perceive it to be, and what the system could be. To bridge this gap, agents need to embrace and harness complexity to find ways to better understand, map, monitor, and promote reforms in IP and biomedical innovation systems.

Understanding the interplay between law and science is especially important today because the COVID-19 pandemic has exacerbated existing problems arising from the interaction of these two systems and brought new ones to light. Examples abound, varying from discussions about the importance of science (and research and academic communities) in pandemic responses to power relations and political articulations that have led to vaccine nationalism and an unequal vaccine rollout around the globe. In this scenario, developing and least-developed countries' populations are the most harmed.[38]

In fact, debates about IP waivers and the use of other WTO-TRIPS agreement flexibilities have become common in COVID-19 times, with countries taking different positions. While some have issued emergency laws and declarations supporting the waiver, others have questioned the need and legitimacy

[37] In this dissertation, I assume that agents do not know—or have a limited understanding of—all the short and long term effects of IP law and policy on innovation, access to knowledge (including access to data, information, knowledge, research materials, and tools), access to health-related inventions (such as medicines, vaccines and, diagnostic tests), technology transfer (from universities to the private sector and between diverse nations), and social and economic development. This list emerges from the complementary work of different scholars. See, initially: Rebecca S Eisenberg, "Noncompliance, Nonenforcement, Nonproblem - Rethinking the Anticommons in Biomedical Research Patent Law in Perspective: Institute for Intellectual Property & Information Law Symposium" (2008) 45 Houst Law Rev 1059–1100; Gold et al, "The unexamined assumptions of intellectual property", *supra* note 4; Timothy Caulfield, Shawn HE Harmon & Yann Joly, "Open science versus commercialization: a modern research conflict?" (2012) 4 Genome Med 17; S Tina Piper, "The Tools and Levers of Access to Patented Health Related Genetic Invention in Canada" (2009) 30:1 Wash Univ J Law Policy 043–077; Arti K Rai, "Engaging Facts and Policy: A Multi-Institutional Approach to Patent System Reform" (2003) 103 Columbia Law Rev 1035; Stuart Minor Benjamin & Arti K Rai, "Fixing Innovation Policy: A Structural Perspective" (2008) 77 George Wash Law Rev 1; PACEOMICS, *supra* note 34.

[38] For discussions on these topics, see: Matt Apuzzo & David D Kirkpatrick, "Covid-19 Changed How the World Does Science, Together", *N Y Times* (1 April 2020), online: <https://www.nytimes.com/2020/04/01/world/europe/coronavirus-science-research-cooperation.html>; COVID-19 Therapeutics Accelerator, "Advancing research into accessible coronavirus treatments", online: *COVID-19 Ther Accel* <https://www.therapeuticsaccelerator.org/>; Galvão-Castro et al, "HIV/Aids and COVID-19 in Brazil", *supra* note 7; Christopher Morten & Matthew Herder, "We Can't Trust Big Pharma to Make Enough Vaccines" (31 May 2021), online: <https://www.thenation.com/article/world/covid-vaccines-pharma/>; *Public lies and public goods : ten lessons from when patents and pandemics meet*, Working Paper, by Peter Drahos, cadmus.eui.eu, Working Paper (European University Institute, 2021) Accepted: 2021-06-03T12:15:47Z.

of these instruments. Issues have also been raised regarding some countries' ability to produce health technologies, especially vaccines.[39] These issues further connect to debates about the need to de-colonize global health, problems of localized supply chains of active pharmaceutical ingredients, lack and insufficiency of local manufacturing capacities, and the need for adequate knowledge and technology transfer to facilitate local manufacturing and scaling-up of vaccine production.[40]

Additionally, the development of several SARS-CoV-2 vaccines also illustrates the complexity of different stakeholders' interactions in developing health technologies and the role of IPRs in advancing science. At the same time, this highlights the role of public funding, procurement, and tax incentives in developing technologies. Examples precede COVID-19, the development of the Ebola vaccine and the CRISPR-Cas 9 gene-editing tool, in turn, underscores the role of public universities and research centres in the different stages of health technologies development and the public sector support for late-stage R&D of new drugs.[41]

All these examples demonstrate how important agents' behaviours are in shaping the outcomes of IP and biomedical innovation systems, how uncertainty is an enduring element that needs to be accounted for and adequately dealt with, and how reform can arise from strategies and agents that are not traditionally considered. The complex interaction between IP and biomedical innovation systems further shows that

[39] Council for Trade-Related Aspects of Intellectual Property Rights, *supra* note 8; Enria et al, *supra* note 8; note 13.
[40] See, specially: Lurie, Keusch & Dzau, "Urgent lessons from COVID 19", *supra* note 24; Drahos, *supra* note 38; W Nicholson Price, Arti K Rai & Timo Minssen, "Knowledge transfer for large-scale vaccine manufacturing" (2020) 369:6506 Science 912–914.
[41] Rahul K Nayak, Jerry Avorn & Aaron S Kesselheim, "Public sector financial support for late stage discovery of new drugs in the United States: cohort study" (2019) 367 BMJ l5766; Rahul K Nayak et al, "Public-sector Contributions to Novel Biologic Drugs" (2021) JAMA Intern Med, online: <https://doi.org/10.1001/jamainternmed.2021.3720>; John Brooks, "Making Sense of the CRISPR Patent Dispute Between the University of California and Broad", (20 February 2019), online: *KQED-Sci* <https://www.kqed.org/science/1938007/making-sense-of-the-crispr-patent-dispute-between-the-university-of-california-and-broad>; "CRISPR: The New Frontier of Biotechnology Innovation | Section of Intellectual Property Law", online: <https://www.americanbar.org/groups/intellectual_property_law/publications/landslide/2017-18/january-february/crispr-new-frontier-biotechnology-innovation-digital-feature.html>; Matthew Herder, Janice E Graham & Richard Gold, "From discovery to delivery: public sector development of the rVSV-ZEBOV Ebola vaccine" (2020) 7:1 J Law Biosci, online: <https://doi.org/10.1093/jlb/lsz019>; Matthew Herder, Janice Graham & E Richard Gold, "The public science behind the 'Merck' Ebola vaccine", (16 January 2020), online: *STAT First Opin* <https://www.statnews.com/2020/01/16/public-science-behind-merck-ebola-vaccine/>.

coordination, decentralization, and diversity of agents and responses are keen to target problems and promote a balanced innovation ecosystem that primes access and innovation.

Research Question, Hypothesis, and Scope

This dissertation's research question is as follows: how should the legal system frame the rights to access to knowledge and innovation given the interactions of the IP and biomedical innovation systems? To answer this question, we must examine the dynamic relationship between IP and biomedical innovation systems and how agents[42] mediate between them. This dissertation is premised on the argument that one can better understand legal responses and propose reforms to ensure access and innovation by applying an agent-based understanding of IP and biomedical R&D.

The IP system is "locked in perpetual coevolution with [its] regulatory targets,"[43] the biomedical innovation system, to create a global innovation ecosystem.[44] While the interaction of IP and biomedical innovation systems also touches on other systems—economic, political and cultural—it is this interaction that most prominently raises questions of access and innovation. I thus focus on the relationship between law and science, recognizing that I leave much out that will need to be excavated through future research.

[42] In this dissertation, I mostly use the term 'agent' (or 'population of agents') even though this term might be interchangeable for 'stakeholder' or 'actor.' An agent is any element (not exclusively a person, but also, a group of people organized into an institution) that acts on, interacts with, creates expectations for and influences the system, its other elements, and the broader environment. For initial ideas on these concepts, see: Melanie Mitchell, *Complexity: A Guided Tour* (Oxford: Oxford University Press, 2011); Melanie Mitchell, "How Can the Study of Complexity Transform Our Understanding of the World?", (20 January 2014), online: *Big Quest Online* <https://www.bigquestionsonline.com/content/how-can-study-complexity-transform-our-understanding-world> 8p.; Robert Axelrod & Michael D Cohen, *Harnessing Complexity*, reprint edition ed (New York: Basic Books, 2001); Herbert A Simon, "The Architecture of Complexity" (1962) 106:6 Proc Am Philos Soc 467–482; Herbert Simon, "Alternative Views of Complexity" in Mark A Bedau & Paul Humphreys, eds, *Emergence Contemp Read Philos Sci* (The MIT Press, 2008) 249; John H Miller & Scott E Page, *Complex Adaptive Systems: An Introduction to Computational Models of Social Life: An Introduction to Computational Models of Social Life* (Princeton University Press, 2009).

[43]Originally stated by Rulh, Katz, and Bommarito as: "Legal systems are locked in perpetual coevolution with their regulatory targets." J B Ruhl, Daniel Martin Katz & Michael J Bommarito, "Harnessing legal complexity" (2017) 355:6332 Science 1377–1378 at 1377.

[44] IP systems have multiple and diverse regulatory targets that are regulated by different categories of IPRs (patents, copyrights, trademarks, trade-secrets, biodiversity and traditional knowledge (TK), etc.), simultaneously or not. These different regulatory targets range from biomedical R&D and technology (in the most varied fields) to music, arts, culture, trade, etc.

Providing legal agents with an understanding of scientific processes enables law to regulate science more effectively, in the same way, that the research and academic community needs to understand legal rules for the proper operation and protection of intangible assets. This co-construction of meanings and communication between law and science is dynamic and ever-evolving. Neither of the systems supersedes the other or dictates rules of operation; they are equal partners in constructing ecosystems and common spaces (niches) in which agents interact to accomplish common goals. If these systems are unable to cross-communicate, they are less able to address society's problems. Taking this further, achieving the precise alignment of goals between IP and biomedical innovation systems would facilitate their interaction and coevolution. Therefore, seeing old problems through new lenses and promoting a dialogue between law and science is essential.[45]

Theoretical Framework

CAS theory is part of a broad range of theories from different fields united through the idea of complexity. "Complexity theory involves the study of many actors and their interactions."[46] As Axelrod and Cohen explain, there is no unified theory in complexity. Instead, recurring topics such as agents, strategies, and interactions appear in systems studies across various disciplines. This research combines

[45] As previously mentioned, scholars from different fields are engaging in new methodologies to solve complex problems, even though they use different terminologies to name the complexity of systems. Examples of these new methodologies can be found in other areas besides complex adaptive systems theory. For some examples, see: Rittel & Webber, *supra* note 18; Bubela, Gold & Morin, "Wicked Issues for Canada at the Intersection of Intellectual Property and Public Health", *supra* note 18; Leslie A Curry, Ingrid M Nembhard & Elizabeth H Bradley, "Qualitative and Mixed Methods Provide Unique Contributions to Outcomes Research" (2009) 119:10 Circulation 1442–1452; Sarah Earl & Fred Carden, "Learning from complexity: the International Development Research Centre's experience with outcome mapping" (2002) 12:3–4 Dev Pract 518–524; Sarah Earl, Fred Carden & Terry Smutylo, *Outcome Mapping: Building learning and reflection into development programs* (International Development Centre of Canada (IDRC), 2001).

[46] Axelrod & Cohen, *supra* note 42; Robert Axelrod, Robert Levin & Steven Strogatz, *The Complexity of Cooperation: Agent-Based Models of Competition and Collaboration*, 1 edition ed (Princeton, N.J: Princeton University Press, 1997) at 3; Robert Axelrod, "Syllabus. Complexity Theory in the Social Sciences", (2003), online: *Univ Mich* <http://www-personal.umich.edu/~axe/PS793.htm>; Hadfield, *supra* note 2; Edgar Morin, "The Concept of System and the Paradigm of Complexity" in Magoroh Maruyama, ed, *Context Complex* (Springer New York, 1992) 125.

these recurrent topics in an attempt to answer the problem of "analyzing interventions in a world that is hard to predict because it is complex."[47]

CAS are systems composed of interconnected parts (agents and populations of agents), each pursuing its own goals, whether those goals be the same or different. The interaction between these parts leads CAS to be dynamic, adaptable, and highly dependent on information flows. CAS give rise to emergent behaviours—or *emergence*—as a result of the interaction of parts of the system that is neither designed nor predictable: they emerge as the system operates. Prediction is impossible in CAS because of the large number of possibilities that emerge from interactions between the parts of the system and our lack of knowledge about them and their likelihood to happen. This characteristic makes observing CAS through patterns of interaction more realistic than trying to establish clear cause and effect relationships from their operation. In this sense, "the whole of the system is more than the sum of its parts."[48]

By showing that IP and biomedical innovation systems should be seen as CAS, this dissertation proposes an analysis that allows for their innovative understanding, co-design, and reform through bottom-up approaches.

Methodology and Method of Study

This dissertation engages primarily in theoretical research to reframe how agents think about IP and biomedical innovation systems. In particular, it applies CAS theory to law with the goal of uncovering hidden patterns of interaction between agents participating in those two systems. This improved understanding facilitates legal and policy design and opens opportunities for reform.

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[47] Axelrod & Cohen, *supra* note 42 at 15-20 (specifically, 17); Edgar Morin, "From the Concept of System to the Paradigm of Complexity" (1992) 15:4 J Soc Evol Syst 371–385 at 371–385; Morin, *supra* note 46; Warren Weaver, "Science and Complexity" (1948) 36:4 Am Sci 536–544; A-L Barabasi, "The Architecture of Complexity: From Network Structure to Human Dynamics" (2007) 27:4 IEEE Control Syst 33–42; Mitchell, *supra* note 42 at 14; Brian Castellani, "Map of Complexity Sciences", online: <http://www.art-sciencefactory.com/complexity-map_feb09.html>.

[48] See: Simon, *supra* note 42; Axelrod & Cohen, *supra* note 42; Mitchell, *supra* note 42.

In this dissertation, I focus on how individual agents or a population of agents (mainly expert communities[49]) affect law and biomedical R&D—the two central CAS I explore—and their ability to influence, change, and reform those systems. This dissertation is particularly interested in assessing the perspective of experts within those research, academic, and legal communities who are situated, for the most part, at the base of the organizational structure of IP and biomedical innovation systems. Most of these experts work at publicly funded universities and research institutions. I focus on expert communities because of the central role played by these agents in terms of their ability to engage in bottom-up systemic reform, to clarify the relationship between law and science (since they are the ones often performing biomedical R&D), and to experiment with creating new biomedical RD&I models.

Among the many lenses and insights provided by CAS theory and its models, this research draws inspiration from the literature on Agent-Based-Models (ABMs) and, in particular, discussions of 'agent-centred evaluations.' As explained in Chapter One, these agent-centred evaluations apply to the combined study of IP and biomedical innovation systems.[50]

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[49] By expert communities (or communities of experts) I mean the agents situated at the bottom organizational layers of IP and biomedical innovation systems that are mainly members of publicly funded universities and research centres. The expert community is also a good example of the multiple and dynamic roles an agent can play. Experts may be part of research and academic institutions which can be private or public, as well as agents interacting in settings and niches that combine both elements such as public-private partnerships. They may also be internal agents to governments, considering there are research institutes that integrate the government infrastructure such as Fiocruz Foundation in Brazil. They are academics and researchers engaging in biomedical R&D and legal experts that advise these communities on the design of IP strategies applied to their activities. Examples of these legal experts are members of Universities' Technology Transfer Offices (TTOs). In evaluating agents' behaviours, interactions, and expectations, I may also name them 'legal agents' and 'non-legal agents' while referring to the fact that they have or do have not formal legal training.

[50] Briefly explained, ABMs are computer models created to simulate the behaviour (interactions and actions) of different agents that comprise a CAS and are particularly interested in the role of individual agents in these systems. In developing ABMs, after selecting the most important factors interfering in a complex issue, one might determine the agents that participate in this issue, delimiting the time and scope (context) in which these agents interact and determining the conditions of their interaction, then, a computational model (ABM) is created to simulate the selected interaction. As the model operates over time and context, emergent patterns of behaviours that were not foreseen by the person analyzing that CAS may arise. This dissertation does not engage in computer simulations, although, it acknowledges their value. Rather, this study is limited to translating CAS theory and ABMs concepts to legal theory and extracting elements from the interaction and coevolution of IP and biomedical innovation systems that are relevant to clarify the manner these systems relate to each other and to understand better the problems arising in the biomedical innovation ecosystem. Chapter One explains better ABMs. For initial information about ABMs, see: Eric Bonabeau, "Agent-based modeling: Methods and techniques for simulating human systems" (2002) 99:suppl 3 Proc Natl Acad Sci 7280–7287; Robert Axelrod & Leigh Tesfatsion, "Appendix A: A Guide for Newcomers to Agent-Based Modeling in the Social Sciences" in *Handb Comput Econ* (Elsevier, 2006) 1647.

Moreover, in engaging in CAS analysis of social systems, it is critical to maintain awareness of the risk of operationalizing the study of these systems while taking their human characteristics seriously. This can be accomplished by focusing on agents that work within and between systems. As dynamic entities, human agents can play any number of roles within a system. Still, they will always be systems' participants while using and benefiting from the outcomes of these systems' interactions. It is in their interest to guarantee that access and innovation problems are effectively addressed.

As methods of analysis, this research engages in descriptive, analytical, and conceptual evaluations. This dissertation uses bibliographical, legislative, and case studies review to examine the interaction and coevolution of IP and biomedical systems and recount their coevolutionary story.

Failures in Understanding and Analysing Intellectual Property and Biomedical Innovation Systems and the Need for New Approaches

Current approaches to understanding and reforming IP systems are insufficient to address societal problems for several reasons:

(i) They have a static view of these systems and their interaction with regulated systems, and they generally focus on applying norms in abstract. As such, they do not consider the interactions and behaviours of agents that determine the shape and content of these systems and even less so of agents working within regulated systems (herein, the biomedical innovation system).

(ii) They are insufficient to promote multi-systemic evaluations and are not always tailored to specific social, cultural, and economic contexts, especially in developing and least-developed countries.

(iii) They do not combine evaluations of the normative content with the organizational features of interacting systems, nor do they evaluate how the structure and intrinsic characteristics of systems' organization may influence content.

(iv) They usually happen through top-down instead of bottom-up approaches, focusing on hierarchized and centralized policy and legislative reform processes. Agents conducting these processes are generally distant from the target problems. Mechanisms that promote feedback about the application and effects of the law (norms) in real-life to those engaging in law and policymaking are rare, and so it is the observation of emergent behaviours of agents in answering to problems. There is also a lack of communication and collaboration between legal and non-legal agents who participate in regulated systems to understand how those systems interact and coevolve.

(v) They tend to disregard uncertainty arising from agents' interactions and its impacts on problems response, understanding of multi-systemic settings, and planning reforms.

In summary, to promote solutions that address both problems of access and innovation, it is paramount to develop a novel approach that prompts agents always to consider the interconnectedness of those problems. While these problems occur within systems (such as IP and innovation systems), agents seldom tackle them systematically under the dominant framework. Agents thus rarely consider the interactions and behaviours between different agents and within systems that lead to these problems. They also disregard uncertainty and emergent behaviours within these systems that directly influence their understanding and reform. A CAS evaluation applied to the legal system and its regulatory targets provides a new and dynamic understanding of these systems' interactions and evolution by studying their agents' expectations and behaviours.

In support of this new approach, there is a demand for more empirical evidence, more engagement of the academic and scientific communities in the law and policymaking processes, the development of new methodologies to study the effects of uncertainty and IPRs' protection in access and innovation, and for more and newer metrics to evaluate the successes or failures of different laws and

policies in the regulation of science. The prevailing approach to understand the interaction of law and science has resulted in legal and policy responses to scientific endeavours that are not thoughtful and systemic. A different, more effective response would be to admit the degree of uncertainty created by complexity and then consider how this complexity should influence the design of dynamic, resilient systems to harness it properly. This research posits that applying CAS theory to IP and biomedical innovation systems might be one of the solutions to this problem of increased complexity.[51]

Moreover, applying CAS theory and agent-centred approaches allows for an evaluation of interconnected systems that combines the content of law and policy and the organizational features of those systems. Different agents have various levels of comprehension about the commands and sanctions that flow from the legal system. Accounting for the diversity within these systems, rather than the average of what happens within them, is essential to answer problems. This diversity of understanding partly results from the degrees of agents' overall knowledge about the legal system and its rules of operation and partly from the divergence of experts' interpretations of the law and its interactions. CAS theory assumes that agents' comprehension of the system and their problems is incomplete and influenced by biases.[52] Intuition and assumptions about previously successful strategies of other agents often have more influence on the decision-making of agents participating in CAS than legal scholars consider in their analysis and proposals to reform legal systems.[53] In bridging the gap between IP and biomedical innovation systems through CAS theory and agent-centred evaluations, one must keep in mind that agents are building blocks

[51] For a critical assessment of IPRs, see: Jean-Frédéric Morin, Kevin Daley & E Richard Gold, "Having Faith in IP: Empirical Evidence of IP Conversions" (2011) Available SSRN 1950541, online: <http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1950541>; Jean-Frédéric Morin, "Mapping Prevailing Ideas on Intellectual Property" (2013) Available SSRN 2278423, online: <http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2278423>.

[52] Richard H Thaler, "Behavioral Economics: Past, Present, and Future" (2016) 106:7 Am Econ Rev 1577–1600; Daniel Kahneman, *Thinking, Fast and Slow*, eighth edition ed (Anchor Canada, 2013) at 411–413.

[53] W Brian Arthur, "Inductive Reasoning and Bounded Rationality" (1994) 84:2 Am Econ Rev 406–411; Daniel Kahneman, "Maps of bounded rationality: Psychology for behavioral economics" (2003) 93:5 Am Econ Rev 1449–1475; Daniel Kahneman, "A perspective on judgment and choice: mapping bounded rationality." (2003) 58:9 Am Psychol 697.

to understanding the world's complexity around them. For effective reform, it is critical to uncover and evaluate agents' decision-making processes, emergent behaviours, and assumptions about 'what the legal regulation is' and 'what it ought to be.'

A CAS analysis also enables the creation of new methodologies to evaluate problems and aggregates more elements into this analysis. It allows whoever studies these systems to assess their structures—or CAS organizational framework—and identify components that contribute to tackling complex problems. The importance of the system's organizational framework is generally overlooked in legal analysis, while agents are more concerned with content. The same for how the constituent parts of systems (agents) build these CAS through behaviour and not only norms. Even though content evaluation is not a concern for CAS theory, I intend to extend my study to a combined evaluation of organizational features and content and inquire how structure influences or even determines agents' behaviours and, consequently, systems' contents. Knowing CAS's organizational framework uncovers new pathways to understanding and reform and explains the rationale for suggesting bottom-up approaches and testing new models to regulate these systems.[54]

Law and science have different rules and principles that guide their operation. However, no system exists and works in isolation. Multidisciplinary research and the development of a dialogue between the agents comprising these systems to identify shared features that facilitate their interaction and joint functioning is part of a system evaluation and reform strategy. Thus, it is also necessary to identify or

[54]As Gillian Hadfield states: "To increase our capacity to invent and build the legal infrastructure we need throughout the complex global economy—in both rich and poor places—we have to think differently about how we produce rules and rule systems. (…) Today the rules are designed almost exclusively in top-down fashion by elected officials and civil servants, often with the "help" of well-heeled lobbyists and the politically connected. Our legal systems are operated by lawyers and judges who make up a legal profession that faces only muted competition from innovators who might come up with better ways of getting law done." Hadfield, *supra* note 2 at 5–6.

create a common language to improve collaboration between different systems and their agents and common principles that inform the interaction and coevolution of diverse CAS.[55]

IP and biomedical innovation systems also operate as an ecosystem formed by many agents engaged in constant interactions directed to pursue their objectives—for example, agents working on a specific open drug development project or initiative to develop a new medicine. Within this ecosystem, agents create niches to adjust how they interact, communicate, and experiment.[56] Niches have a contained organizational structure and comprehend a selection of rules and agents of the systems enabling their operation and the pursuit of goals. They are places where agents can experiment and improve their knowledge about the systems in which they operate, other agents, communication processes enabling interaction, and identify common traits of these systems. Data, information, and knowledge allow communication among agents and within systems.[57] Improving and guaranteeing processes and mechanisms that would enable agents to share data, information, knowledge, and the results of their research are conditions for systems' operation and reform. This is why informed decision-making and more effective communication between agents and systems are crucial to their functionality and reform.

IP systems are created to enable the protection of intellectual assets by different agents. For example, diverse agents (private sector and universities) acquire and exercise IPRs to achieve varied goals. The way agents use IP to protect their intellectual assets and their choices about how, when, and what they protect through IPRs and who has access to them determine the impact of these rights in other agents and the overall functionality and results of different CAS. IPRs are instruments that, by themselves, do not harm or prevent access to knowledge or innovation; however, the behaviours and choices of agents towards these rights might. The question is how to equip agents to make better decisions that safeguard

[55] See Chapter One for more details about it. For initial thoughts, see: John H Holland, *Signals and Boundaries: Building Blocks for Complex Adaptive Systems*, reprint edition ed (The MIT Press, 2012).
[56] See Chapter One for further information about how agents and systems communicate and interact.
[57] See: Holland, *supra* note 55.

access to knowledge and innovation while pursuing broader social and economic benefits from exercising these rights. Clarifying the rules and principles guiding the interactions and behaviours of agents within IP and biomedical innovation systems is critical to understanding these systems and, consequently, informing agents' decision-making while setting IP strategies, policies, and practices. If there is a dissonance in the relationship between law and science—and how agents communicate through them—decision-making processes are impaired.

An example of the lack of harmony between these systems relates to patent infringement and the need to establish clear boundaries for research activities through research exception rules. Research exception rules impose legal limits on the behaviour of the research community while doing research. If the ownership of data, information, and knowledge is absolute, then research activities encounter a restrictive environment and do not progress. Research exception rules are in place to enable the advancement of science in non-commercial research, and these rules allow researchers to perform their activities without infringing third parties IPRs. However, the definition of non-commercial purposes is debatable, as it is determining which technology will have commercial value at an early stage of research. As a result, scientists generally ignore legal rules around what research is acceptable, relying instead on informal norms and behaviour.[58] On occasion, agents resort to strict legal rules[59] causing uncertainty in the scientific community. Science needs the freedom to operate, and excessive ownership of intellectual assets derails this freedom; hence, agents must rethink applying the law (IPRs) to accommodate this need. IPRs are dynamic rights that can promote both openness and closedness towards intellectual assets. There is a need to reassess and recount the story about the interaction and coevolution of IP and biomedical innovation systems to identify the effects of this interaction on access and innovation.

[58] See: Wesley M Cohen & John P Walsh, "Real Impediments to Academic Biomedical Research" (2008) Innov Policy Econ Vol 8 1–30.
[59] *Madey v Duke University*, 2002 United States Court of Appeals for the Federal Circuit 1351.

Moreover, a CAS approach spurs further experimentation in legal theory by promoting empirical and multidisciplinary research and supporting the development of new models representing and evaluating the regulation of biomedical RD&I by IPRs. These models not only provide a more nuanced understanding of these systems' interactions (that is, they are pictures presented from a specific point of view) but can also simulate a broader range of agents' interactions over time and context. Thus, they suggest variations on these new models that can better achieve access and innovation goals.[60]

Understanding and reforming IP and biomedical innovation systems have long been a challenge. Any applied model will be an imperfect representation of reality. However, models can be valuable instruments that explain the world around us, expand our assessment of it, and promote multidisciplinary research and collaboration among disciplines.[61] In analyzing IP and biomedical innovation systems, agents need to consider the usefulness of seeing them as CAS. Learning to identify similarities and shared responses to problems in those systems can assist in solving some of society's most challenging problems.[62]

For too long, developing countries (and their agents) have been afflicted by limited access to knowledge and innovation, which in turn affects their legal and public policy choices and hinders multidisciplinary strategic thinking about these issues. It is time to correct these distortions by promoting more participatory, transparent, and accountable IP and biomedical innovation systems while enabling critical and local leadership. Drawing more explicit connections between law and science can lead to better outcomes from these systems' operations that would guide more comprehensive legal and policy reforms in the long term. Enabling these connections requires assessing agents' expectations and behaviours that

[60] Even though modelling is an important element of CAS, this dissertation does not engage in development of computational models to understand the coevolution and interactions of IP and innovation systems. For specific modelling techniques in social systems and the limitations of it, see: Miller & Page, *supra* note 42.
[61] Richard Gold, "Structural Dynamic Theory of Law, A" (1991) 16 Queens Law J 347; Axelrod & Cohen, *supra* note 42.
[62] J B Ruhl, "Is Law a Complex Adaptive System?", (25 July 2006), online: *Jurisdynamics* <http://jurisdynamics.blogspot.ca/2006/07/is-law-complex-adaptive-system.html>; Ruhl, Katz & Bommarito, *supra* note 43.

result in these systems' content, organization, and structure. When these connections are enhanced, law and science should respond more effectively to the challenges of complexity and work towards cooperative goals. Thus, law and science need to interact and establish a shared language that permits their dynamic and complementary interaction.[63]

As a global and dynamic pandemic, Covid-19 demonstrated how societies are at once fragile and resilient and, in doing so, highlighted the characteristics that make society a CAS. It is hard to predict all of the outcomes of the pandemic. Still, several of the fragilities and strengths of IP and biomedical innovation systems and society's response to problems have again been exposed. Society will move forward and, more than ever, will need to look for new ways to better address access to knowledge and innovation issues in the broader context of biomedical innovation ecosystems and different health problems. Now is the best time to harness the complexity of CAS and the role of agents, rethinking the challenges of our time while placing people's wellbeing at the centre of these systems. Interestingly, the final review of this dissertation happened in Brazil, where social and economic problems and political instability exacerbated the concerns around the pandemic's response. The Brazilian response to the pandemic further reinforces the importance of local answers, the role of individuals in systems' design and reform (exceptionally, expert communities), and the need to harness CAS complexity for the common good and public interest.

Roadmap

I divide this dissertation into two Parts, transitioning from the theoretical to practical (case studies and legislative and policy analysis) while identifying the interplay of agents as crucial elements that create,

[63] *WHO | Public health, innovation and intellectual property rights: Report of the Commission on Intellectual Property Rights, Innovation and Public Health*, by World Health Organization (WHO) (Geneva: World Health Organization, 2006); Røttingen et al, *supra* note 15; *Toward New Models for Innovative Governance of Biomedicine and Health Technologies*, OECD Science, Technology and Industry Policy Papers, by OECD, OECD, OECD Science, Technology and Industry Policy Papers (Paris: Organisation for Economic Co-operation and Development, 2013).

recreate, and reform IP and biomedical innovation systems. The role of agents in these systems—mainly expert communities—crosscuts the discussions in all the chapters and thus serves as a unifying element while reflecting on how to better design and reform these systems.

Part I consists of three chapters and presents the theoretical framework for assessing legal systems and, more specifically, IP systems, as CAS. Chapter One gives an overview of CAS theory and the main characteristics of these systems that are relevant to this research. This chapter examines how these systems (and their agents) learn, adapt, and evolve in light of the information created and exchanged by agents.[64] As this dissertation's analysis focuses on agents of CAS, it employs concepts of ABMs to propose and develop an agent-centred evaluation to study the coevolution and interaction between IP and biomedical innovation systems. Chapter Two contends that legal systems can be seen as CAS. It discusses the current state of CAS theory in legal scholarship while explaining the challenges and opportunities to adapt CAS theory and agent-centred evaluations to legal studies. It further presents theories of legal scholars who have explored this topic—from 'traditional' or 'general' systems theory approaches to scholars who have specifically applied CAS theory to legal scholarship. This chapter also translates elements of CAS theory to legal and policy analysis based on selected characteristics of these systems. It finally incorporates insights from behavioural theory into the analysis due to this dissertation's interest in the role of individual agents in CAS. Chapter Three presents the IP system as a CAS. It provides background information, theories, and justifications for granting IPRs that may influence the relationship of this system with its diverse regulatory targets, especially the biomedical innovation system. Information is, according to this chapter, critical in connecting evaluations of content and structure regarding IP systems. In summary, Part I presents the theoretical background for this dissertation and provides the methodological starting point

[64] For explanations about CAS as an entity that can learn, adapt, and evolve, see, generally: Axelrod & Cohen, *supra* note 42.

to evaluate IP and biomedical innovation systems' interactions, especially in developing countries. Part I also advances the debate on how to translate CAS concepts into legal theory as a dynamic tool.

Part II has four chapters that describe the complexity of multi-systemic analysis. This part studies the interaction and coevolution of IP and biomedical innovation systems, moving from theory to real-world problems encountered by agents participating in those systems. It completes the picture by presenting the components that form the biomedical innovation ecosystem while highlighting the uncertainty that emerges from those systems' operations and interactions. Chapter Four presents the complexity of science, its normative structure, and the reasons to classify the biomedical innovation system as a CAS. It explains concepts related to biomedical RD&I and its regulation by IPRs that enable connecting the structure and content of these systems. This chapter aims to contextualize legal agents' understanding of the elements of regulated systems and how they engage agents within these regulated systems to reform them. Chapter Five evaluates the interaction and coevolution of IP and biomedical innovation systems while revisiting the 'tragedy of the anticommons' hypothesis in biomedical research[65] and provides other examples. The tragedy of the anticommons provides an example of how agents behave in designing, strategizing, and reforming IP and biomedical innovation systems based on assumptions that do not necessarily represent the reality occurring within those systems. This chapter also illustrates agents' traditional views and patterns of behaviour while engaging in IP systems' reform, mainly referring to legal transplantation and the importance given to patents in universities and research centres. Chapter Six studies the role of agents in reforming biomedical R&D systems. It asserts that behaviours and interactions

[65] Briefly, the tragedy of the anticommons states a hypothesis (the likelihood of something happen) in which too much early and broad patent protection over basic research in the biomedical field can negatively affect innovation and product development. This is because to develop a product (a medicine, for instance) the private sector would have to negotiate with multiple patent owners of 'small' inventions that are needed to develop its final product. It refers to how ownership (more specifically, patenting) in early stages of research can interfere in the advancement of science and innovation. Heller and Eisenberg stated a hypothesis of something that could happen. Later-on several scholars engaged in empirical research to see if this actually happened, as described in Chapter Five. M A Heller & R S Eisenberg, "Can patents deter innovation? The anticommons in biomedical research" (1998) 280:5364 Science 698–701; Michael A Heller, "The Tragedy of the Anticommons: Property in the Transition from Marx to Markets" (1997) 111 Harv Law Rev 621.

of agents situated at the bottom layers of these systems (expert communities) are critical for these systems' reform. It mainly presents Brazil as a case study and illustrates how coordination, diversity, and experimentation are essential to solving problems of access and innovation. Chapter Seven examines the idea of openness in law and science through the lens of CAS theory. It asks whether openness is a component or characteristic of the biomedical innovation ecosystem, a common guiding principle of RD&I activities, or an emergent phenomenon reflecting agents' behaviours and patterns of interaction. It further illuminates how the idea of openness manifests itself in different RD&I models and initiatives, in specific institutional practices and policies, and legal provisions in developing countries, using Brazil as an example. This chapter aims to understand better how different agents interact to create niches within biomedical innovation systems that may lead to systemic change.

Part II narrows this dissertation's analytical focus to developing countries (with primary examples from Brazil) as it considers the experiences of developing countries in designing and reforming IP and biomedical innovation systems. This focus is justified because of the need to advance discussions about these countries' social and economic development and IP systems. Brazil is not only a key player in the biomedical RD&I scene, but focusing on it allows me to contribute to critical debates in this area in my country and participate in discussions that may result in creative solutions at the local and global levels.

PART I—GENERAL AND LEGAL THEORY ON COMPLEX ADAPTIVE SYSTEMS

CHAPTER ONE—COMPLEX ADAPTIVE SYSTEMS: FOUNDATIONS OF ANALYSIS

1.1. Overview: Definitions, General Concepts, and Ideas

Imagine a colony of ants, an amoeba, the human body, the law, a city, a country or the universe. Think about these entities in terms of their organization and common features. They can all be classified as systems despite their clear dissimilarities. The Oxford Dictionary defines a system as: "[a] set of things working together as parts of a mechanism or an interconnecting network; a complex whole." [66] Ludwig von Bertalanffy defines systems as "complexes of elements standing in interaction"[67] while formulating the claims for a 'General Systems Theory'[68] and exposing trends related to it in different fields. He states:

> It is necessary to study not only parts and processes in isolation, but also to solve the decisive problems found in the organization and order unifying them, resulting from dynamic interaction of parts, and making the behavior of parts different when studied in isolation or within the whole.[69]

The concept of 'system' is an intuitive human understanding of complex organizations. In this work, I define systems as being composed of different parts that are related, interact, coevolve, and function together.[70]

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[66] Oxford Dictionaries, "Definition of system in English by Oxford Dictionaries", online: *Oxf Dictionaries Engl* <https://en.oxforddictionaries.com/definition/system>.

[67] Ludwig Von Bertalanffy, *General System Theory: Foundations, Development, Applications*, revised edition ed (New York: George Braziller Inc., 1969) at 33.

[68] Bertalanffy, *supra* note 67; Ludwig Von Bertalanffy, "An Outline of General System Theory" (1950) I:2 Br J Philos Sci 134–165.

[69] He complements: "(…) Thus, there exist models, principles, and laws that apply to generalized systems or their subclasses, irrespective of their particular kind, the nature of their component elements, and the relations or "forces" between them. It seems legitimate to ask for a theory, not of systems of a more or less special kind, but of universal principles applying to systems in general." Bertalanffy, *supra* note 67 at 31–32.

[70] For foundational and general aspects of CAS theory applied to different fields, as well as general features of complexity theory, see: Mitchell, *supra* note 42; Mitchell, *supra* note 42; Miller & Page, *supra* note 42; Axelrod & Cohen, *supra* note 42; Tamas Vicsek, "Complexity: The bigger picture" (2002) 418:6894 Nature 131–131; Yanner Bar-Yam, "Why Complexity is Different | NECSI", (16 March 2017), online: *N Engl Complex Syst Inst* <http://www.necsi.edu/research/multiscale/whycomplexity>; Y Bar-Yam, *Dynamics of Complex Systems* (Westview Press, 2003); Murray Gell-Mann, "Complex adaptive systems" (1994) Complex Metaphors Models Real 17–45; Stuart A Kauffman, *Investigations*, 1st ed (Oxford ; New York: Oxford University Press, 2000); Edgar Morin, *On Complexity* (Hampton Press, 2008); Morin, *supra* note 46.

The basis of Systems Theory is to identify properties of different systems (for example, physical, biological, and social systems) and abstract common features and patterns. Details about the system's properties, behaviour, and elements may be uncovered more easily in some systems than in others, and the observation of one system may improve the analysis of others. This property is known as *universality in systems theory*, which starts from the position that no matter how distinct some systems appear to be, when compared to others, they function under universal rules of organization.[71] Thus, Systems Theory focuses on the properties and features of the system without necessarily specifying the content that is created by complexity.

In this and the following sections, I will set out (i) definitions, general concepts, and ideas that are key to understanding complex adaptive systems (CAS), comprehending and identifying their comprising elements, and the role of information in these systems, (ii) the characteristics of CAS that emerge from the interaction of its elements, and; (iii) the importance of agents in CAS and specific points to be considered while studying them. I conclude by stating the importance of harnessing complexity as a way to improve CAS design and reform.

1.1.1. Complex Systems and Complex Adaptive Systems

A system is *complex* when it is composed of multiple and large number of parts that interact in a non-simple way. It is complex because the dynamic and interrelated features of the different elements that constitute the system cannot be derived simply by adding each element together. Understanding the whole

[71] General considerations about systems theory and universality, see: Bertalanffy, *supra* note 67 at 32–33; Bar-Yam, *supra* note 70 at 1–5; Simon, *supra* note 42.

system requires examining the patterns of interaction between its elements; this helps to turn chaos into manageable complexity.[72]

A system is not only *complex* but also *adaptive* when its interacting parts can respond to changes in external or internal environments and adapt. Because a CAS consists of a variety of different parts (agents and populations of agents), a CAS adapts through the internal behaviours of those parts and interactions between them.[73] That is, the system 'learns' through its interactions by *feedback mechanisms* that enable it to assess the result of interactions and change or adapt in the future to better respond to problems. The modifications generated by the system (and its agents) may be temporary or definitive and are a consequence of systemic actions of learning, selecting, adapting, and evolving.[74] Interaction in CAS, between agents and within systems, is what leads to complexity and, consequently, uncertainty, and emergent behaviours—these elements are explained in detail in section 1.2.

Therefore, problem-solving may start by understanding which type of system agents interact with and where problems arise; this influences the strategies agents apply to solve problems. Distinguishing complex systems from simple or complicated systems is a helpful clarification to adopt systems' thinking approaches tailored to situations and contexts. The differences between these concepts are briefly described in the table below.[75]

[72] Simon explains: "I shall not undertake a formal definition of 'complex systems". Roughly, by a complex system I mean one made up of a large number of parts that interact in a non-simple way. In such systems, the whole is more than the sum of the parts, not in an ultimate, metaphysical sense, but in the important pragmatic sense that, given the properties of the parts and the laws of their interaction, it is not a trivial matter to infer the properties of the whole." Simon, *supra* note 42 at 467–468.
[73] Miller & Page, *supra* note 42 at 6.
[74] For general considerations, the definition, and characteristics of CAS, see: Axelrod & Cohen, *supra* note 42 at 20; Miller & Page, *supra* note 42 at 4–31; Mitchell, *supra* note 42.
[75] Table available at: Bev Holmes et al, "Systems Thinking in Dissemination and Implementation Research" (2012) Dissem Implement Res Health Transl Sci Pract at 31.

Differences between simple or complicated and complex systems[76]	
Simple or Complicated Systems	**Complex Systems**
Homogeneous: identical / indistinguishable structural elements	**Heterogeneous**: large number of structural variations
Linear: a relationship with constant proportions	**Nonlinear**: cause does not produce a proportional effect
Deterministic: same result always occurs for a given set of circumstances; predictable	**Stochastic**: an element of randomness leads to a degree of uncertainty about the outcome
Static: nothing changes over time	**Dynamic**: changes over time; past has an impact on the future
Independent: subsystems are not influenced or controlled by other parts of the system	**Interdependent**: subsystems are interconnected or interwoven, not just interacting
No feedback: open chain of cause and effect	**Feedback**: a closed chain of causal connections
No adaptation or self-organization	**Adaptation and self organization**: ability of a system to structure itself, to create new structure, to learn, or diversify
No connection between levels or subsystems	**Emergence**: collective behavior that cannot be simply inferred from the behavior of components

Illustrating the lack of uniformity in the definition of CAS, Melanie Mitchell describes a CAS as "a system in which large networks of components with no central control and simple rules of operation give rise to complex collective behavior, sophisticated information processing and adaptation via learning or evolution" or "a system that exhibits non-trivial behavior." [77] Mitchell elaborates on her definition by noting the impossibility of providing a unique description of CAS and instead calls attention to their properties. First, Mitchell notes that CAS have complex collective behaviours and work in large networks of individual components, where each component follows simple rules with no central control. The collective actions and interactions of components make them hard to predict, as well as being subject to changing patterns of behaviour. Second, CAS makes use of signalling and information processing, i.e.,

[76] Table adapted from: Diane T Finegood, "The Complex Systems Science of Obesity" in *Oxf Handb Soc Sci Obes* (2011).
[77] Mitchell, *supra* note 42 at 13.

they use information and signals of their internal and external environments to operate and communicate with other systems—I will examine this further below. Third, CAS adapt and change behaviour in a manner that tends to improve their chances to succeed and survive.[78] These are important characteristics of CAS for this dissertation, given its focus on the coevolution and interaction of different CAS, and how these systems communicate.

Scott Page and John Miller introduce the idea of 'the interest in between' to explain complexity science and, ultimately, CAS theory while acknowledging the relative infancy of this theory in social science. 'The interest in between' is an assessment tool proposed by the authors to appreciate complexity.[79] To understand the idea of 'the interest in between,' one can imagine a world in which interactions between agents range from total connectedness (i.e., a direct and reliable cause-and-effect pathway that is undisturbed by other factors) to total disconnectedness. In a perfectly connected world, there is no complexity. This is because everything that happens in the system could be mapped or explained by tracking back to previous causes, consequences, and interconnections. However, a complete lack of connectedness does not necessarily characterize complexity because, when parts of the system do not communicate or exchange information, they still operate within their own closed reality. Such isolation results in a lack of interaction and, consequently, the system becomes a predictable system, which is the opposite of a CAS. In this sense, a complex world is formed 'in between' total and inexistent connectedness, and this inspired the authors to coin the term 'the interest in between.'[80]

[78] *Ibid*.
[79] Miller & Page, *supra* note 42 at 7-8-27-218–230.
[80] Clarifying this idea, the authors assert: "The science of complex systems and its ability to explore the interest in between is especially relevant for some of the most pressing issues of our modern world. Many of the opportunities and challenges before us—globalization, sustainability, combating terrorism, preventing epidemics, and so on—are complex. Each of these domains consists of a set of diverse actors who dynamically interact with one another awash in a sea of feedbacks. To understand, and ultimately to harness, such complexity will require a sustained and imaginative effort on the part of researchers across the sciences. (…) The science of complex systems is not a new way of doing science but rather one in which new fantasies can be indulged." *Ibid* at 7–8.

Even though there is no unifying theory of complex systems and CAS, the figures below provide some guidance on the study of CAS. They represent 1) a visualization of theoretical and conceptual routes that influenced complex systems theory, and 2) the place of complexity theory while considering different theoretical approaches.[81]

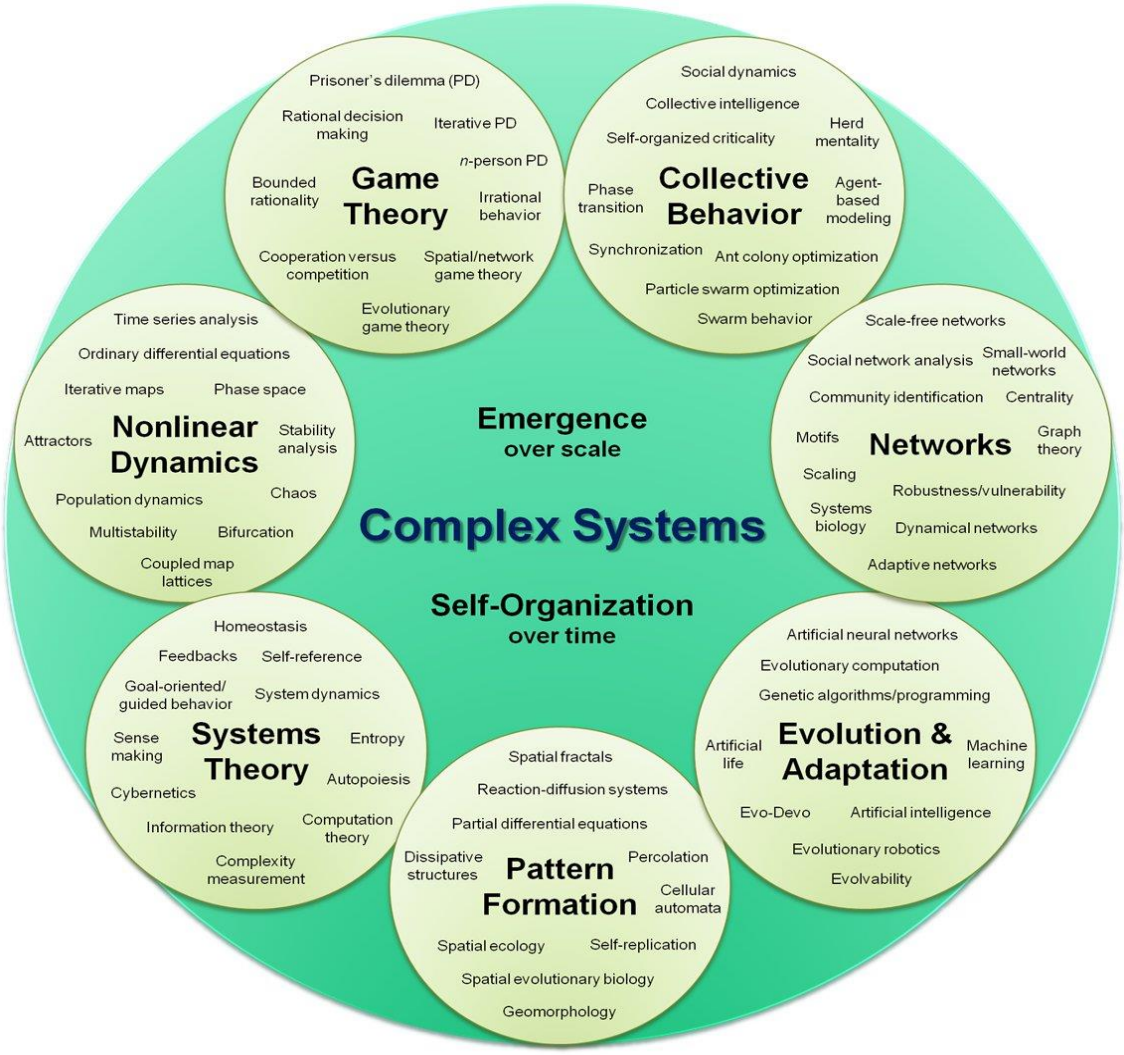

Figure 1: Visual, Organizational Map of Complex Systems Broken into Seven Sub-Groups. Created by Hiroki Sayama, D.Sc., Collective Dynamics of Complex Systems (CoCo), 2010.[82]

[81] For another useful tool to visualize some connections between different theories, concepts, and the work of different scholars studying complexity science, see: Castellani, *supra* note 47.

[82] Hiroki Sayama, *Visual, organizational map of complex systems broken into seven sub-groups* (Collective Dynamics of Complex Systems (CoCo), 2010).

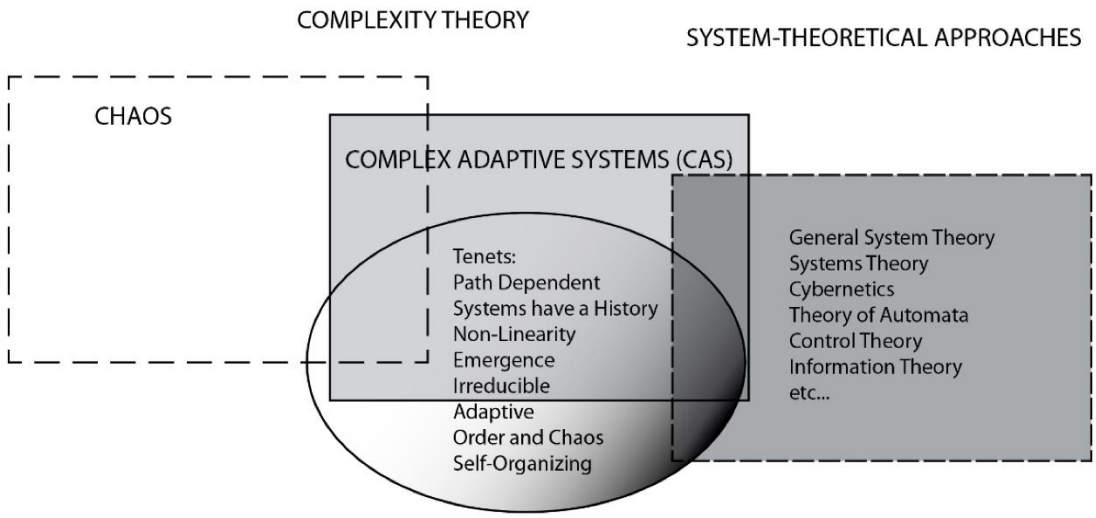

Figure 2: "Complexity theory and theoretical system approaches"[83]

1.1.2. Multiplicity of Elements Comprising Complex Adaptive Systems

For my work, three elements are important in studying a CAS and its characteristics: (i) the overall idea about the system and its main characteristics, its interactions with other systems—I have defined CAS above and item 1.2. explains better selected characteristics of it; (ii) the agents (or parts) making up these systems and determining a CAS's dynamic emergent behaviour that leads to uncertainty due to the rules of interaction between these parts; and, (iii) the external environment in which different systems operate, interact, and coevolve and the internal environment of each system. This research examines CAS through the perspective of its agents (and, consequently, their behaviours and interactions with other agents). It further considers how CAS analysis can assist agents in promoting change and reform in and within these systems.

[83] John R Turner & Rose M Baker, "Complexity Theory: An Overview with Potential Applications for the Social Sciences" (2019) 7:1 Systems 4 at 12.

(i) The System as a Whole: CAS Main Characteristics and its Interactions with Other Systems (and Agents)

As previously mentioned, the whole of the system is more than the sum of its parts. CAS do not exist or work in isolation. To better design and propose reforms of these systems, one needs to understand how they operate, interact, and coevolve with other systems. Therefore, there is a need to develop a dialogue between different systems and the agents comprising them and to identify shared features that facilitate their interaction and joint functioning that affect the whole of the system.[84] While interacting, CAS create niches—common spaces—within their ecosystem, which are comprised of agents of different systems. For example, agents working on a specific project to develop a new drug constitute a niche. Niches have a contained organizational structure and include rules and agents of the systems enabling their operation. Niches are where agents can experiment and improve their knowledge (and communication) about the systems and information about other agents. I will further explain these ideas in section 1.3.3 below.

(ii) Agents in CAS

Agents create, transform, re-create, and influence the system. Agents within a system can often number in the many thousands. In the context of this dissertation, key agents of IP and biomedical innovation systems include states, the private sector, NGOs, individuals, international organizations, groups of people (for instance, patients), and institutions.

An agent is "an individual that exhibits the capacity to achieve a goal or to effect an outcome. Often the term 'agent' implies that an agent operates within a population and interacts with other agents as well as with a more passive environment."[85] Agents have properties such as location, capabilities, and memory. Agent's strategy, or "the way an agent responds to its surroundings and pursues its goals,"[86] may

[84] See, especially: Holland, *supra* note 55.
[85] Santa Fe Institute, "Glossary of Terms", online: *Complex Explor - St Fe Inst* <http://www.complexityexplorer.org/explore/glossary#dynamical-system>.
[86] Axelrod & Cohen, *supra* note 42 at 4.

change as the agent evaluates the impact of its actions against its goals and the behaviour and strategy of other agents. Agents may pursue goals individually or in a group of similar agents, sometimes joining a group permanently or only for a specific purpose. For instance, some developing countries tend to negotiate together in international trade settings such as the World Trade Organization (WTO), as do developed countries.[87] Agents not only act in conjunction with other agents but also act in relation to artifacts—tools or objects—in the environment that result from their actions or assist them in achieving goals. For instance, IP artifacts include protected assets such as medicines and different kinds of products and processes.[88]

Moreover, agents evaluate the system and their role in it through both subjective and objective measures of success. For instance, the economic gain or royalty fees that result from licensing a patented medicine is an objective measurement of success. However, evaluating whether research-peers admire an inventor and how this admiration may drive his/her behaviour towards collaboration or competition while doing science is a subjective measurement. Measurements are selected, and selection presupposes choice, which is highly influenced by beliefs, biases, and knowledge that agents have about the system, other agents, and the goals they choose to pursue in that system. Indicators can also vary over time and context[89], but they should further indicate the success or failure of agents in achieving predetermined goals in different systems. For this dissertation, access and innovation are intrinsically connected goals, and, as such, they should be equally pursued. Therefore, the design and reform of these systems and measurements and evaluations of their performance should consider these goals.

[87] *Ibid* at 3–5.
[88] *Ibid*.
[89] *Ibid* at 119–127.

The agents making up these systems engage in reasoning that is subject to the rules of interaction that guide these systems' operation.[90] In the case of social CAS (as opposed to natural CAS, such as the weather or natural environments), agents interact with one another through connections but also act independently through their cognitive processes, applying the information they have available.[91] In section 1.3, I explore the behaviours and interactions of agents.

(iii) Systems' Environments and Boundaries

The study of systems implies recognizing that any system exists within an environment where the creation, receipt, and exchange of information actively occurs. The *external environment* is the location for interactions with other systems. The *internal environment* is where the interaction between the components/parts of a system takes place (or between the subsystems of a major system). The boundaries delimiting a system's internal and external environment may change over time and context. Therefore, one must be aware of the need to redefine these boundaries when studying or observing the system.[92]

In deepening the evaluation of systems in relation to their environmental interaction, one may differentiate between types of systems. For this dissertation, it is important to assess whether a system is open or closed.[93] A closed system is isolated from its environment, and changes happen within its internal

[90] I will discuss the decision-making processes of agents in CAS and their imperfect reasoning (bounded rationality) later in this Chapter and the impossibility of analyzing these systems by taking an average of their agents' interactions and behaviours as a parameter.

[91] In this sense: "The remarkable thing about social worlds is how quickly such connections and change can lead to complexity. Social agents must predict and react to the actions and predictions of other agents. The various connections inherent in social systems exacerbate these actions as agents become closely coupled to one another. The result of such a system is that agent interactions become highly nonlinear, the system becomes difficult to decompose, and complexity ensues." Miller & Page, *supra* note 42 at 10.

[92] About the elements that forming the system and their environment, see: Axelrod & Cohen, *supra* note 42; Bar-Yam, *supra* note 70.

[93] Clarifying this notion: "Closed and open are relative terms, of course: no living system is either totally open or totally closed. A living system is open to matter/energy and information (in the case of a human being, for air, food, communication with the environment, other people), but also closed in the sense that a human being is not open to everything—having a defined identity also means having boundaries which articulate self- and not-self. So every living system is both open and closed, again one of those paradoxical, both/and relationships. Open systems tend to be far less stable than closed systems, which are by definition systems in equilibrium, with no exchange with their environment. The openness of the system leads to potential disequilibrium. Open systems are stabilized by flow, but their structural stability is only relative because this structure is gradually, and sometimes quite rapidly, transformed by exchanges with the environment." Alfonso Montuori, "Complexity and Transdisciplinarity: Reflections on Theory and Practice" (2013) 69:4–6 World Futur 200–230 at 206–207.

elements. An open system dynamically interacts with its external environment and receives information from it. The flow of information is what gives some stability to open systems. Changes that occur in open systems result from internal interactions among the parts of the system in its internal environment and information received from its external environment and other systems.[94]

Understood in this way, systems are mental abstractions that agents create to explain, classify, and organize the world around us. They make possible the design of multiple structures and different approaches to address complex problems. To put this another way: one can see systems as models of facts in the world, rather than facts on the ground.

1.1.3. The Role of Information in Complex Adaptive Systems

Information is the fuel for CAS operation and performance. The conceptualization of information used in this dissertation comes from a more colloquial definition, meaning "any medium that presents knowledge or facts."[95] What is at stake here is the creation, communication, and processing of information that feeds or interferes with the operations and performance of these systems and that informs different agents' decision-making processes, interactions, and behaviours. In this sense: "[i]nformation can be understood as a mediator for interaction. Decreasing the costs of its propagation and storage inherently increases possibilities for interaction effects. An Information Revolution is, therefore, likely to beget a complexity revolution."[96]

At least three internal processes are involved in how a CAS manages information: acquiring, processing, and using information that is sourced from the environment and other agents. Agents engage in reasoning in social systems, and this confers a level of subjectivity upon their actions that are based on

[94] Stuart Kauffman, *At Home in the Universe: The Search for the Laws of Self-Organization and Complexity*, reprint edition ed (Oxford University Press, 1999); Bertalanffy, *supra* note 67 at 39–41.
[95] Mitchell, *supra* note 42 at 41.
[96] Axelrod & Cohen, *supra* note 42 at 26.

information they receive from the system's environments and its agents. Agents have the ability to reflect on the information they receive, and this reflection varies enormously depending on agents' backgrounds and reasoning, as well as on their strategic location and interaction with other agents. Nevertheless, there are limitations on agents' ability to acquire, process, and use information because of their cognitive capacity,[97] asymmetrical access to information and analysis based on that information, and the manipulation of information by some agents. Communication of information among agents, the use of adequate and common language or speech, how information flows and is shared among agents, and the quality and reliability of information are some key aspects influencing the structure and operation of CAS.[98]

1.2. Key Characteristics of Complex Adaptive Systems

In this section, I explore selected characteristics of CAS that are relevant to this dissertation in further detail. All these characteristics are critical to improving agents' assessment of the interaction and coevolution of the systems in which they act. In particular, I examine the following characteristics:

(i) The phenomenon of 'emergence' in CAS: seemingly spontaneous features of the system that arise in the absence of central control, resulting in uncertainty;

(ii) Hierarchy;

(iii) Robustness and resilience; and

(iv) Diversity.

[97] Miller & Page, *supra* note 42 at 94–96.
[98] Axelrod & Cohen, *supra* note 42 at 503–515.

1.2.1. Emergence in Complex Adaptive Systems and its Dynamic Nature

Emergent properties or *behaviours* (also known as *emergence*) are aspects of the complex system that arise—seemingly spontaneously—from the interaction of the system's components and are stimulated by the environment and the information available to the system's parts.[99] For example, one could consider the 'rule of law' an emergent feature of a successful legal system. While this emergent feature cannot be derived from any individual part of the system, through the interactions of these parts, they contribute to the overall outcome of the legal system.[100] In this sense, emergent properties lead to inverting the logic that the system as a whole imposes its features on its parts by exercising central control. Instead, complexity views "the global properties of the system as emerging from the actions of its parts, rather than seeing the actions of the parts as being imposed by a dominant central source."[101]

Emergent properties or behaviours of the system render the prediction of outcomes difficult, if not impossible. One way to cope with this uncertainty is to identify patterns of interaction between the parts of the system. This approach stresses the fact that cause and effect are hard to establish in CAS, given that multiple elements interact and because of the incomplete knowledge of agents about the system and their interactions with it.[102] In this sense, understanding how a CAS works in detail is impossible, which leads, in turn, to strategies that focus on identifying patterns of interaction and creating mechanisms that are dynamic and responsive to problems. Viewing systems as CAS means embracing *uncertainty* and changing the focus of analysis from identifying individual cause-and-effect chains to looking at patterns of dynamic interaction.[103]

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[99] For further explanation on emergent behaviour, see: *Ibid* at 20; Miller & Page, *supra* note 42 at 4–31; Mitchell, *supra* note 42.

[100] Axelrod and Cohen further explain: "Complexity often results in features, called emergent properties, which are properties of the system that the separate parts do not have. For example, no single neuron has consciousness, but the human brain does have consciousness as an emergent property. Likewise, a uniform price can emerge in an efficient market of many buyers and sellers." See: Axelrod & Cohen, *supra* note 42 at 14–15; Holland, *supra* note 55 at 108–115.

[101] Axelrod & Cohen, *supra* note 42 at 18; Holland, *supra* note 55 at 108–115.

[102] Morin, *supra* note 70 at 100–103.

[103] Axelrod & Cohen, *supra* note 42.

Emergence is the opposite of equilibrium. While equilibrium tends to a predictable and stable outcome, emergence necessarily entails uncertainty and change. Page and Miller go so far as to say that, in the case of CAS, equilibrium amounts to 'the death of the system.'[104] Emergence and the *difficulty of predicting* outcomes of CAS operation relate to these systems not reaching equilibrium. As Mitchell explains: "Dynamical Systems Theory (or dynamics) concerns the description and prediction of systems that exhibit complex changing behavior at the macroscopic level, emerging from the collective actions of many interacting components. The word *dynamics* means changing, and dynamical systems are systems that change over time in some way."[105] Two characteristics lead to the dynamic nature of CAS: the *absence of central control* and *nonlinearity*.

Absence of central control in CAS is a feature of the multiple interactive parts of the system that operate independently but in interaction with one another. Although some level of control exists, the impossibility of predicting outcomes and behaviours in CAS undermines any real or definitive control of agents participating in it. Despite not being able to control the system, agents can still manage the system by learning how to harness its complexity. As Axelrod and Cohen conclude: "We believe that the difficulty of prediction in complex systems does not make the situation hopeless, although it does require a large shift in the conceptual tactics."[106]

Agents exist in a world of complexity characterized by infinite and *non-linear* possibilities of interaction.[107] As Mitchell explains: "a linear system is one you can understand by understanding its parts

[104] Miller & Page, *supra* note 42 at 83, 141–177; Santa Fe Institute, *supra* note 85.
[105] Mitchell, *supra* note 42 at 15.
[106] Axelrod & Cohen, *supra* note 42 at 67.
[107] "What makes prediction especially difficult in these settings is that the forces shaping the future do not add up in a simple, system wide manner. Instead, their effects include nonlinear interactions among the components of the system. The conjunction of a few small events can produce a big effect if their impacts multiply rather than add. The overall effect of events can be unforeseeable if their consequences diffuse unevenly via the interaction patterns within the system. In such worlds, current events can dramatically change the probabilities of many future events. A collection of complex systems is therefore a kind of dynamical zoo, a "wonder cabinet" of processes that change (or resist change) in patterns wildly unlike the smoothly additive changes of their simpler cousins." *Ibid*.

individually and then putting them together." In contrast, she says: "[a] nonlinear system is one in which the whole is different from the sum of parts." She points out that "[l]inearity is a reductionist's dream, and nonlinearity can sometimes be a reductionist's nightmare."[108] While a previous choice may lead to path dependence and determine or influence the next interaction, emergent features of the system tend to shatter existing patterns. This results in new, unpredictable interactions, which, in turn, lead agents to change their behaviour in response to new information and their learnings about interactions, other agents, and systems. CAS theory can help elucidate agents' understanding of systems through the creation of models that may identify and organize the path of interactions.[109]

It is important to bear in mind the system's *sensitivity to initial conditions* and the fact that even small changes or events can generate unpredictable outcomes in CAS.[110] The sensitivity to initial conditions in a CAS refers to the fact that what happens in this system depends on its initial state, which generates behaviours and interactions of agents that cannot be fully predicted. Thus, a small change in a CAS can have considerable consequences on outcomes, while at the same time, a substantial change may not affect the outcome. This is due to the unpredictability of these systems.

By now, and considering the dynamic nature of CAS, it is clear that achieving certainty and predictability in these systems is impossible. However, achieving some degree of stability in CAS might be possible. Stability is the element that allows agents to recognize and individualize specific systems, considering that certain minimum core features are stable. One of the ways to achieve stability in CAS

[108] Mitchell, *supra* note 42 at 22–23.
[109] Miller & Page, *supra* note 42 at 216, 220–221.
[110] Here, I refer to the 'butterfly effect' that is a characteristic of chaos theory (or chaotic systems) in which sensitivity to initial conditions is extreme. The butterfly effect refers to chaotic systems' sensitivity to initial conditions. Small changes or events in the system that can generate unpredictable outcomes that are felt in distant points of the system or even in subsystems or other systems. Mitchell defines chaotic systems: "(…) The defining idea of chaos is that there are some systems—*chaotic systems*—in which even minuscule uncertainties in measurements of initial position and momentum can result in huge errors in long term predictions of these quantities. This is known as 'sensitive dependence on initial conditions." p. 20. The degree of sensitivity to changes in CAS and chaotic systems differs because CAS have some degree of stability. Mitchell, *supra* note 42 at 20, 34–39.

and avoid large-scale failures is to build redundancy into the system. Redundancy comes from iteration (repetition) of patterns of interaction and behaviours in these systems. In a system's design, creating redundancy can be a valuable tool to assess cases of independent failures in the system. An example of redundancy is that, in writing a bank cheque, one provides both the amount in numbers and in full written form. However, if one element of the system fails or faces challenges, other elements might also fail because they share the same characteristics. Designing solutions to fix failures affecting elements of a system that has some level of dependency is more complicated; redundancy becomes an ineffective strategy to cope with problems in this situation.[111]

Considering interaction and redundancy (iteration), how an agent can address failure in CAS, and which strategies may result in stability in CAS, all encourage reflections on how agents conceive, design, and reform these systems. These are important observations to make, considering the goal of this dissertation is to apply CAS theory and concepts to understand the interactions and coevolution between IP and biomedical innovation systems and further propose strategies to improve the design and reform of these systems. Parts II further presents these points.

1.2.2. The System's Hierarchy and Multiple Levels of Organization

The multiple levels of organization of a system make up its *hierarchy*. Herbert Simon was the first to develop a theory around hierarchical systems. As he explains, "by a hierarchic system, or hierarchy, I mean a system that is composed of interrelated subsystems, each of the latter being, in turn, hierarchic in

[111] Axelrod & Cohen, *supra* note 42 at 106–112.

structure until we reach some lowest level of elementary subsystem."[112] The concept of hierarchy in CAS theory is different from what one may define as legal hierarchy (for instance, hierarchies of different legal sources, jurisprudence or court systems). Hierarchy in CAS does not represent subordination or a formal structure but instead consists of nested concepts that become more general as one moves upward in the hierarchy. Hierarchy means that building blocks make up complex systems, or that subsystems make up a system, and so on. The number of building blocks or constituent parts (agents) of a system and the variation in their organization may suggest that a system is more complex.[113]

Axelrod and Cohen argue that in a system with a hierarchical organization, the upper layers behave differently from the lower ones. This is because the processes that modify upper layers take a long time, while changes at lower layers occur more rapidly. The result is the formation of hierarchical arrangements that operate in terms of time and scale and are key to implementing strategies to design, coordinate, reform and govern the systems."[114]

As relationships evolve, society and different countries created legal infrastructures to enable and govern agents' interactions and solve conflicts. Centralized and top-down approaches resulted in legal systems that allowed a certain degree of stability and predictability to human relations. In these systems,

[112] Going further on the concept of hierarchy in CAS, Simon elaborates: "Etymologically, the word "hierarchy" has had a narrower meaning than I am giving it here. The term has generally been used to refer to a complex system in which each of the subsystems is subordinated by an authority relation to the system it belongs to. More exactly, in a hierarchic formal organization, each system consists of a "boss" and a set of subordinate subsystems. Each of the subsystems has a "boss" who is the immediate subordinate of the boss of the system. We shall want to consider systems in which the relations among subsystems are more complex than in the formal organizational hierarchy just described. We shall want to include systems in which there is no relation of subordination among subsystems. (In fact, even in human organizations, the formal hierarchy exists only on paper; the real flesh-and-blood organization has many inter-part relations other than the lines of formal authority.) For lack of a better term, I shall use hierarchy in the broader sense introduced in the previous paragraphs, to refer to all complex systems analyzable into successive sets of subsystems, and speak of "formal hierarchy" when I want to refer to the more specialized concept". Simon, *supra* note 42 at 468.

[113] The notion of the measure of complexity through its hierarchy comes from another property of hierarchical systems: near-decomposability. This "refers to the fact that, in hierarchical complex systems, there are many more strong interactions within a subsystem than between subsystems. As an example, each cell in a living organism has a metabolic network that consists of huge number of interactions among substrates, many more than take place between different cells." Mitchell, *supra* note 42 at 109–111.

[114] Axelrod & Cohen, *supra* note 42 at 103–104.

citizens minimally know the rules and the consequences of not following those rules, as well as the path to follow or whom to contact to claim their rights. This infrastructure enabled society to prosper and to become more complex.[115] However, in complex societies, the old centralized and top-down approaches to solving problems and reforming systems might not be the most effective, especially in the design of legal systems, as I will present in Chapter Two.[116]

1.2.3. Resilience and Robustness of the System

The concepts of resilience and robustness stand out as features of CAS because they mediate the likelihood of promoting substantial (radical) or incremental changes in the system over the long and short terms. The Santa Fe Institute defines these terms as follows:

> Resilience describes the ability of a system to persist and maintain its core functions and/or purpose in the presence of disturbances, stresses or other changes in its environment.
> (…)
> Robustness describes the ability of a system to maintain a certain behavior, trait, or characteristic regardless of changing environmental conditions. Robustness is often contrasted with optimization, especially in human-constructed systems. This is because the quality of being robust usually requires that one or more components of a system operate at sub-optimal levels in some situations in order to maintain the ability to operate acceptably at any level under most conceivable scenarios. Conversely, a system that is highly optimized typically operates very well under certain conditions but then becomes less than operational if those conditions change.[117]

As described in this definition, resilience relates to flexibility in facing challenges while robustness relates to redundancy—iteration of behaviours and interaction. Resilience and robustness are directly connected. As a system that arises from the interaction of its parts (agents) and adapts, a CAS is robust because it revolves around the dynamic interactions among its core characteristics that generate stability. This dynamic functioning allows the system to self-persevere when a disturbance threatens some of its parts because the other parts remain stable and functioning. Therefore, the level of stability of a CAS also

[115] Hadfield, *supra* note 2 at 200.
[116] See, initially: *Ibid*.
[117] Santa Fe Institute, *supra* note 85.

depends on its resilience—its ability to react to change while preserving its core. These core characteristics are what differentiate one system from others, conferring uniqueness upon it. The degree of robustness of a system is related to its ability to succeed in a determined fashion.

Resilience and robustness are directly related to the ability of agents to respond in the event of disturbance, stress or change in CAS and to processes that lead to change, evolution, and destruction of these systems. Consequently, these two characteristics are crucial to understanding how to propose reforms in CAS. A CAS suffers pressures from its internal and external environments—as well as from other systems—and these pressures may lead to changes and adaptation. In the process of changing and/or adapting, the level of resilience of a CAS can be perceived through its flexible responses to a degree of change. There is, in this sense, a limit to the system's flexibility, i.e., a threshold where resilience ends, and a CAS becomes an entirely different system because its core characteristics no longer remain the same or disappear. However, it is more likely that small and cumulative changes promote a gradual reform of the system over time rather than a large one-time event to which a CAS cannot respond quickly enough and destroy it. Because of this, catastrophic failure is rare and almost impossible to plan for. As a strategy for survival, agents in CAS may increase the diversity and amount of mechanisms needed to respond to disturbance and the degree of readiness and effectiveness while responding to these disturbances. Agents engaging in a system's reform should consider these details to obtain better results from their actions.

The very nature of CAS makes them robust and thus less likely to fail. Robustness, resilience, and emergent behaviour are interconnected features of CAS in processes leading to change, adaptation, or evolution in these systems. When a change or an event disturbing the system occurs, the core features of the system and its functionality remain intact due to its robustness.[118] Identifying the points of the system's structure that are more susceptible to reform and discovering which agents have sufficient power to change

[118] Miller & Page, *supra* note 42 at 214.

and influence rules and other agents are key steps of systemic reforms. Therefore, the concepts like niches and signal-boundary arrangements are elements to operationalize reform in CAS since they allow experimentation on a small scale and facilitate communication among agents.

1.2.4. Diversity in Complex Adaptive Systems

Page and Miller highlight heterogeneity[119] as one of the main features of CAS. CAS are composed of heterogeneous parts—i.e., not only different kinds of agents but agents that have different interests and expectations even though they would qualify as the same type of agents. This leads to a higher degree of complexity as one must consider not only the nature of the agent but also the subjectivity of agents in their decision-making processes and strategies.[120]

"Heterogeneity is often a key driving force in social worlds. (…) If heterogeneity is a key feature of complex systems, then traditional social science tools—with their emphasis on average behavior being representative of the whole—may be incomplete or even misleading."[121] Heterogeneity undermines our ability to predict outcomes as the interaction of actors and their strategies combine exponentially. Instead, one must examine probabilities—not only those that are most likely but the effect of less probable but outlier interactions. By accepting the impossibility of prediction, we move closer to real-world problem-solving. That is, by embracing possibility rather than predictability, agents can respond more promptly to unexpected outcomes.

[119] Heterogeneity and diversity are synonyms in my analysis.
[120] Miller & Page, *supra* note 42 at 238–239.
[121] Deepening the idea, Page and Miller emphasize: "In many social scenarios, differences nicely cancel one another out. (…) While differences can cancel out, making the average a good predictor of the whole, this is not always the case. In complex systems we often see differences interacting with one another, resulting in behavior that deviates remarkably from the average." *Ibid* at 14–15.

Diversity arises through specialization. Specialization allows CAS to be more productive and for agents to be more effective in performing tasks and addressing problems.[122] Diversity arises through the success of the CAS as it evolves to handle ever more problems. For example, a town may have been initially home to a single lawyer who, as a generalist, muddled through any legal problem presented. As the CAS evolved, relationships and interactions became more complex, giving rise to the need for more personalized and detailed answers to specific issues. A demand builds for specialized lawyers across various fields, such as labour, criminal, tax, civil, international, contracts, and IP matters. With more time, lawyers begin to sub-specialize as agents require even more specific knowledge. It may no longer be enough to speak with a generalist IP lawyer but one who specializes in patents, copyrights, or trademarks. The move to ever greater specialization continues, with agents seeking lawyers with specific business knowledge, for instance, someone who understands the intricacies of pharmaceutical, biotechnology, IT, or clean technology industries. Specialization comes at a cost. One consequence of it is that agents may lose sight of the big picture and context. To counter specialization, agents need to consult more broadly and piece advice together.[123] Multidisciplinarity, cooperation, and coordination of efforts are crucial in agents' responses to problems and systems' reform.[124]

Among the several elements that make up the diversity of CAS, I am particularly interested in the multiplicity and diversity of agents, as well as their expectations, behaviours, and interactions. Below, I further develop the role of agents within IP and biomedical innovation systems.

[122] Hadfield, *supra* note 2 at 65–79; "General Features of Complex Systems" Yaneer Bar-Yam, Cambridge, Mass (December 2001); Miller & Page, *supra* note 42 at 210.
[123] Miller & Page, *supra* note 42 at 29.
[124] For further analysis on this topic, see: Scott E Page, *Diversity and complexity* (Princeton, N.J.: Princeton University Press, 2011); Scott E Page, *The Difference: How the Power of Diversity Creates Better Groups, Firms, Schools, and Societies*, new edition with a new preface by the author edition ed (Princeton: Princeton University Press, 2008).

1.3. The Importance of Agents in Complex Adaptive Systems

As explained above, a CAS is comprised of multiplicity of agents. It is the interactions, behaviours, and expectations of those agents that give shape to those systems. I briefly reflect on four aspects of these agents: (i) how agents (and through them, systems) respond to problems; (ii) the decision-making processes of agents; (iii) how agents communicate, and; (iv) a model to capture agent behaviour: Agent-Based Models (ABMs).

1.3.1. How Agents (and Systems) Interact and Respond to Problems

Agents interact with other agents and within systems through the processes of learning, adaptation, and evolution. *Learning* is the process by which agents apprehend information from the system and process it into knowledge that they might use immediately or later. Agents learn by interacting with other agents and by creating new connections. Learning underlines adaptation and evolution. An *adaptation* is any change in the behaviour of an agent and/or structure of the system to conform to a new circumstance or to address different issues. Adaptations constantly happen, both in the internal and external environments and within systems. Much as with natural selection, some of these adaptations are preserved through selection and propagated over time. The adaptations that are selected over time enable the *evolution* of the system. *Adaptation* and *evolution* work in a dynamic pattern of cause and effect, even though these connections may not be entirely apprehended by agents evaluating the system.[125]

Observing and comparing adaptation in biological and social systems also give us insights into mechanisms and processes by which other systems evolve. In biological systems, adaptations generally

[125] A well-known example of adaptation and selection in the natural world is the evolution of butterflies in industrial England from brightly coloured to grey. Due to pollution, colourful butterflies started to stand out in industrial environments, and thus became more easily spotted by predators. By comparison, grey butterflies—an adaptation—flourished in this same environment. As a consequence, grey butterflies eventually replaced colourful ones. For more information, see: Mitchell, *supra* note 42 at 4–14.

occur randomly and are only later selected by the environment. In social systems, adaptations are often formulated as a reaction to a change in the environment, to the behaviour of other agents, or to what an agent anticipates may happen or how another agent might behave. This marks an important distinction. Evolution works in both cases to select favourable adaptations and may assist these systems in thriving. In the case of biological systems, evolution acts on the survival of the organism and its ability to reproduce, whereas in social systems, evolution may favour persistent (even if wrong) ideas. The problem in social systems is that adaptation is permeated by the bounded rationality of agents and the incomplete information they have about the interaction of different systems and agents.[126] This is why designing and reforming law and policy to regulate CAS is so problematic. The actions of designing and reforming systems require one to step outside of it to evaluate the processes and strategies that agents deploy.

Through the interactions of its agents, a CAS learns, adapts, and evolves. Over time, a CAS tends toward an equilibrium—where all forces affecting the system's operation (i.e., mainly agents' expectations and behaviours) are balanced[127]—but never reaches it, given the dynamic nature of CAS and the outsized impact of the accumulation of low probable events (emergence). The result is a CAS that is never entirely determined (unpredictable) but one that retains core features while being flexible and stable. Widespread systemic failures are possible—due to a lack of balance between forces and interests (or agents) that renders adaptation impossible or due to a shock to which a system cannot adjust—but these are rare. When these failures occur, it is important to ask whether agents failed to take advantage of the opportunities presented within the system to learn or adapt. One may also question whether these agents

[126] See: Herbert A Simon, "A Behavioral Model of Rational Choice" (1955) 69:1 Q J Econ 99–118; Herbert A Simon & William G Chase, "Skill in Chess: Experiments with chess-playing tasks and computer simulation of skilled performance throw light on some human perceptual and memory processes" (1973) 61:4 Am Sci 394–403; Herbert A Simon, "Rational Decision Making in Business Organizations" (1979) 69:4 Am Econ Rev 493–513; Herbert A Simon et al, "Decision Making and Problem Solving" (1987) 17:5 Inte Interfaces 11–31.

[127] According to the Glossary of Terms of the Complexity Explorer: "Equilibrium*:* Equilibrium, meaning balance, occurs when all forces or influences on a system are balanced. In physics an example is when the sum of forces on an object result in no change in motion. In dynamical systems, an equilibrium is a solution or behavior of the system that does not change over time (a "fixed point" or "steady state")." Santa Fe Institute, *supra* note 85.

deliberately made choices based on their narrow interests that undermined the balance and stability of the system or could not react quickly enough to address a problem.[128]

One of the critical contributions of CAS theory in analyzing social systems is to understand what failures can tell agents about the system. Failures in CAS demonstrate one of two things: 1) a failure to understand (lack of education or dissemination of ideas); or, 2) an excess of certain interests over others (an imbalance). Agents' strategies, expectations, behaviours, and choices determine the kind of systems being built (as indicated by the routes of systemic failure). These elements also underline the values that guide the system's construction and relate directly to pursuing the ultimate goals of the system.[129] Part II of this dissertation presents how interaction among agents gives rise to emergent behaviours between them, leading to changes and reform on these systems.

Finally, the systems' memory (and agents' and population of agents' memories) informs agents' interactions and behaviours. As with biological systems that preserve old genes and parts that are no longer needed, CAS do not cut out features that were not previously selected as a self-preservation mechanism. Other possibilities for change and adaptation remain in the system's memory, and these will interact with the system and influence it over time. These additional changes can be selected, assessed, and potentially used in the future.[130]

1.3.2. On Agents' Decision-Making Processes

The decision-making processes followed by agents influence the structure/organization of the systems in which they act and, consequently, the possibilities open to agents. Traditional decision-making theories assume agents are instinctively engaged in informed and organized rational methods in their decision-

[128] Axelrod & Cohen, *supra* note 42 at 31–106.
[129] See: Note 37.
[130] Axelrod & Cohen, *supra* note 42.

making processes.[131] However, agent reasoning is limited because agents are subject to biases and incomplete comprehension. There is no perfect rationality—as is assumed in traditional economic theory—nor is there a rational agent ("the economic man") who has perfect knowledge of his or her environment and who works in a static system.[132] Considering this, Hebert Simon proposed the concept of 'bounded rationality,' asserting that the state of information, the decision-maker, and the environment must be considered when assessing decision-making processes and agent choices.[133] Bounded rationality refers to agents' limitations that exist due to their cognitive capacity, the information available about the problem, and the time available to engage in decision-making.[134] Simon argues that agents reach decisions based on presumptions about the consequences of their actions, incomplete information and simplifying assumptions. He highlights that, in assuming a point of view, an agent might be tricked by his/her incomplete perception about the environment, as well as by his/her psychological limits. People assume, Simon argues, that conscious decision-making is better than unconscious action, even though this assumption lacks empirical evidence.

In advancing his argument, Simon proposes a procedure that aims to simplify the evaluation of systems by their agents. This procedure assists us in understanding the processes in which people engage while trying to solve complex problems. First, Simon suggests simplifying reasoning processes that guide agents' choices. To simplify their evaluation, agents might be able to select within easily understandable alternatives without the need to engage in complicated probabilistic assessments about the success of choosing one or another option. Second, he suggests the introduction of 'information-gathering steps' to produce a precise mapping of the various elements that interfere with or might influence agents' decision-

[131] Simon, *supra* note 126 at 103–110.
[132] See: *Ibid* at 99.
[133] For Simon's works on bounded rationality and decision-making, see: Simon, *supra* note 126; Simon & Chase, "Skill in Chess", *supra* note 126; Simon, *supra* note 126; Simon et al, *supra* note 126.
[134] For more information, see: Simon, *supra* note 126 at 99.

making process, alongside the traditional rational choice features. How far this mapping goes depends on an assessment of costs and benefits: if it is not costly, the map might be as detailed as the agent can render it. If it is costly to map processes, then one of the decision-making steps will be to decide how far the mapping might go. The process of gathering information involves the refinement of the mapping over time. Third, Simon suggests a partial ordering of pay-offs to help agents organize elements influencing their decision that are not comparable, so they can try to determine common denominators.[135]

The elements of the decision-making processes involving boundedly rational agents and the procedure suggested by Simon to simplify these processes inspire my analysis in the following chapters. Understanding these processes is the first step in assessing agent behaviours regarding law and policymaking and, consequently, reforming those systems. The merit of Simon's approach lies in its commitment to construct a model of decision-making that is closer to the actual processes in which people engage in complex situations.[136] Knowing the nuances of decision-making and how to adopt procedures that facilitate and inform it may have a considerable impact not only on how law regulates science but also on how new ideas and strategies for regulation arise.

Daniel Kahneman and Amos Tversky also study the bounded rationality of agents while exploring the psychology of intuitive beliefs and choices.[137] They assume that "most judgments and most choices

[135] *Ibid* at 103–110.

[136] Simon highlights specificities of human decision-making such as the fact that, if there are multiple possibilities, the agent does not evaluate or compare them together, but rather considers them in a sequence, which then leads to the likelihood that the first satisfactory possibility will be selected. In this sense, knowing the sequence in which different agents will assess possibilities is key to predicting what will happen (or will not happen) when agents make decisions. In cases where there is no way to figure out the order in which the possibilities will appear, then order prediction becomes impossible, but if the environment presents the options to the agent, then it is possible to know which option will be selected. Simon also stresses the need to consider the aspirational level of different agents while studying their decision-making processes. An agent's expectations about the outcomes of his/her interaction with a system or other agents depend on the knowledge and experience that this agent has about the system and his/her previous history with it and its agents. He also shows that choosing alternatives to a considered pay-off depends not only on considering known options but also on considering alternatives that have been chosen in previous trials by different agents. *Ibid* at 110–113.

[137] Kahneman, "A perspective on judgment and choice", *supra* note 53; Kahneman, "Maps of bounded rationality", *supra* note 53; Kahneman, *supra* note 52; Daniel Kahneman, "A psychological perspective on economics" (2003) 93:2 Am Econ Rev 162–168.

are made intuitively" and "the rules governing intuition are generally similar to the rules of perception."[138] They identify two types of cognitive processes and give them the neutral labels of System 1 (Intuition) and System 2 (Reasoning) and explain that "System 2 monitors the activities of System 1". Kahneman elaborates further:

> The operations of System 1 are fast, automatic, effortless, associative, and often emotionally charged; they are also governed by habit, and are therefore difficult to control or modify. The operations of System 2 are slower, serial, effortful, and deliberately controlled; they are also relatively flexible and potentially rule-governed.
> The difference in effort provides the most useful indications of whether a given mental process should be assigned to System 1 or System 2. Because the overall capacity for mental effort is limited, effortful processes tend to disrupt each other, whereas effortless processes neither cause nor suffer much interference when combined with other tasks.[139]

Kahneman and Tversky's theory shows that "intuition and reasoning are alternative ways of solving problems" and demonstrates how important it is not only to recognize the bounded rationality of agents but also to understand the interplay between System 1 and System 2 in agents' decision-making processes. This recognition enables the creation of a dynamic interaction between these two systems that leads to better results in solving problems. It is essential to recognize that "[t]he central characteristic of agents is not that they reason poorly but that they often act intuitively. And the behavior of these agents is not guided by what they are able to compute, but by what they happen to see at a given moment."[140] Better organization and adoption of procedures to assess what is happening in and within CAS may incentivize agents to make more use of System 2, while building a relationship between law and science can further increase the likelihood of agents to experiment and adopt new biomedical RD&I models and strategies to their regulation.

[138] Original Figure: "Figure One: Three Cognitive Systems." Kahneman, "Maps of bounded rationality", *supra* note 53 at 1451.
[139] *Ibid* at 1451–1452, 1467.
[140] *Ibid* at 1469.

Another critical factor is to consider agents both as individuals and as part of a collective. The influence of other members and institutions on how an individual agent learns, behaves, and perceives the system plays a critical role in how a group of agents affect the overall operation of CAS.[141]

Agents also take on different, sometimes multiple, roles within a single CAS, acting variously as decision-maker, influencer, or rule-follower. These roles may influence how agents evaluate problems or participate in the CAS. The diversity of rules and positions indicates multiple pathways for agents' actions and interactions. Theories and procedures, such as those proposed by Simon, Kahneman, and Tversky, are helpful to map out these interactions.

1.3.3. Communication between Agents and within Complex Adaptive Systems

Page and Miller explain that in all types of CAS (social, biological, or chemical systems) "communication mediates the behavior of the interacting agents, allowing a degree of coordination that can ultimately improve each agent's performance." They also present communication as "strategic phenomena, where agents must consider both, what they will say to others and how they will react to what others say."[142] Understanding communication and how it occurs will ultimately improve agents' performance and the overall outcomes of CAS. It can also help formulate strategies to reform CAS in more transparent, effective, and participatory ways.

Communication is a powerful instrument through which interactions occur in CAS. Communication can enlarge the possibilities open to each agent, allowing each agent to adopt the most effective forms of interaction in a given situation. It also enables agents to differentiate themselves and their behaviours from other agents in the system and organize their decision-making processes.[143]

[141] Herbert A Simon, "Bounded rationality and organizational learning" (1991) 2:1 Organ Sci 125–134.
[142] Miller & Page, *supra* note 42 at 192.
[143] For detailed considerations, see: *Ibid* at 198.

Communication and communication processing intend to make feasible the flow of information between agents and within CAS. However, once communication happens, how information acquires meaning is a challenge to understand.[144]

John H. Holland explains that CAS operate and communicate through "intricate hierarchal arrangement of signals and boundaries." Signals are the means through which an agent communicates with another agent within and between CAS. Examples of signalling devices include language, a cell's protein-based signalling network, and visible actions or behaviour of agents (for instance, moving troops to the frontier with another country in war constitutes a strong signal). Boundaries are the delimitations between agents and/or systems and their environment. Boundaries filter and select information flowing into and out of the system.[145] CAS are dependent on signal-boundary arrangements for interacting with the world. Holland states that "[a]gents are omnipresent in signal/boundary systems"[146] through their internal processing of information.[147] However, Holland recognizes that much work is needed to develop a robust theory about signal-boundary arrangements in different CAS and devotes his book to providing elements that advance those discussions.[148]

Holland explains that the diversity of elements (for instance, agents, behaviours, artifacts) in CAS, results in multiple pathways for interaction and the recirculation of resources. Recirculation of resources enables their recombination in ways that sustain diversity and eventually lead to coevolution between

[144] See, specifically: Mitchell, *supra* note 42 at 179–185.
[145] Holland exemplifies the relationships between agents, signal processing, and communication: "For the Internet, sites act as agents processing messages; for the immune system, antibodies act as agents counteracting invading cells (antigens) through a complicated exchange of signals (proteins); for markets, the agents are buyers and sellers and the signals are bids; for ecosystems (e.g., rainforests), the agents are organisms interacting via complicated resource exchanges; for biological cells, organelles serve as agents interacting via exchanges of proteins; for language, the agents are humans communicating by sequenced utterances; for the central nervous system, agents are clusters of neurons that interact via electrical pulses sent over branching interconnections (axons)." p. 27. See, generally: Holland, *supra* note 55 at 1–30.
[146] *Ibid* at 27–28.
[147] *Ibid* at 8.
[148] *Ibid* at 35-ss.

CAS. Holland calls the place in which recirculation and recombination occurs a niche.[149] According to Holland, "niche designates a tangle of local interactions with recirculation, allowing resources to be used over and over again." He elaborates: "[a] niche is a diverse array of agents that regularly exchange resources and depend on that exchange for continued existence."[150]

While tracking communications and interactions in an entire CAS may be overwhelming, limiting one's examination to specific niches is a more feasible task. For instance, in studying the interaction of IP and biomedical innovation systems, one can examine a niche in which university researchers seek to develop a cancer medicine. We can draw on this and similar niches to better understand agent strategies regarding communication and evaluate the results of their interaction and behaviour in CAS.[151] In this sense, examining niches is conducive to identifying how to improve communication between agents. Niches are also places for experimentation within CAS because the consequences of failure are less traumatic to the systems and their agents due to niches contained features. The processes and actions to repair problems happening in a niche are faster and with fewer constraints. The idea of niche is central to clarifying the relationship between law and science because this is where interaction happens. For this dissertation, biomedical RD&I projects or initiatives are niches. Chapters Five and Seven develop this idea better.

Later, I will draw upon the concepts presented in this section to frame discussions about how legal norms and the 'normative structure of science' (the norms of science) combine and allow multiple systems to co-operate in specific niches. I will also question how agents from diverse backgrounds and different CAS communicate those norms and how accessible the language and rules of operation of a particular system are to agents of another system. Finally, I will question if interactions and communication between

[149] *Ibid* at 11–20.
[150] *Ibid* at 287.
[151] *Ibid* at 16–18.

agents from different CAS taking place in niches result in creating new or combined 'normative structures' and signal-boundary arrangements. These questions will enable the assessment of diverse routes and strategies to better design and reform in CAS.

1.3.4. A Model to Study Agents' Behaviours and Interactions and Improve Complex Adaptive Systems' Design and Reform

CAS theory has developed various models to evaluate problems, which, in turn, connect concepts and theories drawn from mathematics and other fields such as cybernetics, biology, and evolution.[152] Two examples include Agent-Based Models (ABMs) and network analysis. For example, by using an ABM, we can call attention to the role of an individual agent and his or her behaviour towards the adoption of specific regulations and legal reform. On the other hand, network analysis can enlighten the weaknesses and strengths of interactions among agents and the pathways in which those interactions take place.[153]

Among the different models developed by CAS scholars, ABMs inspire this dissertation's methodology considering the need to centre its analysis on the role of individual agents. While ABMs originated as computer models created to simulate the interactions and actions of individual agents that comprise a CAS, they also provide "a mindset more than a technology. The ABM mindset consists of

[152] This dissertation searched for inspiration and guidance in CAS theory and its different models but does not present or develop mathematical or computational models considering its methodological choices and limitations to develop them without robust empirical research. One of the contributions of CAS theory in advancing social science, and legal theory, it is to provide different ways of analysing problems that results in models of thinking which are not necessarily mathematical. As Bertalanffy explains: "The advantages of mathematical models-unambiguity, possibility of strict deduction, verifiability by observed data-are well known. This does not mean that models formulated in ordinary language are to be despised or refused. A *verbal model* is better than no model at all, or a model which, because it can be formulated mathematically, is forcibly imposed upon and falsifies reality. (…) Mathematics essentially means the existence of an algorithm which is much more precise than that of ordinary language. History of science attests that expression in ordinary language often preceded mathematical formulation, i.e., invention of an algorithm. (…) Models in ordinary language therefore have their place in systems theory. The system idea retains its value even where it cannot be formulated mathematically, or remains a "guiding idea" rather than being a mathematical construct." Bertalanffy, *supra* note 67 at 24–25.

[153] For initial considerations about network analysis, see: Barabasi, *supra* note 47; Melanie Mitchell, "Complex systems: Network thinking" (2006) 170:18 Artif Intell 1194–1212; *Knowledge, Complexity and Networks*, Chapters, by Pier Paolo Saviotti, RePEc - IDEAS, Chapters (Edward Elgar, 2011).

describing a system from the perspective of its constituent units."[154] ABMs examine the multiple levels of influence agents wield on each other and different systems and assess the effects of agents' interactions and behaviours on the system. These micro-level evaluations can lead to macro-level consequences over time: *i.e*. they assist agents in inferring the behaviour of other agents or populations of agents and estimating to what degree a single agent can influence the rules of interaction between agents and the whole of the system. Consequently, they can suggest to what degree an individual agent can change a system.[155] However, a challenge for ABMs scientists is to develop models that can have their findings simultaneously generalized and applied to specific cases.[156]

According to Bonabeau, the study of CAS through an ABM approach is especially beneficial to (i) providing a natural description of the system (i.e., a description that is more detailed and focuses on how CAS function through the behaviour of their agents); (ii) enhancing a flexible approach to systems analysis that considers some selected features and parameters (which can vary and be reassessed over time depending on the needs of who evaluates the system); and (iii) studying emergent phenomena, as well as emergent behaviours of agents in CAS, by tracing the interactions of individual agents that are not easily apprehended by observing the whole of the system. This iteration of these emergent behaviours provides new insights into legal and policy reform.[157]

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[154] Eric Bonabeau, "Agent-based modeling: methods and techniques for simulating human systems" (2002) 99 Suppl 3 Proc Natl Acad Sci U S A 7280–7287 at 7280.

[155] For more information about ABMs, see: Bonabeau, "Agent-based modeling", *supra* note 154; Axelrod & Tesfatsion, *supra* note 50; Joshua M Epstein, "Agent-based computational models and generative social science" (1999) 4:5 CPLX Complex 41–60; Hiroki Sayama, *Introduction to the Modeling and Analysis of Complex Systems*, print edition ed (Geneseo (N.Y.): Open SUNY Textbooks, 2015); Robert Axelrod, "Chapter 33 Agent-based Modeling as a Bridge Between Disciplines" in L Tesfatsion and K L Judd, ed, *Handb Comput Econ* (Elsevier, 2006) 1565; Marco Janssen & Elinor Ostrom, "Empirically Based, Agent-based models" (2006) 11:2 Ecol Soc, online: <https://www.ecologyandsociety.org/vol11/iss2/art37/>; John H Miller & Scott E Page, *Complex Adaptive Systems: An Introduction to Computational Models of Social Life*, 1 edition ed (Princeton, N.J: Princeton University Press, 2007).

[156] See: Janssen & Ostrom, *supra* note 155.

[157] As Bonabeau asserts: "[i]n many cases, ABM is most natural for describing and simulating a system composed of 'behavioral' entities. Whether one is attempting to describe a traffic jam, the stock market, voters, or how an organization works, ABM makes the model seem closer to reality. For example, it is more natural to describe how shoppers move in a supermarket than to come up with the equations that govern the dynamics of the density of shoppers. (…) Knowing the actual shopping basket of a customer makes it possible to create a virtual agent with that shopping basket rather than a density of

ABMs are tools to simulate behaviours and interactions within CAS and their components. They provide a good way to picture the system better and simulate how agents interact and strategize with other agents within the system. ABMs can provide multiple possible states from which to study a system to identify points for reform better.[158]

As noted above, CAS tend to assume hierarchical shapes in their organization.[159] However, agents' interactions and behaviours continue to be non-linear and dynamic. Agents are subject to more constraints and interests of other agents when they interact at the system's top layers.[160] ABMs are models used to explain and justify bottom-up approaches to systems' reform while identifying individual agents' rolein them. Bottom-up approaches consider the behaviours of interacting agents and then extract the guiding rules that emerge from these interactions to govern the system. In contrast, top-down approaches impose high-level rules on agents' interactions and then trace back the consequences of these rules on agents' behaviours and the system.[161]

The application of CAS theory and agent-centred evaluations to legal theory is an innovative tool to guide the design and reform of legal systems and their regulatory targets. It can enable the development of new models that connect theory, law, policy, and practice and that are better equipped to deal with the implications of complexity. Moreover, placing agents at the centre of the analysis may result in a more humane view of systems and assist those pursuing reforms to better reflect and balance society and individual needs. It does not matter (for this analysis) whether an agent participates in the system by using innovation, performing R&D, developing public policies or creating laws. Likewise, it does not matter whether an agent is a member of the industry, civil society, government or is simply a citizen. In the end,

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people with a synthetic shopping basket computed from averaging over shopping data." (p.7281) Bonabeau, "Agent-based modeling", *supra* note 50 at 7281.

[158] Bonabeau, "Agent-based modeling", *supra* note 154 at 7280–7281.

[159] I use the terms 'top' and 'bottom' of the systems in terms of organizational hierarchies, not in terms of submission of one part (or agent) to another.

[160] Epstein, *supra* note 155.

[161] Miller & Page, *supra* note 155 at 66.

every agent is a participant[162] in the system and should ideally be able to exercise all their roles fully. In the case of an individual within a population of agents represented by powerful entities or institutions—like a government or corporation—individual voices and opinions may be overwhelmed by the goals of those entities and institutions. In these cases, the degree of influence enjoyed by an agent will determine how much that entity can drive change, such as through cooperation among less influential agents to make their collective opinions heard.

1.4. Harnessing Complexity in the Design and Reform of Complex Adaptive Systems

Most agents dealing with complexity tend to avoid or eliminate it. Unfortunately for them, complexity will never disappear, given the dynamism of society and agents' incomplete knowledge of reality. As Axelrod and Cohen argue, our goal ought not to be the elimination of complexity but rather the exploration of its dynamism to achieve our goals.[163]

This chapter outlined the key theoretical, conceptual, and methodological aspects of CAS and explained features of these systems that are relevant to understanding the relationship between law and science and proposing strategies to better design and reform them. Chapters Two and Three apply these ideas to law, while Part II applies them to specific IP and biomedical R&D interface evaluations.

[162] By participant, I mean the agent in its completeness—the combination of all the roles s/he plays in the system but, especially, the participant that uses and benefits from technological and scientific knowledge, as well as the products, processes, and services that result from this knowledge. It is the agent in its most vulnerable role. This is because, if we consider that technologies related to the public interest such as health technologies do not always have a substitute in the market, their affordability, availability, and adaptability to different agents' needs is a matter of life and death. The idea of seeing agents as participants connects to the need of enhancing systems that are needs-driven instead of market-driven. This is because it is impossible to predict when an agent might participate in the system in his/her most vulnerable role (for instance, as a patient). If we are unable to design these systems based on ethical principles that lead to affordability, availability, and adaptability of health technologies and public interest technologies; we should at least consider that all of us may share the vulnerability of being participants of CAS and enable a design that protects us as individuals.

[163] See, especially: Axelrod & Cohen, *supra* note 42 at 152–160.

CHAPTER TWO—LAW AS A COMPLEX ADAPTIVE SYSTEM

2.1. The Value of Complex Adaptive Systems' Theory to Law

In complex adaptive social systems, commands and signals are translated into norms (informal or formal rules), serving as tools to inform communication among different agents and their behaviours, thus allowing the flow of information within and among systems and the environment.[164] Each legal and scientific (biomedical RD&I or biomedical innovation systems) system has its own internal rules of operation and organization that arise from dynamic interactive processes among the system's agents.[165] What I seek to do in this dissertation is to understand how legal and non-legal actors within these systems interact and influence one another.[166] Through this understanding, I seek to map out a framework for improving legal systems.[167] First, I must show how both law and science are CAS.

This chapter begins this work by arguing that law is a CAS and examining the challenges and opportunities of an agent-centred approach to studying the coevolution of legal systems and their regulatory targets. The goal is to promote a different way of thinking about the legal system that captures its dynamic nature and interactions with other systems (in particular, biomedical innovation systems). Two key questions emerge. The first is whether legal systems are indeed CAS, as stated above. And, in case they are, the second is what this means for our understanding of law and its relationship with other systems (including other CAS).

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[164] Rules are also sources of information that shape the system, selecting the most important aspects and formally regulating agents' interactions, behaviours, and expectations.

[165] These rules are influenced by factors that guide agents' behaviours and expectations.

[166] A legal agent is one who possesses legal training, can analyze the legal system and its technicalities in-depth, and formally interacts with and transform/reform the legal system over time and context. A non-legal agent, in turn, is one who applies the law and abides by it even in the absence of formal legal training or knowledge of the functionality and dynamics of legal systems. In investigating the role of different agents in complex adaptive IP and biomedical innovation systems, Part II develops this distinction further to argue for the importance of improving the understanding of non-legal agents about law and how legal systems work, as well as legal agents understanding of regulated systems among them science.

[167] This is further investigated in Chapter Three and Part II.

2.2. Law as a System and Its Interaction with Other Social Systems: General Thoughts

Law is a social institution that can be understood in different ways, for example, as rules, as an instrument of social control, or as a system.[168] This dissertation focuses on studying law as a system and what this means to evaluate expectations, behaviours, and interactions among agents acting within it. Legal systems emerge from the interactions of agents (individually and/or collectively), adapt to agents' beliefs and expectations, and support society based on those interactions, beliefs and expectations. As a human creation, law regulates the natural world.[169]

Legal systems can also be seen as a subsystem of society and, more specifically, as a CAS, as argued in this dissertation. Niklas Luhmann, the first to apply systems theory to law noted:

> The legal system is a differentiated functional system *within* society. Thus in its own operations, the legal system is continually engaged in carrying out the self-reproduction (autopoiesis) of the overall social system as well as its own. In doing so, it uses forms of communication that, for all their esoteric quality, can never be so abstract as to be completely removed from normal, comprehensible meaning. This means not only that the legal system fulfills a function for society—that it "serves" society—but also that the legal system participates in society's construction of reality, so that in the law, as everywhere in society, the ordinary meanings of words (of names, numbers, designations for objects and actions, etc.) can, and must, be presupposed.[170]

Luhmann's model is a simplified one, where a single level of law exists comprised of yes/no answers to legal questions but no meta-rules on how to resolve conflicts between principles. Even though law exists within and in relation to society, there is a clear separation that he sees as necessary for the operation of the legal system. This is why Luhmann argues that legal systems are operationally closed. As presented and criticized below, there are four key concepts in Luhmann's theory: *self-differentiation*, *closedness*, *communication*, and *autopoiesis*.

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[168] See: H L A Hart, *The Concept of Law*, 3 edition ed (Oxford, United Kingdom: Oxford University Press, 2012); Lon Fuller, "Law as an Instrument of Social Control and Law as a Facilitation of Human Interaction" (1975) 1975:1 BYU Law Rev 89–96; Niklas Luhmann, "Law As a Social System" (1988) 83 Northwest Univ Law Rev 136.

[169] Gold, *supra* note 61; Robert Axelrod, "An Evolutionary Approach to Norms" (1986) 80:4 Am Polit Sci Rev 1095–1111; Hadfield, *supra* note 2; J B Ruhl, "Law's Complexity: A Primer" (2007) 24 Ga State Univ Law Rev 885; Ruhl, Katz & Bommarito, *supra* note 43.

[170] Luhmann, *supra* note 168 at 138–139.

2.2.1. Self-Differentiation and Closedness of Legal Systems

Clear boundaries are essential to Luhmann's model. Assuming a *self-referential closedness* to enable law to differentiate itself from other systems, the legal system autonomously predetermines the elements of its operation and impedes the inclusion of other elements into its internal environment. Closed (and self-differentiated) systems reduce internal complexity by putting aside interactions with other systems. Even if potentially open to external systems, the legal system must close itself off from outside influence to maintain autonomy.[171] *Operational closedness* establishes a clear separation between the legal and other systems or the environment, isolating the law from society.[172]

Luhmann relies on the idea that the boundaries of the legal system can be firmly enforced. But like in any other system, law's boundaries are conceptual and change over time and context. Because every system is part of an environment where exchanges occur, there can be no truly closed system. As Richard Nobles and David Schiff explain, boundaries are permeable, allowing ideas and content to enter and leave through interactions with other systems and the environment. The elements that a given system allows to enter and remain within its boundaries are what differentiate it from other systems.[173]

In CAS theory, the system redefines itself over time, so boundaries are changeable or even permeable to the external environment's and other systems' influences and interactions. In acting and making cumulative decisions over time, legal agents set the contingent boundaries of the law. Law's open structure leads to the flexibility that is necessary to accommodate novel and unregulated areas. For instance, the Internet and information technologies (IT) bring new legal issues such as data privacy, data ownership, security, individual rights and autonomy, and the right to be forgotten. In addition, the

[171] *Ibid* at 137–138.
[172] See: Niklas Luhmann, "Operational Closure and Structural Coupling: The Differentiation of the Legal System" (1992) 13 Cardozo Law Rev 1419–1441.
[173] Richard Nobles & David Schiff, *Observing Law through Systems Theory* (Bloomsbury Publishing, 2012) at 4–5 Google-Books-ID: _H3bBAAAQBAJ.

emergence of artificial intelligence (AI), biotechnology, nanotechnology, personalized medicine, and assisted reproduction redefines the way agents interact and behave and creates new business models (UBER, Facebook, and YouTube) that require flexible boundaries of legal systems in order to evaluate agents' interactions and behaviours and successfully incorporate new rules.

To effectively answer society's contemporary needs, the legal system's boundaries must be flexible enough to receive information and allow interactions with other systems, different agents, and the external environment. "[L]aw is just another way in which people make rules,"[174] but, at the same time, "law needs to be something understood and designed by economists, policymakers, entrepreneurs, business leaders, and ordinary people, not just lawyers."[175] For society to extract the best results from law, it must be seen as a joint enterprise designed by multiple agents, enabling interactions and the pursuit of competing goals within society. This idea of law as co-creation is critical for systems' design and reform, illuminating the relationship between law and science. To provide effective solutions to today's fast-changing challenges, agents must innovate in the way they think about and create law, embracing the idea that the legal system dialogues with its regulatory targets. One way to achieve that is by using the diversity of multiple CAS and their agents as an instrument to harness complexity and amplify the spaces from which the legal infrastructure arises.

2.2.2. Law as an Autopoietic System

Another central element in Luhmann's theory is the idea of *autopoiesis.*[176] An autopoietic system is one that creates, recreates, and maintains itself through time. For Luhmann, autopoiesis means self-

[174] Hadfield, *supra* note 2 at 19.
[175] *Ibid* at 20.
[176] Maturana and Varela were the firsts to develop a concept of autopoietic systems in the fields of biology and chemistry. Humberto R Maturana, Francisco J Varela & Humberto R Maturana, *Autopoiesis and cognition: the realization of the living* (Dordrecht, Holland; Boston: D. Reidel Pub. Co., 1980) at 86.

reproduction not only of the law but also of the social system as a whole. This gives legal systems a dual role where legal systems simultaneously serve society and participate in society's construction of reality.[177]

Reflecting on autopoietic systems in law, Gunther Teubner proposes an alternative view.[178] Because he is more concerned with the process that enables law's operation, and not only law's capacity to create, recreate, and maintain itself through time, Teubner connects *autopoiesis* to *legal communication*, shifting the emphasis away from rules.[179] Instead of operational closedness and self-differentiation, Teubner's concept of *legal communication* focuses on whether "law arbitrarily 'invents' social reality" or whether this act of "inventing" may be reciprocal. Law creates situations that would not be easily respected or exist in its absence,[180] but at the same time, law is also invented (or at least influenced) by social reality and other systems.

Autopoiesis also relates to the ideas of adaptation and evolution in systems. In Luhmann's theory of *self-referential autopoietic systems*, successful differentiation leads to evolution and, consequently, to self-reproduction. Because the need to promote internal consistency makes autopoietic systems unable to use all signals they receive from the environment thoroughly, they restrict their own evolution.[181] In law, interaction, variation, and selection lead to learning, adaptation, and evolution. These are particularly

[177] The IP system, for example, is one of the many subsystems forming the legal system. As Chapter Three shows in further detail, the fact that IP systems protect knowledge, data, and information confers them a strategic role in the design of other systems.

[178] See: Gunther Teubner, "How the Law Thinks: Toward a Constructivist Epistemology of Law" (1989) 23:5 Law Soc Rev 727–757 at 738.

[179] For Teubner: "Law is defined as an autopoietic social system, that is, a network of elementary operations that recursively reproduces elementary operations. The basic elements of this system are communications, not rules; law is not, as analytical-normativist legal theories have it, a system of rules. (…) Law as an autopoietic social system is made up neither of rules nor of legal decision makers, but of legal communications, defined as the synthesis of three meaning selections: utterance, information, and understanding. These communications are interrelated to each other in a network of communications that produces nothing but communications. This is what is basically meant by autopoiesis: the self-reproduction of a network of communicative operations by the recursive application of communications to the results of former communications. Law as a communicative network produces legal communications." *Ibid* at 732.

[180] One example are IPRs designed to protect and contain knowledge, which is non-rivalrous and non-excludable. As a public good, knowledge can be used by different agents at the same time and this use does not diminish its value. These ideas are further discussed in Chapter Three. See, initially: Joseph E Stiglitz, "Case Studies - Knowledge and Information: Knowledge as a Global Public Good" in Inge Kaul, Isabelle Grunberg & Marc Stern, eds, *Glob Public Goods Int Coop 21st Century* (Oxford University Press, 1999) 308.

[181] Luhmann, *supra* note 168 at 146–150.

complex processes because of the uncertainty in multiple selecting options from different agents' expectations, behaviours, and interactions. Due to the difficulty in maintaining selected options in cases of conflict, these processes cannot be easily ignored by the system, as Luhmann's reductionistic view might indicate.

For Luhmann, law evolves to diminish uncertainty, as when courts apply the law to conflicts. There is a search for stability, which tends to restrain evolution by encouraging the legal system to remain the same for an extended period.[182] But since law's evolution involves other agents besides courts (legal and non-legal), Luhmann's evaluation disregards the complexity of the system and the diversity of parties involved. As further explained below, evolution also happens when norms change the type and level they occupy in the legal system. And if one considers law as a CAS, unnecessary system elements cannot be discarded overtime during autopoietic reproduction or evolution. This is because CAS preserve elements, or at least their memory, even when they are not necessary at a given moment. A system's element that is considered unnecessary in a particular situation and time may become key to the operation of the system in the future.

2.2.3. Communication in Legal Systems

Luhmann presents law as a binary code of expectations that allows agents to communicate. A binary code is a positive or negative command emanating from the legal system, such as when courts say who has a right in a lawsuit. These binary codes enable communication inside and from the system towards other systems, in relation to the law's functionality in translating agents' expectations and determining their actions. They also check for consistency and clarify contradictions executed by the courts. Over time, a collection of codes builds the system's memory about how, and under which rules, the system functions.

[182] *Ibid*.

This memory is then updated continuously as information changes and is assessed by courts. Therefore, the process of checking for consistency relates to the system's autopoietic reproduction because unnecessary elements may be forgotten, allowing the system to perform auto-reflection and regulate itself over time.[183]

Nobles and Schiff note that "[h]aving only two sides to the code allows for an easy move from one side of the code to the other."[184] However, a binary coding system is an oversimplification of social relations and the diversity of CAS. For instance, in the face of unclear norms, the binary codes 'legal'/'illegal' might have to be supplemented by a third option of 'maybe,' or 'it depends.' And even if a norm results in a binary code represented by opposite signals, there can be many binary codes for different applications of that norm. As social complexities increase, the diversity and number of codes vary, and discovering which code an agent will use, as well as subsequent choices in applying a norm, becomes impossible. For instance, one might figure out whether an inventor will enforce his/her patent right, but which solution unfolds and whether the parts will settle in a given case is not so simple. This renders the legal system unpredictable. Acknowledging the interactions among multiple agents (legal and non-legal) not only amplifies agents' understanding of these systems, but also enlarges the places and processes by which law is created. This is essential to develop strategies to design and reform legal systems and guide their interaction with their regulatory targets.

Finally, Luhmann's theory completely disregards 'the interest in between,' as explained in Chapter One.[185] Since the 'interest in between' relates to the diversity of elements (for instance, agents, norms, and signal-boundary arrangements) in CAS, analyzing only extremes or averages of components cannot represent the dynamic processes happening within CAS.[186] Once agents accept the complexity in CAS and

[183] Luhmann, *supra* note 168; Nobles & Schiff, *supra* note 173 at 16.
[184] Nobles & Schiff, *supra* note 173 at 120–121.
[185] See: Miller & Page, *supra* note 42 at 7-8-27-218–230.
[186] See Chapter One, for specific considerations and more generally, see: Miller & Page, *supra* note 155.

the diversity of interactions and agents, they must also recognize that binary codes cannot express them. Due to unpredictability, they can only identify a few causes and consequence connections, encountering a combination of behaviours, expectations, facts, and interactions that is much richer than a binary code description.

2.2.4. The Importance of Agents in Building the System

As outlined above, Teubner defines law as an autopoietic system without disregarding the importance of the individual (or agents) in the system's creation.[187] By criticizing Luhmann's replacement of the "autonomous individual, not with supra-individual entities, but with communicative processes,"[188] Teubner argues that "Luhmann completely separates psychic processes from social ones and perceives the human individual in society as a communicative artifact, as a product of self-observation of social autopoiesis."[189] Luhmann's view of the agents forming the legal system is problematic because, for Teubner, communication and signals are abstract entities that exist independently of the agents creating them. As such, the creation of legal systems is attributed exclusively to legal agents, namely courts.[190]

Teubner, in turn, defines law as both a system of communication and a social process,[191] integrating the role of individuals (agents) in interacting with the law, and its autopoietic process. Autopoiesis, in his view, decenters individuals as the prime figures of the system by promoting "an epistemic autonomy of multiplicity of social discourses."[192] Communication and cognition processes are built up by different sets of agents and, when combined in each setting, create and enable the functionality of a system.[193] Although

[187] See: Teubner, "How the Law Thinks", *supra* note 178 at 738.
[188] *Ibid*.
[189] *Ibid*.
[190] Luhmann, *supra* note 168.
[191] Teubner, "How the Law Thinks", *supra* note 178 at 739.
[192] *Ibid* at 741.
[193] *Ibid*.

communication remains even after individual agents have vanished, it would not exist or be transformed without the existence of agents—human beings—and their cognitive processes.

In CAS theory, due to its universality principle, different systems are studied despite their content. But, the content and structure of CAS are directly connected, exercise mutual influences upon each other, and might be strategically considered while planning the reform of systems. This is particularly true in social systems, and, therefore, legal systems. As such, in legal systems, the influence of the content in the structure of the system (and vice versa) cannot be ignored.

Thus, the structure or organization of a system influences its content and vice-versa. For instance, the structure of a system may influence or even determine agents' interactions, as well as the flow of information in, within, and about the system. This may even impact the content of norms, as the position of an agent in the system determines the amount and type of information received, influencing his/her actions and understanding of the system. This means a norm can determine the organizational rules of a system and thus affect agents' interactions and behaviours and the flow of and access to information among agents. These factors and dynamics further influence the structure and content of the system.

In terms of content in legal CAS, the behaviours of agents, while interacting with one another and with and within systems, might not coincide with formal rules. The influence of agents' behaviours in shaping the system and their ability to influence law and policymaking processes, and vice versa, shows that the system is ever-changing.

2.2.5. Moving Forward in Legal System Analysis, Design, and Reform

Several of Luhmann's methodological choices render it unsuitable for a dynamic understanding of the law and legal systems. The way he presents self-differentiation implies that the boundaries between the law and other systems, and between the law and the environment, are clear and static, as well as the sources

and agents creating the law. The way the law operates suggests a constant flow of information and communication moving between legal systems and society, which turns Luhmann's operational closedness into an artificial attempt to remove external influences, and complexity, from the system. Even though Luhmann's view of autopoiesis requires some level of variation, interaction, and selection, in order to allow the system to learn, adapt, and evolve, these processes would be limited in a closed system because closedness limits the sources that would ensure the legal system to thrive against challenges.

Finally, being able to differentiate between systems does not mean that complete separation exists. Differentiation is an abstract construction that might allow agents to understand society better, but the complexity of interactions among agents prevents them from determining clear and/or fixed boundaries. While Luhmann might be right, that "[o]nly the law can say what is lawful and what is unlawful, and in deciding this question it must always refer to the results of its own operations and the consequences for the system's future operations,"[194] it is the dynamic interaction among agents in and between systems that feeds the legal system through the constant recreation of 'what is law.' Our dynamic societies require that legal systems be open, constantly observing their regulatory targets, interacting with internal and external agents, and filtering and incorporating new information to improve or create new regulations. As such, the legal system's boundaries need to be flexible and permeable to society and agents' influences and information, serving more as a filter to aspects of life that must be regulated by law and those that must not. With such a reconceptualization of the law, it is possible to promote effective innovation in legal design and reform.

[194] Luhmann, *supra* note 168 at 139.

2.3. The Need for New Models to Regulate Complex Societies

An increasing number of scholars have been searching for theories that explain the law's role in regulating today's complex social world, including CAS theory. Developing a new understanding of legal systems requires considering the commands (or content) of norms, the behaviours of agents, the organizational features of the systems, as well as foreseeing the dynamic between legal and other systems.

Connecting the abstract and philosophical frameworks for law discussed previously with the way legal systems work, evolve and coevolve in practice (through systemic interactions and co-creation by different agents), this section presents the legal system as a CAS. As such, it shows how an agent-centred approach based on a dynamic and strategic evaluation of agents and their behaviours can serve as a better foundation for tailor-made strategies for legal system reform.

2.3.1. Experimentation in Legal System's Design and Reform

Legal theory taking a CAS approach remains sparse. There is even less work on empirical analyses and modelling of law within a CAS paradigm. But the gap is narrowing. Through multidisciplinary research, legal scholars have been further exploring CAS methods and models related to law.[195] Rulh, Katz, and Bommarito note four factors that suggest that legal systems are CAS: (i) the diversity of their constituting elements (institutions, norms, actors, and instruments); (ii) interconnections between their multiple elements via processes that are not determinable in advance (leading to probabilistic evaluations of interactions); (iii) their self-organizing properties, and; (iv) their agents' bounded rationality.[196]

[195] Some examples of these scholars and studies are: Ruhl, Katz & Bommarito, *supra* note 43; J B Ruhl & Daniel Martin Katz, "Measuring, Monitoring, and Managing Legal Complexity" (2015) 101 Iowa Law Rev 191; *Quantitative Legal Prediction – or – How I Learned to Stop Worrying and Start Preparing for the Data Driven Future of the Legal Services Industry*, SSRN Scholarly Paper, by Daniel Martin Katz, papers.ssrn.com, SSRN Scholarly Paper ID 2187752 (Rochester, NY: Social Science Research Network, 2012); Jean Frédéric Morin, Joost Pauwelyn & James Hollway, "The Trade Regime as a Complex Adaptive System: Exploration and Exploitation of Environmental Norms in Trade Agreements" (2017) 20:2 J Int Econ Law 365–390; Hadfield, *supra* note 2; Gold, *supra* note 61; Ruhl, "Law's Complexity", *supra* note 169.
[196] Ruhl, Katz & Bommarito, *supra* note 43 at 1377.

Gillian Hadfield adopts a definition of complexity in line with that of Page and Miller and highlights the interactions among multiple agents in creating society and its complex systems. Hadfield refuses to define legal systems exclusively as a set of state-based rules since such a statist view has been historically shown to be inaccurate or useless for policy development.[197] Considering social norms, she focuses on the creation and evolution of legal infrastructures directed at developing platforms for regulation.[198] For her, law is everywhere, and what society wants and the people need are legal infrastructures that allow for safe interactions.[199] As the levels of complexity in society and economies rise, more robust regulatory platforms are required to facilitate social interactions and processes. There is a high demand for legal innovation to incentivize open competitive markets that can create and deliver more sophisticated legal infrastructures tailored to tackle complex problems in a technology-driven world.[200]

Hadfield describes CAS as working through positive feedback loops to evaluate the impacts of agents' interactions and behaviours after the application of rules governing them. She argues for using diversity to develop smarter and more suitable solutions—what she calls to harness legal innovation.[201] It is the sense that this research approaches the relationship between law and science, proposing increased diversity in law and policymaking processes through the inclusion of non-legal agents.

Another aspect of Hadfield's analysis is her discussion of the bottom or base of the pyramid (BoP) and legal transplantation. BoP consists of that part of the population who live in vulnerable socioeconomic conditions, without access to legal platforms and at the margin of the rule of law, which is a significant

[197] Hadfield adopts Fuller's definition of law ("the enterprise of subjecting human conduct to the governance of rules") and shifts her evaluation from what law does and does not to what law looks like. In doing so, she opens up the possibilities to rethink and built the legal infrastructure governing CAS. Hadfield, *supra* note 2 at 19–20.
[198] By legal infrastructure, she means what produces legal conduct on the ground, thus affecting the capacity of any entity to address problems and how people behave towards them. See: Hadfield, *supra* note 2.
[199] She does not disregard the role of state-based rules in regulating societies but advocates for diversification in the participation of agents building and delivering law, as well as creating its content. See: *Ibid*.
[200] *Ibid*.
[201] *Ibid*.

portion of developing and least-developed countries.[202] Legal transplantation refers to the adoption or importing of legal institutions or rules from one country to another that are not necessarily tailored to local realities and needs.[203] In Hadfield's case, the transplant is from developed to less developed countries.

Robert Axelrod studies norms from an evolutionary perspective.[204] According to Axelrod, for a norm to exist, the individual has to act upon it.[205] The most common types of norms comprise expectations, values, and behaviours.[206] Behavioural norms are at the centre of his analysis because they provide a more accurate picture of what happens within systems. Assuming that "effective strategies are more likely to be retained than ineffective strategies,"[207] Axelrod claims that his evolutionary approach helps minimize problems of agents' reasoning while studying social systems. Specifically, in the law-making process, he explains that agents tend to follow strategies that seem to be the most successful. Yet, they must be aware that the notion of success varies according to context and the perceived goals of each agent.[208] When agents do not interact with one another or are not incentivized to think outside of the box of existing 'successful strategies,' they are likely to reproduce the same strategies. This is why increasing diversity and the flow of information in CAS is so important.[209]

Following Axelrod, the behavioural norms are present in the execution and coordination of biomedical RD&I practice. As IPRs regulate biomedical RD&I, behavioural norms also stem from agents'

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[202] BoP highlights poor living conditions, costs of building a legal infrastructure and later implementing and maintaining it, as well as the need to create and disseminate a culture about the rule of law. See: *Ibid*.
[203] *Ibid* c 12.
[204] He argues that, to fully understand a norm, one needs to grasp how the norm evolves over time. His analysis of the "evolution of norms" looks into the emergence and stability of behavioural norms ("metanorms") and their enforcement by agents. Specifically, he focuses on norms regulating group conflicts, by which he means conflicts arising between two or more agents without a central authority. Axelrod, *supra* note 169 at 1097.
[205] Axelrod clarifies that "how often the action is taken and just how much often someone is punished for not taking it." *Ibid*.
[206] Accordingly to Axelrod: "A norm exists in a given social setting to the extent that individuals usually act in a certain way and are often punished when seen not to be acting in this way." *Ibid* at 1097.
[207] *Ibid* at 1097–1098.
[208] Axelrod, *supra* note 169.
[209] Recalling ideas exposed in Chapter One and combining them with Axelrod's evaluation, specifically see: Miller & Page, *supra* note 155; Axelrod & Cohen, *supra* note 42; Simon, *supra* note 126; Kahneman, "Maps of bounded rationality", *supra* note 53.

application of IP norms. But the behaviour of individual agents may not always coincide with the norm and may sometimes limit a norm. Axelrod's ideas can significantly contribute to the analysis of IP and biomedical innovation systems by clarifying systemic interaction and coevolution.

Axelrod's evolutionary approach is not, however, enough, as it is essentially passive. Actual agents may also actively try to change other actors' behaviours to attain their goals. Towards this end, agents may consider: (i) evaluating agents' past behaviours; (ii) simulating agents' interactions within multiple options of legal regulation; and (iii) monitoring system changes while choosing diverse options. Complementary approaches such as these could amplify agents' knowledge of systems, inspiring them to create new models to regulate biomedical RD&I and even overcome obstacles to adopt models like open science and open drug development.

Richard Gold has also studied law as a CAS, and his evaluation combines elements of cognitive science (mathematics, psychology, and philosophy) to propose a "Structural Dynamic Theory of Law."[210] He states that individuals view reality in an inherently limited and partial manner and, consequently, they are unable to apprehend the whole of reality. Gold explains that two kinds of legal theory have tried to understand and analyze law: the first at the specific level, centred on individual rules, and the second, broader theory that locates law in relation to society and ideology. The first theory fails to describe how law became what it is, while the second fails to identify "where opportunities for change are, or the nature of the small actions which may have large effects."[211]

Gold argues that law is not stable and consistent but evolves over time. It does so, however, too slowly for most actors to observe any wholesale change. For him, "[e]ssentially, a legal system consists

[210] Gold, *supra* note 61.
[211] *Ibid* at 347.

of an interconnected set of expectations."[212] Borrowing from Luhmann, Gold contends that "an expectation is no more than a person anticipates will happen."[213] Expectations can either be about outcomes (primary norm) or how and when other expectations about law can be deployed (meta-norm).

One of the most crucial and relevant points of Gold's theory is how he describes the richness of interactions in the system and the constant changes that may happen within it. He asserts that nothing is static or permanent in legal systems and that norms may change in nature, content, and level. Even hierarchically organized norms change place in a system that is not static; a meta-norm today may be a primary norm tomorrow. The importance of society and agents—and their dynamic interaction with law—in Gold's theory presents law as a fluid and dynamic entity.

Agents behave differently when society changes, and through iteration, their behaviour may eventually stabilize and evolve into norms. This is a coevolutionary process between behaviours and norms that is subject to the bounded rationality of agents. Legal agents may strategically evaluate the benefits of formalizing behaviour into legal rules.

So far, the scholars presented above share similar viewpoints about the dynamic relationship between law and society and the need to include agents in the process of designing law, policy, and institutions.[214] The dynamic between social and legal norms that results in their mutual support and interaction above presented highlights social influences as critical drivers to comprehending how legal

[212] Gold's working definition of legal systems is: "Essentially, a legal system consists of an interconnected set of expectations. These expectations, whether primary, secondary, tertiary, etc., are held by legal actors practising within the system. Legal actors or legal practitioners means lawyers, judges, legal academics, and legislators. That is, the legal system consists of all those expectations held by legal actors which are held by such actors while practising law. While there is an evident circularity to this definition (that is, whether a legal actor holds an expectation in the actor's capacity as a legal practitioner is the subject of an expectation which lies both inside and outside the system at the same time), it provides a useful starting point." *Ibid* at 353.
[213] *Ibid* at 352.
[214] As Axelrod states: "In short, social norms and laws are often mutually supporting. This is true because social norms can be formalized into laws and because laws provide external validation of norms. They are also mutually supporting because they have complementary strengths and weaknesses. Social norms are often best at preventing numerous small defections where the cost of enforcement is low. Laws, on the other hand, often function best to prevent rare but large defections because substantial resources are available for enforcement." Axelrod, *supra* note 169 at 1107.

systems operate and evolve. In the same way, the importance of a constant flow of information moving between legal and social systems distances these scholars' theories from that of Luhmann in terms of how they view closedness and how they adopt openness as a characteristic of legal systems.

There is a need to connect norm development to the notion of emergence in legal systems and how behaviour may lead to norms. An evolutionary study of the interaction of legal systems and their regulatory targets can indicate the emergence of behaviours leading to the creation of norms. Constant observation, assessment, and monitoring of the legal system through the interaction of its multiple agents may assist in the identification of emergence.

In engaging in multisystemic studies, one must be aware that interaction in CAS happens at the agent level of a system and between different systems and their agents. I have asserted that legal systems are CAS and, as such, they interact with and regulate other systems that are also CAS and others that are not. This dissertation studies the interactions and coevolution between different CAS, i.e., legal and innovation systems (specifically, IP and biomedical innovation systems). As Rulh, Katz, and Bommarito state, "[l]egal systems are locked in perpetual co-evolution with their regulatory targets."[215] This statement indicates that any attempt to understand legal systems in isolation from the CAS they regulate will tend to remain at an abstract level and will not address real-world problems.

In sum, the analysis of agents' behaviour, interaction, iteration of behaviours, and emergence informs this dissertation's agent-centred evaluation. These features facilitate the identification of commonalities between law and science that help to clarify the interaction and coevolution of these systems.

[215] Ruhl, Katz & Bommarito, *supra* note 43 at 1377.

2.3.2. Legal Complexity's Challenges and Opportunities

There are at least three challenges to studying law through the lenses of CAS. First, CAS concepts need to be translated into legal scholarship. Second, CAS methods require adaptation to be applied to legal systems, which in turn requires training legal scholars in multidisciplinary research and picking the best CAS method for their research target. Third, there is the need to build a robust dataset to enable the application of CAS approaches to law through the proper development of models and support empirical legal research.

Rulh, Katz, and Bommarito compare CAS theory to traditional empirical approaches, highlighting modelling's potential to address social problems while evaluating systems in their coevolutionary interaction. According to them, a CAS approach stands out because it simultaneously considers the evolution of agents' strategies and the system's structure; that is, it portrays a dynamic situation.[216] In discussing possible applications of CAS theory to law, these scholars stress the need to harness and collect data about legal systems.[217] A solid theoretical and empirical foundation for legal complexity can allow for different applications through projects, while real-time monitoring of legal systems can facilitate adaptation and identification of problems.[218]

In another study, Katz and Rulh present and evaluate the efforts of legal scholars while engaging in descriptive, prescriptive, and ethical models in their evaluation of law as CAS.[219] Descriptive models[220]

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[216] *Ibid*.

[217] Rulh, Katz, and Bommarito also note that there is already a considerable amount of data that needs to be organized and made available in open-source repositories to allow further evaluations. This is important because information is what feeds CAS and informs its operation. Therefore, better access and organization of data and information may enable harnessing complexity within different CAS. The authors further stress the need to build foundations for CAS research in legal systems that will set an agenda to advance CAS legal theory and empirical research. *Ibid* at 1378.

[218] They conclude: "Research questions are largely limited in their ambition by the capacity of existing theoretical and empirical approaches. A complexity science agenda in legal research may open new horizons of important research questions. So long as complex and coevolving legal systems are exogenized from social systems research, our understanding and management of human societies will remain incomplete and policy-making will fall short." *Ibid*.

[219] Ruhl & Katz, *supra* note 195.

[220] *Ibid* at 204, 207.

consist of describing, translating, and mapping components of complexity into a legal analysis map. The authors note that diverse legal fields (for example, administrative law, mediation, dispute resolution, tax law, health law, and IP law) have been subject to descriptive models. Considering this, they conclude by establishing "a robust descriptive model of legal systems as complex adaptive systems."[221] Katz and Rulh further assert that "[a]nyone with training in law can easily map this framework onto the legal system."[222] By 'framework,' they mean the components of legal systems (such as institutions, laws, regulations, and cases) and their interactions and interconnections.

The prescriptive model[223] goes beyond the description of elements from CAS theory to legal theory and examines how the legal system targets other CAS for regulation. Therefore, the design of legal systems should consider human interaction and complexity.[224]

Finally, the ethical model examines the "ethical implications of seeing legal systems as CAS."[225]. The ethical model accounts for how the structure of the legal system and its interaction with regulatory targets may affect society and the fact that agents do not have complete control of these societal effects, considering the complex characteristics of CAS.

After recognizing the contributions of these three approaches—descriptive, prescriptive, and ethical—and the fact that they rely on intuition, analogy, and exemplification, Rulh and Katz point to the next step, which is a legal-complexity theory to "respond to the critic's demand of empirical proof." This

[221] *Ibid* at 207.
[222] *Ibid* at 203.
[223] The authors further explain: "Hence, legal complexity theory has worked on designing legal institutions and instruments that seem to fit well with complex adaptive system attributes. The theoretical premise is not that complexity is necessarily normatively good and should be promoted, but that some structural designs are less likely to disrupt the complexity dynamics of the system and are more likely to work well within the system as a whole and, perhaps as important, to facilitate the legal system's interaction with other complex social systems. The operative principle is that the legal system should be designed with its complexity in mind. "*Ibid* at 209.
[224] *Ibid* at 207–210.
[225] *Ibid* at 210–211.

legal-complexity theory should demonstrate the complexity of legal systems in different empirical experiments and develop a set of necessary metrics and methods to evaluate legal complexity.[226]

Rulh and Katz's explanations and criticisms of the three approaches deserve attention. The authors note that there are a fair number of studies combining CAS and legal theory across different legal fields.[227] However, there is a need and space for theoretical evaluations and studies of specific contexts connected to diverse areas of law, the same for in-depth analysis of some of the already studied topics.[228]

Legal scholars still have a considerable amount of work to understand the subtleties of CAS theory and methods applied to legal theory and the ethical implications of a CAS model of law. Collaboration and multidisciplinary studies between legal and CAS scholars can facilitate this endeavour. One also needs to consider that the level of technical knowledge in investigating the legal system alongside its regulatory targets varies depending on each field.[229]

The level of sophistication in the legal analysis of a specialist differs from that of a generalist, without even discussing or considering the quality of legal education. Not everyone with general legal training can accurately map and evaluate the legal landscape in highly specialized and technical fields, such as the IP and biomedical innovation systems. In my view, applying CAS theory, concepts, and methods still requires further training of legal scholars and their willingness to engage in interdisciplinary practices and projects. This type of study becomes even more challenging in developing and least

[226] *Ibid* at 211–212.
[227] They mention 22 (twenty-two) studies dealing with the subject law as CAS in different legal field. *Ibid* at 206.
[228] At the time of their article (2015), Katz and Rulh mention two studies in IP systems and CAS theory (Chapter Three presents more details about them). However, none of them provides a comprehensive analysis of IP systems as CAS, an in-depth translation of theoretical concepts from CAS to legal or IP theory, or innovative development of models and use of CAS methods or consider developing and least developed countries perspectives. The studies mentioned by Ruhl and Katz are: Andrea M Matwyshyn, "Organizational Code: A Complexity Theory Perspective on Technology and Intellectual Property Regulation Foreword" (2006) 11 J Technol Law Policy xiii–xviii; Deborah Tussey, "iPods and Prairie Fires: Designing Legal Regimes for Complex Intellectual Property Systems" (2007) 24 105–130.
[229] This point also connects to Hadfield's explanations about the level of legal expert knowledge and multidisciplinary and multi-agent approach to promote legal innovation. She also highlights the difficulty of finding and forming legal professionals that understand all the intricacies of legal systems in different jurisdictions and contexts and that can navigate complexity. See: Hadfield, *supra* note 2.

developed countries, where resources and qualified and specialized professionals are still limited and extremely expensive.

A final point about the challenges and opportunities of applying CAS theory to legal theory is to think about the place and capability of computer models and simulations to advance our understanding of different CAS interactions and coevolution.[230] Jean Frédéric Morin, Joost Pauwelyn, and James Hollway analyzed trade agreements to argue that the trade regime has evolved into a CAS.[231] One interesting point from their research is that they did not rely on a computer model but instead relied on human coders to analyze the legal and substantive relationship between norms. The reason for this methodological choice is the absence of computational capacity to perform such a task, considering that legal analysis is subject to interpretation and ambiguity.[232]

So far, I have highlighted some of the challenges of translating CAS theory and methods to social systems (primarily legal systems), and I share the opinion (implied in Morin's, Pauwelyn's, and Hollway's methodology) that analyzing the human component is still essential in an empirical analysis of legal CAS. Even though technology and computer sciences have evolved, especially in the realm of AI, there is still a long way to go. Currently, AI cannot accurately perform the same evaluations as do legal agents. This conclusion also justifies why I proposed strategies and developed conceptual and theoretical analysis instead of engaging in computer simulations for this dissertation project.

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[230] Computer models and simulations may be tools to improve the governance and experimentation in the regulation of IP and biomedical innovation systems. However, there is still a significant challenge for current computational models to properly portrait the bounded rationality of agents and the complex interplay between agents' behaviours and norms when modelling legal systems. This is one of the reasons I chose to not develop models. Additionally, the development of these models would require a dataset and empirical analysis tailored to specific questions and problems that are not developed given this dissertation's scope.

[231] The authors classify trade regimes as CAS by identifying six elements of CAS (multiple heterogeneous elements, no central coordination, interdependency, simple rules of operation, multiscale structure, and openness). In their study, they looked for insights in CAS theory and applied network analysis to understand "how law coevolves with other complex social and natural systems as well as how legal systems grow and sustain themselves." They engaged in empirical analysis—researching a network of countries' memberships in 680 bilateral, plurilateral, and multilateral trade agreements—and identified 280 environmental norms. Morin, Pauwelyn & Hollway, "The Trade Regime as a Complex Adaptive System", *supra* note 195 at 365.

[232] *Ibid* at 366.

2.3.3. Mirroring General Complex Adaptive Systems' Features into Legal Systems

In sum, the core aspects of CAS theory as set out in Chapter One and of CAS theory applied to law as set out in this chapter, and which will be used in this dissertation are:

(i) Legal systems are CAS;

(ii) Legal systems result from the combination and interaction of multiple agents (parts);

(iii) Legal systems are dynamic in their creation, operation, and reform;

(iv) Legal systems' operation, design, and reform are highly dependent on information flow and access;

(v) Legal systems' resilience and robustness, as well as their structure and reform, depend on diversity;

(vi) Legal systems are open systems in the sense that they are deeply connected to and influenced by society and their agents' expectations and behaviours;

(vii) Legal systems are locked in coevolutionary processes with their regulatory targets;

(viii) Legal systems are unpredictable but, nevertheless, stable;

(ix) Legal systems are inherently complex, requiring strategies that harness complexity rather than attempt to eliminate it.

In Chapter One, I highlighted features of CAS (emergence, hierarchy, robustness and resilience, and diversity) that are useful in analyzing legal systems, especially IP systems. Below, I transpose these features to legal systems to help agents understand some elements that influence these systems' design and reform and their coevolution and interaction with science.

(i) Emergence

CAS theory holds that interactions within and between systems (and their agents) and the environment occur in a non-linear and unpredictable way without central control. Even though agents

could arguably control the first legal outcome, as in applying a norm, it is practically impossible to track all other results and paths of interactions that this first application triggers. Likewise, these interactions happen in non-trivial ways, making it impossible to predict their content with certainty or assess how they might influence others.

(ii) System hierarchy translated into multiple levels of organization

As explained in Chapter One, 'hierarchy' does not mean 'subordination' in CAS. However, in legal systems, hierarchy deserves better attention concerning the content and structure of the law and how hierarchy influences systems' reform strategies. Legal systems are hierarchical not only in their structure and organization but also in their content. What law defines influences the evaluation of content and other hierarchies, as well as the interplay between different types of norms and their evolutionary process, given that legal systems combine diverse elements in dynamic ways (formal and informal rules, agents, institutions, behaviours, and expectations).

In terms of content, formal norms (legislation and case law) follow a hierarchy that entails subordination. For example, a constitution under federalism can set the primary rules for society, dictate principles for federal, provincial, and municipal legislation, and assign law-making power to each level of government. However, as complexity results in unpredictability and dynamic change, there will always be legal gaps, and conflicts may arise both between and within legislation. These inconsistencies may be solved in different ways and then incorporated into norms, or not at all. The choice of constantly amending legislation may not be the best strategy in light of the changing pressures on lawmakers and the specialized nature of regulatory targets, such as cutting-edge technologies. Sometimes, it might be more appropriate to wait for relations between content and agents to stabilize before formally changing the law.

Hierarchy in legal systems also determines formal routes to legal reform, where different procedures or even a single one might lead to different types of legislation. A view of CAS hierarchy that

considers the generality of content in the legal system, and the existence of normative gaps that make it difficult to predict and regulate outcomes, can enable innovative systems' design and bottom-up reforms in areas such as biomedical RD&I.

(iii) The robustness and resilience of the system

The way law organizes and reproduces itself complements the goal of achieving some predictability and promoting a stable legal system. Even in times of crisis, the legal system operates. But there are cases in which extreme situations may entirely alter the legal system. To address problems, some rules may change, and others appear. In more robust and resilient systems, the core rules remain, however. Studying resilience and robustness can reveal the system's structure in terms of its core and incidental norms. It can also allow for discovering norms that are more fragile and susceptible to change and supporting groups of agents that are open to new ideas and strategies to reform the system.

Moreover, agents must assess cohesion, coherence, and consistency in legal systems if they consider that legal systems are 'artificial' systems: a translation from the world of ideas to the real world. Sometimes law does not match reality; for example, the way it seeks to regulate science often does not match the purpose and effect of the scientific discovery or invention in society. Sometimes, the legal regulation of science does not facilitate how biomedical R&D happens and may directly (and negatively) affect follow-on innovation and access to knowledge. The value of being a 'fabricated' system or model of thinking is that argumentation and evidence can change the course of legal regulation. For example, as knowledge is not easily contained once the invention or creation that expresses it is available to the public, it is necessary to create rights to protect it. IPRs give the creator or inventor some control of who and under which terms can access and use his/her invention or creation. The arguments used to justify granting and/or extending IPRs, as well as the benefits related to them, vary. Changing the justifications of IP systems and the means of granting different IPRs could create entirely different systems.

(iv) Diversity: highlighting the role of agents in CAS

Diversity matters in legal systems and is crucial for understanding and reforming the law. As Rulh states:

> Throughout the legal system, agents interact in ways suggesting that the differences between agents matter, because they do. Complex adaptive systems theory is about building models for moderate number contexts in which agent heterogeneity can and usually does influence outcomes, and as such it is worth exploring how it might inform our understanding of the legal system.[233]

Law relates to the world as it 'ought to be,' while dealing with the world as it 'is.' In creating and reforming the law, agents (both legal and non-legal) reduce the space between these two worlds.

In law and policymaking, there is a tendency to search for an equilibrium point at which all interests are fairly balanced. But in a dynamic system, equilibrium is ephemeral. CAS are, by their very nature, unable to lock into an equilibrium. No outside forces are needed to cause a disturbance; the internal dynamics of these systems, including agent interactions, make equilibrium impossible. In developing countries, as later explained, equilibrium in IP and biomedical innovation systems is even harder due to weak socioeconomic conditions and transplantation of 'successful' strategies from developed countries that are inadequate for the local reality.

Law reform requires accommodating the diversity of experiences, perceptions, realities, and knowledge not only from legal agents but also from non-legal agents. This is evident when considering the "perpetual co-evolution between law and its regulatory targets."[234] To expand the sources that inspire regulation, it is essential to improve non-legal agents' knowledge of the law.[235] Moreover, legal agents should move towards other agents and build a dialogue to understand how other systems function and communicate and the rules and principles they operate. In doing so, different agents in legal systems and

[233] Ruhl, "Law's Complexity", *supra* note 169 at 890.
[234] Ruhl, Katz & Bommarito, *supra* note 43.
[235] Reflecting upon different agents' roles in system design and reform, their knowledge of, position (location), and influence on different systems and other agents, and their ability to assume diverse roles in different situations must be part of any evaluation. Part II discusses these issues, by presenting legal and non-legal agents, and their different roles as decision-makers, influencers, and rule-followers.

their regulated systems can optimize communication (signal-boundary arrangements) and, consequently, enable better outcomes within these systems. In essence, agents need to harness complexity to face the challenge of studying multilayered (or multilevel) and multi-agent systems.

Therefore, diversity is critical because one must be aware that evaluating and designing CAS by accounting for the average of agents' behaviours and strategies do not represent what happens in these systems. In this sense, complex evaluations that recognize the understanding of agents about CAS and the diversity of agents, strategies, and behaviours taking place in these systems are required to assess these systems closer to their reality.

Although CAS theory, methods, and models might have limitations, like any other approach, they provide a very useful tool for different agents to interact and exchange ideas, assumptions, and hypotheses about how to best regulate a given system. Because of internal biases and cognitive limitations, multidisciplinary and agent-centred approaches inspired by CAS theory become even more vital. In a not-so-distant future, this perspective could even be applied to computer simulations to improve the governance of (and experimentation in) IP and biomedical innovation systems in order to enhance related law and policy-making. Non-legal agents involved in biomedical RD&I could, for example, simulate different implementations of legal rules in designing their IP strategies. Combining an agent (and multi-discipline)-based approach for regulating new technologies would allow for dynamic collaboration between different agents and facilitate the work of diverse teams involving legal experts, scientists, coders, and programmers.

CHAPTER THREE—INTELLECTUAL PROPERTY SYSTEMS AS A COMPLEX ADAPTIVE SYSTEM

3.1. Initial Thoughts about the Complexity of Intellectual Property Systems and its Interaction with Biomedical Innovation Systems

IPRs regulate the conduct of R&D in the biomedical field in complex ways and directly influence access to knowledge and innovation. There is a critical balance to be pursued in the relationship between these two systems. IPRs can work as tools to enhance these outcomes or as barriers to achieving them. The relationship between IPRs and biomedical R&D is especially critical when considering its impact on global health in developing and least-developed countries.[236]

The complexity of the regulation by IPRs of biomedical R&D results from at least three factors: (i) the technical nature of scientific discourse, (ii) the structure and nature of law, and (iii) the relationship between the first two factors. First, as a form of science, biomedical RD&I requires high levels of technological and personnel specialization and infrastructure. It functions under specific business and research models that are determined by rules of interactions among agents. Second, the law regulates biomedical RD&I through various mechanisms at state and international levels, creating a multilayered system. IPRs are only one of the legal instruments that apply to this area. Others include competition law, innovation law, tax law, administrative law, and regulatory law. All these legal frameworks combine to establish the complex legal environment in which RD&I takes place. There is also the issue of whether traditional forms of IPRs (such as patents and copyrights) are appropriate for regulating cutting-edge technologies such as biotechnology. Third, experience indicates that people legislating, developing public policy, and managing technology tend to have difficulty understanding the relationships that exist between law and science and can fail to develop a common language for integrating them. Thus, they tend to

[236] See, initially: Røttingen et al, *supra* note 15; Barton et al, *supra* note 4; Stiglitz et al, *supra* note 5; Maskus, Lahouel, & others, *supra* note 5.

develop policies and strategies within a limited framework that ignores how the law actually applies to difficult scientific questions. For example, debates over the patenting of human DNA sequences often break down into disputes between those who see DNA as nothing more than a biological molecule and a source of health information and those who see it as an early stage of knowledge that, if protected, will block future invention.[237] This second level of dispute arises because of the broad range of scientific information, agents' interests, expectations and behaviours towards the protection of biomedical R&D and public policy needs that are part of the biomedical innovation system.

Thus, this third factor—what I describe as the relationship between law and science—lies at the heart of the problem I discuss in this dissertation. Investigating how these two CAS and their agents interact and coevolve and how law arises make up the following chapters' discussions. Below I provide the building blocks for understanding the characteristics of the IP system and the reasons for classifying it as CAS.

3.2. Overview of Intellectual Property Systems

This section presents four important points to generally understand the IP system and guide its evaluation as a CAS. These points are: (i) a basic definition of the IP system and the rights that are granted under it; (ii) the logic behind and functionality of the international IP system and how different IP systems (or regimes) relate to each other; (iii) the role of IPRs in society and, particularly in biomedical innovation systems; and (iv) the importance of IPRs as sources of information. Subsequent chapters will deepen the

[237] To discussions about gene patents, the protection of personalized medicine by IPRs, and the ethical, legal, social and economic issues related to it, see: *Gene Patents*, From Birth to Death and Bench to Clinic: The Hastings Center Bioethics Briefing Book for Journalists, Policymakers, and Campaigns (Garrison, NY: The Hastings Center, 2008); Piper, *supra* note 37; Robert Cook-Deegan & Christopher Heaney, "Patents in Genomics and Human Genetics" (2010) 11:1 Annu Rev Genomics Hum Genet 383–425; Ricardo Meléndez-Ortiz & Vicente Sánchez, *Trading in genes development perspectives on biotechnology, trade, and sustainability* (London; Sterling, VA: Earthscan, 2005); Caulfield, Harmon & Joly, "Open science versus commercialization", *supra* note 37; Yann Joly, "Open biotechnology: licenses needed" (2010) 28:5 Nat Biotechnol N Y 417–9; PACEOMICS, *supra* note 34.

technical discussions about the particularities of the regulation of biomedical RD&I by IPRs and its impact on access to knowledge and innovation, especially in developing countries.

3.2.1. Basic Definition and Different Categories of Intellectual Property Rights

According to the World Intellectual Organization, "[i]ntellectual property (IP) refers to creations of the mind, such as inventions; literary and artistic works; designs; and symbols, names and images used in commerce."[238] This definition serves as a starting point to present the two traditional categories (copyrights and related rights and industrial property) created to protect the results of inventive and creative minds. Copyrights protect expressive works and related rights, and the industrial property category includes trademarks, geographical indications, industrial design, patents, layout designs (topographies) of integrated circuits. IP systems also contemplate the protection of undisclosed information (trade and industrial secrets) and the control of anti-competitive practices in contractual licences.[239] Apart from traditional categories, there is the protection of biodiversity assets and traditional knowledge and discussions about how appropriate the traditional categories are to protect cutting-edge technologies such as biotechnology, nanotechnology, and AI.

The protection of biomedical R&D by IPRs is a complex endeavour for the reasons explained in subsection 3.1. above. To better understand the dynamic interaction of these systems through the perspective of CAS theory and an agent-centred approach, some background information is presented below.[240]

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[238] World Intellectual Property Organization, *What is Intellectual Property?*, WIPO Publication 450 (E) (Geneva: WIPO) at 2.
[239] World Intellectual Property Organization, *WIPO Intellectual Property Handbook.* (2008); World Intellectual Property Organization, *supra* note 238; *Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS Agreement)*, Annex 1C of the Marrakesh Agreement Establishing the World Trade Organization, signed in Marrakesh, Morocco on 15 April 1994 (15 April 1994).
[240] IP is an extremely technical and field-specific area of law; Part II provides further details and examples that connect to this dissertation hypothesis.

3.2.2. The International Intellectual Property System: The Logic Behind Different Intellectual Property Systems

In 1995, the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS agreement) of the WTO established a multilateral system that determines *minimum standards* for the protection of IPRs by its Member-States.[241] Consequently, Member-States must adapt their national legislation to the minimum levels of protection predicted in the TRIPS agreement—if a Member-State wants to provide higher IP protection than that set out in the agreement, it is allowed to do so but must extend those rights to all Member State actors fairly.[242] Even though international minimum standards guide the design and reform of IP national legislation, the examination and grant of IPRs occur locally. The local examination and granting of different categories of IPRs aim to guarantee countries' sovereignty to shape their laws considering their local needs and realities.[243] This allows countries to tailor their evaluations for granting IPRs in light of local needs. For instance, some countries do not grant patents for second-medical use.[244]

The TRIPS agreement further determines that Member-States cannot discriminate which technological field to protect. This means that areas that IPRs did not previously protect in some Member-

[241] *Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS Agreement)*, *supra* note 239.

[242] Before the WTO, the discussions about IPRs and related international agreements (for instance, Paris and Berne Convention) were managed by UN-WIPO forum. The WTO-TRIPS placed the discussion about IPRs on international trade and created a Dispute Settlement Body for matters involving these rights and guarantee enforceability. Currently, both forums share the space on IP matters, even though these institutions had distinctive priorities and mandates. The discussion about the protection of human rights and social and economic development was also brought to the umbrella of international trade. With time, and because of the difficulty to accommodate diverse interests and reach consensus, the multilateral system suffered pressures and redefinitions especially due to the emergence of bilateralism and plurilateralism. For more information about IP and global health at the international level, see: Benjamin Coriat, Fabienne Orsi & Cristina d'Almeida, "TRIPS and the international public health controversies: issues and challenges" (2006) 15:6 Ind Corp Change 1033–1062; World Health Organization (WHO), *supra* note 63; World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22; World Health Organization, World Intellectual Property Organization & World Trade Organization, *supra* note 17; UNCTAD-ICTSD, *Resource Book on TRIPS and Development* (Cambridge: Cambridge University Press, 2005).

[243] There are systems that facilitate the request of IP protection in multiple countries at the same time. Some examples are the Patent Cooperation Treaty (PCT) and the Madrid Protocol administered by WIPO that respectively facilitate the deposit of patents and trademarks. However, the examination and granting phases of IPRs happen at the national level and follow standards of examination of each country. World Intellectual Property Organization, "WIPO | Madrid – The International Trademark System", online: *World Intellect Prop Organ* <https://www.wipo.int/madrid/en/index.html>; World Intellectual Property Organization, "PCT – The International Patent System", online: *World Intellect Prop Organ* <https://www.wipo.int/pct/en/index.html>.

[244] *Guidelines for the examination of patent applications relating to pharmaceuticals*, by Carlos María Correa (United Nations Development Programme (UNCTAD), 2016) at 13–17, 42–44.

States, such as pharmaceutical, agriculture, and food-related products, are now subject to protection.[245] It also established a different period (transitional period) for Member-States to adapt their national legislation to its requirements considering their diverse social and economic development levels.[246]

The general principles mentioned above—alongside other principles of the TRIPS agreement and international agreements—constrain national IP systems' structure and reform. In this sense, there were multiple combinations of how different countries could implement the TRIPS agreement's requirements into their national legislations. Nonetheless, several developing and least-developed countries followed the apparent success of the legislation of developed countries, opting for partial or total legal transplantation. However, they were not tailored for their developmental needs.[247] Both at the time that the TRIPS agreement was negotiated and later when countries engaged in legislative reform, little in the way of empirical evidence existed on the impacts of IP protection in different countries.[248]

Considering the various developmental levels and needs of WTO-Member-States, the TRIPS agreement provides countries with exceptions and limitations in implementing IPRs nationally, generally referred to as 'TRIPS flexibilities.'[249] The objective of these flexibilities is to allow countries to protect the public interest, public order, health, and environment in their countries and protect against abuse of IPRs. Some examples of TRIPS flexibilities are transition periods to adapt national laws to the TRIPS agreement, compulsory licensing, and government use (for instance, public non-commercial use of

[245] *Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS Agreement)*, *supra* note 239.
[246] *Ibid*.
[247] For discussions on the TRIPS agreement negotiations and other international negotiations related to IPRs, biomedical RD&I, and global health, see: Christopher May & Susan K Sell, *Intellectual property rights: a critical history* (Boulder, Colo.: Lynne Rienner Publishers, 2006); Susan K Sell, "TRIPS Was Never Enough: Vertical Forum Shifting, FTAs, ACTA, and TPP" (2011) 18 J Intellect Prop Law; Abbott, Correa & Drahos, *supra* note 5; Stiglitz et al, *supra* note 5.
[248] Several developing countries opposed to a more protective version of IPRs in the TRIPS agreement's negotiations. One of the reasons for their claims was based on historical evidence that developed countries did not have restrictive IP laws at their early social and economic development period. These same countries guaranteed that legal instruments (flexibilities) to protect their social and economic needs and the public interest were incorporated to the TRIPS agreement. For more details about these issues, see: Drahos & Braithwaite, *supra* note 4; May & Sell, *supra* note 247; Sell, *supra* note 36.
[249] World Trade Organization (WTO), 33 I.L.M. 1197, *Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement)*, 1869 U.N.T.S. 299 (15 April 1994).

patents), the Bolar exception to allow research for regulatory purposes, and parallel importations. Flexibilities also help avoid a 'one-size fits all' approach to IP regulation and assist countries in overcoming problems that emerge from the interaction of the IP system and its regulatory targets.[250]

Beyond the TRIPS agreement, the international multilateral IP system born in the 19th century contains principles that guarantee the balance between IP protection and the public domain and public interest. Even though the Preamble of the TRIPS agreement recognizes IPRs as private rights,[251] a holistic interpretation of the overall framework of the agreement and its guiding principles show the underlying protection of the public interest. IPRs might be private rights, but they are granted by a public entity representing society. Unless those rights operate in a balanced way that fulfills that brings benefits to society, the reasons for justifying IPRs no longer exist. Thus, the granting of IPRs emerges from complex interaction sites among agents and is guided by general principles.[252]

Following the same logic, the objectives and principles stated by the TRIPS agreement relate the IP protection with the promotion of technological innovation, transfer and dissemination of technology, the use of knowledge to ensure social and economic welfare while protecting the public health and nutrition, and the promotion of the public interest. Therefore, these principles balance rights and obligations among Members of the agreement and ultimately the owners of IPRs.[253]

Technology continues to evolve, but trade agreements are static. This raises two points. First, the IP system needs to keep pace with technological change and provide flexible and smart solutions to the

[250] Barton et al, *supra* note 4; Benjamin Coriat, Fabienne Orsi & Cristina d'Almeida, "TRIPS and the international public health controversies: issues and challenges" (2006) 15:6 Ind Corp Change 1033–1062; Carolyn Deere, *The Implementation Game : The TRIPS Agreement and the Global Politics of Intellectual Property Reform in Developing Countries* (OUP Oxford, 2008); Sell, "TRIPS Was Never Enough", *supra* note 247.
[251] *TRIPS Agreement*, *supra* note 249.
[252] See: Sell, *supra* note 36; Stiglitz, *supra* note 180; Reichman & Maskus, *supra* note 4; Joseph E Stiglitz, "Knowledge as a global public good" (1999) 1:9 Glob Public Goods 308–326; Stiglitz, *supra* note 4.
[253] These ideas are found in several parts of the agreement and directly relate to openness in science and law. See especially, articles 7 and 8 of the TRIPS Agreement *TRIPS Agreement*, *supra* note 249.

regulation of emerging technologies. Second, traditional IPRs categories may prove inadequate for the appropriate regulations of emerging technologies.[254]

The TRIPS agreement does not provide specific or detailed rules for regulating different scientific areas such as biotechnology and nanotechnology. Under the logic of *minimum standards*, the responsibility for providing clear legal parameters to regulate knowledge by IPRs in any field rests on each Member-State and can vary among them. A Member-State can either specify the protection for an area or not make any distinction. However, it cannot favour any Member State to the detriment of others while doing so.[255] Countries are not free, however, to refuse to provide protection for a field of technology, given the prohibition of discrimination by technical field. The impact of providing technology-specific regulations and policies to specific areas as a strategy to obtain better results from the IP system is still under evaluation, even though the need for tailored approaches is recognized.[256]

The manner in which countries shape their domestic IP systems and the level of IP protection they choose to adopt is a function of their level of industrialization and their research and innovation.[257] Below, I compare the strategies of each of Brazil and India in adapting their domestic legislation to TRIPS agreement requirements, especially in technological sectors—pharmaceutical, food, and agriculture—in which they had not previously provided IP protection.[258]

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[254] *Toward a new era of Intellectual Property: from confrontation to negotiation. A Report from the International Expert Group on Biotechnology, Innovation and Intellectual Property*, by Richard Gold et al (Montreal: The Innovation Partnership, 2008); Dan L Burk & Mark A Lemley, "Biotechnology's Uncertainty Principle" in BT-Advances in Genetics, ed, (Academic Press, 2003) 305; David Vaver, "Need Intellectual Property Be Everywhere: Against Ubiquity and Uniformity" (2002) 25 Dalhous Law J 26.

[255] See, specifically, article 4 of the TRIPS agreement. *TRIPS Agreement*, *supra* note 249.

[256] For additional information on these topics, see: Dan L Burk & Mark A Lemley, "Is Patent Law Technology-Specific" (2002) 17 Berkeley Technol Law J 1155; Dan L Burk & Mark A Lemley, "Policy Levers in Patent Law" (2003) 89 Va Law Rev 1575–1696; Burk & Lemley, *supra* note 254.

[257] *Promoting Innovation and Access to Health Technologies*, by United Nations Secretary-General's High-Level Panel on Access to Medicines (New York: United Nations, 2016).

[258] Graziela Ferrero (org) Zucoloto & Rogério Edivaldo Freitas, *Propriedade Intelectual e aspectos regulatórios em biotecnologia* (Rio de Janeiro, Brasil: Instituto de Pesquisa Econômica Aplicada (Ipea), 2013); UNCTAD-ICTSD, *supra* note 242; Carlos María Correa, *Integrating Public Health Concerns into Patent Legislation in Developing Countries* (Geneva: South Centre, 2000).

Rather than take advantage of the transition period set out in the TRIPS agreement, Brazil adopted new IP laws in 1996, only one year after the agreement. This decision had a considerable impact on the Brazilian national pharmaceutical industry and, in particular, on the production of generic products, which further impacted the Brazilian government's capacity to cover the costs of health technologies provided by its public health system.[259] In contrast, India used the entire ten-year transition period provided by TRIPS to revise its laws in 2005. India decided to protect its generic industry, the leading supplier of drugs to developing and least-developed countries, rather than to accommodate global pharmaceutical firms.[260] These two examples illustrate that countries have options in how and when to adapt national IP laws.

Focusing on whether and how developing countries use TRIPS flexibilities to formulate domestic IP law[261] misses the fact that the R&D process starts much earlier. At that earlier stage, it is possible to tackle access to knowledge and innovation issues from a different perspective and design IP strategies that prioritize access, cooperation, and openness. I am interested in this phase of the process and in how agents interact on the ground. There are few empirical studies evaluating these interactions, especially when considering the behaviours and interactions of legal and non-legal agents in these CAS and the relationship

[259] César et al, *supra* note 7; Paulo Marchiori Buss, José da Rocha Carvalheiro & Carmem Phang Romero Casas, *Medicamentos no Brasil: inovação e acesso* (Rio de Janeiro, Brasil: Editora Fiocruz, 2008); Pedro Paranaguá, "A Revisão da Lei de Patentes: o Brasil como mero consumidor de conhecimento ou produtor de inovação?" (2014) 10:4 Pontes 14–18; Priscilla M D G César, Monica Guise Rosina & Fabricio Polido, "Propriedade Intelectual: Potencialidades e fragilidades do ambiente jurídico-institucional brasileiro para a inovação" in *Direito E Desenvolv Um Diálogo Entre Os BRICS* Coleção Direito, Desenvolvimento e Justiça: Direito em Debate - (Sao Paulo: Editora Saraiva, 2012) 137 Google-Books-ID: YbC5NAEACAAJ; *A Revisão da Lei de Patentes: Inovaçãoem prol da Competitividade Nacional*, by Newton Lima et al, Estudos Estratégicos 1 (Brasília: Câmara dos Deputados, Centro de Estudos Estratégicos, 2013).

[260] Graham Dutfield & Uma Suthersanen, "Harmonisation or differentiation in intellectual property protection? The lessons of history" (2005) 23:2 Prometheus Routledge 131–147 at 139–141; Kevin Outterson, "Fair followers: Expanding Access to Generic Pharmaceuticals for Low- and Middle-income Populations" in Jillian Clare Cohen, Patricia Illingworth & Udo Schüklenk, eds, *Power Pills Soc Ethical Leg Issues Drug Dev Mark Pricing* Social, Ethical and Legal Issues in Drug Development, Marketing and Pricing (Pluto Press, 2006) 164; Priscilla M D G César, *Análise crítica da proteção das patentes de invenção farmacêuticas e biotecnológicas: perspectiva dos países em desenvolvimento* (text, Universidade de São Paulo, 2011) [unpublished]; César et al, *supra* note 7; Correa, *supra* note 13; Correa, *supra* note 258.

[261] Some examples of these studies are: Correa, *supra* note 13; Correa, *supra* note 258; Stiglitz et al, *supra* note 5; Chaves, Vieira & Reis, "Access to medicines and intelectual property in Brazil", *supra* note 7; Oliveira et al, *supra* note 7; César et al, *supra* note 7.

between law and science. This lack is particularly noticeable in respect of developing and least-developed countries.[262]

Given the national nature of IP systems, there is space to innovate the content and structure of IP laws, a topic I will cover in subsequent Chapters.

3.2.2.1. The Dynamic Framework of Intellectual Property Systems: Power Relations and Politics at the Top-Layers of Systems

Agents exercise multiple roles within CAS and interact with other agents in various layers of these systems, thus opening possibilities for learning and adaptation from multiple sources and places. For instance, researchers often sit as experts on advisory boards or special commissions at international organizations.[263] Participating in different decision-making instances or being aware of discussions and decisions at the top layers of RD&I systems enlarges agents' overall knowledge and positions them to engage in more sophisticated IP strategies to regulate biomedical innovation. Increasing agents' overall understanding of CAS may help them innovate in managing and organizing biomedical R&D activities at the bottom layers what can result in more effective upper layer reforms. As biomedical RD&I becomes a global enterprise, coordinating bottom-up and top-down approaches to legal and policy design and reform becomes not only a strategy but a need.

Power relations and politics complicate both international and domestic discussions about IP law. Power relations and politics play dual roles in the structure of systems and influence those systems in various ways. Therefore, agents need to learn how to identify and evaluate these factors' influence to understand how IP and biomedical innovation systems interact and coevolve to promote changes and

[262] Chapter Five presents some of these studies through the lenses of CAS.
[263] One example of this are several members of the *Consultative Expert Working Group on Research and Development:* Financing and Coordination (CEWG) at the World Health Organization (WHO). See: Røttingen et al, *supra* note 15; John-Arne Røttingen & Claudia Chamas, "A New Deal for Global Health R&D? The Recommendations of the Consultative Expert Working Group on Research and Development (CEWG)" (2012) 9:5 PLOS Med e1001219.

reforms in these systems. In assessing these factors, agents will be better equipped to strategize and influence other agents' behaviours, expectations, and strategies toward these systems.

International negotiations concerning IP occur within multiple fora covering different topics, for example, IP itself, international trade, the environment, culture, indigenous rights and so on. Even though the main actors in the international scene are states that operate through international organizations, the decision-making processes that result in international law and policy usually engage various non-state actors, for example, the private sector and NGOs. Each of these groups has its agenda. Even though it is possible to identify the main arguments driving their conduct, the process of their interactions lacks transparency and suffers from the influence of power relations and politics among agents.[264]

The situation becomes more complex when one considers the high degree of regime-shifting that occurs with respect to IP. The decline of multilateralism (mostly WTO fora) and the ascension of bilateralism, plurilateralism, and regionalism have resulted in new negotiation dynamics. As a result of the WTO becoming a site of debate on social and economic development, several developed countries, such as the US, members of the European Union (EU), and Japan, have shifted negotiations to bilateral, plurilateral, and regional negotiations to increase the rights of IP holders. The combination of change of focus of international fora and forum-shifting leads to the difficulty of reaching consensus on controversial matters. It is not a surprise that the WTO Doha Round of Negotiations has not progressed due to a lack of consensus.[265] Similar dynamics exist in fora covering other subject areas, all displaying a dynamic and complex set of relations between actors, both state and non-state.

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[264] See, e.g.: Jean-Frédéric Morin & Amandine Orsini, "Regime Complexity and Policy Coherency: Introducing a Co-adjustments Model" (2013) 19:1 Glob Gov Rev Multilateralism Int Organ 41–51; Laurence R Helfer, "Regime shifting in the international intellectual property system" (2009) 7:01 Perspect Polit 39–44; Laurence R Helfer, "Regime shifting: the TRIPS agreement and new dynamics of international intellectual property lawmaking" (2004) 29 Yale J Intl L 1; Susan K Sell, *Cat and Mouse: Forum-Shifting in the Battle over Intellectual Property Enforcement* (2009); Yu, *supra* note 36.

[265] See, e.g.: Helfer, *supra* note 264; Helfer, "Regime shifting", *supra* note 264; Morin, Daley & Gold, "Having Faith in IP", *supra* note 51; Jean-Frédéric Morin, "Multilateralizing TRIPs-Plus Agreements: Is the US Strategy a Failure?" (2009) 12:3 J World Intellect Prop 175–197.

Given the complexities and interests involved, promoting informed, transparent, country-specific, and developmental needs-based approaches to law and policy is challenging. This situation worsens at the upper layers of these systems' organization where the number of agents involved (and representing the interests of a larger number of agents sitting at lower levels of these systems) is high, and the interests and expectations are more diverse. Agents need to be strategic by foreseeing the positive and negative aspects of complexity in any given situation and try to collect as much information as possible from different perspectives to ground their decision-making processes properly.

Combining the above insights, we can highlight three main considerations that frame agent decisions about negotiating IPRs: (i) the perspective from which an agent observes the system (including with whom that agent discusses her or his perspective); (ii) the ideal shape of the system (from that agent's perspective), and; (iii) the type and amount of information about the system to which the agent has access (including the agent's understanding of other agents' behaviours, expectations, and strategies). The ability to reassess decisions is also essential because what is significant or problematic today might not be tomorrow. The information an agent currently holds about the system may change over time.

For developing countries, adjusting to other agents' interests (especially developed countries) can have problematic consequences for their long-term social and economic development. Accommodating different agents' interests through the standardization of law and policy in IP and biomedical innovation systems may appear to facilitate trade and cooperation in diverse fields. However, accommodation and standardization can result in a disproportionate burden on developing and least-developed countries where meeting international or contractual obligations becomes more critical than addressing local needs.[266]

[266] Stiglitz et al, *supra* note 5; Røttingen et al, *supra* note 15; Vaver, "Need Intellectual Property Be Everywhere", *supra* note 254.

3.2.2.2. The International Debates on Systems Reform and New Research and Development Models

The decline of multilateralism, the rise of plurilateralism and bilateralism, and the creation of new cooperative schemes among countries have redefined the geopolitics of power relations and politics in IP and biomedical innovation systems. These facts directly impose challenges to strategize toward these systems' reform, fragment the debate, harm coordination aiming for multilateral systemic reform at the top layers of these CAS, and challenge legal and policy governance and agents' strategies to defend their interests in this field, especially developing and least developed countries.[267]

Long-term debates about the use of TRIPS flexibilities and their effective adoption by national laws have been at the centre of the discussion on IP systems' reform at the international level. Through the years, TRIPS flexibilities, as instruments to protect the public interest and address global health problems in different countries, have also taken on greater and lesser importance in declarations and debates by WTO Members. The WTO Doha Round of Negotiations, known as the round for development, resulted in several declarations and decisions stating the importance and legality of TRIPS flexibilities. These negotiations also brought to light the different needs of countries in adapting or reforming domestic legislation to international IP standards, their productive capacity to address health problems and the urgency of technology transfer and capacity building.[268]

New articulations and collaborations among different stakeholders—for instance, the trilateral cooperation among the World Trade Organization (WTO), the World Intellectual Property Organization (WIPO), and the World Health Organization (WHO)—also set the stage for discussions about how to

[267] World Health Organization, *Public health related TRIPS-plus provisions in bilateral trade agreements: a policy guide for negotiators and implementers in the WHO Eastern Mediterranean Region* (2010) Accepted: 2014-06-17T12:32:03Z; Jean-Frédéric Morin, "Tripping up TRIPS debates IP and health in bilateral agreements" (2006) 1:1 Int J Intellect Prop Manag 37–53; World Health Organization, *supra* note.

[268] 4th Doha Ministerial Round WTO, *Doha Declaration on the TRIPS Agreement and Public Health* -, (14 November 2001); General Council, *Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and public health*, WT/L/540 and Corr.1 (1 September 2003); *Amendment of the TRIPS Agreement*, WT/L/641 (6 December 2005); World Trade Organization (WTO), "WTO | Intellectual Property (TRIPS) - TRIPS and Public Health", online: <https://www.wto.org/english/tratop_e/trips_e/pharmpatent_e.htm#declaration>.

create incentives to address global health problems and failures in respect of IP and biomedical innovation that will inform reforms on these systems.[269] Debates gravitate from proposing the de-linkage of the IPRs from the results of biomedical innovation systems, the creation of an international R&D treaty, the need to create alternative ways to reward those involved in biomedical innovation (for instance, the establishment of prizes for drug development), to declarations stating the need for transparency of markets for health-related technologies.[270]

Among several topics that underline the debate of better strategies to design and reform IP systems and promote new RD&I models, openness in law and science is a crucial element.[271] There is still no multilateral international instrument regulating or devoted explicitly to openness and clarifying the different models and conceptualizations (like open science, open-source biotechnology, and open innovation) through which it takes place. However, some international organizations, like the United Nations Educational, Scientific and Cultural Organization (UNESCO), have promoted discussions. During an intergovernmental meeting of Member States experts, UNESCO held consultations with different stakeholders and issued a Report on "UNESCO Recommendation on Open Science" in March 2021. The draft Recommendation was submitted to the Member States and adopted by 193 countries at the 41st General Conference in November 2021, becoming the first international framework on open

[269] World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22; World Health Organization, World Intellectual Property Organization & World Trade Organization, *supra* note 17.
[270] Tim Hubbard & James Love, "A New Trade Framework for Global Healthcare R&D" (2004) 2:2 PLOS Biol e52; Médecins Sans Frontières (MSF), "Member States adopt the resolution on 'Improving the transparency of markets for medicines, vaccines, and other health products' at WHA today", (28 May 2019), online: *Médecins Front Access Campaign* <https://msfaccess.org/member-states-adopt-resolution-improving-transparency-markets-medicines-vaccines-and-other-health>; Seventy-Second World Health Assembly, *A72/A/CONF./2 Rev.1. Improving the transparency of markets for medicines, vaccines, and other health products* (World Health Organization (WHO), 2019); Aidan Hollis, "The Health Impact Fund: A Useful Supplement to the Patent System?" (2008) 1:2 Public Health Ethics 124–133; The Health Impact Fund, "The Health Impact Fund (HIF)", (14 December 2015), online: *Health Impact Fund* <http://healthimpactfund.org/>; Røttingen & Chamas, *supra* note 263.
[271] Chapter Seven specifically targets this concept.

science.[272] UNESCO's view of open science highlights the need to modify the entire scientific process to answer planetary and socio-economic challenges. The UNESCO Recommendation defines open science as:

> "[A]n inclusive construct that combines various movements and practices aiming to make multilingual scientific knowledge openly available, accessible and reusable for everyone, to increase scientific collaborations and sharing of information for the benefits of science and society, and to open the processes of scientific knowledge creation, evaluation and communication to societal actors beyond the traditional scientific community. It comprises all scientific disciplines and aspects of scholarly practices, including basic and applied sciences, natural and social sciences and the humanities, and it builds on the following key pillars: open scientific knowledge, open science infrastructures, science communication, open engagement of societal actors and open dialogue with other knowledge systems."[273]

Specifically, concerning the relationship between IPRs and open science, the UNESCO Recommendation recognizes the importance of the existing IP international legal frameworks that include the rights of scientists to their scientific productions. It further acknowledges that open science practices are based on the values of collaboration and sharing that build on existing IPRs. Therefore, open approaches connected to open licensing[274], availability of materials in the public domain, and IPRs' flexibilities are essential to amplify access to knowledge, enhance the benefits of science to society, and innovation and participation in the co-creation of knowledge.[275]

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[272] See: United Nations Educational, Scientific and Cultural Organization (UNESCO), *Preliminary study of the technical, financial and legal aspects of the desirability of a UNESCO recommendation on Open Science. General Conference. 40th Session, Paris, 2019. 40 C/63* (UNESCO Digital Library, 2019); "Draft text of the UNESCO Recommendation on Open Science - UNESCO Digital Library", online: <https://unesdoc.unesco.org/ark:/48223/pf0000376893?posInSet=7&queryId=64f6c09b-9508-4258-82a1-e195d9d38368>; "Preliminary report on the first draft of the Recommendation on Open Science - UNESCO Digital Library", online: <https://unesdoc.unesco.org/ark:/48223/pf0000374409.page=10>; United Nations Educational, Scientific and Cultural Organization (UNESCO), *UNESCO Recommendation on Open Science (SC-PCB-SPP/2021/OS/UROS)* (UNESCO, 2021) publisher: UNESCO; United Nations Educational, Scientific and Cultural Organization (UNESCO), "UNESCO sets ambitious international standards for open science", (25 November 2021), online: *UNESCO* <https://en.unesco.org/news/unesco-sets-ambitious-international-standards-open-science>.

[273] See: United Nations Educational, Scientific and Cultural Organization (UNESCO), *supra* note 272.

[274] The UNESCO Recommendation on Open science generally mentions open licensing and explicitly mentions its application to copyrights and software. However, it lacks specific mention to open licensing applied to patents, which does not impede a more extensive interpretation that includes this category of IPRs.

[275] See, specifically: United Nations Educational, Scientific and Cultural Organization (UNESCO), *supra* note 272.

As the UNESCO Recommendation on Open Science faces challenges to its implementation, one of the proposed areas of action in this instrument is the promotion of a shared understanding about open science and the different paths that lead to its implementation. Two points directly related to the discussions taking place at the dissertation. First, the recommendation that Member-States ensure that "publicly funded research is undertaken based on the principles of open science." Second, these states should enable "open multi-stakeholder discussions on open science benefits and its real and apparent challenges," including linking open science and IPRs.[276]

Still, given that the idea of openness in science relates to the obligation and right to share scientific knowledge and promote the flow of information, it has received indirect attention in other international instruments for human rights protection. These instruments highlight the importance of access to knowledge and the sharing of scientific advancements among nations.[277] Chapter Seven discusses the importance of openness in science and law for access to knowledge and innovation and analysis its emergence in CAS.

Finally, aligned with the above discussions are the UN Sustainable Development Goals (SDGs). The SDGs are part of the United Nations (2015) Resolution adopted by the General Assembly on 25 September 2015 ("Transforming our world: the 2030 Agenda for Sustainable Development"). The UN General Assembly established 17 interconnected goals as a guide for the action of Members-States to transform the world and accomplish a better and more sustainable future for society.[278] Targets and

[276] See, specifically: *Ibid*.
[277] Some examples of these instruments are: Article 27 of the Universal Declaration of Human Rights (1949) states the right of everyone to "share in scientific advancement and its benefits." Article 15 of the International Covenant on Economic, Social and Cultural Rights (1966) states the right of everyone to "enjoy the benefits of scientific progress and its applications" and "benefit from the protection of the moral and material interests resulting from any scientific, literary or artistic production of which he is the author." Article 15 of the UNESCO Universal Declaration on Bioethics and Human Rights (2005) declares the importance of sharing benefits that result from the scientific enterprise while stating the importance of guaranteeing access and promoting capacity building. See: United Nations General Assembly, *Universal Declaration of Human Rights*, Resolution 217 A (10 December 1948); UNESCO's General Conference, *Universal Declaration on Bioethics and Human Rights*, (19 October 2005); *International Covenant on Economic, Social and Cultural Rights*, United Nations General Assembly, 1966.
[278] *Transforming our world: the 2030 Agenda for Sustainable Development*, A/RES/70/1.

indicators envision the implementation of these goals and are monitored every year. Several SDGs rely on scientific input and the scientific community's work to be accomplished, making the debate about open science, access to knowledge, and innovation even more prominent and connected to the need for effective action.[279]

3.2.3. The Role of Intellectual Property Systems in Access to Knowledge and Innovation

The failures of IP and biomedical innovation systems to adequately address access to knowledge and innovation issues have been extensively debated in various fora.[280] Calls for technology-specific regulations and empirical research on the effects of IPRs' protection on access to knowledge and innovation demonstrate a challenge to the 'one size fits all' view of IPRs regulation.[281] There is also a growing acknowledgment that IP systems have not promoted access to knowledge and innovation—even

[279] For initial discussions on SDGs and their implementation, see: Frank Biermann, Norichika Kanie & Rakhyun E Kim, "Global governance by goal-setting: the novel approach of the UN Sustainable Development Goals" (2017) 26 Curr Opin Environ Sustain 26–31; Alicia Bárcena, "De-colonizing the 2030 Development Agenda Moving Towards a Universal Partnership for Sustainable Development" in *Glob Gov Dev José Antonio Ocampo* (Oxford Scholarships, 2016); John H Knox, "Human Rights, Environmental Protection, and the Sustainable Development Goals" (2015) 24 Wash Int Law J 517–536; Martin S Edwards & Sthelyn Romero, "Governance and the Sustainable Development Goals: Changing the Game or More of the Same?" (2014) 34:2 SAIS Rev Int Aff 141–150.

[280] For deeper discussions on these failures, see: Barton et al, *supra* note 4; Gold et al, "The unexamined assumptions of intellectual property", *supra* note 4; Gold et al, *supra* note 254; Drahos & Braithwaite, *supra* note 4; Stiglitz, *supra* note 4; Reichman & Maskus, *supra* note 4; Bessen & Meurer, *supra* note 4; Heller, *supra* note 4; Murray & Stern, "When Ideas Are Not Free", *supra* note 4.

[281] In this sense, Yochai Benkler states: "The efficiency of regulating information, knowledge, and cultural production through strong copyright and patent is not only theoretically ambiguous, it also lacks empirical basis. The empirical work trying to assess the impact of intellectual property on innovation has focused to date on patents. The evidence provides little basis to support stronger and increasing exclusive rights of the type we saw in the last two and a half decades of the twentieth century. Practically no studies show a clear-cut benefit to stronger or longer patents." Yochai Benkler, *The Wealth of Networks: How Social Production Transforms Markets and Freedom* (Yale University Press, 2006) at 39–40.

in the developed world—but instead have aggravated health crises and given IPRs a detrimental and harmful global status.[282]

From the perspective of advocates seeking to address crises in access to knowledge and innovation, the problems associated with limited access to data, information, knowledge, medical technologies, and innovation are significant consequences of multiple failures of IP and biomedical innovation systems. The results are decreased levels of innovation and increased access gaps (in all dimensions). The debate on this topic has reached the point where different agents are discussing (at national and international levels) the need to implement alternative models to guide biomedical R&D. These same agents are even contesting whether IPRs are the best instrument to regulate biomedical R&D.[283]

IPRs are tools that may hinder or stimulate innovation and access to knowledge depending on how agents implement them and design policies and strategies for their deployment. Peter Drahos and John Braithwaite stated that it is not a matter of propagating an "anti-intellectual property tract," but instead promoting democratic IPRs in a society that is aware of these rights' effects, especially in developing and least-developed countries. They explain that knowledge has been dominated by a corporate elite, which has resulted in high social costs, mainly for developing countries and least-developed countries and created what they call an era of 'Information Feudalism.'[284] They clarify:

> Information Feudalism is a regime of property rights that is not economically efficient, and does not get the balance right between rewarding innovation and diffusing it. Like feudalism, it rewards guilds instead of inventive individual citizens. It makes democratic citizens trespassers on knowledge that should be the common heritage of humankind, their educational birthright. Ironically, information

[282] In a specific evaluation of the patent system, Josh Lerner explains that strengthening patent protection does not lead to benefits in the country adopting it. There is evidence that countries with lower standards of protection in the beginning of their industrial development have greater economic development. Studies present similar findings and back 50 years, starting with Edith Penrose (1951) and being corroborated by different authors like Mazzoleni & Nelson (2000). An interesting point raised by Penrose is that, if thought today, the patent system would maybe not exist. However, given its current complexity, making a case for abolishing it is very difficult. See: *Patent Protection and Innovation Over 150 Years*, Working Paper, by Josh Lerner, National Bureau of Economic Research, Working Paper Series Working Paper 8977 (National Bureau of Economic Research, 2002); Edith Penrose, *The Economics of the International Patent System.* (Pp. xv. 247. Johns Hopkins Press: Baltimore, 1951); *150 Years of Patent Protection*, Working Paper, by Josh Lerner, National Bureau of Economic Research, Working Paper Series Working Paper 7478 (National Bureau of Economic Research, 2000).
[283] Burk & Lemley, *supra* note 256; Barton et al, *supra* note 4; Drahos & Braithwaite, *supra* note 4; Krattiger, *supra* note 16.
[284] Drahos & Braithwaite, *supra* note 4.

> feudalism, by dismantling the publicness of knowledge, will eventually rob the knowledge economy of much of its productivity.[285]

As mentioned in Chapter Two, a considerable number of developing and least-developed countries' population still lives at the BoP[286] and, therefore, at the margin of the rule of law in fragile social and economic circumstances. This population also bears a higher cost of the legal (including IP) system that generally does not serve their interests and developmental needs but those of foreign investors. For instance, in Brazil, there is a predominance of patent applications from foreign holders as opposed to from Brazilian citizens and firms.[287] Additionally, the Brazilian Public Health System often feels the burden of costly patented health technologies necessary to face health challenges afflicting its population.[288] Likewise, diseases that predominantly affect developing countries' populations, such as neglected diseases, face insufficient investment.[289]

Developing and least-developed countries also face significant challenges in harnessing and benefiting from IP and biomedical innovation systems. Many of these countries are still designing or improving their law, policy, and governance mechanisms to meet their needs and international obligations. Their law and policy design processes often need ongoing work to overcome the lack of transparency, address increased citizen participation, and ensure accountability.[290] These difficulties create a risk that

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[285] *Ibid* at 219.
[286] See: Hadfield, *supra* note 2.
[287] Zucoloto & Freitas, *supra* note 258; *Research in Brazil. A report for CAPES by Clarivate Analytics*, by Di Cross, Simon Thompson & ALEXANDRA Sinclair (Clarivate Analytics, 2017).
[288] Buss, Carvalheiro & Casas, *supra* note 259; Mazzucato & Penna, *supra* note 35.
[289] Drugs for Neglected Diseases (DNDi), *supra* note 27; *G-Finder-2019- Neglected Disease Research and Development: Uneven Progress*, by Dr Nick Chapman et al, Zotero, G-Finder (Policy Cures Research, 2019).
[290] This scene has changed through the years given the work of NGOs and other stakeholders including research and academic communities. An example of it is the policy and advocacy to approve a TRIPS waiver legislation during COVID-19 Pandemic. However, this same story shows the difficult faced by Brazilian citizens given the chaotic pandemic response and that Bill could have been issued at the beginning of the pandemic by the President. The same reasoning applies for the current lack of support from Brazil in access to medicines debates taking place in the WTO forum. This shows uncertainty in these systems and the higher impacts on developing countries like Brazil that have other factors like corruption and denial of science besides law adding complexity to pandemic response. About the Brazilian response to the Covid-19 pandemic, see: Conectas Human Rights, *supra* note 6; Ventura & Reis, *supra* note 6; Ventura, Aith & Reis, *supra* note 6; Ventura, Aith & Reis, *supra* note 6; Galvão-Castro et al, "HIV/Aids and COVID-19 in Brazil", *supra* note 7; Carvalho, *supra* note 9.

developing and least-developed countries overlook, misunderstand or underestimate the complexities of IP and biomedical innovation systems and fail to identify the critical points of these systems that need reform. Therefore, there is a risk that they might design laws or policies that do not respond adequately to complexity.

Moreover, given the limitations of resources and time, vulnerable developing and least-developed countries may opt to transplant laws and policies from other countries—mainly developed countries—to regulate their IP and biomedical innovation systems. However, these mechanisms are often unsuited to their economic structure, levels of education and resources, and pressing health and social needs. Aligning different sets of national policies such as industrial, innovation, IP, and health and organizing them into a network of common (urgent and less urgent) targets are critical factors to redesigning these systems with efficiency and equality in mind. How to appropriately design and reform IP systems considering these developmental needs and the specificities of different regulated systems requires a better understanding, mapping, and monitoring of the interaction and evolution of IP systems and the diverse regulated systems.

As highlighted in Figure 3 below, the role of IP systems in promoting access to knowledge and innovation while regulating biomedical R&D must be evaluated in the context of multiple law and policy intersections.[291] These intersections generate interactions among agents within different systems that are hard to monitor and complex to understand. Therefore, the IP system is not the only part of the equation but a vital piece to answer these challenges.

[291] Figure available at: World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22 at 15.

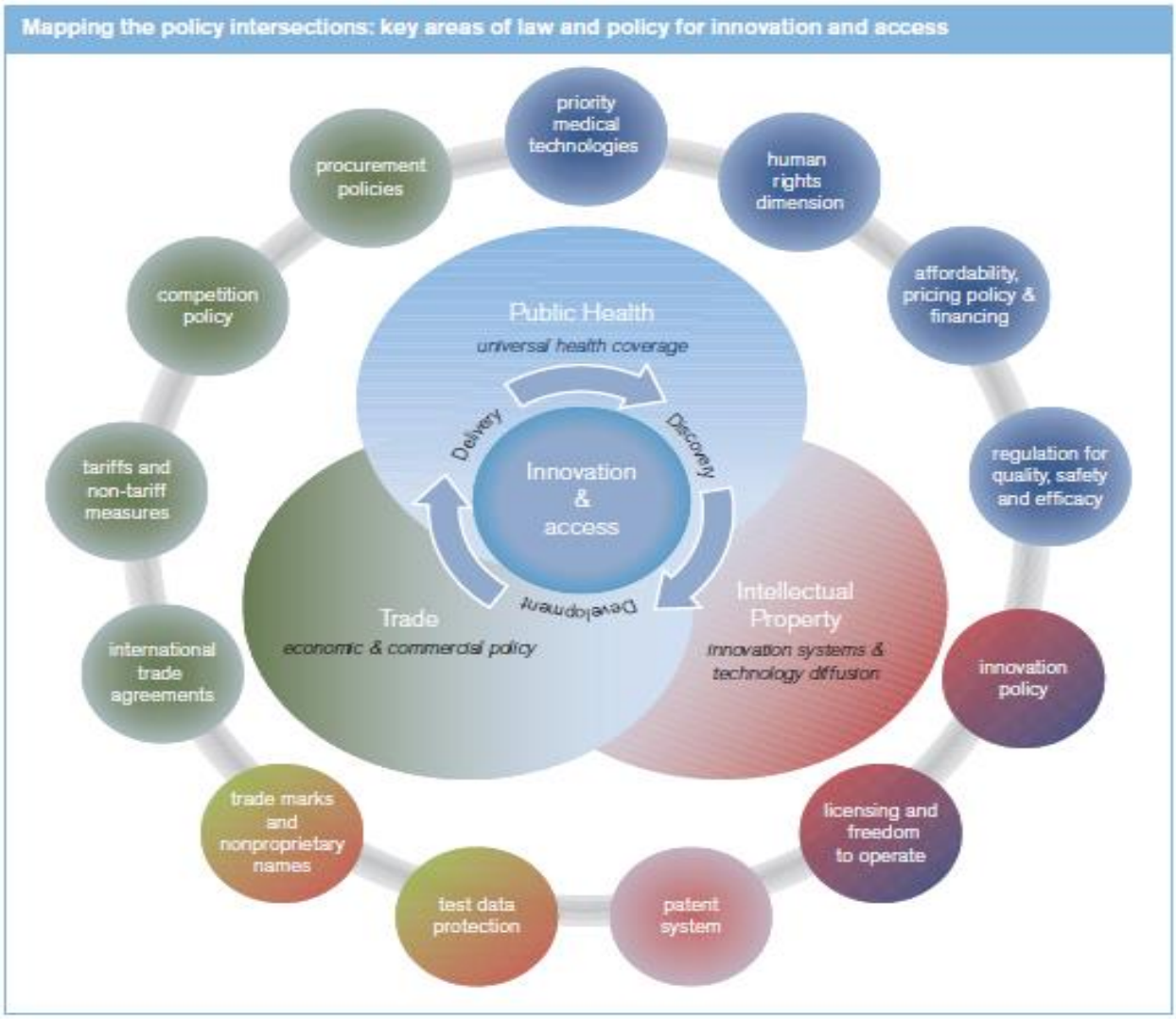

Figure 3: *WTO, WIPO, WHO. Mapping the policy intersections: Key areas of Law and policy for innovation and access.*[292]

Finally, in designing and reforming these systems, one must be aware that IP systems are highly susceptible to politics and power relations throughout their organizational structure. Even at the lower levels, where fewer interests are in place, the interests of expert communities encounter the interests and motivations of different stakeholders. Thus, evidence-based decision-making, participation, and

[292] Figure available at: *Ibid*.

transparency must guide the design and reform of CAS; in doing so, the agents comprising IP systems may help to promote access to knowledge and innovation.

3.2.4. Intellectual Property Rights as Sources of Information

IP systems play a dual role in respect of information. First, these systems protect knowledge, data, and information, a condition that elevates the importance of IP in other systems. Second, the intangible assets protected by IP are also sources of information.[293]

Information is critical in knowledge economies to create further knowledge, innovation and other benefits. For example, disclosing information in patent documents aims to allow other agents to replicate the object of the patent (the invention) and advance RD&I.[294]

Patents, like other IPRs, function as sources of information for the academic and research communities. The description of the invention sets out previous knowledge ('prior art') on which that

[293] Yochai Benkler states: "This second quirkiness of information as a production good makes property-like exclusive rights less appealing as the dominant institutional arrangement for information and cultural production than it would have been had the sole quirky characteristic of information been its nonrivalry. The reason is that if any new information good or innovation builds on existing information, then strengthening intellectual property rights increases the prices that those who invest in producing information today must pay to those who did so yesterday, in addition to increasing the rewards an information producer can get tomorrow. Given the nonrivalry, those payments made today for yesterday's information are all inefficiently too high, from today's perspective. They are all above the marginal cost—zero. Today's users of information are not only today's readers and consumers. They are also today's producers and tomorrow's innovators. Their net benefit from a strengthened patent or copyright regime, given not only increased potential revenues but also the increased costs, may be negative. If we pass a law that regulates information production too strictly, allowing its beneficiaries to impose prices that are too high on today's innovators, then we will have not only too little consumption of information today, but also too little production of new information for tomorrow." Benkler, *supra* note 281 at 37–38.

[294] In this sense, Stiglitz states: "For instance, to get a patent you have to disclose enough information that somebody could replicate what is being patented (though often firms try to get away with disclosing as little as possible). Disclosure has long been an important part of the patent and intellectual property regime; it is one of the reasons why IPR can enhance innovation: people can build on that knowledge. Knowledge is the most important input into knowledge." Joseph E Stiglitz, "Economic Foundations of Intellectual Property Rights" (2008) 57:6 Duke Law J 1693–1724 at 1698.

invention builds, which works as an essential source of information. This can, with appropriate training in IP, advance and facilitate R&D.[295]

There are, however, imperfections in the IP system that limit its ability to disseminate knowledge optimally. Patents are not easy documents to read, and strategies used in their drafting purposely make it harder for people to fully appreciate the invention. Similarly, the high level of technicalities and dialogue with multiple scientific fields render the IP system challenging to navigate for a non-specialist. Finally, it is rare the case in which a single patent captures an invention.[296]

Disclosing and sharing information enables peer-review assessment and practices that support the scientific endeavour. However, how knowledge has been shared and disclosed by research and academic communities has been subject to criticism by these same communities. There are questions on the rules and principles guiding the disclosure and sharing of biomedical R&D activities and the metrics used to evaluate the performance of researchers and academics. Poor research enterprise management and the influence of IP practices, policies, and business models (like the pharmaceutical industry) that under-incentivize competition and promote secrecy have resulted in bad research practices. These practices include the duplication of research efforts because of insufficient or absent sharing of negative results of R&D activities among agents.[297]

Disclosure further works as a mechanism that creates a record or memory of data, information, knowledge, and inventions that are part of the biomedical innovation ecosystems and enable scientific

[295] *Addressing a Gap in Canada's Global Innovation Strategy: Capacity Building in IP Literacy, IP Strategy and Access to Affordable IP Legal Services*, Special Report, by Myra J Tawfik, www.cigionline.org, Special Report (Waterloo, Canada: Centre for International Governance Innovation (CIGI), 2016); Paul David, "The Economic Logic of 'Open Science' and the Balance between Private Property Rights and the Public Domain in Scientific Data and Information: A Primer" in *Role 27111946Sci Tech Data Inf Public Domain Proc Symp M Esanu Paul F Uhlir Ed* (Washington, D.C.: The National Academies Press, 2003) 19; *Using IP for development*, by World Intellectual Property Organization (Geneva, Switzerland: World Intellectual Property Organization (WIPO), 2017).

[296] World Intellectual Property Organization, *supra* note 295; Nancy Gallini & Suzanne Scotchmer, "Intellectual Property: When Is It the Best Incentive System?" (2002) 2 Innov Policy Econ 51–77.

[297] Daniele Fanelli, "Negative results are disappearing from most disciplines and countries" (2012) 90:3 Scientometrics 891–904.

progress. Therefore, disclosed information needs to be accessible and available in the public domain. Particularly in discussions about data and open science, research and academic communities disseminate under principles the vision that data must be findable, accessible, interoperable and reusable (FAIR Data Principles). These FAIR Data Principles aim to support scientific progress and create a global infrastructure that allows proper data management, publishing, discovery, sharing and re-use.[298] Scholars and scientists have raised questions about how fair these principles are in data-driven research and society and the need to go beyond technical and incorporate normative and ethical dimensions on this debate.[299] Even though FAIR Data Principles and open science are related, they are not a condition to each other. A more elaborated discussion is needed to enhance both and establish mechanisms for their implementation.[300]

3.3. Theories and Justifications

The reasons for granting IPRs and supporting the development of IP systems vary among agents and are not universally accepted. These reasons include recognizing IPRs as natural rights of inventors or creators, IPRs as incentives to promote innovation, IPRs as rewards to the intellectual and economic efforts of inventors and creators, and IPRs as instruments to advance science, technology, and innovation (ST&I).

[298] See: Mark D Wilkinson et al, "The FAIR Guiding Principles for scientific data management and stewardship" (2016) 3:1 Sci Data 160018.

[299] In this sense, see: Martin Boeckhout, Gerhard A Zielhuis & Annelien L Bredenoord, "The FAIR guiding principles for data stewardship: fair enough?" (2018) 26:7 Eur J Hum Genet 931–936 Bandiera_abtest: aCg_type: Nature Research Journalsnumber: 7Primary_atype: Reviewspublisher: Nature Publishing GroupSubject_term: Ethics;GeneticsSubject_term_id: ethics;genetics.

[300] In this sense: "The FAIR principles do not specify what would constitute legitimate means of controlling access. More extensive guidance within open science frameworks and policies about how data should be made available 'as open as possible, as closed as necessary' is urgently needed. (…) The FAIR principles are a powerful way of making true on the ideal of a more open science, which could stimulate researchers to take issues related to data stewardship and wider accessibility and reusability on board in an early stage. Their strength also rests in their simplicity and flexibility, providing common ground for developing shared agendas and courses of action in research data stewardship and the development of community-wide data and metadata standards. The FAIR principles thereby provide a necessary stimulus to a data-driven research culture for actually facilitating reuse of data in a transparent fashion. The articulation of standards for data, metadata and access conditions is a core principle in this regard." *Ibid* at 933, 935.

The theory used by an agent to justify the grant of IPRs influences his/her IP strategy, the goals this agent aims to achieve from the IP system's operation, and how and why this agent interacts with other agents. This section does not present in-depth theoretical discussions but, instead, provides a glimpse of the diversity of these discussions and their influence on CAS design and reform.

William Fisher III highlights four main theoretical approaches to justify IPRs: the utilitarian approach, the Lockean approach (or Labour Theory), the personality theory, and the social planning theory approach. The *utilitarian approach* states that the goal of IPRs is to maximize social welfare.[301] This approach relies on the notion of increasing economic benefits from the granting of rights while limiting the costs of doing so. The *Lockean approach* relies on the idea that the person who worked towards creating or inventing something has a property right (a natural right) over that creation or invention. The *personality approach* holds that creations of the mind form part of an individual's personality and thus ought to be protected by private property (and, hence, IPRs).[302] Last, the *social planning theory approach* justifies granting IPRs as an incentive to achieve a just culture. This approach has similarities to the utilitarian approach but relies more on the award that results from social benefits generated by the creation or invention rather than only on economic benefits. Fisher notes that these different approaches can be identified in the arguments of a diverse group of agents (such as judges, lawyers, and legislators) when they interact with the IP system and apply its rules. Thus, identifying the nuances of these agents' beliefs about IPRs is key to understanding how agents design IP systems and set their strategies.[303]

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[301] William W Fisher III, "Theories of Intellectual Property" in *New Essays Leg Polit Theory Prop Stephen R Munzer Ed* Cambridge Studies in Philosophy and Law (Cambridge, United Kingdom: Cambridge University Press, 2001) 168 at 170.
[302] In this sense: "[T]hat private property rights are crucial to the satisfaction of some fundamental human needs; policymakers should thus strive to create and allocate entitlements to resources in the fashion that best enables people to fulfill those needs. From this standpoint, intellectual property rights may be justified either on the ground that they shield from appropriation or modification artifacts through which authors and artists have expressed their 'wills' (an activity thought central to 'personhood') or on the ground that they create social and economic conditions conducive to creative intellectual activity, which in turn is important to human flourishing." *Ibid* at 172.
[303] Fisher III, *supra* note 301.

Of the above, the utilitarian justification is most commonly held and is generally subsumed within a general law and economics understanding of IP.[304] William Landes and Richard Posner explain that contrary to the economic reasons for granting physical property, the economic justification for IPRs requires a balance between incentives and access to knowledge.[305]

Stiglitz explains that IP systems provide incentives to agents to invent by allowing them to restrict the use of the knowledge they produce in exchange for financial returns while charging people to access that knowledge. Contrary to Landes and Posner, Stiglitz argues that IP is less important as an incentive than commonly he thought. He points out that some of the most significant ideas (for instance, the Alan Turing's 'Turing Machine' that resulted in the creation of the computer) are not protected through IPRs. Instead, he argues, many of these ideas are born in universities backed by government funding. In those settings, monopolies over knowledge are not efficient and hinder rather than support the progress of science. Stiglitz highlights other incentives to conduct research and development, such as reputation and contributing to society. IPRs only account for a small portion of the diversity of motivations that underlie innovation. Overreliance on a narrow economic view of IP does not capture the true complexity of scientific and technological motivations.[306]

Fundamentally, Stiglitz asks us to understand the role of IP systems more broadly within innovation systems. He starts by arguing that knowledge is a public good[307] and asserts that creating incentives for innovation is dynamic. Hence, there is a need to balance the interaction of IP and innovation systems, given that the efficient use of knowledge requires that it is freely available. IPRs circumscribe

[304] For in-depth evaluation of economic foundations of IPRs and different views about it, see: William M Landes & Richard A Posner, *The economic structure of intellectual property law* (Cambridge, Massachusetts: Harvard University Press, 2003); Stiglitz, *supra* note 294; *Intellectual Property*, SSRN Scholarly Paper, by Peter S Menell & Suzanne Scotchmer, papers.ssrn.com, SSRN Scholarly Paper ID 741424 (Rochester, NY: Social Science Research Network, 2005); Robert P Merges, "Economics of intellectual property law" (2014), online: <http://papers.ssrn.com/sol3/Papers.cfm?abstract_id=2412251>.
[305] Landes & Posner, *supra* note 304 at 11–36.
[306] Stiglitz, *supra* note 294 at 1696–1700.
[307] This idea is presented later in this chapter.

and restrict, however, the use of knowledge, thus undermining efficiency. Further, they support the creation of monopolistic power over knowledge and, consequently, further lessen use. These conclusions, he argues, should lead us to reform IP systems in a manner that promotes access to knowledge.[308]

Drahos presents a view similar to Stiglitz. He advocates for an instrumental view of IP in which a broader moral theory and values frame the limits and goals of these rights. He asserts:

> Instrumentalism would require a strongly articulated conception of the public purpose and role of intellectual property. The juristic development of intellectual property law would have to adhere rigidly to that purpose. Instrumentalism would require an old-fashioned way of talking: the language of property rights would be replaced by the language of monopoly privileges. The grant of these monopolies would be tied to the idea of duty. Duty-bearing privileges would form the heart of an instrumentalism of intellectual property. Under instrumentalism, intellectual property would be located in the context of some broader moral theory and set of values. Property rights would be morality's servants and not its drivers. Finally, an instrumentalist theory of intellectual property would rest upon a naturalistic empiricism. Legislative experiments with these rights would be driven by information about their real-world costs and abuses.[309]

The combination of Stiglitz's and Drahos's views supports the case for looking at different principles and justifications to guide the design and reform of IP systems. They call attention to the diversity of agents and goals in interacting systems and the need to look beyond the current presumptions about the role of IP in innovation systems and society. Their views also support seeing IPRs as instruments to uphold agents' objectives within systems driven by a sense of public purpose. This dissertation aligns with these views. Independently of the reasons agents choose to justify IP protection, they should promote IP systems that respond to societies' needs and balance the interests of different agents.

[308] Stiglitz, *supra* note 294 at 1696–1700.
[309] Peter Drahos, *A Philosophy of Intellectual Property*, 1 edition ed (Routledge, 2016) at 231–265, 265.

3.4. Connecting the Dots: Intellectual Property Rights, the Public Domain, Proprietary and Non-Proprietary Approaches to Knowledge Regulation, and the Idea of Openness in Law

The study of openness in law and science can have different approaches. For this dissertation, openness works as a characteristic and a guiding principle of these systems. Openness plays a fundamental role in enabling a balanced biomedical innovation ecosystem.[310] Specifically, the idea of openness in law requires reflecting on the adequate level of IP protection needed in different circumstances and for regulating specific scientific fields and technologies. Openness highlights the necessity of promoting dialogue between legal and policy domains and science to achieve society's goals concerning innovation and access to knowledge.

3.4.1. The Context: Network Societies and Knowledge Economies

Intellectual property is at the heart of the knowledge economy, as Stiglitz affirms:

> Intellectual property has become one of the major issues of our global society. Globalization is one of the most important issues of the day, and intellectual property is one of the most important aspects of globalization, especially as the world moves toward a knowledge economy. How we regulate and manage the production of knowledge and the right of access to knowledge is at the center of how well this *new economy*, the knowledge economy, works and of who benefits. At stake are matters of both distribution and efficiency.[311]

Knowledge economies use 'knowledge' as their prime asset to generate tangible and intangible goods. Network societies arose with the advent of the Internet and IT and are characterized by a shift in how agents relate, communicate, and deal with information—how they see the world around them.[312] The main assets agents trade are knowledge, data, and information. The value of these intangible assets extends

[310] Chapter Seven discusses these ideas in detail.
[311] Stiglitz, *supra* note 294 at 1695.
[312] Gustavo Cardoso, "Chapter 2 -Societies in Transition to the Network Society" in Gustavo Cardoso & Manuel Castells, eds, *Netw Soc Knowl Policy* (Washington, DC: Center for Transatlantic Relations, Jhu-Sais, 2006) 23; Manuel Castells, "Chapter 1: The Network Society: from Knowledge to Policy" in Gustavo Cardoso & Manuel Castells, eds, *Netw Soc Knowl Policy* (Washington, DC: Center for Transatlantic Relations, Jhu-Sais, 2006) 03.

far beyond economic revenues. Owning or accessing these assets affects agents' capacity to interact with other agents and their environment, overcome dependency on other agents, and succeed in their goals.

IPRs play an essential role in networked societies and knowledge economies by mediating how agents in those societies access and share intangible assets. The choices agents make regarding their IP strategy directly affect how costs and benefits are distributed. Therefore, agents need to look for effective ways to improve the interaction and coevolution of IP and biomedical innovation systems and regulate these systems to enable them to succeed in these complex environments.[313]

The public goods nature of knowledge[314] renders any equivalency between IP and 'traditional' property inappropriate.[315] Stiglitz argues that the public goods and nonrivalrous nature of knowledge "is at the core of understanding efficiency in the use of knowledge. It is more efficient to distribute knowledge freely to everybody than to restrict its use by charging for it."[316] IP systems render, according to Drahos and Braithwaite, knowledge into an 'impure public good' because it sometimes becomes excludable. IP holders seek to further diminish the public goods aspect of knowledge by lobbying for an ever-greater scope of protection. Overprotection may increase individual profits but translates into a lower efficiency of the innovation system and access to its benefits through decreased competition and a more restricted ability to build on knowledge.[317] In this sense, the level and terms of protection offered by IPRs on data,

[313] See: Gustavo Cardoso, "Chapter 2 -Societies in Transition to the Network Society" in Gustavo Cardoso & Manuel Castells, eds, *Netw Soc Knowl Policy* (Washington, DC: Center for Transatlantic Relations, Jhu-Sais, 2006) 23; Manuel Castells, "Chapter 1: The Network Society: from Knowledge to Policy" in Cardoso & Castells, *supra* note 8; Joseph E Stiglitz, "Case Studies - Knowledge and Information: Knowledge as a Global Public Good" in Inge Kaul, Isabelle Grunberg & Marc Stern, eds, *Global Public Goods Int Coop 21st Century* (Oxford University Press, 1999) 308.
[314] Knowledge—as a good—is non-excludable and non-rival. Essentially, these terms mean that different agents can use knowledge simultaneously without diminishing the asset's value, regardless of the number of agents making use of it. For more information about it, see: Stiglitz, *supra* note 294.
[315] See: Fisher III, *supra* note 301; Drahos, *supra* note 309.
[316] Stiglitz, *supra* note 294.
[317] Drahos & Braithwaite, *supra* note 4 at 215–216.

information, knowledge, creations, and inventions and the impact of these rights on the public domain must be considered in any modification of the biomedical RD&I regime.[318]

Beyond IPRs, agents are limited in their ability to use knowledge based on their level of education and their access to background information. In this sense, the gap separating those who can use knowledge from those who cannot is more extensive in developing and least-developed countries, particularly cutting-edge technologies and science. This indicates the importance of guaranteeing equal access to education to improve knowledge access, use, and exchange.[319]

For our purposes, information is more than just the fuel for biomedical RD&I: it is the object of regulation by IP systems and the source of dynamism, adaptation, and evolution for IP and biomedical innovation systems (or any CAS). What predominates is a question of power.[320] The power encompassed by IP protection goes beyond common-sense assumptions. It can restrict the information about the IP system itself and how IP works, interacts, and coevolves with other systems. Therefore, information (encompassing data and knowledge) is vital to better regulate and design systems of any kind.

3.4.2. Openness in Law and the Public Domain

The idea of openness in law and science (biomedical RD&I) relates to the relationship between IPRs and the public domain and, more specifically, their interaction. Openness means sharing data, materials, tools and outcomes of R&D, including the right to use them and improve upon them. Everything from basic research, drug targets, potential drugs and other interventions, clinical data and associated know-how can be shared without limitations imposed by IP. As Paul David explains:

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[318] See: Stiglitz, *supra* note 294; Peter Drahos, "The Regulation of Public Goods" (2004) 7:2 J Int Econ Law 321–339.
[319] Castells, *supra* note 312; Cardoso, *supra* note 312; Stiglitz, *supra* note 180.
[320] See: Gustavo Cardoso, "Chapter 2 -Societies in Transition to the Network Society" in Gustavo Cardoso & Manuel Castells, eds, *Netw Soc Knowl Policy* (Washington, DC: Center for Transatlantic Relations, Jhu-Sais, 2006) 23; Manuel Castells, "Chapter 1: The Network Society: from Knowledge to Policy" in Cardoso & Castells, *supra* note 8; Joseph E Stiglitz, "Case Studies - Knowledge and Information: Knowledge as a Global Public Good" in Inge Kaul, Isabelle Grunberg & Marc Stern, eds, *Global Public Goods Int Coop 21st Century* (Oxford University Press, 1999) 308.

> The elision effected by the application of the metaphor of "property" to the domain of ideas has been fruitful in many regards. But there is a danger in permitting those who are enthusiastic for more and stronger IPR to employ this as rhetorical device as a way of avoiding the burden of proof. They should be asked to show that the moves already made in that direction have not been economically damaging, that further encroachments into the public domain of scientific data and information would not be still more harmful, and that society would not benefit by adopting a policy that was just the opposite of the one they support.[321]

Creating openness means restricting or limiting proprietary approaches to knowledge regulation, relying instead on a more substantial public domain and commons.[322]

As James Boyle explains, "[t]he public domain is the material that is not covered by intellectual property rights."[323] 'Commons,' on the other hand, is "a resource over which some groups have access and use rights—albeit perhaps under certain conditions."[324] The result is that there are no IPRs in the sphere of the public domain, but they can exist in terms of outsiders of a 'commons.'[325]

IPRs and the public domain are intrinsically connected:[326] they are 'two sides of the same coin,' and they work together to pursue objectives such as access to knowledge and follow-on innovation. Boyle exposes the connection between these concepts and stresses the importance of creating mechanisms to achieve balance in their operation.[327]

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[321] David, *supra* note 295 at 33.
[322] James Boyle, *The Public Domain: Enclosing the Commons of the Mind* (New Haven & London: Yale University Press, 2008).
[323] *Ibid* at 38.
[324] *Ibid*.
[325] *Ibid* at 38–41.
[326] Reinsuring these definitions Boyle affirms: "Our markets, our democracy, our science, our traditions of free speech, and our art all depend more heavily on a public domain of freely available material than they do on the informational material that is covered by property rights. The public domain is not some gummy residue left behind when all the good stuff has been covered by property law. The public domain is the place we quarry the building blocks of our culture. It is, in fact, the *majority* of our culture. Or at least it has been." *Ibid*.
[327] The limits and the relationship between public domain and IPRs have suffered an imbalance by what some authors use to denominate the 'second enclosure movement'—the tendency of some agents to overprotect intangible assets. This tendency may result in the tragedy of anticommons, as discussed in Chapter Five. The 'first enclosure movement' would be an answer to the 'tragedy of commons.' Hardin describes the tragedy of commons as the situation in which the multiple ownership and management of land would result in an overuse of the land resources considering each individual owner would try to maximize her/his own use of the land. The problem of the common use of resources was solved by the delimitation of the land's use. See: Garrett Hardin, "The Tragedy of the Commons" (1968) 162:3859 Science 1243–1248; Boyle, *supra* note 322 at 42–53.

Seeing diversity in how we regulate knowledge leads to a more sophisticated assessment of the IP system. IPRs are instruments that can either enable the public domain by providing incentives to create or lead to overprotection and decreased innovation and access. That is, IP strategies can range from maintaining knowledge in the public domain, passing by the idea of commons, and applying different levels for protecting intangible assets.

Openness in respect of biomedical RD&I means building a system that enables multiple approaches and possibilities for regulation and allows the flow of information through its boundaries, feeding the system to achieve greater innovation.

Several variables influence the adoption of proprietary and non-proprietary approaches to knowledge regulation, including (i) the knowledge of agents regarding the application of IP law in different scientific fields; (ii) agent understanding and assumption about the relationship between IPRs and the public domain; (iii) whether agents view knowledge as being cumulative and cooperative; (iv) the reciprocity in which agents share or provide access to other agents to information, data, knowledge, and intangible assets and their incentives for doing so; (v) the instruments (for example, contracts, material transfer agreements, and licenses) and institutions that enable sharing; and (vi) the ease with which it is possible to separate public from private knowledge. Law and policymakers and those defining IP strategies, policies, and practices at universities and research centres must be aware of these variables while reforming IP and biomedical innovation systems.[328]

Finally, Nelson and Eisenberg analyze science and technology as a joint enterprise, not as separate activities.[329] The overlap between science and technology in biotechnology also justifies, according to

[328] Chapters Six and Seven further develop these points.
[329] Rebecca S Eisenberg & Richard R Nelson, "Public vs. proprietary science: a fruitful tension?" (2002) Acad Med 1392–9.

them, new approaches to knowledge regulation that differs from traditional proprietary views.[330] As just discussed, openness does not imply the absence of IP protection but a more targeted approach to it within IP strategies, practices, and policies that enable agents to achieve goals such as access to knowledge and innovation.

3.5. Intellectual Property Systems as Complex Adaptive Systems

Few scholars have specifically studied IP systems as CAS.[331] Nevertheless, there exist multiple issues related to evaluating the IP system and its interaction with other systems.[332] In this dissertation, I examine the relationship between IP and biomedical innovation systems in developing countries through the lenses of CAS theory.

David A. Harper is one of the few who examines the IP system as a CAS in order to map out the evolution of IPRs' structural complexity with time.[333] He applies an evolutionary approach to property rights by focusing on the behaviours of entrepreneurs who combine IPRs into new arrangements

[330] Additionally, Art Rai explains that the non-commercial characteristic of molecular biology determined the ways it was funded. The research was conducted in academic institutions, funded by governments and non-profit institutions, and after licensed to the private sector. At this time, commercialization and IPRs start to influence scientific research. In this sense, see: *Ibid* at 90–92; Robert Merton, *The Sociology of Science: Theoretical and Empirical Investigations* (University of Chicago Press, 1979); Donald E Stokes, *Pasteur's Quadrant: Basic Science and Technological Innovation* (Washington (DC): Brookings Institution Press, 1997); Arti Kaur Rai, "Regulating Scientific Research: Intellectual Property Rights and the Norms of Science" (1999) 94 Northwest Univ Law Rev 77–152 at 88–89.

[331] Some of these scholars and studies are: Matwyshyn, "Organizational Code", *supra* note 228; Tussey, *supra* note 228; David A Harper, "Property rights as a complex adaptive system: how entrepreneurship transforms intellectual property structures" (2014) 24:2 J Evol Econ 335–355; David A Harper, "Intellectual Property as a Complex Adaptive System" in Andreas Pyka & John Foster, eds, *Evol Econ Innov Syst* Economic Complexity and Evolution (Cham: Springer International Publishing, 2015) 309.

[332] There is also a growing interest of the academic community in the study of IP systems as CAS. An example of this is the activities of the European Intellectual Property Institutes Network-Innovation Society (EIPIN-Innovation Society) that have engaged in multidisciplinary research to examine the role of IP as a CAS in innovation. Among their activities there is a specific 'Work package' for doctoral students who want to study IP as CAS. For more information, see: EIPIN, "Intellectual Property as a Complex Adaptive System", online: *EIPIN Innov Soc* <https://www.eipin-innovationsociety.org/research/intellectual-property-as-a-complex-adaptive-system/>.

[333] For Harper: "The property rights system is a web-like network of rules that exhibits increasing structural complexity as it evolves. This network consists of nodes and channels through which information, materials and energy flow." His analysis is interested in the structure of the system and ability of the system to combine and create new organizational arrangements. He does not assess normative and content relation questions, he is interested in the IPRs structures that are amendable and changeable. Harper, *supra* note 331 at 313–314.

(specifically patent pools[334]) while incorporating capital to make their businesses more profitable. Harper explains that entrepreneurs work in the gaps of the IP systems by combining building blocks to propose new routes to address problems.[335] That is, entrepreneurs act on the world through transformation by combining rules and resources to innovate. "They do not start from a blank slate devoid of rules."[336] He pays particular attention to the parts of the system (agents/entrepreneurs and patents) and how they dynamically combine to present new solutions to problems that IP systems intend to solve.

Harper's analysis of legal rules as capital goods helps to understand their effects in society and how "legal entitlements affects who (i.e. which entrepreneur) gets to select the uses of capital goods and what decisions they make to transform, combine, regroup or scrap capital goods."[337] After acknowledging the impact of legal entitlement and access to the legal rules and infrastructure, Harper finds a deep network of interactions, behaviours and application of rules, allowing the IP system to thrive. Harper's view that IP is a network of "combinatorial, relational, structural and heterogeneous"[338] capital goods relates to this dissertation's analysis. Like Harper, I am interested in the building blocks of the IP systems that, combined with the blocks of the biomedical innovation systems, generate possibilities for regulation and solutions.

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[334] A patent pool is an organizational framework that intends to facilitate the licensing process and, therefore, the access to patented inventions. Patents from different owners are licensed to the pool and third parties interested in the inventions contact the pool that has the right to sub-license them. The pool facilitates the transactional costs of licensing, especially in fields that require several patents with potentially different owners to develop an invention. Health technologies, airplane industries, digital video compression technology used in digital television and DVDs are examples of areas in which patent pools have been applied. For Harper, law and IP are complex capital goods ("property rules are an integral part of the knowledge structure that mobilizes and guides the transformation (manufacture, transportation, and storage) of materials, energy and information in the economic system"). He further states, patent pools "constitute a new level of economic organization within the economy wide network of rules." In the health field, the Medicines Patent Pool (MPP) has emerged as a key institution to optimize licensing and increase access to health technologies. *Ibid* at 310; "Medicines Patent Pool (MPP)", online: *Med Pat Pool* <https://medicinespatentpool.org/>.

[335] He explains: "The system of property is a structure in the sense that its heterogeneous elements are connected and interact. It is not a mere aggregate or stock. There is some patterning in the diverse array of property rights. These rules cannot be combined arbitrarily; they have to fit together and mesh with other types of inputs. They are like blocks of Lego that can be mixed and matched in particular ways to yield endless combinations. In addition, the property rights system exhibits a great deal of structural patterning at more than one level. It emerges as a nested multi-layered structure—a system of systems in which interrelated subsystems in turn consist of lower-level subsystems and connections between them." Harper, *supra* note 331 at 311.

[336] *Ibid* at 314.

[337] *Ibid* at 313.

[338] *Ibid* at 333–334.

All the scholars mentioned above may choose different frames, but all are in a common search for a new lens to address problems, in our case, the regulation of biomedical R&D by IPRs. Those scholars who treat IP systems as CAS have in common their attention to the parts of the system, its diversity, and emergent behaviours. However, much work is still required to develop CAS legal and IP scholarship into a cohesive whole. There is also a need for more multi-systemic and empirical analysis in this field.

Two main reasons suggest why analyzing IP systems as CAS is productive. First, doing so recognizes the diversity of elements within IP systems,[339] for example, the existence of multiple agents and institutions (lawyers, judges, patent and trademark officers, Courts, Intellectual or Industrial Property Offices, etc.), and multilevel regulatory arrangements and legal instruments (at the international, regional, federal, provincial, municipal, and institutional levels). These IP rules are also present in IP-specific legislation and other fields (for instance, IP rules in investment and biodiversity treaties). The variety of types of IPRs (patents, copyrights, trademarks, industrial design, plant variety rights, geographical indications, trade secrets, traditional knowledge) combines and overlaps in a manner that leads to complexity. Second, the elements within the IP system interact in non-linear and decentralized ways leading to unpredictability in this system's operation due to its dynamic nature and the emergent behaviours of its agents.

[339] Recalling the discussions in Chapter Two, specially: Ruhl, Katz & Bommarito, *supra* note 43; Hadfield, *supra* note 2.

PART II—CLOSING GAPS AND ADVANCING MULTISYSTEMIC ANALYSIS

CHAPTER FOUR—THE REGULATORY TARGET: BIOMEDICAL INNOVATION SYSTEMS AS COMPLEX ADAPTIVE SYSTEMS

4.1. The Complexity of Science

This chapter focuses on three points. First, it explains concepts and general aspects related to how and under which rules biomedical R&D takes place and clarifies the attributes that make the biomedical innovation system a CAS. The normative structure of science—the norms and principles by which the scientific endeavour happens—and the manner in which agents communicate within this system are the foundations for thinking of biomedical R&D as a CAS.[340] Second, the chapter presents organizational features of biomedical R&D that illustrate its evolution. Third, it concludes with explanations and examples about the protection of biomedical R&D by IPRs to set up a more detailed discussion of how these two CAS interact and coevolve in subsequent chapters.

4.1.1. The Normative Structure of Science[341]

In a sociological evaluation of science, Robert Merton presented the 'Republic of Science' and reflections on the 'normative structure of science.'[342] According to Merton:

> Science is a deceptively inclusive word which refers to a variety of distinct though interrelated items. It is commonly used to denote (1) a set of characteristic methods by means of which knowledge is certified; (2) a stock of accumulated knowledge stemming from the application of these methods; (3) a set of cultural values and mores governing the activities termed scientific; or (4) any combination of the foregoing.[343]

[340] Other systems also comprise the biomedical ecosystem alongside biomedical innovation and IP systems. Some of them are public health systems, tax systems, funding systems, and regulatory systems. This research focuses only on the interaction and coevolution of the first two.

[341] This chapter does not aim to deeply discuss aspects of Science, Technology, and Society Studies (ST&S) that relate to the normative structure of science nor thoughts of their scholars in depth. Its goals are to present a general idea that informs the existence of such structure that further connects to legal norms' structure and enables agents from different CAS to interact, communicate, and evolve, as well as to create common normative structures and operate in niches. This dissertation also does not intend to discuss the evolution of these norms regarding their content, as it is highly dependable on time and context and would require empirical research, the assessment of different agents' impressions and expectations about it.

[342] Merton, *supra* note 330 at 267–278.

[343] *Ibid* at 268.

Merton's theory presents science as an institution whose primary goal is promoting 'the extension of certified knowledge,' and is governed by norms and values. Four institutional imperatives comprise the ethos of science: universalism, communism, disinterestedness, and organized skepticism.[344] These institutional imperatives guide the scientific community's behaviour and, therefore, enable the evolution of the scientific enterprise.

Universalism means that objectivity, accuracy, and impersonal character guide scientific claims. Merton states that universalism is a 'dominant guiding principle' in the ethos of democracy. It determines impersonal criteria to limit the ability of actors or groups of actors to pursue personal advantage rather than overall welfare. He highlights that "[u]nder changing conditions, new technical forms of organization must be introduced to preserve and extend equality of opportunity."[345]

Communism relates to joint ownership of the results of the scientific enterprise. This imperative directly relates to IPRs and ideas such as commons, collaboration, and openness. Merton affirms that IP protection must be the exception and not the rule in the scientific enterprise. To the extent that it exists, it ought to function primarily to recognize the contribution of scientists.[346] Merton also asserts the 'status of scientific knowledge as common property.' He clarifies:

> The institutional conception of science as part of the public domain is linked with the imperative for communication of findings. Secrecy is the antithesis of this norm; full and open communication its enactment. The pressure for diffusion of results is reenforced by the institutional goal of advancing the boundaries of knowledge and by the incentive of recognition which is, of course, contingent upon publication.[347]

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[344] *Ibid* at 268–170.
[345] *Ibid* at 270, 273.
[346] Specifically, about IP and its relationship with the principle of communism, Merton affirms: "Property rights in science are whittled down to a bare minimum by the rationale of the scientific ethic. The scientist's claim to 'his' intellectual 'property' is limited to that of recognition and esteem which, if the institution functions with a modicum of efficiency, is roughly commensurate with the significance of the increments brought to the common fund of knowledge. (…) Scientific ethic goes beyond guaranteeing that property rights are in a bare minimum but also in the role of scientific community to guaranteeing that any invention produced by them is bided by ethical concerns and consequently accessible and affordable." *Ibid* at 273–275.
[347] *Ibid* at 274.

Disinterestedness refers to the fact that scientists should guide their activities for the benefit of the scientific enterprise. "Disinterestedness is not to be equated with altruism nor interested action with egoism."[348] Merton warns that the institution of disinterestedness can be distorted and misdirected by personal interests and states that it is the role of social institutions to defend against this.[349]

Finally, *organized skepticism* is interrelated with the other imperatives and supposes that science should be independent of other belief systems. As Merton explains, there is "[t]he temporary suspension of judgment and the detached scrutiny of beliefs in terms of empirical and logical criteria have periodically involved science in conflict with other institutions."[350]

Merton's theory grounds the understanding of the norms and principles by which science operates. Although these norms are not formally codified, they inform the scientific community's expectations, behaviours, and interactions. Consequently, they impact agents and systems that are not part of this community but interact with it. Further, they compose and enable communication in different niches and assist in the discussion of why biomedical science is a CAS.

4.1.2. Innovation and National Innovation Systems as Complex Adaptive Systems

Neither defining innovation nor measuring it are simple tasks. This is because of the infinite number of elements and agents that are involved in the innovation process. The Organisation for Economic Co-operation and Development (OECD) Oslo Manual defines innovation as "the implementation of a new or significantly improved product (good or service), or process, a new marketing method, or a new organisational method in business practices, workplace organisation or external relations."[351] The Manual

[348] *Ibid* at 275.
[349] *Ibid* at 275–277.
[350] *Ibid* at 277–278.
[351] OECD & Eurostat, *Oslo Manual* (Paris: Organisation for Economic Co-operation and Development, 2005) at 46.

categorizes innovation into main types: product innovation, process innovation, marketing innovation, and organizational innovation.[352]

Joseph Schumpeter first discussed the definition of innovation in his exposition of the 'process of creative destruction'[353] that is inherent in capitalist societies. Innovation, he says, is the process by which a system recreates itself through a set of organic interactions that cannot be fully described. Schumpeter explains that "[t]he fundamental impulse that sets and keeps the capitalist engine in motion comes from the new consumers' goods, the new methods of production or transportation, the new markets, the new forms of industrial organization that capitalist enterprises create."[354] Through the destruction, creation, and transformation of structures, institutions, and relations, innovation becomes a critical engine of growth—an evolutionary process. This process can occur in both disruptive (radical) or incremental ways. For Schumpeter, technological and organizational changes are the driving forces of innovation and are cumulative.

More than two decades ago, Bengt-Åke Lundvall coined the term 'National Innovation System' to capture the network of actors and processes that lead to domestic innovation:

> The national innovation system is an open, evolving and complex system that encompasses relationships within and between organisations, institutions and socioeconomic structures which determine the rate and direction of innovation and competence building emanating from processes of science-based and experience-based learning.[355]

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[352] Briefly explained, the Oslo Manual asserts: "A **product innovation** is the introduction of a good or service that is new or significantly improved with respect to its characteristics or intended uses. This includes significant improvements in technical specifications, components and materials, incorporated software, user friendliness or other functional characteristics. […] A **process innovation** is the implementation of a new or significantly improved production or delivery method. This includes significant changes in techniques, equipment and/or software. […] A **marketing innovation** is the implementation of a new marketing method involving significant changes in product design or packaging, product placement, product promotion or pricing. […] An **organisational innovation** is the implementation of a new organisational method in the firm's business practices, workplace organisation or external relations." *Ibid* at 48–52.

[353] Precisely about the process of creative destruction of Schumpeter, see: Joseph A Schumpeter, *Capitalism, Socialism, and Democracy: Third Edition*, 3 edition ed (New York: Harper Perennial Modern Classics, 2008) at 83–84.

[354] *Ibid* at 83.

[355] Chris Freeman, "The 'National System of Innovation' in historical perspective" (1995) 19:1 Camb J Econ 5–24 at 9.

Lundvall situates his analysis in systems theory and highlights that innovation systems are dynamic social systems in which the central activity is learning and interaction between agents through feedback and evolution. Lundvall emphasizes the importance of the nation-state to structure these systems and clarifies that globalization and internationalization make it possible for national innovations systems to reach other levels and organizations.[356]

It is also important to clarify that innovation and invention are related but different concepts. An invention is the materialization of a new idea into a concrete form. Innovation is the process by which an invention is brought to the market. That is, innovation involves the real-life application and use of an invention. It follows that some inventions never become innovations due to various factors, including market demand, quality, cost, management, and marketing.[357] In the pharmaceutical domain, in fact, most inventions—the creation of a new molecule—never become innovations due to, among other things, lack of efficacy or safety, lack of funding, poor clinical study design, or cost.[358]

Multiple interconnected historical, economic, sociological, cultural, and political factors shape innovation systems and their various subsystems. Analyzing all of them in-depth goes beyond the scope of this work. Instead, this dissertation focuses on evaluating the coevolution and interactions between IP and biomedical innovation systems and how these systems integrate into an innovation ecosystem—a

[356] Bengt-Åke Lundvall, *National systems of innovation toward a theory of innovation and interactive learning* (London; New York, NY: Anthem, 2010) at 1–19. [First edition in 1992]

[357] In this sense, Jan Fagerberg clarifies: "Invention is the first occurrence of an idea for a new product or process, while innovation is the first attempt to carry it out into practice. Sometimes, invention and innovation are closely linked, to the extent that it is hard to distinguish one from another (biotechnology for instance). In many cases, however, there is a considerable time lag between the two. In fact, a lag of several decades or more is not uncommon. (…) To be able to turn an invention into an innovation, a firm normally needs to combine several different types of knowledge, capabilities, skills, and resources. For instance, the firm may require production knowledge, skills and facilities, market knowledge, a well-functioning distribution system, sufficient financial resources, and so on." Jan Fagerberg, "Innovation: A Guide to the Literature" (2006) Oxf Handb Innov, online: <http://www.oxfordhandbooks.com/view/10.1093/oxfordhb/9780199286805.001.0001/oxfordhb-9780199286805-e-1> at 03.

[358] See, specially: David B Fogel, "Factors associated with clinical trials that fail and opportunities for improving the likelihood of success: A review" (2018) 11 Contemp Clin Trials Commun 156–164.

system of systems—globally, in specific countries, or through particular niches (for example, in public-private partnerships (PPPs) and research projects).

Finally, by applying Schumpeter's and Lundvall's rationales, this dissertation sees innovation systems as learning systems that rely on information to define their organization, rules, goals, and performance. Information also determines the ability of innovation systems to respond quickly to problems through feedback mechanisms. Legal regulation is one of several components of innovation systems and includes the interplay between IP laws and policies[359] that apply to knowledge created in CAS, such as biomedical R&D and the translation of R&D outcomes into the market.

As contemporary discussions of innovation systems expand beyond national borders, we can contemplate the idea of global innovation systems. Such a move enables us to think about biomedical innovation in terms of addressing global health needs and mechanisms through which to quickly and efficiently respond to those needs. It opens the opportunity to examine new arrangements to organize R&D through collaborative, complementary, and coordinated efforts. These concepts are important to set the stage for a joint analysis of IP and biomedical innovation systems.

4.2. Biomedical Innovation Systems as Complex Adaptive Systems

There are a number of reasons to justify analyzing biomedical innovation systems through the lens of CAS. These include:

(i) the multitude and diversity of elements constituting these systems (institutions, rules of operation, agents, inventions, and creations, etc.). This diversity translates into specialization and

[359] This dissertation also recognizes the role of public policy and governance mechanisms in IP and biomedical innovation systems as tools to achieve the objectives of these systems. However, it focusses on legal systems' evaluation. For considerations about public policy as CAS, see: Liz Johnson, "Complexity modelling and application to policy research (Chapter 10)" in *Handb Complex Public Policy Ed Robert Geyer Paul Cairney* Handbooks of Research on Public Policy series (150-170: Edward Elgar Publishing, 2015) 150; Bernardo A Furtado, Patricia Sakowski & Mariana Tóvolli, *Modeling Complex Systems for Public Policies* (Brasília: Institute for Applied Economic Research-IPEA, 2015).

segmentation of functions that create space for niches directed at specific goals such as developing new medicines for particular diseases and the advancement of scientific knowledge in specific areas;

(ii) the interactions among these elements occur in nonlinear and decentralized ways, setting the stage for emergent behaviours, and;

(iii) the multiple levels of organization in which these systems operate enable different types of organizational arrangements. These arrangements—and, especially, the niches in which diverse CAS combine—translate into new and open R&D models that are conducive to experimentation and essential to addressing the challenges faced by society.

The above characteristics underlie the discussions in the sections below in which I establish the foundation for the multisystemic examinations in the following chapters.

4.2.1. Overview of Biotechnology and Biomedical Research and Development

According to the Organisation for Economic Co-operation and Development (OECD), biotechnology is: "[t]he application of science and technology to living organisms, as well as parts, products, and models thereof, to alter living or non-living materials for the production of knowledge, goods and services."[360] The National Institute of Health (NIH) defines biomedical research as "[r]esearch that is conducted to increase fundamental knowledge and understanding of the physical, chemical and functional mechanisms

[360] This definition comes with a non-exhaustive, interpretative, and constantly developing 'list definition' of biotechnology techniques that aims to operationalize the single definition for measurement purposes. For more information and the 'list definition', see: Organisation for Economic Cooperation and Development (OECD), "Biotechnology, Single Definition", (2 November 2001), online: *OECD Gloss Stat Terms* <https://stats.oecd.org/glossary/detail.asp?ID=219>; Organisation for Economic Co-operation and Development (OECD), "Biotechnology, list based definition", (7 November 2001), online: *OECD Gloss Stat Terms* <https://stats.oecd.org/glossary/detail.asp?ID=218>.

of human life processes and diseases."[361] Biotechnology is characterized by highly specialized infrastructure and human resources, with new developments coming from various fields, including genomics and personalized medicine.[362] Most biotechnology R&D happens in research institutions, universities, and start-ups that are often heavily publicly funded. In this context, different partnerships and R&D arrangements have been developed to maximize results and minimize risks.[363]

As biotechnology's frontiers and organizational features expand, different groups have debated issues such as ownership of the results of R&D, the possibility of using traditional categories of IPRs (e.g. patents) to protect biotechnology inventions, and the fairness of licensing practices and policies considering the significant public investment.[364] As innovation productivity decreases in traditional pharmaceutical research, biotechnology has been seen as a promising field for new treatments for several diseases.[365] In the same way, it is a source of hope to populations worldwide that are facing global health crises. Global health problems do not always coincide, however, with business and market priorities. Often, the countries most in need—especially developing and least-developed countries—have little

[361] To other definitions of biomedical research (Canadian Institutes of Health Research and OECD), see: Canadian Institutes of Health Research Government of Canada, "Biomedical Research - CIHR", (24 November 2014), online: <http://www.cihr-irsc.gc.ca/e/48804.html>; National Institute of Health (NIH), "U.S. National Library of Medicine - Collection Development Manual: Biomedical Research", online: <https://www.nlm.nih.gov/tsd/acquisitions/cdm/subjects16.html>; Organisation for Economic Co-operation and Development (OECD), "OECD Glossary of Statistical Terms - Biomedical research Definition", online: <https://stats.oecd.org/glossary/detail.asp?ID=217>.

[362] A current example of this is the discussion surrounding the gene-editing tool CRISPR-CAS9. For more information, see: Heidi Ledford, "CRISPR, the disruptor" (2015) 522:7554 Nat News 20; Sheila Jasanoff, J Benjamin Hurlbut & Krishanu Saha, "CRISPR Democracy: Gene Editing and the Need for Inclusive Deliberation" (2015) 32:1 Issues Sci Technol 37.

[363] For general information on it, see: Arti K Rai & Rebecca S Eisenberg, "Bayh-Dole Reform and the Progress of Biomedicine" (2003) 66 Law Contemp Probl 289.

[364] Gary P Pisano, *Science Business: The Promise, the Reality, and the Future of Biotech*, 1 edition ed (Boston, Mass: Harvard Business School Press, 2006); E Richard Gold et al, "Needed: models of biotechnology intellectual property" (2002) 20:8 Trends Biotechnol 327–329; Halla Thorsteinsdóttir et al, "Health biotechnology innovation on a global stage" (2011) 9:2 Nat Rev Microbiol 137–143; Tania Bubela et al, "Patent landscaping for life sciences innovation: toward consistent and transparent practices" (2013) 31:3 Nat Biotechnol 202–206; Jorge Niosi, Tomas G Bas & Julieta Flores Amador, "Biopharmaceuticals in Latin America: challenges and opportunities" (2013) 3:1 Innov Dev 19–36.

[365] For considerations about the biotechnology and pharmaceutical companies business models, promises, and challenges, see: Bountra, Lee & Lezaun, *supra* note 22; Pisano, *supra* note 364; Thorsteinsdóttir et al, *supra* note 364; Niosi, Bas & Amador, "Biopharmaceuticals in Latin America", *supra* note 364; Jorge Niosi & Maureen McKelvey, "Relating business model innovations and innovation cascades: the case of biotechnology" (2018) 28:5 J Evol Econ 1081–1109.

influence over decisions concerning which diseases and areas ought to be priorities for R&D and investments or about how R&D should be regulated.[366]

4.2.2. Basic versus Applied Research: Are Some Classifications and Differentiations Still Appropriate?

The OECD Frascati Manual describes the categories in which R&D efforts fall:

> The term R&D covers three types of activity: basic research, applied research and experimental development. Basic research is experimental or theoretical work undertaken primarily to acquire new knowledge of the underlying foundations of phenomena and observable facts, without any particular application or use in view. Applied research is original investigation undertaken in order to acquire new knowledge. It is, however, directed primarily towards a specific, practical aim or objective. Experimental development is systematic work, drawing on knowledge gained from research and practical experience and producing additional knowledge, which is directed to producing new products or processes or to improving existing products or processes.[367]

These categories are more permeable than may at first appear. This is particularly true of biotechnology (or biomedical R&D), given the scope of research problems addressed, organizational complexity, and the multiple agents who engage in it. That is, the reality of biomedical R&D implicitly contests current definitions and modes of understanding science and the organization of RD&I.[368] For

[366] Developing countries have a huge potential to contribute to the biotechnology field, especially considering the biodiversity in their territories. Even though these countries have urgent problems and basic needs to overcome, they must decide how and how much to invest in cutting-edge research specially to tackle their pressing health problems, such as neglected diseases. They also have to consider how to frame their IP and biomedical innovation systems to respond to their local needs while participating in the global R&D system. Setting expectations higher in terms of developing countries' potential in biomedical R&D and locally investing to achieve it may be ways to advance social and economic outcomes in these countries. See, initially: Røttingen et al, *supra* note 15; Morel et al, *supra* note 23; Årdal et al, *supra* note 20; Yamey & Morel, "Investing in Health Innovation", *supra* note 28; Drugs for Neglected Diseases (DNDi), *supra* note 27.

[367] OECD, *Frascati Manual 2015*, The Measurement of Scientific, Technological and Innovation Activities (OECD Publishing, 2015) at 45. Additionally, it is also common to see a different nomenclature for these terms. Basic research is referred to as upstream research and applied research as downstream research or applied technology.

[368] Sheila Jasanoff deepens this discussion: "The idea of 'science' as a unified field of activity also began to break down as it became clear that scientific practices varied considerably both across disciplines and across institutional settings. In particular, regulatory science produced to support increasingly complex state efforts to protect the public was recognized as a radically different enterprise, entailing different kinds of public supervision and access, from research driven by scientists' collective curiosity. At the same time, observers of science and society began questioning whether the accepted categories of basic and applied research held much meaning in a world where the production and uses of science were tied to each other, as well as to larger social and political interests, through dense networks of relationships among researchers, patients, venture capitalists, the stock market, regulatory agencies, lawyers, politicians, and private companies." Sheila Jasanoff, "The Life Sciences and the Rule of Law" (2002) 319:4 J Mol Biol 891–899 at 896.

instance, there are an increasing number of researchers in universities and research centres doing basic research that results in groundbreaking products or services, such as the CRISPR-Cas9 tool for gene editing.[369] This fact raises questions about the expansion of the role of academic and research communities in the biomedical innovation ecosystem and, consequently, their power to influence the rules by which their interactions with other agents occur.[370]

Donald Stokes presents a schematic, called 'Pasteur's Quadrant,' to contest traditional views about science and the concepts and classifications that form society's beliefs about how science operates.[371] Pasteur's Quadrant situates different 'types' of research and shows how interconnected they are in reality. Rather than describe a linear, static model in which science flows as a sequence from old to new technology,[372] Stokes sees research and innovation as intrinsically linked: more of a circle than a line. He understands science to be—the intersection of non-linear behaviours—in constant evolution.

Fiona Murray and Scott Stern draw on 'Pasteur's Quadrant' to better explain the dynamic interactions between basic and applied research. They highlight the importance of 'dual knowledge'—

[369] For more details about the CRISPR-Cas9 and the patent dispute around it, see: Heidi Ledford, "Pivotal CRISPR patent battle won by Broad Institute" (2018) Nature, online: <http://www.nature.com/articles/d41586-018-06656-y>; Ledford, *supra* note 362; Brooks, *supra* note 41; Kery Grens, "UC Berkeley Team to Be Awarded CRISPR Patent", (11 February 2019), online: *Sci Mag* <https://www.the-scientist.com/news-opinion/uc-berkeley-team-to-be-awarded-crispr-patent-65453>; Jasanoff, Hurlbut & Saha, "CRISPR Democracy", *supra* note 362.

[370] For more details about personalized medicine, its promises and IP practices, see: Marc Dammann & Frank Weber, "Personalized medicine: caught between hope, hype and the real world" (2012) 67 Suppl 1 Clin São Paulo Braz 91–97; Matthew Herder, "Patents & (and) the Progress of Personalized Medicine: Biomarkers Research as Lens" (2009) 18 Ann Health Law 187; PACEOMICS, *supra* note 34.

[371] The types of research that make up the quadrant are: pure basic research (which "includes basic research that is guided solely by the quest for understanding without thought of practical use"); pure applied research ("research that is guided solely by applied goals without seeking a more general understanding of the phenomena of a scientific field"); use-inspired basic research (that "includes basic research that seeks to extend the frontiers of understanding but is also inspired by consideration of use"); and the not empty quadrant ("research that is inspired neither by the goal of understanding nor by the goal of use"). See: Stokes, *supra* note 330 at 73–74.

[372] Specifically about biotechnology Stokes states: "Certainly the modern biological sciences are difficult to bring within the traditional, either-or view of basic and applied research. The revolution in molecular biology has posed questions such as how interferon works, that were enormously important both for the advance of fundamental knowledge on recombinant DNA and for major applications—some of which will be immensibilly profitable. A similar observation can be made about the nonmolecular parts of modern biology. Some of the fundamental problems in population dynamics, such as biology underlying recruitment processes and stock densities in fish, have applications that have inspired the most innovative research in the field." *Ibid* at 70–89.

"ideas that are simultaneously of value as a scientific discovery and as useful inventive construction"[373]—in analyzing how agents develop and implement IP strategies. The implications of this are profound, perhaps foremost in understanding the university's role in research and innovation.[374] Murray and Stern clarify:

> The dual knowledge framework challenges one of the core assumptions of the linear model: Science and technology are not necessarily substitutes but can be jointly produced in a single research project. Moreover, commercial incentives (such as property rights) may not erode the incentives for basic research in fact, they have the potential to shift research towards Pasteur's Quadrant and the production of dual knowledge, with implications for scientists, research organizations, and policymakers.[375]

Richard Nelson and Rebecca Eisenberg argue that, especially in biotechnology, basic scientific research and technology (applied research) are joint enterprises that cannot be separated. They challenge the assumption that basic research is a venture only for the public sector, that research should be broadly available as a source of knowledge, that applied research should be undertaken only by the private sector, and that applied research should be the subject of more restrictive IPRs.[376] They assert that the investments and partnerships necessary to accomplish, for example, the Human Genome Project (HGP) and how public and private institutions organized themselves to map the human genome defy strict classifications. This overlapping nature of basic and applied research and the multitude of funding mechanisms available argue for a new approach to regulating knowledge and new ways to promote RD&I in this field.[377]

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[373] Well-known examples of inventions that lie on the idea of dual knowledge are the research on fermentation of Louis Pasteur and the Harvard oncomouse. The authors further explain: "The discovery and exploitation of the Oncomouse offers a rather different perspective on the relationship between science and technology—and the university-industry divide—than traditional policy models. By and large, most policy analysis assumes that science is an important input into the process of technological innovation, and that instrumentation and measurement technologies (such as the computer) can provide important feedbacks (in the form of tools) into scientific discovery itself. In contrast, the Oncomouse highlights the possibility that a single discovery can simultaneously serve as a scientific discovery and a technological innovation. This insight raises questions about how researchers (and those who fund them) manage the collision between the norms of "open science" and the proprietary incentives of commercialization, and the role played by formal intellectual property rights in the development and diffusion of dual-purpose knowledge." Murray & Stern, "When Ideas Are Not Free", *supra* note 4 at 34–35.

[374] Bellow and in subsequent chapters I will provide some insights about the relationship between university and industry and the role of universities in biomedical R&D and access to knowledge and innovation.

[375] Murray & Stern, "When Ideas Are Not Free", *supra* note 4 at 43–44.

[376] Eisenberg & Nelson, "Public vs. proprietary science", *supra* note 329.

[377] *Ibid*.

4.2.3. Public Research versus Private Technology: Who Produces and Owns the Knowledge

Biotechnology challenges the division of 'public research' from 'private technology,' as if the public sector should be solely responsible for developing basic research and the private sector for technology and innovation. Within the field of biotechnology, IPRs are available in both academic and industrial labs. In summarizing previous empirical research, Murray and Stern conclude that this is often beneficial to innovation as IPRs "facilitate the creation of a market for ideas, encourage further investment in ideas with commercial potential, and mitigate disincentives to disclose and exchange knowledge which might otherwise remain secret."[378] They further stress that university-held IPRs help to ensure that inventions reach the market to actualize social and economic benefits.[379] However, accessing the benefits and harms IPRs protection in access to knowledge and innovation and how to better tailor IP practices, policies, and strategies in the context of developing and least developed countries, as well as by different agents (universities and research centres and private sector) must consider various factors.[380]

Additionally, the coevolution of IP and biomedical innovation systems shows the constant tensions between proprietary and non-proprietary approaches to knowledge regulation and the ideas of openness versus closedness and cooperation versus competition. Universities and research centers produce not only knowledge but also a broad range of intangible assets, some of which constitute inventions. The exercise of IPRs by these institutions depends on their policy and practices, as well as their institutional missions and values. The propagation of a proprietary view of IPRs, a trend to include patent grants in

[378] Murray & Stern, "When Ideas Are Not Free", *supra* note 4 at 36.
[379] *Ibid* at 35–36.
[380] Chapter Five further develops these discussions and provides concrete examples about the role of publicly funded universities and research centres in access to knowledge and innovation and problems arising when legal transplantation takes place in developing and least developed countries and IP practices and policies are driven by commercialization principles. See, initially: Dutfield & Suthersanen, "Harmonisation or differentiation in intellectual property protection?", *supra* note 260; Jean-Frédéric Morin & Edward Richard Gold, "An Integrated Model of Legal Transplantation: The Diffusion of Intellectual Property Law in Developing Countries" (2014) 58:4 Int Stud Q 781–792; May & Sell, *supra* note 247; David Mowery et al, *Ivory Tower and Industrial Innovation: University-Industry Technology Transfer Before and After the Bayh-Dole Act*, reprint edition ed (Stanford Business Books, 2015); Anthony D So et al, "Is Bayh-Dole Good for Developing Countries? Lessons from the US Experience" (2008) 6:10 PLOS Biol e262.

university and grant peer review processes, and the adoption of missions that include the translation of knowledge to the market all influence access and innovation outcomes.

Eisenberg and Rai claim that "[t]he tradition of open science has eroded considerably over the past quarter-century" in publicly funded universities.[381] They explain that universities have adopted more aggressive IP practices and policies, narrowing the distance between them and the industrial sector. Not only do universities patent more, but they import knowledge through patent licences from the private sector in order to access research tools and materials. This has created a shift toward greater protection, more licenses and more negotiation while ignoring other mechanisms to share and build knowledge. These changes in the economic structure and organization of research show that patents are not the only or most critical intangible asset. There is a web of IPRs surrounding biomedical R&D activities that overlap and need to be understood and well managed to enable the success of these activities.[382] Chapter Six evaluates the role of agents in complex adaptive IP and biomedical innovation systems focussing on the expert communities.

4.2.4. Research and Business Models in the Biomedical Field

Information, data, and knowledge play a critical role in biomedical R&D and interact in cumulative and interactive ways that take place over time. How particular biomedical R&D systems organize themselves in respect of information depends on which actors are participating, the goals and expectations of those agents, and the institutions involved (local, regional, national, and international). There is a long road of both successes and failures, from basic exploratory research to the insertion and translation of technologies and processes into the market (innovation).

[381] Rai & Eisenberg, *supra* note 363 at 294–295.
[382] *Ibid*.

Biomedical R&D is risky, costly, time-demanding, and uncertain; its success and failure depend on the interactions of multiple agents and factors.[383] Each actor pursues its own interests within the system, anticipating the actions of others to the limit of their experience and knowledge. Like a sports gain between two teams, each with a game-plan based on expectations of the other, the outcome is not only unpredictable, but actors change strategies midstream as a result of changes by others. In this process, actors are constantly recreating the biomedical R&D system. The problem is, however, that there is no guarantee that the sum of agent activity and strategy will result in the efficient production of health interventions.

Pharmaceutical firms increasingly rely on biotechnology firms to develop new compounds while the pharmaceutical firms take responsibility for conducting clinical trials and scaling up production and distribution.[384] For example, the relationship between Pfizer and BioNTech regarding the development, manufacture and sale of their mRNA vaccine against SARS-CoV-2 follows this pattern.[385]

Under this model, a pharma company seeks technologies from diverse partners (mainly universities, research centres, and start-ups) and engages in product development partnerships (PDPs), licensing schemes, and technology acquisition to reach world markets. However, the pharmaceutical

[383] For initial considerations about these details see: Hoen, *supra* note 25 c 6; DiMasi, Grabowski & Hansen, "Innovation in the pharmaceutical industry", *supra* note 25; Love, *supra* note 25; John R Graham, "Crisis In Pharma R&D: It Costs $2.6 Billion To Develop A New Medicine; 2.5 Times More Than In 2003", online: *Forbes* <https://www.forbes.com/sites/theapothecary/2014/11/26/crisis-in-pharma-rd-it-costs-2-6-billion-to-develop-a-new-medicine-2-5-times-more-than-in-2003/>; Chapman et al, *supra* note 289.

[384] Pisano, *supra* note 364; Gary P Pisano & David J Teece, "How to Capture Value from Innovation: Shaping Intellectual Property and Industry Architecture" (2007) 50:1 Calif Manage Rev 278–296; OECD, "The future of science, technology and innovation policies" in *OECD Sci Technol Ind Outlook* (Organisation for Economic Co-operation and Development, 2014) 23; Janet Hope, *Biobazaar: The Open Source Revolution and Biotechnology* (Harvard University Press, 2009) Google-Books-ID: TXpR0SHRLu8C; Thorsteinsdóttir et al, *supra* note 364.

[385] See: Mario Gaviria & Burcu Kilic, "A network analysis of COVID-19 mRNA vaccine patents" (2021) 39:5 Nat Biotechnol 546–548; Health Canada, "Pfizer-BioNTech COVID-19 Vaccine (tozinameran)", online: *COVID-19 Vaccines Treat Portal* <https://covid-vaccine.canada.ca/pfizer-biontech-covid-19-vaccine/product-details>; Elie Dolgin, "The tangled history of mRNA vaccines" (2021) 597:7876 Nature 318–324 Bandiera_abtest: aCg_type: News Featurenumber: 7876publisher: Nature Publishing GroupSubject_term: SARS-CoV-2, History, Intellectual-property rights, Vaccines; Norbert Pardi et al, "mRNA vaccines — a new era in vaccinology" (2018) 17:4 Nat Rev Drug Discov 261–279 Bandiera_abtest: aCg_type: Nature Research Journalsnumber: 4Primary_atype: Reviewspublisher: Nature Publishing GroupSubject_term: Cancer;Drug discovery;Infectious diseases;RNA vaccinesSubject_term_id: cancer;drug-discovery;infectious-diseases;rna-vaccines.

industry's business strategies have not been enough to deliver innovation, sustain its productivity levels, restrain cost increases, and develop new technologies.[386]

While an ideal starting point for discussions about rendering the biomedical RD&I system more efficient would be a clear idea of the costs involved in developing a new drug, this information is not available due to secrecy.[387] We do know that taxpayers and public funds bear a significant portion of drug development, yet the financial rewards fall to the private sector.[388] The cumulative revenue of the 35 large pharmaceutical companies was, by way of illustration, US$11.5 trillion, and their cumulative net income was US$1.9 trillion from 2000 to 2018.[389]

According to the Association of the British Pharmaceutical Industry (ABPI), "[t]he global pharmaceutical industry invested over $1.36 trillion in R&D in the decade from 2007 to 2016 and forecasts predict an annual investment of $181 billion by 2022. Investment is growing at an average of 4% per annum, with the most recent annual growth increasing to 6%."[390] While increasing significantly, the industries and other stakeholders argue that this amount of funding remains insufficient to address global

[386] World Health Organization, *supra* note 23 at 27–28; Bountra, Lee & Lezaun, *supra* note 22; *Advancing Health Through Innovation: New Drug Therapy Approvals 2019*, by FDA's Center for Drug Evaluation and Research's (CDER), Zotero (Silver Spring, MD: USA Food and Administration (FDA), 2020) at 11.
[387] Hoen, *supra* note 25; DiMasi, Grabowski & Hansen, "Innovation in the pharmaceutical industry", *supra* note 25; Love, *supra* note 25.
[388] Ekaterina Galkina Cleary, Matthew J Jackson & Fred D Ledley, "Government as the First Investor in Biopharmaceutical Innovation: Evidence From New Drug Approvals 2010–2019" (2020) 133 Inst New Econ Think, online: <https://www.ineteconomics.org/research/research-papers/government-as-the-first-investor-in-biopharmaceutical-innovation-evidence-from-new-drug-approvals-2010-2019>; Liji Thomas, "Big Pharma more profitable than most other large public firms" *News Med Life Sci* (3 March 2020), online: <https://www.news-medical.net/news/20200303/Big-Pharma-more-profitable-than-most-other-large-public-firms.aspx>; Fred D Ledley et al, "Profitability of Large Pharmaceutical Companies Compared With Other Large Public Companies" (2020) 323:9 JAMA 834–843.
[389] Ledley et al, *supra* note 388; Becky Brickwood, "Pharma companies are more profitable than most S&P 500 companies", (3 March 2020), online: *Health Eur* <https://www.healtheuropa.eu/pharma-companies-are-more-profitable-than-most-sp-500-companies/98229/>.
[390] Association of the British Pharmaceutical Industry (ABPI), "Worldwide pharmaceutical company R&D expenditure | ABPI", online: <https://www.abpi.org.uk/facts-and-figures/science-and-innovation/worldwide-pharmaceutical-company-rd-expenditure/>.

health crises and that it is too risky to invest in some types of research, particularly cutting-edge fields such as personalized medicine and genomics.[391]

The lack of transparency of the pharmaceutical industry's business model is evident in its failure to disclose its investments in R&D. According to a study presented by the Tufts Center for the Study of Drug Development, the cost to develop a new medicine through to market approval—which may take between 7 to 10 years—is US$2.6 billion.[392] However, this number (and study) has been highly criticized for its methodology and the fact that the data used in conducting the study are not publicly available and that the study fails to account for public investments.[393] In particular, the study does not address the costs in respect of the following: (i) the labs of public universities and research centers; (ii) the skills and knowledge of academic and research communities acquired during the years under public funding and scholarships; (iii) the hospitals that run clinical trials, and; (iv) the patients' data that underlies studies and clinical trials that is essential to registration and approval of health technologies.

Industry claims of the high costs inherent in drug discovery are further undermined by publicly oriented efforts, such as DND*i*. Based on its fifteen years of experience in drug development through PDPs, DND*i* estimates "that it can develop and register new treatments based on existing drugs at a cost of €4-32 million, and new chemical entities for €60-190 million." These numbers include the attrition costs (the costs of failure in every stage of drug discovery and development).[394]

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[391] In this sense, see: DiMasi, Grabowski & Hansen, "Innovation in the pharmaceutical industry", *supra* note 25; Love, *supra* note 25; Pisano, *supra* note 364; Marcia Angell, *The Truth About the Drug Companies: How They Deceive Us and What to Do About It*, 1 edition ed (New York: Random House Trade Paperbacks, 2005); Amy Maxmen, "Busting the billion-dollar myth: how to slash the cost of drug development" (2016) 536:7617 Nat News 388; Drugs for Neglected Diseases (DNDi), *supra* note 27; Marcela Fogaça Vieira, *Research Synthesis: Cost of Pharmaceutical R&D* (Global Health Centre, Graduate Institute, 2020).
[392] DiMasi, Grabowski & Hansen, "Innovation in the pharmaceutical industry", *supra* note 25.
[393] Love, *supra* note 25.
[394] One could also argue that DND*i*'s work concentrates on compounds already identified, what contributes to put the costs down. However, even if so, the business models of initiatives such as DND*i* demonstrate that transparency and cooperation are critical to improving the results of the biomedical innovation system. Drugs for Neglected Diseases (DNDi), *supra* note 27 at 18.

The private sector focuses almost all of its R&D efforts on 'profitable' diseases that are generally prevalent in developed countries. So-called 'neglected diseases' that mainly affect poor populations are ignored. Governments and philanthropists bear the costs of addressing these diseases.[395]

As CAS, biomedical innovation systems are comprised of multiple agents, often with overlapping and multiple roles. Pharmaceutical companies, biotechnology firms, start-ups, governments, public and private universities and research centres, researchers, academics, entrepreneurs, and patients work separately and collaboratively on R&D projects. In observing this complex network of agents and their interactions, the question of whether the biomedical RD&I model is increasingly more collaborative and open rather than competitive, closed, and isolated arises.[396]

More recently, actors in the biomedical R&D system have begun to experiment by developing new models of how and with whom they generate and share knowledge. These new models include open science, open-source, open innovation, and open drug development.[397] What these open models have in common is that they use IP to enhance sharing and to create a robust public domain.[398] Chapter Seven discusses them in detail.

Finally, in conducting its business, the pharmaceutical industry has been using the IP system, especially the patent system, strategically, even predatorily. Its business model has become well-known for its lack of transparency and anti-competitive practices that directly affect the prices and access to health technologies and restrain access to data, information, and knowledge essential to advancing innovation.[399]

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[395] Policy Cures Research, *supra* note 20; Drugs for Neglected Diseases (DNDi), *supra* note 27.
[396] For initial thoughts about publicly funded R&D in universities (Mowery et al and Piper) and about biotechnology business model (Pisano), see: Mowery et al, *supra* note 380; Piper, *supra* note 37; Pisano, *supra* note 364.
[397] I have briefly defined these models in the Introduction and Chapter Seven discusses them and the idea of openness in depth.
[398] For initial thoughts about these models, see: David, *supra* note 295; Sarah E Ali-Khan et al, "Defining Success in Open Science" (2018) 2 MNI Open Res 2; Henry Chesbrough, "Open innovation: a new paradigm for understanding industrial innovation" (2006) Open Innov Res New Paradigm 1–12; Hope, *supra* note 384.
[399] FM Scherer, "Patents, Monopoly Power, and the Pricing of Pharmaceuticals in Low-Income Nations" in Daniele Archibugi & Andrea Filippetti, eds, *Handb Glob Sci Technol Innov* (John Wiley & Sons, Ltd, 2015) 443; Angell, *supra* note 391; Ledley et al, *supra* note 388; Médecins Sans Frontières (MSF), *supra* note 270.

The pharmaceutical industry also engages in substantial lobbying toward regulating its activities and areas related to its business. Its powerful influence has contributed to shaping the international IP system and national legislations, which consequently impacted access and innovation.[400] The section below further discusses these issues.

4.3. On the Protection of Biomedical Research and Development by Intellectual Property Rights

IP strategies change depending on the phase of the biomedical R&D pipeline and the particular products, processes, and services involved.[401] Effective IP strategies must be tailored to meet the needs and specificities of these R&D stages and the expectations and goals of agents involved in them. These strategies must consider agents individually and populations of agents representing diverse groups and institutions and, consequently, institutional missions, visions, and values that affect agent interactions and expectations.

4.3.1. Overview: Illustrating Complexity

The three figures below illustrate the complexity of biomedical R&D.[402] Figure 4 provides an idealized, simplified, and linear schematic of the R&D pipeline for drug development in the biomedical sector.

[400] Bountra, Lee & Lezaun, *supra* note 22 at 6,9; Outterson, *supra* note 260; Stu Woolman, Elliot Fishman & Michael Fisher, "Evidence of Patent Thickets in Complex Biopharmaceutical Technologies" (2013) 53 IDEA Intellect Prop Law Rev 1; Moon, Bermudez & Hoen, "Innovation and Access to Medicines for Neglected Populations", *supra* note 23; Angell, *supra* note 391.
[401] For discussions and clarification on the need of an integrative approach between IP strategy and management, see: William W Fisher III & Felix Oberholzer-Gee, "Strategic Management of Intellectual Property: An Integrated Approach" (2013), online: <https://www.hbs.edu/faculty/Pages/item.aspx?num=45271> at 158–159.
[402] John Wagner et al, "A dynamic map for learning, communicating, navigating and improving therapeutic development" (2018) 17:2 Nat Rev Drug Discov 150–150; John A Wagner et al, "Application of a Dynamic Map for Learning, Communicating, Navigating, and Improving Therapeutic Development" (2018) 11:2 Clin Transl Sci 166–174; National Center for Advancing Translational Sciences (NIH), "Drug Discovery, Development and Deployment Maps", (9 December 2017), online: *Natl Cent Adv Transl Sci* <https://ncats.nih.gov/translation/maps>.

Figure 4: *Therapeutic development chevron diagram. Traditional chevron diagram representation of therapeutic development. Colors in this chevron correspond to the associated "neighborhoods" on the Drug Discovery, Development, and Deployment Map. FDA, US Food and Drug Administration*.[403]

The simplifying assumption of linearity may be useful in developing a diagram, but it does not represent reality where linearity is the exception, not the rule. R&D is messy, with feedback loops, wrong turns, and reassessments. Distinct phases may result in 'small' inventions that are part of or necessary to produce another invention in the pipeline. Drafting an IP strategy in this context requires that one considers each process and phase individually and within the pipeline as a whole.

Figures 5 and 6 provide a more realistic picture of drug development and its complexity in respect of, respectively, small molecules and biologics.[404] These Drug, Discovery, Development and Deployment Maps (4DM) highlight the non-linearity of the biomedical R&D pathway involving multiple agents, interactions, and feedback loops.

[403] Figure and more information available at: Wagner et al, *supra* note 402 at 167.
[404] "Small molecule drugs are chemically manufactured compounds of relatively low molecular size that make up the vast majority of drugs on the market today. Biologic drugs are large complex molecules manufactured by a living system, such as a microorganism, or plant or animal cells, and include antibodies and vaccines." National Center for Advancing Translational Sciences (NIH), *supra* note 402.

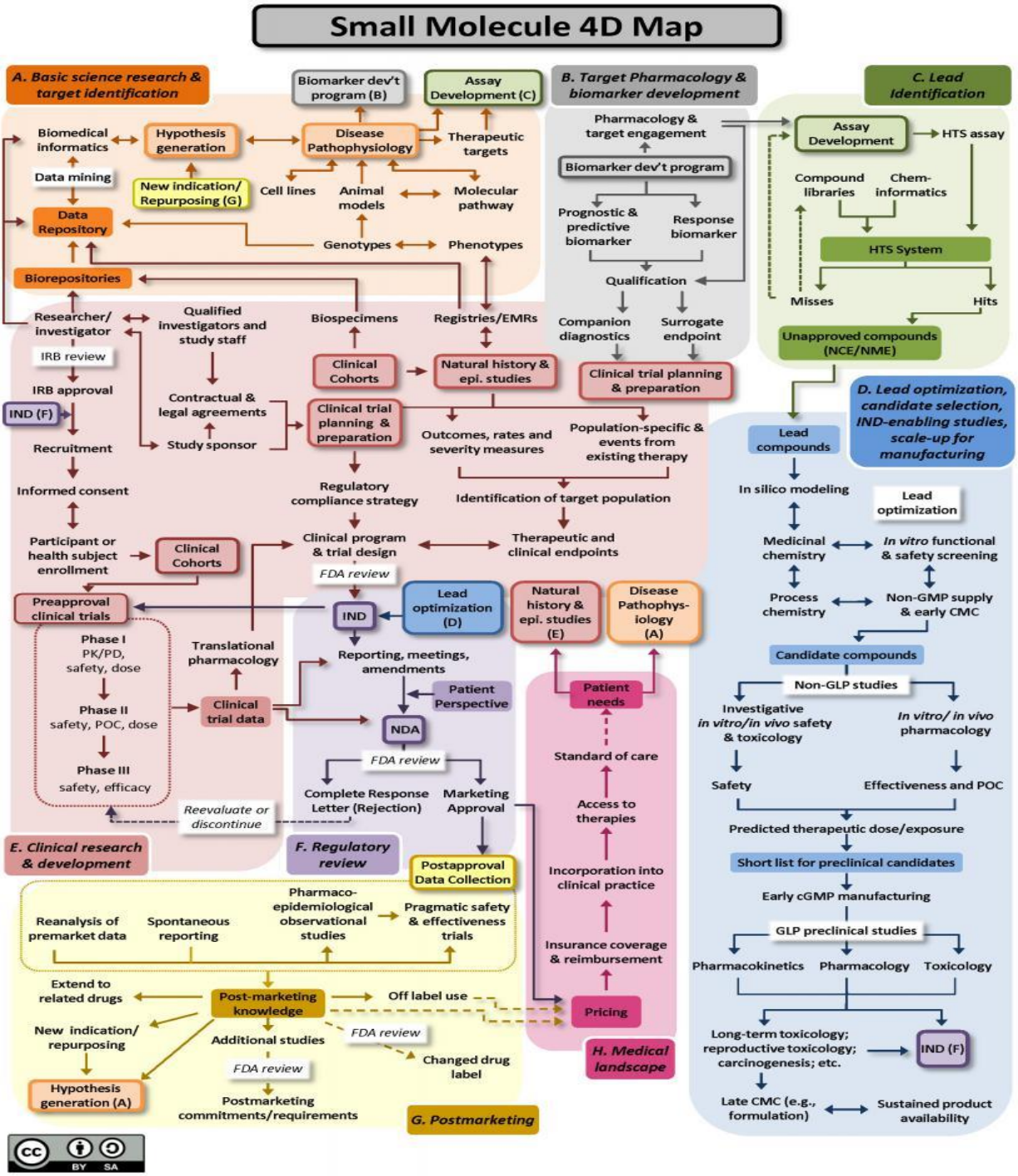

Figure 5: *4DM Small Molecules Map*. Wagner JA, Dahlem AM, Hudson LD, Terry SF, Altman RB, Gilliland CT, DeFeo C, and Austin CP. Drug Discovery, Development and Deployment Map (4DM): Small Molecules. Available at <https://ncats.nih.gov/translation/maps>. Last updated in November 2017.[405]

[405] Figure and more information available at: National Center for Advancing Translational Sciences (NIH), "Figure- 4DM Small Molecules Map", online: *Drug Discov Dev Deploy Maps* <https://ncats.nih.gov/files/Figure%20A%20-%204DM%20Small%20Molecules%20Map.jpg>; National Center for Advancing Translational Sciences (NIH), *supra* note 402; John A Wagner et al, *Drug Discovery, Development and Deployment Map (4DM): Small Molecules* (2017).

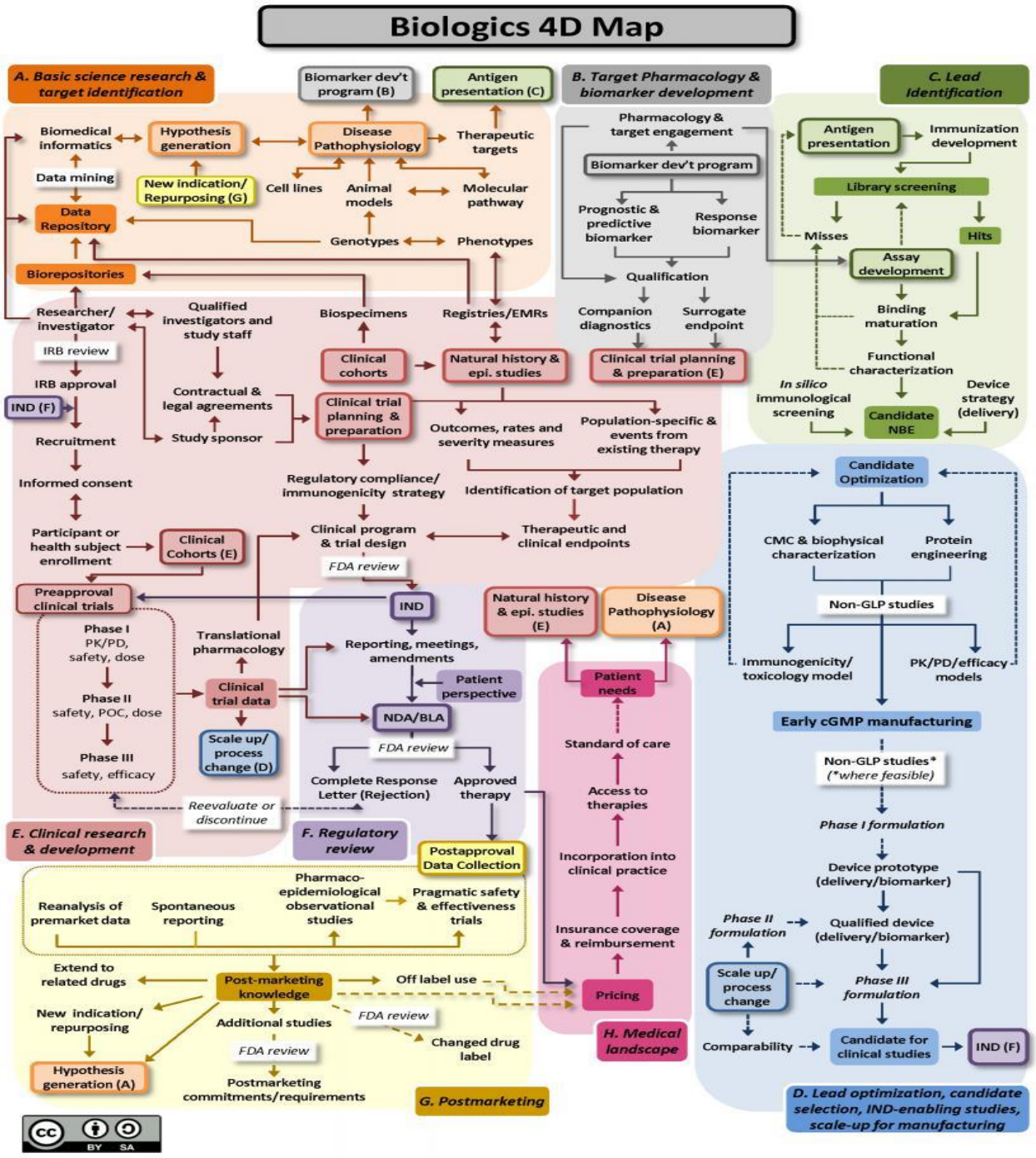

Figure 6: *Biologics 4 D Map.* Wagner JA, Dahlem AM, Hudson LD, Terry SF, Altman RB, Gilliland CT, DeFeo C, and Austin CP. Drug Discovery, Development and Deployment Map (4DM): Biologics. Available at <https://ncats.nih.gov/translation/maps>. Last updated in November 2017.[406]

[406] Figure and more information available, at: National Center for Advancing Translational Sciences (NIH), "Figure- 4DM Biologics Map", online: *Drug Discov Dev Deploy Maps* <https://ncats.nih.gov/files/Figure%20B%20-%204DM%20Biologics%20Map.jpg>; National Center for Advancing Translational Sciences (NIH), *supra* note 402; John A Wagner et al, *Drug Discovery, Development and Deployment Map (4DM): Biologics* (2017).

There is a diversity of legislation and policies that inform the interaction and coevolution of IP and biomedical innovation systems in different countries. Predicting the exact IP strategy that an agent will adopt in each of his/her projects is difficult. Many collaborative arrangements among agents while engaging in R&D activities amplify the number of possible IP strategies.

In a well-balanced IP system, researchers and firms can follow the signals—the areas of high activity and gaps—in R&D. IPRs also send signals to legal experts about the trends followed by other agents in protecting IPRs and their adopted business and R&D models. Disclosure and flow of information are critical to advance science and increment legal and policy strategies.[407]

The value of IP assets is uncertain and ever-changing due to uncertainties in the underlying science and the activities of other agents. For example, a promising drug patent may suddenly lose value should another firm develop a better drug aimed at the same condition. Examining biomedical R&D through the lens of CAS provides a mechanism to account for this uncertainty. In particular, doing so leads to discussions of whether existing regulations and strategies work.[408]

The degree of sophistication and understanding of an agent about IPRs and strategies determine his/her ability to engage with other agents effectively and the type of interests the agent pursues. Given this, the IP strategy of public universities may (and should) differ from those of the pharmaceutical

[407] IP systems can help to manage uncertainty in biomedical R&D. This is because IPRs work as signals to the academic and research communities (and other agents such as the private sector) about R&D pathways that are likely successful. Monitoring these rights also assists in the identification of gaps in the scientific knowledge that need to be answered to enhance innovation. Possible technological trajectories that lead to technological learning and the assessment of knowledge and information contained in IPRs have signalling functions. Maria Alessandra Rossi & Fabio Pammolli, "Intellectual property, technological regimes and market dynamics" (2005) 2005/2:2 Econ E Polit Ind, online: <https://econpapers.repec.org/article/fanpolipo/v_3ahtml10.3280_2fpoli2005-002005.htm>.

[408] On the discussions about the importance of feedback for CAS operation and evolution, and especially about legal systems, Hadfield highlights the isolation of legal professionals in their current practices that limits them to test solutions and receive feedback about the implementation of legal regulation and strategies. Therefore, these agents have limited resources to discover how well their proposed solutions and regulations are working. She points out: "Lawyers can be expected to come up with ideas for how to streamline procedures or write somewhat easier-to-read contracts. But they can't be expected to come up, all on their own, with entirely novel ways to coordinate economic arrangements or resolve conflicts. (…) Legal practitioners are significantly walled off from feedback from those who use and implement the legal infrastructure they produce." (p. 230). Hadfield, *supra* note 2 at 224–248.

industry. For example, it is common for pharmaceutical corporations to buy or license (preferentially with exclusivity) IP portfolios of universities and biotechnology start-ups. Generally, they do so to amplify their innovative capacity while anticipating market trends and business opportunities or to block competitors.[409] On the other hand, universities seek to create and transmit knowledge[410] as a central element of their mission[411] while leveraging their IP assets to finance future R&D.[412]

There is no 'one size fits all' IP strategy. Instead, agents need to analyze IP strategies and management on a case-by-case basis. Below I briefly explain the regulation of biomedical R&D by the 'traditional' categories of IPRs mentioned in Chapter Three and some regulatory specificities of this field.[413]

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[409] The monitoring and detailed description of known IP strategies and simulation of new strategies that demonstrate how and in which phase of R&D pipeline agents could apply certain norms differentially can also assist in characterizing the nuances of IP protection in different biomedical R&D scenarios. This would incentivize agents to experiment in IP strategies and biomedical R&D models and move towards a new era of IP and openness. For more details about IP strategy and the business models of pharmaceutical industries, see generally: Angell, *supra* note 391; Woolman, Fishman & Fisher, *supra* note 400; Fisher III & Oberholzer-Gee, "Strategic Management of Intellectual Property", *supra* note 401.

[410] There are different types of knowledge. Tacit (or implicit) knowledge is the "knowledge that you do not get from being taught, or from books, etc. but get from personal experience, for example when working in a particular organization." Explicit knowledge is the "knowledge that can be expressed in words, numbers, and symbols and stored in books, computers, etc." Even though, the two types of knowledge are part and essential to biomedical R&D, it is in the tacit knowledge that most of the potential to innovate relies on. Tacit knowledge is more difficult to be created, transferred, and measured as it requires a higher degree of interaction and cooperation among agents, and relates to know-how. As different institutions, and especially universities and research institutes, set in place their IP and knowledge management strategies, they need to consider the value of their tacit knowledge to those looking for partnerships. This value enables them to attract more investments to their R&D activities and gives them power to better negotiate and decide how they will protect their R&D. For these definitions and further discussions, see: Cambridge English Dictionary, "Tacit Knowledge definition", online: <https://dictionary.cambridge.org/us/dictionary/english/tacit-knowledge>; Cambridge English Dictionary, "Explicit Knowledge definition", online: <https://dictionary.cambridge.org/us/dictionary/english/explicit-knowledge>; E Richard Gold, "Should Universities Get Out of the Patent Business?", (3 April 2019), online: *Cent Int Gov Innov* <https://www.cigionline.org/articles/should-universities-get-out-patent-business>; David, *supra* note 295.

[411] Considering this research mainly focuses on the behaviours and interactions of agents situated at the bottom layers of IP and biomedical innovation systems (academic, research, and legal communities), the question of whether universities and research centres should be concerned with post-commercialization issues leads to a positive answer in my point of view. These institutions have their missions and activities connected to the public interest, the advancement of science and count with a substantial amount of publicly funded R&D. Therefore, they must consider responsible IP practices and policies. Additionally, the roles of agents change alongside the redefinition of concepts like basic and applied research, as previously explained in this chapter.

[412] Myra Tawfik, Francine Schlosser & Wissam Aoun, "Strategies and Practices for Overcoming Obstacles to the Effective Commercialization of Student Innovation on University Campuses" (2012) Law Publ, online: <https://scholar.uwindsor.ca/lawpub/26>; Piper, *supra* note 37.

[413] For initial considerations, see: World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22 at 53–75; UNCTAD-ICTSD, *supra* note 242.

4.3.2. The Patent Debate

Patents have been the star in discussions about the effects of IP protection in biomedical R&D, and, consequently, access to knowledge and innovation.[414] A patent protects an invention (product or process) that fulfills the criteria of novelty, inventiveness (non-obviousness), and usefulness (or industrial application) in any field of technology for at least 20 years.[415] A country may exclude from patentability inventions in order "to protect *ordre public* or morality including to protect human, animal or plant life or health or to avoid serious prejudice to the environment."[416]

Patents are territorially bounded: each country has sovereignty over the criteria, granting and enforcement of patents. That is, despite international treaties, each country has the freedom to interpret and adapt international standards to its national needs by setting specific guidelines for patent examination in their national Patent Offices. For example, some countries do not grant patents for the second medical use of medicines—the use of a previously discovered drug to treat a different condition.[417]

Like any IPR, patents are not absolute rights; their grant and extension are subject to limitations and exceptions, such as compulsory licenses, parallel importation, and research exemptions.[418] A patent confers its holder with the exclusive right to exploit the invention, that is, with the ability to prohibit third

[414] Additionally, as reported by WIPO, WTO, and WHO, the last decades have shown an increase in the number of patents related to health technologies, especially in emerging economies. It is important to recall that the majority of these patents are not owned by these countries' nationals but developed countries and might have substantial impact on their biomedical R&D activities and social and economic development. World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22 at 55–56.

[415] See article 27 for patentable subject matter and criteria and art. 33 for the term of protection of the TRIPS Agreement. *TRIPS Agreement*, *supra* note 249.

[416] See, art.27 of the TRIPS Agreement for full information about patentable subject matter and the exclusions of it. *Ibid*.

[417] For more information about these guidelines and, specifically in Brazil, see: World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22 at 57–61; Correa, *supra* note 244; *Guidelines for the examination of pharmaceutical patents: Developing a public health perspective*, by Carlos M Correa, DOI.org (Crossref) (Geneva, Switzerland: International Centre for Trade and Sustainable Development, 2007); Instituto Nacional de Propriedade Industrial (INPI), *Brazil: Guidelines for the Examination of Patent Applications in the areas of Biotechnology and Pharmaceutical Filed after December 31, 1994*; Instituto Nacional de Propriedade Industrial (INPI), *Brazil: Guidelines for Examination of Patents*.

[418] For the limitations and exceptions to patent rights, see art. 30 and 31 of the TRIPS Agreement. See also: World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22 at 60–61; *TRIPS Agreement*, *supra* note 249.

parties from making, using, offering for sale, selling, or importing the invention. The patent also confers the right to assign, transfer by succession, and conclude licensing contracts.[419] As the counterpart to the exclusive granted, the patent holder must disclose the knowledge embedded in the invention through the patent document.[420] As I mentioned in Chapter Three, justifications for granting this exclusive right relate to rewarding inventors' inventive efforts and allowing the recovery of investments. However, in areas where there is no substitute in the market for the invention, such exclusivity can result in a monopoly. The effects of patents on the prices of health technologies have been extensively discussed, and how the entry of their generic versions in the market affects their price and access.[421] This also shows distortions in the IP system and often anti-competitive pharmaceutical industry practices, especially in developing countries.[422]

Many considerations go into the decision of whether, what, and how to patent an invention well beyond one's legal entitlement to do so. Agents should examine, for example, whether applying for a

[419] See, article 28 of the TRIPS Agreement. *TRIPS Agreement*, *supra* note 249.

[420] For the conditions on patent applicants and disclosure requirements, see Art. 29 of the TRIPS Agreement. In some jurisdictions, insufficient disclosure or absent information of some details related to invention are grounds for patent invalidation. In talking about the importance of quickly releasing information in the public domain for the advancement of science, depending on the filing system chosen to request a patent the information related to it might be in secrecy for a period. For instance, by the rules of the Patent Cooperation Treaty (PCT) there is a period of 18 months in between the patent application and its publication in which the patent information remains in secrecy, and it is only accessible by the Patent Offices—the International Phase. Additionally, the patent application date is what determines the 'priority date', the beginning of the patent term, and the date to assess the 'prior art' that determines the novelty and inventiveness of a patent. In this sense and for additional information, see: *Ibid*; World Intellectual Property Organization, *supra* note 243; World Intellectual Property Organization, "PCT FAQs-Protecting your Inventions Abroad: Frequently Asked Questions About the Patent Cooperation Treaty (PCT)", online: *World Intellect Prop Organ* <https://www.wipo.int/pct/en/faqs/faqs.html>.

[421] Specifically on access to HIV/Aids medicines, for the past 20 years, MSF has been issuing an annual report that presents patent barriers, and the availability and prices of antiretroviral medicines (ARV) practiced by pharmaceutical companies and generic industries worldwide. These reports show the progress on access to medicines, the challenges to achieve it, and the market segmentation that functions under differential prices' policies practiced by the pharmaceutical industries affects developing and least developed countries differently. To the complete list of MSF Reports on it, see: Médecins Sans Frontières (MSF), "Report Series: Untangling the Web of Antiretroviral Price Reductions", online: *Médecins Front Access Campaign* <https://msfaccess.org/utw>.

[422] See, generally: Hoen, *supra* note 25; Outterson, *supra* note 260; Joseph E Stiglitz & Arjun Jayadev, "Medicine for Tomorrow: Some Alternative Proposals to Promote Socially Beneficial Research and Development in Pharmaceuticals" (2010) 7:3 J Generic Med 217–226; World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22 at 53–77; Calixto Salomão Filho, "Uma perspectiva jurídica neo-estruturalista para a análise do poder econômico / A neo-structural legal perspective to economic power analysis" (2016) 7:4 Rev Direito E Práxis 447–482.

patent best promotes their objectives, considering the related costs and benefits and the goals they want to achieve from the protection. Moreover, the grant of a patent does not mean that the invention will reach the market. For example, in the biomedical field, the registration and approval for commercialization of health technologies by Health Authorities, such as the Food and Drug Administration (FDA) in the US and the National Health Surveillance Agency (Anvisa) in Brazil, is mandatory.[423]

Some advocates of open science or open drug development hold that the balance of costs and benefits argues against patenting.[424] Nevertheless, the decision to set knowledge free still requires a strategy about IPRs to avoid other agents appropriating the products of knowledge by patenting it themselves. Especially in developing and least-developed countries, there is another point to consider: the pressures and demands for acquiring intangible assets and building IP portfolios are more attractive for investors and undermine public institutions' ability to maintain a public domain.

Health technologies are also generally protected by several patents over a series of 'small inventions' that result in the final product and the processes to produce it. For an agent, trying to identify the patented health technologies is not easy given the level of technicality involved in patent searches and the fact that patents are territorial. Thus, in talking about improving the relationship between law and science, one needs to consider building an infrastructure that allows different agents to access this information and the costs related to building, accessing, and maintaining it. Some databases provide this

[423] Regulatory requirements also generate intangible assets that can be protected in some cases and legislations. For instance, the data generated by clinical trials (test data) that basis the registration and market approval of a health product in a Heath Authority is subject to data protection—data exclusivity regimes. To approve a generic product, the generic pharmaceutical company relies on this original data (pharmacological, toxicological, and clinical test data) that was filled by the pharmaceutical company that owns the patent or the license to commercialize it. However, there are cases in which the data protection remains after the patent term expiration and can delay the entry of generic medicines in the market. Related to this issue, it is also one of the exceptions to IPRs of the TRIPS Agreement (article 30) that some countries have adopted as a regulatory review exemption (the 'Bolar' exception). This exception allows generic companies to start the regulatory approval to their product before the patent term expiration and use the test data. It is a guarantee that no artificial extension of patent protection will happen by data protection clauses. For more information, see: World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22 at 63–67, 174; *TRIPS Agreement*, *supra* note 249.

[424] Gold, *supra* note 410; E Richard Gold et al, "An open toolkit for tracking open science partnership implementation and impact" (2019) 3 Gates Open Res 1442; Bountra, Lee & Lezaun, *supra* note 22; Zeeshaan Arshad et al, "Open Access Could Transform Drug Discovery: A Case Study of JQ1" (2016) 11:3 Expert Opin Drug Discov 321–332.

information and are critical to inform decisions regarding future biomedical R&D activities and public policies related to issues such as industrial sector planning on generic medicines or public procurement of these health technologies, especially in public health systems.[425]

The proliferation of patents (and, too often, their lack of quality) diminishes access to knowledge and follow-on innovation. The increasing number of patents creates patent thickets around some inventions or technological fields and leads to litigation (or the threat of doing so by its owners).[426] However, considering the difficulties of a highly specialized field and the burden and costs of IP litigation, deciding these issues in the courts should be the last alternative—in some cases, it is not an alternative considering the lack of economic power of agents involved to engage in this type of litigation.[427] Also, in a sensitive area such as healthcare, letting the public interest and public health be at the mercy of predatory market practices is a risk that developing and least developed countries should not take.[428]

Specific domains would also require tailored strategies and discussions about patent law being technology-specific.[429] For instance, there are highly technical debates about applying the same (traditional) patentability criteria to biotechnological inventions. This is because the assessment of novelty

[425] For instance, the USA FDA Orange Book gives information relating patents and active ingredients, formulations, compositions, and methods of use of medicines. Health Canada provides a list of patents that claim protection towards health technologies. MedsPaL, the database of MPP, provides information about patents, patent families, and licenses of selected medicines in low and middle-income countries. WIPO also has a recent database, PAT-INFORMED, that gives information about patents related to medicines' International Non-Proprietary Name (INN) in different countries. For more information about these databases, see: Food and Drug Administration (FDA), "Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations", online: <https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm>; Health Canada, "Patent Register", (9 December 2002), online: <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/patent-register.html> Last Modified: 2017-04-06; Medicines Patent Pool (MPP), "MPP-MedsPaL", online: <https://medicinespatentpool.org/what-we-do/medspal/>; World Intellectual Property Organization, "Pat-INFORMED", online: <https://www.wipo.int/patinformed/>.

[426] In this sense, see: Gallini & Scotchmer, "Intellectual Property", *supra* note 296; Woolman, Fishman & Fisher, *supra* note 400; Bessen & Meurer, *supra* note 4; Carl Shapiro, "Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard Setting" (2000) 1 Innov Policy Econ 119–150.

[427] See, generally: Bessen & Meurer, *supra* note 4.

[428] Rebecca Eisenberg, "Patents and the Progress of Science: Exclusive Rights and Experimental Use" (1989) 56:3 Univ Chic Law Rev, online: <https://chicagounbound.uchicago.edu/uclrev/vol56/iss3/2>; Gallini & Scotchmer, "Intellectual Property", *supra* note 296; J H Barton, "Policy forum: intellectual property rights. Reforming the patent system" (2000) 287:5460 Science 1933–1934; Drahos, *supra* note 38.

[429] Burk & Lemley, *supra* note 256; Burk & Lemley, *supra* note 256; Burk & Lemley, *supra* note 254.

in biotechnology is relative as inventions from this field copy some mechanisms of living organisms or the entire debate about patenting genes.[430] These discussions raise the bar in understanding, acquiring, and managing IPRs.

Additionally, patent landscapes provide a picture of the patent situation for different types of technologies. Therefore, these landscapes delimit the freedom to operate of researchers (and other agents like pharmaceutical companies) and determine the risks of IPRs infringement by them.[431] While discussing patent landscapes in the Covid-19 response and the difficulties to free access knowledge in this regard, Drahos asserts: "We have created a world in which scientists have to wander legal labyrinths to find out their degree of research freedom. For an exponentially reproducing virus looking for new hosts to infect, this (politically manufactured) slow response is a replication opportunity."[432]

Legal rules are more likely to influence agent behaviour if those rules resonate with agent conceptions of appropriate behaviour towards peers rather than by imposing counterintuitive assumptions of the norms of science on them.[433] The redefinition of boundaries between basic and applied research,

[430] Rebecca S Eisenberg, "Proprietary Rights and the Norms of Science in Biotechnology Research" (1987) 97 Yale Law J 177; Burk & Lemley, *supra* note 254.

[431] About the complexity of the patent system and landscapes and some examples of them, see: Bubela et al, "Patent landscaping for life sciences innovation", *supra* note 364; Woolman, Fishman & Fisher, *supra* note 400; Murray & Stern, "When Ideas Are Not Free", *supra* note 4; World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22 at 136–137; *Patent Landscape Report on Ritonavir*, by Landon IP, 946/1E (Geneva: World Intellectual Property Organization (WIPO), 2011); *Patent Landscape Report on Atazanavir.*, by Thomson Reuters IP Solutions, IP Consulting Group, 946/2E (Geneva: World Intellectual Property Organization (WIPO), 2011) 946/2E; World Intellectual Property Organization, "Patent Landscape Reports by Other Organizations", online: *World Intellect Prop Organ* <https://www.wipo.int/patentscope/en/programs/patent_landscapes/plrdb.html>; World Intellectual Property Organization, "Publications: Patent landscape reports", online: *World Intellect Prop Organ* <https://www.wipo.int/publications/en/series/index.jsp?id=137>.se

[432] Drahos further explains: "Mapping patent landscapes requires access to fee-charging databases (for example, those accessible thorough Derwent Innovation) and specialist expertise. No serious player in this field would rely on PATENTSCOPE's COVID-19 search facility. In the world of high stakes patent litigation this would be suicide. PATENTSCOPE is a nice place for amateurs to have a go. The more important message of PATENTSCOPE is the one to be found blaring in its title; researchers need to scope patents before they begin to research." Drahos, *supra* note 38 at 6.

[433] Axelrod, *supra* note 169; Eisenberg, "Noncompliance, Nonenforcement, Nonproblem - Rethinking the Anticommons in Biomedical Research Patent Law in Perspective", *supra* note 37.

new R&D and organizational arrangements, and what may lead to innovation, especially in cutting-edge technologies, require unique views and strategies about IPRs. [434]

Finally, there continues to be no robust or definitive empirical evidence of the positive effects of strong patent protection on access to knowledge and innovation, especially in developing and least-developed countries. A historical evaluation of patent systems suggests the opposite, considering the adoption of less protective regimes (not only regarding patents but other IPRs, such as copyrights) by developed countries during their own industrial development periods.[435]

4.3.3. Other Categories of Intellectual Property Rights and Regulatory Specificities Applied to Biomedical Research and Development

Beyond patents, other categories of IPRs such as trade secrets, trademarks, copyrights, and, in some jurisdictions, specific protection over genetic resources and traditional knowledge (TK) apply in the biomedical field. Contract law and health regulations, data protection and privacy (for example, over patient data) form part of legal regulation of access to and control over biomedical R&D.

Trade secrets consist of information that is not widely shared, has some value, and in respect of which the holder takes reasonable steps to prevent dissemination.[436] Secrecy is generally obtained by a combination of contracts among those who have access to the invention and security measures that ensure secrecy. This protection is possible for hard-to-copy inventions, given that reverse engineering allows others to discover how the inventor ended up with a technical solution to a problem or invented something. There is no time limitation for the protection of trade secrets. However, once released into the public domain, there is no going back. Where an idea can be copied (if the agent copying it has the resources and

[434] In this sense, see Eisenberg, *supra* note 430 at 231.
[435] Some studies corroborating these points are: Lerner, *supra* note 282; Lerner, *supra* note 282; Penrose, *supra* note 282; Burk & Lemley, *supra* note 256; Woolman, Fishman & Fisher, *supra* note 400; Hoen, *supra* note 25.
[436] UNCTAD-ICTSD, *supra* note 242; World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22.

know-how to do so) by reverse engineering, agents generally opt-out of the trade secrecy regime, choosing patent protection instead.[437]

"Trademarks allow manufacturers and traders to distinguish their goods from those of competitors. They help consumers make informed choices, and they aim to prevent consumer deception."[438] While trademarks do not play a role in protecting inventions; they serve to distinguish between brand names and generic versions of biomedical products. For instance, Trastuzumab is the generic name of the trademarked Herceptin held by Roche.

Books, papers, research notebooks, and educational materials are automatically protected by copyright on creation and do not require registration. They are also generally the most effective manner of communicating R&D findings, sharing knowledge and information, and promoting a peer review and quality assessment of the research activities. However, copyright's goal of inducing rapid dissemination can be undercut by delays caused by the novelty requirement of patent law. In order to secure patent protection, inventors hold off on publishing results until they can file their patents. Thus, legal advice is essential to manage these IPRs' technical details and guarantee adequate circulation and share of research and scientific information.[439]

Software—a critical tool in coordinating, sharing, and accessing publications, data, and research materials (such as blood samples)—is also subject to copyright. The practices and policies governing libraries, journals, and publications around the world and educational tools also have an enormous impact on advancing RD&I and interact with copyright law, creating complex interactions.[440]

[437] UNCTAD-ICTSD, *supra* note 242; World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22.
[438] World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22 at 67.
[439] UNCTAD-ICTSD, *supra* note 242; World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22.
[440] UNCTAD-ICTSD, *supra* note 242; World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22.

Copyright also applies to databases, albeit in a modified form. Databases are critical for biomedical research, storing patient and experimental data, information, and knowledge. Even though data itself is not copyrightable, the manner in which an agent organizes information into a database can be protected.

This quick survey of other IPR regimes—not to mention the contracts dealing with them and the practices surrounding their use—illustrates those debates concerning access to knowledge and innovation go far beyond patents.[441] Access to and dissemination of knowledge that feeds biomedical innovation systems depends on the sum and interactions among IP laws, practices and policies adopted by different institutions. In this sense, while claiming responsible patenting and licensing practices and policies is essential, knowing the impacts of other IPRs and contractual practices on access and innovation is also critical. For instance, affordability or free access to data, information, educational materials, and scientific publications must be part of the claims of the expert communities to address access and innovation problems and advance the scientific enterprise more efficiently and sustainably.[442]

So far, I have touched on a few nuances of IPRs protection applied to the biomedical field to illustrate the complexity surrounding its understanding. In the following chapters, I will deepen the analysis of a specific jurisdiction (Brazil) to show that the diversity of components translated into IP legislation, policies, and practices increases the possibilities of combination and complexity.

[441] Rai & Eisenberg, *supra* note 363 at 294–295.

[442] These issues are related to the notions and discussions of open access, open data, open innovation, and open science and further developed in Chapter Seven. See, initially: Arshad et al, "Open Access Could Transform Drug Discovery", *supra* note 424; James MacGregor, Kevin Stranack & John Willinsky, "The Public Knowledge Project: Open Source Tools for Open Access to Scholarly Communication" in *Open Sci* (Springer, Cham, 2014) 165; E Richard Gold, "Accelerating Translational Research through Open Science: The Neuro Experiment" (2016) 14:12 PLOS Biol e2001259; Leslie Chan, Barbara Kirsop & Subbiah Arunachalam, "Towards Open and Equitable Access to Research and Knowledge for Development" (2011) 8:3 PLOS Med e1001016; Dagmar Sitek & Roland Bertelmann, "Open Access: A State of the Art" in *Open Sci* (Springer, Cham, 2014) 139; Paul A David, "The Economic Logic of 'Open Science' and the Balance between Private Property Rights and the Public Domain in Scientific Data and Information: A Primer" in Julie M Esanu & Paul F Uhlir, eds, *Role Sci Tech Data Inf Public Domain Proc Symp* (Washington (DC): National Academies Press (US), 2003) 19.

CHAPTER FIVE—ON THE INTERACTIONS AND COEVOLUTION OF COMPLEX ADAPTIVE INTELLECTUAL PROPERTY AND BIOMEDICAL INNOVATION SYSTEMS

5.1. Assumptions versus Reality in Complex Adaptive Intellectual Property and Biomedical Innovation Systems

In previous chapters, I argued that we can analyze IP and biomedical innovation systems as CAS. I noted the characteristics of these systems that are essential to understand their functionality, interaction, and coevolution. This included, notably, the diversity of components, agents, their behaviours, and interactions.

In this chapter, I take the next step in the analysis by examining more closely what agents know (and do not know) about these systems and how their knowledge influences the functioning of those systems. This is critical because there can be no sensible system reform without acknowledging and becoming comfortable with uncertainty. Uncertainty is part of the complex world and is one of the main features of CAS. Law and policy seek to manage uncertainty and guide agents through multiple factors, cause-consequence relations, and interaction patterns that emerge from human interaction. Embracing uncertainty may be disruptive because of the often-illusory idea that achieving control is more valuable than realizing that limited control over the world is the norm.

This chapter addresses three points. First, as just noted, it highlights the importance of recognizing uncertainty as a central characteristic of seeing IP and biomedical innovation systems as CAS. Second, it illustrates uncertainty through target examples that prove how these CAS' reform is often based on assumptions and not observations of what happens within them. In doing so, I present the debate over the tragedy of the anticommons hypothesis in biomedical research and subsequent empirical research, followed by discussions about how agents tend to assume that legal frameworks and policies implemented in developed countries are suited for developing and least developed countries. I also briefly raise

questions about legal transplantation in general and IP policies and practices affirming that the best way to transfer ideas from universities and research centres to the private sector is through patents. I do so while inquiring what CAS theory and concepts could have added to agents' understanding of the interactions between IP and biomedical innovation systems. My goal is to show a pattern in which legal experts (and other agents engaging in law and policymaking) evaluate problems in a wrong or simplistic fashion and propose CAS as a methodology to address these problems. Emergent behaviour appears as a critical issue to explain why looking at problems through the lens of CAS is so helpful. The issues emanating from this chapter's evaluation also relate to the importance of minimizing agents' bounded rationality that increases uncertainty in these systems; therefore, their solution relates to this dissertation's hypothesis on clarifying the relationship between law and science. Third, this chapter concludes by pointing out some of the elements that make clarifying the relationship between law and science difficult and how to assist agents in overcoming those elements.

5.1.1. Uncertainty in Complex Adaptive Intellectual Property and Biomedical Innovation Systems

As I previously explained, CAS are uncertain because of the richness of interactions that occur within them in a multi-layer, multi-agent, and multi-factorial context. By accepting uncertainty rather than fighting against it, agents can better manage and guide these dynamic systems. After embracing uncertainty, agents need to thoroughly observe these systems and minimize the noise that impairs or misguides them in their comprehension of these systems. To do so, agents need to create mechanisms that minimize external and internal influences such as bias, power, politics, rhetoric, and ideology, as well as confront their bounded rationality when interacting within these systems and with other agents.

I have argued that IP and biomedical innovation systems not only coexist but also coevolve and communicate. Law and science create signal-boundary arrangements that enable agent communications

and interactions, leading to these systems' adaptation and coevolution. Agent behaviours and expectations influence the construction of these signal-boundary arrangements and the nature and content of the information these agents have access to. However, expectations and behaviours may or may not always coincide with legal norms that arise in these systems. These systems also co-create niches that provide contained spaces for experimentation between legal and non-legal agents as they test new ways to achieve their goals within these systems. Thus, aligning the goals of agents acting within IP and biomedical innovation systems influences systemic success and failure.

Due to cognitive limitations, the agents working on IP and biomedical innovation systems—as is true of any system—have a limited understanding of the interactions and processes internal to those systems. To manage this limited understanding, agents build models of how those systems work. If we are to minimally address the limits of understanding and make headway against uncertainty, we need to develop new methodologies that respond flexibly and dynamically to the complexity of these systems. To do so, we must engage in multidisciplinary evaluations and multi-agent views of these systems to revise the framework through which we analyze their interactions. Through such an understanding, we can suggest ways through which agents can better achieve the system's goals.

Complexity science is not only about results but is also interested in the journey and models of thinking that respond to different problems emerging from the interaction of agents. In a world characterized by uncertain and complex interactions, relying on simple strategies to solve problems may no longer be either possible or desirable.[443] We can replace simple strategies calling for either stricter or more flexible IP protection with voices situated 'in between' these two opposing positions. These voices suggest that agents do not know, and may never know with certainty, what is the best IP strategy to regulate

[443] As previously commented, different scholars have defined problems that are similar to complex problems in other theories and suggested different strategies to address them. For more information, see: Rittel & Webber, *supra* note 18; Bubela, Gold & Morin, "Wicked Issues for Canada at the Intersection of Intellectual Property and Public Health", *supra* note 18.

biomedical R&D or how to strike the right balance between protection and openness—that agents will never have a general golden recipe for success, that there is no 'one size fits all' approach. This space in between leads us to recognize that agents might never know, or—more precisely—that they will never be able to predict all of the effects of IP law and policy that apply to real-life issues, such as the regulation of science and the impact of this regulation on access to knowledge, medical technologies, and innovation.[444]

The point of highlighting uncertainty in decision-making is to reveal the significance of less visible factors that play a significant role in forming the outcomes of the IP and biomedical R&D systems. Uncertainty represents a gap in agent understanding of what the system is. We can fill some of these gaps by developing empirical evidence on the functioning of these systems, including through greater engagement with expert communities (academic, research, and legal). Accompanying these new methodologies is the need to develop new metrics to evaluate the successes or failures of laws and policies that aim to regulate science in different countries going forward.[445]

[444] For initial thoughts, see: Eisenberg, "Noncompliance, Nonenforcement, Nonproblem - Rethinking the Anticommons in Biomedical Research Patent Law in Perspective", *supra* note 37; Gold et al, *supra* note 254; Gold et al, "The unexamined assumptions of intellectual property", *supra* note 4; Caulfield, Harmon & Joly, "Open science versus commercialization", *supra* note 37; Piper, *supra* note 37; Rai, "Engaging Facts and Policy", *supra* note 37; Benjamin & Rai, "Fixing Innovation Policy", *supra* note 37; PACEOMICS, *supra* note 34.

[445] Morin, Daley & Gold, "Having Faith in IP", *supra* note 51; Morin, *supra* note 51; Gold et al, *supra* note 254; Gold et al, "The unexamined assumptions of intellectual property", *supra* note 4.

5.2. A Tale of Complexity: Revisiting the Tragedy of the Anticommons Hypothesis in Biomedical Research and Subsequent Studies on It

In 1998, in a parallel to the 'tragedy of the commons,'[446] Michael Heller coined the concept of 'the tragedy of the anticommons.'[447] He described it as follows:

> In an anticommons, by my definition, multiple owners are each endowed with the right to exclude others from a scarce resource, and no one has an effective privilege of use. When there are too many owners holding rights of exclusion, the resource is prone to underuse—a tragedy of the anticommons. Legal and economic scholars have mostly overlooked this tragedy, but it can appear whenever governments create new property rights.[448]

Later on, in the same year, Heller and Eisenberg applied the idea of 'the tragedy of the anticommons' to the biomedical field.[449] They argued that too much early and broad patent protection over basic research in biomedicine had the potential to reduce the amount of downstream research and product development (or follow-on innovation). As Heller and Eisenberg hypothesized, actors initially sought to create a competitive advantage against others by obtaining as broad protection as possible. The result of this activity would be that, faced with these patents, others would be unable to improve on inventions or carry out follow-on innovation without seeking approval from multiple patent holders, leading to an anticommons problem. In particular, those looking to develop a new medicine or diagnostic kit would be blocked from doing so.[450]

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[446] About the 'tragedy of commons', Heller explains: "More generally, one can understand anticommons property as the mirror image of commons property. In a commons, by definition, multiple owners are each endowed with the privilege to use a given resource, and no one has the right to exclude another. When too many owners have such privileges of use, the resource is prone to overuse—a tragedy of the commons. Canonical examples include depleted fisheries, overgrazed fields, and polluted air." See: Heller, "The Tragedy of the Anticommons", *supra* note 65 at p.623-624; Hardin, *supra* note 327.

[447] As explained in Chapter Three, see: Hardin, *supra* note 327.

[448] Heller, "The Tragedy of the Anticommons", *supra* note 65 at 624.

[449] Heller & Eisenberg, "Can patents deter innovation?", *supra* note 65.

[450] As mentioned in Chapter Four, especially in the biomedical field, a single invention (a medicine, for instance) encompasses several patents that do not necessarily have the same owner. The number of patents required to produce this invention will require several licensing agreements to enable the product to reach the market. See: Bubela et al, "Patent landscaping for life sciences innovation", *supra* note 364; Woolman, Fishman & Fisher, *supra* note 400; Murray & Stern, "When Ideas Are Not Free", *supra* note 4.

Since 1998, the anticommons hypothesis has become a buzzword—Eisenberg notes this in her later evaluation of the initial paper[451]—but it also has been misconceived as empirical fact rather than a hypothesis.[452] People reading the paper assumed that anticommons actually existed, endangering innovation and derailing future R&D activities; however, patents are only one piece of an IP strategy and are not the only category of IPRs to be taken into account. In 2008, Eisenberg revisited the tragedy of the anticommons in biomedical research. In her later analysis, she evaluates empirical research that attempted to verify the existence of the anticommons' effect on biomedical R&D in different countries. She concludes as follows:

> The results suggest that, overall, intellectual property has presented fewer impediments to research than policymakers may have projected on the basis of early salient controversies. Most scientists report no difficulties in attempting to acquire IP-protected technologies, and only a small percentage report significant delays in research or having to abandon a project because of IP issues. Even in fields characterized by extensive patenting, many academic researchers seem to be either oblivious to the patents they might be infringing or unconcerned about potential infringement liability. More significant to researchers than patents as such have been practical restrictions on access to materials and data, such as requirements for institutional assent to the terms of materials transfer agreements (MTAs).[453]

The studies reported by Eisenberg relate to agent behaviours (mostly expert communities) and illustrate that the interaction and coevolution of complex adaptive IP and biomedical innovation systems may yield unexpected results. These studies further show that assumptions about how and why agents

[451] Eisenberg, "Noncompliance, Nonenforcement, Nonproblem - Rethinking the Anticommons in Biomedical Research Patent Law in Perspective", *supra* note 37.
[452] *Ibid*.
[453] She further elaborates on these findings and links them to the behaviour of agents: "After all, patents are more like property rights than the combination of self-help and contract used to control access to materials and data. Patents confer a legal right to exclude all others-including researchers who make the same thing independently-from making, using, selling, or importing an invention without the permission of the patent owner. By contrast, researchers are free to duplicate unpatented materials and data without legal liability. As property rights, patents might seem more likely to threaten an anticommons than the less absolute rights held by those in possession of unpatented materials and data. But it is transaction costs and risks of bargaining failure that set the stage for an anticommons; what matters is thus not the property-like character of the underlying rights, but rather the need to negotiate multiple agreements. As a matter of law, a user needs to get permission from the patent owner before using a patented invention. But as a matter of practice, both owners and infringers routinely ignore patents in the context of upstream research. Would-be users thus readily gain access to patented technology without having to engage first in costly bargaining, a fact that minimizes the risk of an anticommons arising from a proliferation of patents alone. On the other hand if, as the data also suggest, exchanges of materials and data are encumbered by costly negotiations and risks of bargaining breakdowns, then a proliferation of MTAs and database access agreements could potentially give rise to an anticommons even without patents." *Ibid* at 1061–1062, 1084–1085.

behave and the impact of their behaviour on IP protection is more nuanced than may appear. Eisenberg connects the original hypothesis to a new concept that she calls 'the burden of inertia.' In doing so, she makes an argument about non-compliance and non-enforcement of IPRs while observing non-legal agents' (researchers) behaviours and interactions with those who own IPRs. The 'burden of inertia' results from the idea of 'practical excludability.'[454]

'Practical excludability' means that a patent by itself does not entail the exclusion of an agent (for instance, a researcher) of the use of a resource. In some situations, the patent holder may be the only one with the practical ability to produce the resource, forcing researchers to negotiate access with that holder. In other situations, the researcher has the means to produce the patented resource without the assistance of the patent holder but would violate the patent by doing so. In a third scenario, while the resource is not patented, the researcher does not have the ability to produce the physical resource without the collaboration of the agent with physical control over that resource.[455] Only in the first and third scenarios is the researcher practically blocked from access as long as the researcher is willing to ignore (or be blind to) legal rights.

The implications of 'practical excludability' to the tragedy of the anticommons hypothesis is that one must go beyond an analysis of legal rights to understand the knowledge, ability to produce the physical resource by him/herself, and motivations of agents. For instance, in the second scenario above, agents' need for a given intangible asset influences their willingness to negotiate with the IP owner or assume the risk of using the asset without authorization or a legal right (for instance, research exception). There are also circumstances in which a researcher uses the intangible asset and does not realize that there is a patent legally prohibiting use.

[454] In this sense, see: *Ibid* at 1085–1088; Cohen & Walsh, *supra* note 58 at p.12-14.
[455] In this sense, see: Eisenberg, "Noncompliance, Nonenforcement, Nonproblem - Rethinking the Anticommons in Biomedical Research Patent Law in Perspective", *supra* note 37 at 1085–1088; Cohen & Walsh, *supra* note 58 at p.12-14.

According to Eisenberg, a 'burden of inertia' exists when a barrier impedes or limits an agent from accessing scientific research. After considering all options, costs, and risks, an agent will decide to overcome his/her inertia and use the resource—despite the barrier, whether a patent or otherwise. Similarly, an agent who holds patent rights to the asset will decide whether to enforce the patent after evaluating the transaction costs s/he may incur.[456] For instance, it is unlikely that a patent owner would enforce IPRs when facing minor infringements resulting from academic research due to the poor cost-benefit ratio, where the cost primarily consists of direct litigation costs and bad publicity. The benefits of threatening legal action would be small, especially in an academic setting where damages are likely to be nominal. Thus, in the end, a dynamic interaction happens between industry and the research community as they work on different phases of the R&D pipeline. However, by presuming that patent holders are unlikely to enforce a patent, some researchers tend to ignore the existence of IPRs during the research phase.[457]

Eisenberg describes the scenario generated by the ideas of 'practical excludability' and 'burden of inertia' as a 'non-enforcement, non-compliance, non-problem.' This scenario results in agents operating according to behavioural norms within the IP system. There remains the risk that they could be found to have infringed an IPR, but they are willing to take this risk. There are a large number of empirical studies, many of which Eisenberg surveyed that further illustrate the complexity of how actors handle the problem of legal, but not practical, excludability.[458]

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[456] Eisenberg, "Noncompliance, Nonenforcement, Nonproblem - Rethinking the Anticommons in Biomedical Research Patent Law in Perspective", *supra* note 37.
[457] *Ibid*.
[458] More information about research exceptions and flexibilities of IPRs, see *WIPO Standing Committee on the Law of Patents. Exclusions from Patentability and Exceptions and Limitations to Patentees' Rights*, by Lionel Bently et al, SCP/15/3 (Geneva: World Intellectual Property Organization (WIPO), 2010); World Intellectual Property Organization, "Exceptions and Limitations to Patent Rights", online: *World Intellect Prop Organ* <https://www.wipo.int/patents/en/topics/exceptions_limitations.html>; Correa, *supra* note 13; Ellen 't Hoen et al, "Medicine procurement and the use of flexibilities in the Agreement on Trade-Related Aspects of Intellectual Property Rights, 2001–2016" (2018) 96:3 Bull World Health Organ 185–193.

Eisenberg pointed out a small snapshot of biomedical R&D compared to its global perspective that needs to be further evaluated. All the empirical studies mentioned in her analysis refer to developed countries. However, it is possible to identify few studies that theoretically mention the tragedy of the anticommons hypothesis without providing examples, engaging in empirical analysis in those countries, or adding to the discussion the ideas of 'burden of inertia' and practical excludability.'[459] This fact shows the gap of empirical studies that precisely assess the likelihood of the tragedy of anticommons happening in developing and least-developed countries.

Therefore, more empirical studies and monitoring tools would be helpful to those devising IP strategies and those promoting new ways of doing science, especially in developing countries. As Eisenberg's 2008 reanalysis of the tragedy of the anticommons hypothesis illustrates, agents are often unaware of the details of interactions between IP systems and their regulatory targets. Such evaluation indicates the need for constant reassessment of the interaction between CAS and their agents to inform tailored legal and policy reform.

5.2.1. Lessons Learned from the Tragedy of the Anticommons Hypothesis

The tragedy of the anticommons hypothesis and subsequent research on it is illustrative of agents' bounded rationality. It illustrates how agents tend to generalize assumptions and are too quick to draw conclusions without first obtaining an empirical basis for their claims. Thus, it is easier to affirm that patents hinder or incentivize innovation and access to knowledge than to evaluate the dynamic interactions between agents and the results generated by the protection of inventions by patents and other IPRs. These assumptions

[459] For some of these studies, see: César, Rosina & Polido, *supra* note 259; César, *supra* note 260; André Luís Menegatti, "Pools de Patentes: Entre uma Possível Solução à Tragédia dos Anticomuns e Ameaças à Concorrência" (2013) 1:1 Rev Def Concorr 16–51; Alfredo Canavese, "Temas en el Análisis Económico de Los Derechos de Propiedad" (1) 1 Rev Econ Política B Aires, online: <http://ojs.econ.uba.ar/index.php/REPBA/article/view/234>.

filter out beyond academia to influence law and policymaking processes, the IP strategies of different agents, the adoption (or not) of new biomedical RD&I models such as open science, and court decisions.

The anticommons illustration set out above also highlights the central focus agents place on patents as opposed to other interactions within biomedical innovation systems. There is no doubt that patents are important, but they are not the whole story and often, as in the anticommons case, are heavily modulated by other elements in the system. It is time, therefore, to place patents within a broader view of biomedical R&D.

5.2.2. Applying Complex Adaptive Systems Theory and Agent-Centred Evaluations to the Tragedy of the Anticommons Hypothesis

Imagine the situation in which Researcher A must decide whether to share (freely or with payment of royalties) a research tool (such as a genetically modified mouse to test a cancer drug) or enforce her right against another agent in case of infringement. On the other side of this relationship, Researcher B needs to use the research tool to advance her research. There are several aspects to consider in this situation. First, for Researcher A (a non-legal agent) to understand her rights, she must know the IP strategy and IPRs that protect this research tool. The same applies to Researcher B. Both researchers may benefit from the advice of a legal agent. If these researchers are part of a university or research centre, they may request assistance from its Technology Transfer Office (TTO). However, in many cases, this dialogue and assistance do not occur, either because Researchers A and B are not used to seeking legal advice or because the service is not offered (or if it is, overworked professionals do not have the time to provide detailed attention to each researcher and project).

Researcher A's decision to share the research tool may rely on subjective factors such as her history of collaboration or competition with Researcher B and the possibility of cooperating in future projects. Sharing also requires an infrastructure that enables it. This infrastructure involves physical (for instance,

databases or biobanks) and legal or personal assets and knowledge (such as the drafting and negotiation of MTAs and confidentiality agreements) to work and implies costs for its operation and maintenance. Agents most likely engage in a cost-benefit evaluation of sharing and collaborating in these settings, drawing on what they understand of the system in which they act. Behavioural factors (such as the role of reciprocity) may also play a role in determining an outcome in this case. As such, a strict normative evaluation of the situation does not fulfill the need for a balanced interaction among agents within IP and biomedical innovation systems.[460]

Biomedical R&D is an activity that relies on cumulative information, data, and knowledge built up over time through the dynamic interactions of various agents. If information, data, and knowledge do not flow appropriately within systems, they may not operate to their full potential and achieve their goals. The same reasoning applies to products and processes resulting from this flow of information, data, and knowledge. The ideas of cooperation and competition and sharing information, data, and knowledge underlie the dynamic interactions between agents. Agent choices to contain intangible assets by protecting them by IPRs can negatively affect biomedical R&D systems if the IP strategy is not balanced and designed to achieve long-term results. Cooperation and competition and different degrees of IPRs protection directed by the idea of openness in science are at the core complex issues affecting the regulation of biomedical R&D.[461]

[460] Refer to Chapter One for insights on behavioural analysis in CAS.
[461] For issues related to cooperation see Axelrod's work on it. Robert Axelrod, *The Evolution of Cooperation: Revised Edition*, revised ed. edition ed (New York: Basic Books, 2006); Robert Axelrod, "The Emergence of Cooperation among Egoists" (1981) 75:02 Am Polit Sci Rev 306–318.

5.2.3. The Interplay between Agent Behaviours and Norms and the Importance of Communication for Understanding the Evolution of Legal Systems

As noted in Chapters One and Two, it is impossible to predict all the outcomes of the interaction between CAS and their agents. However, even though CAS might be unpredictable, they are stable in their core functions and features. Complex adaptive IP and biomedical innovation systems reach stability and increase robustness and resilience by incentivizing repetition (iteration) or directing and compelling agents to behave consistently. As Gold notes, "iteration holds the key to the unity of legal systems."[462] From a normative standpoint, repetition refers to the reiterated use and compliance with norms.

Not everyone follows the law, and there are pockets of obscurity and lacunae in the law as well as a continuous interplay between norms of different types leading to change and evolution in legal systems. Behavioural norms are, in this sense, essential elements of legal systems. The repetition of patterns of interaction among agents relates to the robustness of the system. The increase of iteration of agents' behaviours that are not predicted by a norm may indicate an adaptation of agents in a system, within systems, or in a specific niche.

Adaptation occurs either because a norm is not applied or does not appropriately respond to a situation. An increase of iteration of behaviours that are not predicted by a norm may lead to the evolution of the legal system, resulting in new or emergent behaviours. In some cases, the behaviours of agents do not necessarily infringe norms and may respond to situations where norms are not yet in place.

The scholarship related to the tragedy of the anticommons hypothesis and related empirical studies shows that a large number of agents behave in opposition to what is prescribed by law and, consequently, build a system based more on behaviour than on law. It also shows the diversity of sources that lead and influence legislative design and reform.

[462] *Ibid* at 349.

Applying an agent-centred evaluation to the situation in which behaviour influences the creation or modification of the law, one may consider other factors apart from the content of the law to understand that phenomenon. Proximity (not only physical but through communication) of agents and their ability to influence the behaviour of others is a crucial factor. Proximity increases the likelihood that other agents will replicate a new behaviour, thereby entrenching it. Another factor is the position of authority or power that an agent has over others and the likelihood that the latter agent follows the dictates of the first. In any event, because of the system's complexity, many of the behaviours that emerge would not have been predictable at the start.

5.2.4. The Importance of the Tragedy of the Anticommons Hypothesis and Related Discussions to Advance Multisystemic Analysis, Design, and Reform

In light of the above, viewing the tragedy of the anticommons hypothesis in biomedical research through the lens of CAS and applying agent-centred evaluation provides a window to the interaction between law and science and between legal and non-legal agents. In particular, it illustrates the activity occurring in 'the space in between' the IP and biomedical innovation systems. The empirical studies give us a small picture of the behaviour of agents, which varies over time within IP and biomedical innovation systems. This variation and adaptation depend on multiple factors, such as the technological field and the country where the interaction occurs.

In promoting bottom-up approaches to understanding IP and biomedical innovation systems, some details are essential. First, one needs to be aware of the dynamic interactions of agents and how their expectations lead to their behaviour. Second, agents' position and degree of influence within the system and the information flow that enables decision-making are critical to outcomes. Third, diversity in how agents think about and experience biomedical R&D provides the force needed to overcome the burden of inertia.

Because of the size and complexity of these systems, it is not possible for agents to fully appreciate all the factors at play in expectations and behaviours within IP and biomedical innovation systems, nor the connections between multiple elements of these systems. Actions and changes in strategy are in constant flux, making it impossible for agents to set definitive IP strategies and goals for these systems. Our collective ability to understand and improve biomedical R&D will operate poorly unless we include in our analyses not only formal laws and informal norms but the ways in which these norms work together with often unanticipated results.

The anticommons problem illustrates the importance of thinking about law and science as CAS at a larger scale. It focuses our attention on evaluating the interaction and behaviours of agents deciding to apply—or not—IPRs. Focusing either on the existence of patent rights or ignoring problems caused by patents misses the important interactions occurring in between. Without a systemic understanding of the biomedical R&D systems, we limit our understanding of the complex interactions among agents that shape outcomes. A CAS approach allows us to investigate how agents develop norms through their behaviours that soften the effects of patents but in unpredictable ways. So, while IPRs, and more specifically patents, turn out not to be a problem, MTAs and the protection of research materials and tools may be in the broader scenario in which agents do research. Enlarging agents' knowledge about this biomedical innovation ecosystem and creating strategies to minimize the effects of their bounded rationality may improve its operation and enable changes and reforms that more adequately address problems.

Those analyzing the tragedy of the anticommons also have assumed that agents and situations posed by the environment were homogeneous. They did not count for the diversity of agents, behaviours, interactions, and problems within IP and biomedical innovation systems and assumed those agents behave at the average. They did not think about the burden of inertia or unpredictability of these CAS. These acknowledgment needs to combine with IP literacy, multidisciplinary assessment, dialogue and

cooperation among legal and non-legal agents, observation and mapping of behaviours and interactions to inform law and policy reform.

Finally, we should not assume that the tragedy of the anticommons does or does not occur in developing and least-developed countries simply because we lack empirical analyses. Nor should we guess how agents in those countries might behave given the burden of inertia. Several developing countries possess complex IP laws and policies, and institutions that would allow empirical studies to evaluate the current state of the relationship between law and science and the level of understanding of legal and non-legal agents about these CAS. Chapter Six develops this thought further, using Brazil as an example. An essential factor in analyzing the tragedy of the anticommons and, more broadly, the effects of IP protection in biomedical innovation systems in developing and least-developed countries is that a substantial amount of IPRs in those countries are held by developed countries' agents. Therefore, the challenges to developing and least-developed countries to establish IP and biomedical innovation systems that serve their developmental needs and interests may differ from those in developed countries.

This section provided a targeted example of how CAS theory and agent-centred evaluations enable us to assess claims about how the biomedical R&D system operates critically. It allows us to understand the levels at which agents within these systems overcome problems, such as the anticommons, and create others, such as those arising from restrictive contracting. In doing so, this approach positions us to not only better critique the system, develop empirical studies to assess that system, and create solutions that might otherwise have eluded us.

5.3. Legal Transplantation and Intellectual Property Practices and Policies at Universities and Research Centres

Complementing the above presented and pointing out that what occurs in these systems is often different from what people assume to happen, I briefly explain two points. First, the assumption that IP legislation,

policies, practices, and strategies that are good for developed countries are similarly suitable for developing and least-developed countries and how this may lead to legal transplantation and harmonization that are not necessarily beneficial. Second, the assumption that the best way to transfer ideas and knowledge from the university to the private sector is through IPRs, particularly patents. This section illustrates a behavioural pattern of legal and policy experts getting the interaction of IP and biomedical innovation systems wrong and without context, similarly to what happened in the tragedy of the anticommons hypothesis. Emergent behaviour seems to be a key element in explaining why looking at the problem through the lens of CAS is helpful and how it can diminish the gap between theory and reality applied to law and policy design and reform in different countries.

Chapter Three briefly presented discussions about the harmonization of IPRs, and the adoption of minimum IP protection standards established by the WTO-TRIPS agreement. Even though adopting minimum standards may be helpful in a global economy and facilitate international trade, incorporating the ideas behind it without criticism and a sense of local needs and realities is troublesome. Minimum standards do not mean that all countries may adapt their laws equally. The TRIPS agreement and posterior declarations, such as the Doha Declaration, have exposed the need to incorporate flexibilities in national laws, acknowledge different countries' developmental levels, and pursue different strategies and tailored regulations. However, when it comes to legislative and policy practices, power relations and politics, and the appearance of success of developed countries' legal and policy instruments play critical roles in CAS reform. As mentioned before, this situation is further aggravated by developed countries' bilateral and plurilateral negotiation practices that try to impose more restrictive IP protection standards on other countries.[463]

[463] On harmonization, especially considering developing and least-developed countries perspective, see: May & Sell, *supra* note 247; Sell, "TRIPS Was Never Enough", *supra* note 247; Dutfield & Suthersanen, "Harmonisation or differentiation in intellectual property protection?", *supra* note 260.

Graham Dutfield and Uma Suthersanen call attention to the strategy of developed countries trying to impose on developing and least developed countries high IP protection standards that are different from those they adopted while developing (for instance, Switzerland, Germany, Japan, and the USA). The authors do not claim that differentiation is better than harmonization or advocate stronger or weaker IP protection. Instead, they argue for a tailored approach to evaluate innovation and creativity geography that is different in various types of industry and areas, as well as does not fit in the North-South divide. They further see legislative and policy developments in developing countries beyond minimum standards—like global IP harmonization for patents and dynamic responsiveness for copyright—undermining their possibilities of adopting IP flexibilities in national legislation.[464] They conclude:

> In reflecting on the implications for policymaking and diplomacy, history would appear to indicate two things that are worthwhile considering. First, the developed countries can justifiably be accused of hypocrisy when they demand that the rest of the world adopt their own patent and other IP standards. Second—and this is much more important—their demands are preventing the developing countries from adopting appropriate patent and copyright standards for their levels of development, a freedom today's rich countries made sure not to deny themselves when they were developing countries themselves, and may well adopt again if they find themselves being overtaken in certain strategic business sectors.[465]

Gold and Morin also highlight the problem of legal transplantation[466] of exogenous rules by countries in their national legislation even when those rules violate their specific interests. They explain that "legal transplantation lies not in any single causal mechanism but in the succession and reinforcement of multiple mechanisms" while acknowledging multicausality and context-conditionality and using IP as "an example of the dynamics of legal transplantation under asymmetric interests." They further clarify that the term transplant "fails to adequately capture the subtle process of adaptation involved in taking a legal concept developed in one context and incorporating it into another" and acknowledge that legal

[464] Dutfield & Suthersanen, "Harmonisation or differentiation in intellectual property protection?", *supra* note 260.
[465] *Ibid* at 144.
[466] The authors clarify that "legal transplantation is a process through which the adopter implements a rule formulated in and for the originator country" and engage in quantitative research to evaluate 121 developing countries over more than 14 years. Morin & Gold, "An Integrated Model of Legal Transplantation", *supra* note 380 at 782.

scholars still have to explain the mechanisms leading to it.[467] Therefore, CAS theory and agent-based approaches can assist in identifying causes that led agents to transplant law and policy that are not necessarily beneficial to their reality.

Shifting our attention to the lower organizational layers of complex adaptive IP and biomedical innovation systems, the discussion about legal transplantation and harmonization takes on a concrete form and becomes more concerning when publicly funded research is explicitly tied to commercialization through patents. The *Bayh-Dole Act* (P.L. 96-517, *Patent and Trademark Act Amendments of 1980*) was adopted in the US[468] to give institutions—primarily universities—the mandate of obtaining and dealing with IPRs emanating from federally funded research.[469] Even though the *Bayh-Dole Act* arose in the specific context and history of the US, many countries (including Brazil)[470] adopted similar legislation, known as Bayh-Dole analogues.[471] The tendency of agents to adopt strategies that they see as successful might be one reasonable explanation for this, but transplantation without local context, especially in developing and least developed countries, may not always lead to desired results.[472]

[467] *Ibid* at 781.
[468] For the Bayh-Dole Act and initial discussions and criticism about it, as well as its transplantation in different countries' legislation, see: Bill Pub. L. 96-517, *Bayh-Dole Act: 35 U.S. Code Chapter 18 - Patent Rights in Inventions Made with Federal Assistance*, 1980, Part II Patentability of Inventions and Grant of Patents; Association of University Technology Managers (AUTM), "Bayh-Dole Act: Landmark Law Helped Universities Lead the Way", online: *Assoc Univ Technol Manag AUTM* <https://autm.net/about-tech-transfer/advocacy/legislation/bayh-dole-act>; Mowery et al, *supra* note 380; Rai & Eisenberg, *supra* note 363.
[469] For further considerations, see: Mowery et al, *supra* note 380; Rai & Eisenberg, *supra* note 363; Bhaven N Sampat, "The Bayh-Dole Model in Developing Countries: Reflections on the Indian Bill on Publicly Funded Intellectual Property" *UNCTAD - ICTSD Proj IPRs Sustain Dev* (October 2009) 1; So et al, "Is Bayh-Dole Good for Developing Countries?", *supra* note 380.
[470] Chapter Six presents some details about the Brazilian Innovation Law that regulates the relationship between public universities and research centres and the private sector, this law can be seen as a Bayh-Dole analogue legislation.
[471] Same examples of countries that have adopted similar Bayh-Dole legislation (Bayh-Dole analogues) are Brazil, China, Denmark, Finland, Germany, Italy, Japan, Malaysia, Mexico, Norway, Philippines, Russia, Singapore, South Africa, South Korea, and the United Kingdom. For more details about it, see: Association of University Technology Managers (AUTM), *supra* note 468.
[472] Morin & Gold, "An Integrated Model of Legal Transplantation", *supra* note 380.

Consider, for example, the attempt to adopt a Bayh-Dole analogue in India in 2010.[473] Several NGOs (MSF, DND*i*, and UAEM) and the Indian academic and research communities expressed concern about adopting a *Bayh-Dole* clone that failed to include any counterbalancing provisions of the US legislation, such as 'march in rights.'[474] They pointed to the lack of public participation in drafting the legislation and the Indian government's lack of transparency of its content. In the end, through their advocacy, the critics convinced the government to suspend approval of the amendments and guarantee public participation.[475] This example shows the importance of agents, mainly expert communities, participating in the design of legislation that directly affects their R&D activities and access to their results.

Debates over the role of IPRs in universities and research centres biomedical R&D activities (primarily publicly funded) further determine the shape of law and policy in these settings. These same debates indicate the tendency of law and policymakers and legal agents to adopt regulation without context and IP strategies that do not serve their goals. Some defend high levels of protection by IPRs to generate revenues through licenses and royalties to the university. Others argue that IPRs decrease knowledge diffusion and innovation by imposing barriers to sharing and increasing the costs of accessing knowledge. A third group supports knowledge dissemination within and beyond the academic community but is afraid of the risks of knowledge appropriation; their opinion and strategy stand for 'defensive' protection of IPRs as a manner to guarantee public control over inventions. Claims for new strategies arise as few examples

[473] For initial considerations, the Indian Bill (The Protection and Utilisation of Public Funded Intellectual Property Bill, 2008) and other documents related to it, see: Rajya Sabha (Parliament of India), *The Protection and Utilisation of Public Funded Intellectual Property Bill, 2008*, LXVI (2008); Annette Lin et al, *UAEM White Paper on the Proposed Indian Bayh-Dole Analogue* (Universities Allied for Essential Medicines (UAEM), 2008); *The Protection and Utilisation of Public Funded Intellectual Property Bill, 2008*, *supra* note.

[474] The Bayh-Dole Act allows universities and research centres that are publicly funded to patent inventions and negotiate them in their name. However, paragraph 203 of the Bayh-Dole Act predicts the 'march in rights' which refers to the right of the USA Federal Government (the Federal agency that funded the research) to request that an exclusive license related to a publicly funded invention to become non-exclusive. This request intends to guarantee that the invention is available to the public under reasonable terms. *Bayh-Dole Act: 35 U.S. Code Chapter 18 - Patent Rights in Inventions Made with Federal Assistance*, *supra* note 468; Lin et al, *supra* note 473.

[475] Lin et al, *supra* note 473; Sampat, *supra* note 469; So et al, "Is Bayh-Dole Good for Developing Countries?", *supra* note 380.

of successful university inventions have generated significant licensing revenue to balance the costs of IP protection, especially in developing and least-developed countries.[476]

University IP is not only contested in developing countries. Gold argues, for example, that "[t]o improve Canadian innovation, universities need to get out of the patent business."[477] He concludes that "universities are poor patent managers"[478] and notes that "university patenting is an example of a policy that was developed for the right reason but fails in practice."[479] Gold elaborates on his criticism of university patented by pointing to the time and money involved in obtaining and negotiating university IP and the delays in research and translation into products and services that this entails. Canadian university patents provide, overall, low benefit in Canada as the most valuable IP is transferred out of the country.[480] He argues for a return to open science principles.[481] Gold's points further show the importance of

[476] In this sense, see: Gold, *supra* note 410; Catherine McIntyre, "Universities earned just $75 million from IP in 2017, but spent $5.7 billion on R&D: Report", (29 April 2019), online: *The Logic* <https://thelogic.co/news/universities-earned-just-75-million-from-ip-in-2017-but-spent-5-7-billion-on-rd-report/>; Karima Bawa, "After Failing to Commercialize, Universities Learn to Set Ideas Free", (25 April 2017), online: *Cent Int Gov Innov* <https://www.cigionline.org/articles/after-failing-commercialize-universities-learn-set-ideas-free>; Renato Dagnino & Rogério Bezerra da Silva, "As patentes das universidades públicas" (2009) 5:3 Rev Econ Tecnol, online: <http://revistas.ufpr.br/ret/article/view/27147>; Rogério Bezerra da Silva & Renato Dagnino, "Universidades públicas brasileiras produzem mais patentes que empresas: isso deve ser comemorado?" (2009) 5:2 Rev Econ Tecnol, online: <https://revistas.ufpr.br/ret/article/view/27269>.

[477] Gold, *supra* note 410 at 1.

[478] He complements: "Evidence from as far back as the 1980s indicates that universities—while they have many strengths—are poor patent managers. For example, they are weak at identifying market needs; recognizing ideas that meet those needs; obtaining the right form of IP rights on the right things; and finding partners to build up the Canadian innovation ecosystem. It is not necessarily true that universities are any worse at IP management than most firms. The real issue is that universities suffer no adverse consequences for producing so little IP that stays in Canada. Firms face pressure to perform well in managing their IP. Those that do so badly usually go out of business, and those that are overly aggressive face regulations or adverse court decisions. Failed university technology transfer policies face no such fate." *Ibid* at 1–2.

[479] *Ibid* at 1.

[480] *Ibid*.

[481] The main costs mentioned by Gold are the delays in advancing research because of patent negotiations, the premature patenting of technologies in universities that makes difficult to find partners and create start-ups companies or engage in better licensing agreements, and the narrow and limited scope of licenses which also include tacit knowledge that could benefit other fields of research. He also shows that the goals of increasing revenue from licensing practices in universities in Canada have failed considering the substantial expenditures to afford the infrastructure that allows it. He highlights: "Despite the promise of tripling commercialization revenue, total commercialization revenues only rose from $52.5 million in 2001 to $67.4 million in 2009, or roughly 28 percent over the period. During the same period, however, expenditures almost doubled, from $28.5 million to $56.6 million. The increase in cost seems largely due to greater expenditures on personnel and the ling of more patent applications per protected invention. The result: net revenues actually fell during the period, from approximately $24 million to $10.7 million." *Ibid* at 4.

monitoring the effects of IP law, policy, and strategies and creating feedback mechanisms to assess their impact on science.

Years before Gold, Matthew Herder and Jocelyn Downie had alerted about the emphasis given to the commercialization of research in public institutions worldwide and specifically in Canada. They pointed out that Canadian public universities have been harnessing IP by holding patents, filing patents, engaging in PPPs, licensing agreements, creating spin-offs, and being driven by funding agencies and governmental policies. They called attention to the need for a large-scale debate about the benefits and harms of commercialization in publicly funded universities and the uncertainty surrounding its impacts on society and specific research areas.[482] Even though progress has happened since then in understanding the role of public universities and research centres and information, their conclusions still apply to different countries:

> A great deal of information is required to make informed decisions about whether this grand social experiment in the commercialization of research in public institutions is a good idea, and is being conducted well. If we never gather and gain access to the information about the realization of potential benefits and harms, we may never get from indeterminate to determinate and from uncertain to certain. There are still further problems with respect to weighing the potential harms and benefits of the commercialization of research in public institutions. There is both a lack of public debate about the relative value of the various potential harms and benefits, and a lack of independent expert advice in relation to public policy and practice regarding commercialization.[483]

I am not saying that academic and research communities should not devote efforts to solving society's problems and aim to commercialize their research. However, if these communities over-promote the idea that commercialization is the central element of their activities and that patents are *per se* good instruments to transfer knowledge to society, they might lose opportunities to innovate while regulating their intellectual assets. There must be room for diversification and experimentation of IP strategies in universities and research centres as critical elements to inform IP practices and policies at these CAS

[482] Jocelyn Downie & Matthew Herder, "Reflections on the Commercialization of Research Conducted in Public Institutions in Canada" (2007) 1:1 McGill J Law Health 23–44.
[483] *Ibid* at 43.

bottom layers. This may influence more extensive legislative and policy reforms once agents understand these systems better and further minimize uncertainty.

5.4. The Relationship between Law and Science

By regulating other CAS (innovation and biomedical innovation systems), IP systems are in constant coevolution and communication with their regulatory targets. These communications create connections of shared language, information flow, signal-boundary arrangements, niches, and methodologies. In summarizing the relationship between law and science, agents must remember that these systems may sit on two sides of the same coin in terms of how complex issues are solved:

> The need to participate in scientific research and development is universally acknowledged as essential for economic growth; less recognized, but no less necessary, is the need to learn how to critique the institutions and processes by which science and technology are regulated. While the first kind of capacity—the technical—is known to be unevenly distributed around the world, deficits in political and ethical capacity are less widely perceived.[484]

Evaluating science from the normative perspective offered by law allows us to identify and contest the norms and principles that guide science and scientific activities. The existence of a normative structure of science challenges the discourse that law and science will always have a dysfunctional relationship. Once both science and law have 'normative' structures, they become points of connection that enable the identification of commonalities and the development of shared signal-boundary arrangements between these two CAS.[485] How lawyers perceive science to happen and interact with scientists to understand it and create rules to facilitate its operation is an area of overlap and communication. For instance, the behavioural norm guiding scientists to share research materials is communicated by a lawyer through the clauses of an MTA. In a balanced relationship between law and science, these clauses might facilitate the

[484] Jasanoff, *supra* note 368 at 891.
[485] See Chapters One to Four to the discussion on concepts and ideas about how different CAS communicate and the normative structures of law and science.

scientific endeavour through effective processes and translate ethical principles followed by society and scientific communities.[486]

Seeing law and science as CAS allows a dynamic and non-linear approach to tracking the interactions between these systems and minimizing the effects of uncertainty.

5.4.1. Moving Forward in Understanding the Relationship between Law and Science

To better understand the relationship between law and science in developing countries, we need to build models that capture the complexity of that relationship. Here, I identify two elements that will be necessary to accomplish this:

(i) More empirical evidence—case studies, the effectiveness of various collaborations, quantitative evidence of the functioning of IP laws in different contexts, etc.—to ground our understanding of law, policies, and strategies concerning biomedical R&D in developing countries;

(ii) the development of participatory models of critiquing and improving IP systems.

The first factor—the use of empirical evidence to ground law and policy choices and understand how science (biomedical R&D) occurs—is connected to the lack of empirical research assessing the effects of IP protection in biomedical R&D, especially in developing countries. The impact of IP protection applies not only to final products but also to the entire R&D process, including how this protection influences the organization of R&D (for example, access to data, research material, and tools). To better evaluate IP and biomedical innovation systems and propose effective strategies that work in

[486] Migle Laukyte, *Three factor model : some ideas about the relationship between law, science and technology* (2014); Micah L Berman & Annice E Kim, "Bridging the Gap between Science and Law: The Example of Tobacco Regulatory Science" (2015) 43:0 1 J Law Med Ethics J Am Soc Law Med Ethics 95–98; Jasanoff, *supra* note 368; Sheila Jasanoff, *The Fifth Branch: Science Advisers as Policymakers* (Cambridge, Mass: Harvard University Press, 1998).

developing countries, it is crucial to have empirical data suited to the circumstances of developing countries.[487]

Second, too often, IP experts—particularly those from developed countries—control discussions on the role of IP in biomedical innovation systems and the details of IP laws to enable regulated systems operation and achieve goals. By deferring to these experts, developing country governments adopt laws that do not suit either the scientific or normative environments within their countries. As a result of power relations and politics among different agents and institutions, too little attention is paid to local processes. To correct this, developing countries need to develop informed, participatory, and transparent processes to bring a broader range of voices together in determining future laws and policies.[488]

The study of decision-making processes that guide agents' behaviours and expectations within systems may demonstrate the strengths and weaknesses of these systems and explain why they have or have not achieved their goals. The position of agents within CAS—that is, whether one is conducting research, filing patent applications or making policy—influences the construction of biomedical innovation ecosystems and how agents engage with the system.

On the one hand, agents at the bottom of the system engage in activities closely related to science (such as carrying out research) and thus have the most in-depth technical knowledge and understanding of science. These activities tend to involve fewer agents, and their relationship to IP is to implement the institutional rules of their organization narrowly to those activities. Given the speed at which scientists undertake R&D, experimentation in regulation could be more easily implemented at the bottom of the

[487] Julia Lane, "Let's make science metrics more scientific" (2010) 464:7288 Nature 488–489 at 464, 488–489; Morin, Daley & Gold, "Having Faith in IP", *supra* note 51; Benjamin & Rai, "Fixing Innovation Policy", *supra* note 37; Burk & Lemley, *supra* note 256; *Assembling the pharmaceutical R&D puzzle for needs in the developing world: An assessment of new and proposed delinking initiatives aimed at encouraging R&D into neglected and tropical diseases and specific Type II diseases*, by Mario Perez Pugatch, Rachel Chu & David Torstensson (Pugatch Consilium 2015, 2012).
[488] David Kennedy, *A World of Struggle: How Power, Law, and Expertise Shape Global Political Economy* (Princeton University Press, 2016).

system. Bottom-up approaches to regulation may be more effective for testing and embedding new models for regulating R&D that would, perhaps, lead to reforms of the entire system over the longer term.

On the other hand, agents at the top of the system engage in more abstract thinking about IP and biomedical innovation law and policy. Even though the number of law and policymakers may not exceed the number of scientists, academics, research institutions and university personnel who deal with R&D, the number of interests that law and policymakers must balance is significant; It goes beyond the research interests of expert communities. These agents situated at the top layers must translate abstract ideas that guide IP and biomedical innovation systems into principles and general objectives for their organizations. Changes at the top layers are necessarily subject to a longer and more complex implementation process considering they are subject to a greater diversity of agents' expectations and interests than are those instituted at the bottom layers of these systems.

Agent-centred approaches recognize that there are no 'one size fits all' approaches to IP and biomedical innovation systems. This is because agent-centred analysis not only individualizes agents but also places them in the context in which they operate, providing a clearer understanding of the roles of each agent. Although, developing countries—like any country—look to other countries' experiences for inspiration in implementing their IP and biomedical innovation systems, just as researchers investigate other initiatives and models in developing their own IP strategies. Agent-centred approaches can enable simulations of multiple scenarios to enlighten the analysis of these systems. These scenarios can provide the basis for future empirical legal research.[489]

[489] Some ideas of these scenarios are: (i) a scenario in which closedness (competition or over-protection of IP assets) is the absolute rule. None cooperate; (ii) a scenario in which openness is the absolute rule. Openness, however, does not mean the end of competition; (iii) different agents, such as academics and scientists, will compete and cooperate to achieve their goals and fulfill their expectations towards these systems. For instance, they must compete to be the first to publish, to be recognized academically, to get funds. Openness may shape the degree in which competition and cooperation happen, or how they take place; (iv) a scenario in which you have majority (more than 50%) of scientists competing and few of them cooperating; (v) a scenario in which you have majority (more than 50%) of scientists cooperating and few of them competing; (vi) a scenario where you have diverse variations of percentages of people competing versus people cooperating.

Revisiting the interaction and coevolution of complex adaptive IP and biomedical innovation systems and reflecting upon ways to better understand them may be exhausting. We can break down the analysis into smaller steps, such as showcasing new, open, and collaborative biomedical R&D models and their IP strategies. These projects function as contained environments in which it is less risky and time-consuming to experiment with new ideas. Even though one should not extrapolate the findings of one project to another, successful initiatives may inspire the next project. If a project is evaluated as successful, the likelihood of other agents replicating it is higher.

Clarifying the relationship between law and science is a long-term and continuous reassessment project. This is because of the need to consider agent behaviours and changing expectations—agents also evolve in their knowledge about interacting systems and change roles and their degree of influence towards other agents over time and scope. It is a long-term commitment to evaluating the principles that guide the interaction and coevolution of complex adaptive IP and biomedical innovation systems. It is also a commitment to observe if other principles that govern these systems emerge, considering that CAS and their agents are in constant change and the rules by which they operate.

The elements listed above can inspire other agents to develop frameworks of thinking, new methodologies, and computer models to evaluate CAS interaction. Multidisciplinary research is essential to develop these studies. Empirical research is required to assess the impact of IP protection, policies, practices, and strategies in biomedical R&D and, consequently, access to knowledge and innovation. A more detailed assessment of expert communities' understanding of IP and biomedical innovation systems and the degree to which they appreciate the nuanced interactions and rules guiding their behaviour is needed, especially in developing countries.

For instance, the lack or insufficiency of empirical studies makes it impossible to tell if the tragedy of the anticommons hypothesis would or not happen in developing countries and under which

circumstances. Mapping different agents, their roles, and their degree of influence in the various networks they participate in and different biomedical R&D models in various developing countries are necessary steps for multisystemic evaluations.[490] To understand how these systems operate in these countries, there is a need to deepen and refine the information concerning the interaction and evolution of IP and biomedical innovation systems. Subsequent chapters bring specific evaluations and examples about these countries and their agents.

There are no perfect models or ideal IP practices, policies, and strategies; all depend on the goals agents seek to achieve and their specific needs. The suggested approach allows the tailoring of particular projects and acknowledges uncertainty. Therefore, applying CAS theory and concepts and agent-based evaluations to these questions adds elements that are not generally present in legal analysis, especially considering the organizational features that lead to the emergence of law and its interaction with other systems. These organizational features do not depend on the content of law but might influence it in the future. Applying CAS theory may lead to legal innovation.

Finally, I have outlined part of the ecosystem in which multiple IP and biomedical innovation systems interconnect, interact, and coevolve. Even though I assume that the future of biomedical R&D should rely on global collaboration to address access to knowledge and innovation issues, the current scene is formed by multiple national systems, distributed through layers of a global system connected by agents' interactions. This is also why the concept and creation of niches in CAS are so important.

The problem—or the solution, if one considers diversity in CAS to be an asset—is that multiple layers of regulation and systems indicate the existence of various goals and strategies to achieve solutions. Competition is not negative *per se* but to generate positive outcomes, it must be carefully managed. Agents

[490] Especially evaluating the role of developing countries' governments in coordinating and facilitating different agents' interactions and goals also requires further examination to achieve the best results from these systems' operation. However, it is not the scope of this dissertation to do so.

should be able to identify when it is best to compete or cooperate, and when conflict happens, the public interest may also play its role. This is why guaranteeing the flow and access to information in CAS is crucial to improving the efficiency of these systems. Otherwise, repetition of efforts and commitment to non-fully informed strategies will slow down or constrain the realization of agents' full potential and objectives in CAS, among them advancing science.

The following chapters deepen the description of this complex ecosystem by analyzing agents in CAS, narrow down the evaluation to Brazil, and generally provide more examples of the presence and emergence of the idea of openness in these systems.

CHAPTER SIX—THE ROLE OF AGENTS IN COMPLEX ADAPTIVE INTELLECTUAL PROPERTY AND BIOMEDICAL INNOVATION SYSTEMS

6.1. Overview: The Diversity of Agents and Their Dynamic Roles in Systems' Design and Reform

In this chapter, I change the focus from agents operating within the biomedical innovation system to those who study it, manage it, and change it. This chapter provides (i) a brief theoretical reflection on these agents' role (especially the university-industry-government relationship); (ii) an examination of how these agents coordinate action to improve the operations of these systems, and; (iii) a case study of how these agents operate within a developing country—Brazil. This third section aims to illustrate the amount of technical knowledge and information required from legal agents that set up IP policies, practices, and strategies in universities and research centres. I conclude by highlighting the need to coordinate efforts and strategies among expert communities and how their capacity to drive significant changes has so far been underexplored.

6.1.1. Initial Reflections on the Role of Legal Agents and Their Interaction with Other Agents

Those responsible for developing and implementing laws and policies with respect to biomedical RD&I have a particular burden to understanding not only the complexities of science, but of how agents within that system operate. They need to map, monitor and interpret what is happening within the relevant CAS to then engage successfully with those systems. This allows these legal agents to focus not only on applying and analyzing legal rules but on evaluating how these rules interact in reality. This is a dynamic task in which legal agents need to look at agents within the system to develop tools that enable interaction, learning, and coevolution.

Hadfield stresses a critical issue while examining the increase of complexity in a networked economy where everything (from products, parts, and services to information) crosses borders. She points

out that, in these settings, there is an increase in complexity in the legal infrastructure and the need to understand several different legal orders around the world. Legal agents critically require, she states, 'expert navigational judgement' that surpasses the "simple increase in the volume of legal knowledge."[491]

Navigational judgment allows legal experts to effectively interact with other agents in multiple systems. It further enables these experts to assemble the pieces of complex relationships and projects (such as biomedical R&D initiatives) while considering the big picture and envisioning the effects that applying a given regulation may have.[492] Of course, no agent has complete knowledge and perfect information about what happens within different CAS. Uncertainty will always play a role in these settings.[493] However, developing expert navigational judgement assists in harnessing complexity in these systems. One manner of doing so is to improve the relationship between law and science by promoting dialogue and cooperation between legal and non-legal agents in the co-design and reform of CAS.

Legal and non-legal agents' beliefs about the justification behind IP systems and the effects of IPRs protection on access and innovation profoundly influence their decision-making processes. These beliefs vary considerably and embed preconceptions and misunderstandings of how the IP and biomedical R&D system operate in reality. These preconceptions influence agent strategies and interactions and affect the adoption of new approaches to biomedical innovation. Diversity of ideas and shifting and amplifying agents' knowledge of these issues would have an impact on access to knowledge and innovation outcomes.

IP and biomedical innovation systems engage a diversity of agents who respond to stimuli from the environment and other systems differently. Incentivizing agents to become more aware of their multiple roles, collaboration, and diversity is essential to improve the biomedical RD&I. Governments

[491] See: Hadfield, *supra* note 2 at 145–146.
[492] See: *Ibid*.
[493] See, especially Hadfield's comment about the fact that information is an extremely valuable asset which is hard to valuate and contract, given the asymmetric information among agents interacting upon it. This fact increases the importance of designing systems that are transparent, open, peer-reviewed, and enabled by sharing platforms. *Ibid* at 138.

can do so in three ways. First, they can support empirical studies about IP and draw on them to promote informed and empirically based debates about IPRs among agents (legal and non-legal). Second, governments can encourage and improve IP literacy and the use of patent applications as sources of information. Third, they can promote continuous assessments of IP strategies and their evolution in light of emerging R&D models. An agent-centre approach will also encourage reflection on creating mechanisms to solve complex problems.

6.2. Theoretical Insights about the Triple Helix and the Role of Expert Communities

The fact of multiple agents performing different roles in a CAS points to the difficulty in balancing interests in these systems and creating conditions for agents to work together towards common goals. Shifting behaviour in academia shows that researchers started leaving the 'Ivory Tower' long ago.[494] In doing so, researchers more actively engage with other agents and influence decision-making processes that shape society. Agents in universities and research centres have thus been redefining their role in society and rethinking their institutional missions and values while creating new and dynamic niches for interaction. The role these agents (individually and collectively) choose to have integrates these systems' complexity and the routes for their design and reform.

In the 1990s, Loet Leydesdorff and Henry Etzkowitz coined the term Triple Helix to describe university-industry-government relations.[495] They reported the shared interests of various nations in advancing knowledge-based economic and social development. Within the Triple Helix, agents span across institutional boundaries in order to share knowledge with supporting infrastructure and

[494] The "ivory tower" represents an idea or metaphor in which academics and researchers are distant from society and its problems while caught up in their own intellectual pursuits. Mowery et al, *supra* note 380; Henry Etzkowitz et al, "The future of the university and the university of the future: evolution of ivory tower to entrepreneurial paradigm" (2000) 29:2 Res Policy 313–330.

[495] Loet Leydesdorff & Henry Etzkowitz, "Emergence of a Triple Helix of university—industry—government relations" (1996) 23:5 Sci Public Policy 279–286 at 279.

organizational structures. The model and the interactions among agents described by Leydesdorff and Etzkowitz fit the description of a CAS through which one can evaluate these global systems' evolution, enabling knowledge sharing. The authors identify three specific dynamics in these complex systems: "the economic dynamics of the market; the internal dynamics of knowledge production; and governance of the interface at different levels."[496] These dynamics represent and support interaction between markets and science, the functional differentiation between them, the separations between private and public control of structures and relationships, and the place of knowledge within them. They explain:

> The Triple Helix model takes the traditional forms of institutional differentiation among universities, industries, and government as its starting point. The evolutionary perspective adds to this historical configuration the notion that human carriers reflexively reshape these institutions. The model thus takes account of the expanding role of the knowledge sector in relation to the political and economic infrastructure of the larger society.[497]

Leydesdorff and Etzkowitz proposed this model to describe the evolution of relationships among agents within these systems and the mechanism by which knowledge creation evolved. They assert that relationships become more unstable in the Triple Helix model, considering the three sectors involved. How these three sectors interact is not coordinated or linear, increasing complexity in these systems. Even when only two helices interact, the third's presence may influence the other two's behaviour.[498] According to the authors, the helices communicate and engage in selecting and combining multiple possible interactions and behaviours among agents. Even though these systems tend to perform a recursive

[496] *Ibid* at 280.
[497] *Ibid*.
[498] They further explain: "While a co-evolution or a double helix can be stabilized relatively easily (for example, in a biological system), a complex and potentially unstable system emerges when three dynamics interact. A social system is, by definition, in transition, since it is distributed. The distribution contains an uncertainty that provides reflexive actors with emerging options. Under certain circumstances, such as the exigencies of war, governments may be able to harmonize and lead the interactions. In a liberal economy, however, integration occurs ex post and uncoordinated, that is, on the basis of selections by the (sub-) systems upon each other." *Ibid* at 281.

selection, they often recreate themselves and avoid disintegration by organizing and selecting new combinations of behaviours and interactions over time.[499]

These aspects of the Triple Helix highlight how the connections between the helices and the communicative competencies of different agents facilitate and promote each helix's interactions and coevolution.[500] Leydesdorff and Etzkowitz clarify how important it is to understand the "communication structures and culturally encoded messages that are sometimes difficult for outsiders to interpret" used by different institutions and agents to promote "cross-institutional conversations."[501]

Moreover, in the Triple Helix, agents are at an equal level of interaction, with no subordination. Here again, agent expectations and impressions about the interacting systems and agents are critical. The work of Leydesdorff and Etzkowitz describes translation within the Triple Helix and adaptive mechanisms used by agents that result in cross-institutional conversations, corroborating my arguments about the importance of understanding communication between and within CAS and among agents covered in Chapter One.[502]

It is also interesting to note how the scholarship of Leydesdorff and Etzkowitz has contributed to advancing discussions about the emergence of university entrepreneurs. They point out the redefinition of

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[499] "In summary, market mechanisms, technological trajectories, and interactions among reflexive actors in negotiations shape the emerging regime by generating a variety of niches. For example, a new regional innovation environment, such as an industrial district cooperating with universities or other knowledge producing organizations with local government, can be generated with an impact at the network level. The regime at the network level, however, can no longer be localized; it can be considered as the selector for the distribution of niches, and it operates by reproducing somewhat different distributions. Wherever and whenever the various dynamics begin to resonate, flows of energy, resources, and human capital can be absorbed. While a regime is expected to develop on the edge of chaos, niches may crystallize at unexpected places for prolonged periods. Within the niches a reproduction of the differentiation is likely, but potentially in a different order." *Ibid* at 281–282.

[500] "The study of the Triple Helix requires a model that complements the institutional perspective with a focus on interactive operations at the system level. The institutional frameworks can be considered as the fingerprints of communication structures that have been functional hitherto. All the actors and agencies involved are reflexive, that is, recurrently adjusting their positions given institutional constraints and opportunities." *Ibid* at 282.

[501] *Ibid*.

[502] They affirm: "Translations between institutional codes, such as from scientific findings into stock market offerings, are highly specific. Some academic scientists have learned to speak the language of business, while at the same time learning not to divulge too much of the particulars of their science to their industrial interlocutors. Similarly, intellectual property attorneys, even those without a science degree, have acquired a credible facility with scientific jargon in their particular fields. Although many of these people remain in their respective spheres, they have mastered the art of cross-institutional conversations." *Ibid*.

academics and researchers' role in innovation, reflect on their place in these systems, and inquire how knowledge is produced and by whom over time.[503] Their reflection comes with the need to reconsider how science and innovation occur and rethink traditional categories and static classifications, especially those regarding agents' roles in these systems, as presented in previous chapters, and the rise of entrepreneurship among researchers. These entrepreneurial researchers have advanced the scientific enterprise and innovated while rethinking and creating news models for its realization. In this sense, the behavioural and organizational shifts taking place in science as new technologies and fields appear or grow in importance, such as biotechnology, must also be considered while critiquing or reforming law and policy.

Agents perform diverse and multiple roles that depend on the context, the project or activity they engage in each moment, and the degree of influence they have on other agents—as previously discussed. They shift between being decision-makers, influencers, and rule followers. This dynamic of roles, interactions with other agents, and behaviours influence how these agents perceive a system, the information they have about it, and their biases in decision-making processes. The Triple Helix concept shows that there is no prime agent in complex adaptive IP and biomedical innovation systems and that no agent can address complexity alone. From researchers to the private sector, each agent has a role in constructing society. Acknowledging agent's multiple characteristics, roles, and goals may assist in improving CAS operation.

The figure below is the "WIPO's Roadmap on IP Strategies to Academic Institutions."[504] It lists some aspects that these institutions should consider while developing IP strategies and the routes they

[503] Leydesdorff & Etzkowitz, *supra* note 495.
[504] World Intellectual Property Organization, "Upcoming IP Toolkit for Academic Institutions", online: *World Intellect Prop Organ* <https://www.wipo.int/about-ip/en/universities_research/news/2017/news_0001.html>.

should follow while connecting those strategies with the economy and society.[505] The Roadmap illustrates some of the requirements and complexity of setting up an IP strategy for different academic and research activities. It also highlights the amount of technical and legal knowledge needed to regulate institutional activities and define IP strategies.

At the same time, the WIPO Roadmap portrays a linear and traditional view of an IP strategy that misses the nuance I have discussed throughout this dissertation. As mentioned in previous chapters, this linear and traditional view is not likely to lead agents' critical thinking about the routes they choose to protect (or not) intangible assets or adopt alternative views of IPRs and new R&D models.

[505] WIPO has launched several resources to assist academic institutions in drafting their IP strategies and policies and to enable capacity building in knowledge transfer as part of its mandate. Some of these resources include model agreements like MTAs, contract research agreements, license agreements, as well as guidelines for their negotiations. These documents are only available in English though. World Intellectual Property Organization, "New IP Toolkit for Academic Institutions", (20 April 2018), online: *World Intellect Prop Organ* <https://www.wipo.int/about-ip/en/universities_research/news/2018/news_0001.html>; World Intellectual Property Organization, "Database of Intellectual Property Policies from Universities and Research Institutions", online: *World Intellect Prop Organ* <https://www.wipo.int/about-ip/en/universities_research/ip_policies/search.jsp?institution_id=2321&focus_id=&type_id=&territory_id=&language_code=>; World Intellectual Property Organization, "Frequently Asked Questions: IP Policies for Universities and Research Institutions", online: *World Intellect Prop Organ* <https://www.wipo.int/about-ip/en/universities_research/ip_policies/faqs/index.html>; World Intellectual Property Organization, "Frequently Asked Questions: Knowledge Transfer for Universities and Research Institutions", online: *World Intellect Prop Organ* <https://www.wipo.int/about-ip/en/universities_research/ip_knowledgetransfer/faqs/index.html>; World Intellectual Property Organization, "Knowledge Transfer for Universities", online: *World Intellect Prop Organ* <https://www.wipo.int/about-ip/en/universities_research/ip_knowledgetransfer/index.html>.

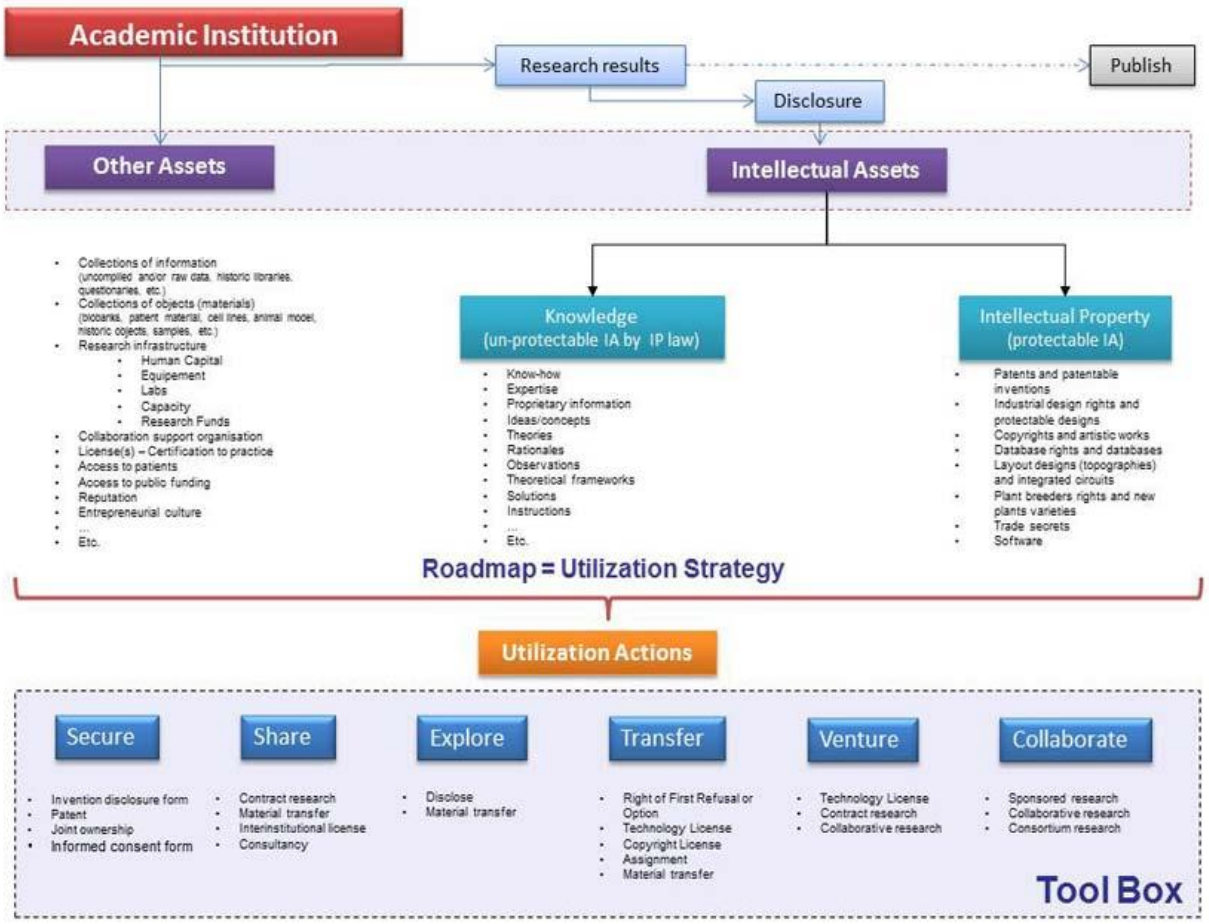

Figure 7: *WIPO. IP Toolkit for Academic Institutions—Connecting Academic Research with Economy and Society. IP Commercialization Roadmap.*[506]

To provide a more realistic view of innovation, the WIPO Roadmap needs to be modified to include evaluations of strategies that enable agents to pay attention to more implicit elements of IP strategies, such as cooperation versus competition, openness versus closedness, and the range of options in between these ideas. If these evaluations are presently missing, agents should rethink how they can integrate them into their discussions about the IP systems. Some of the documents included within WIPO's technical assistance on IP Strategies to Academic Institutions mention open access, open-source (including creative commons licenses and open license), open data, open educational resources (OER),

[506] World Intellectual Property Organization, *supra* note 504.

and open innovation, but only in a limited manner. On the positive side, they do discuss copyrights and software, knowledge dissemination arising from intangible assets, the university-industry relationship, IP and the public domain, and the need to reconcile aspects related to openness and secrecy (trade secrets, publication, and patent strategy).[507] However, they do not provide any detailed or critical assessment of openness or expand this debate to important IPRs categories like patents.

WIPO provides capacity building and technical assistance, especially in legislative and policymaking activities, in developing and least-developed countries, but these fail to capture the complexity of biomedical RD&I. Although these documents are helpful and give guidance for those starting to work with IPRs, they are far from tailored to local needs and do not empower local agents. These documents also fail to address the public goods aspect of the IP system or the public interest more generally.

6.3. Diversity and Coordination of Actions among Agents to Increment Systems' Design and Reform

The case studies below help to illustrate how agents can better understand, study and reform the biomedical RD&I system by using coordination and diversity within CAS.

[507] See: *IP Policy Writers' Checklist: A Mechanism for Kick-starting the Policy Drafting Process*, by Lien Verbauwhede Koglin, WIPO IP Toolkit for Academic and Research Institutions (Geneva, Switzerland: World Intellectual Property Organization (WIPO), 2019) at 08, 11; *Academic Intellectual Assets Map*, WIPO IP Toolkit for Academic and Research Institutions – Connecting Academic Research with the Economy and Society (Geneva, Switzerland: World Intellectual Property Organization (WIPO), 2018) at 17–20; *Guidelines for Customization of the WIPO Intellectual Property Policy Template for Universities and Research Institutions*, by Lien Verbauwhede Koglin, Kerry Faul & Richard Cahoon, WIPO IP Toolkit for Academic and Research Institutions (Geneva, Switzerland: World Intellectual Property Organization (WIPO), 2018) at 04, 47–51, 89; *WIPO Intellectual Property Policy Template for Universities and Research Institutions*, by Lien Verbauwhede Koglin et al (Geneva, Switzerland: World Intellectual Property Organization (WIPO), 2019) at 04, 07, 12–13.

6.3.1. Advocacy and Capacity Building at the Bottom-Layers of Complex Adaptive Intellectual Property and Biomedical Innovation Systems

Two examples illustrate the discussions about coordination, advocacy, and capacity-building strategies of the communities of experts that influence CAS structure and reform. First, I present the case of Universities Allied for Essential Medicines (UAEM). Second, I exemplify how academic and research communities have moved toward greater levels of openness and collaboration in science.

6.3.1.1. Universities Allied for Essential Medicines

Universities Allied for Essential Medicines (UAEM) is an example of coordinated action among students and academic and research communities concerning the role of publicly funded universities and research centres to ensure access to health technologies. UAEM interacts with other agents and tries to influence and change IP and biomedical innovation systems while simultaneously participating in the community of experts and civil society.[508]

In 2001, an essential medicine for HIV/Aids, Stavudine or D4T, was developed by Yale University researchers with public funds and licensed exclusively to the pharmaceutical firm, Bristol-Myers Squibb (BMS). D4T was a critical HIV/Aids treatment but remained unaffordable in Sub-Saharan Africa. At that time, Doctors Without Borders (Médecins Sans Frontières—MSF) provided humanitarian aid in South Africa and engaged in negotiations for a price reduction with BMS. However, negotiations over the price of D4T between MSF and BMS were unsuccessful, resulting in an international campaign led by Yale Law students and MSF to challenge the terms on which the original Yale license to the pharmaceutical company was issued. This case brought to light the issues of publicly funded research and the role of

[508] Several of the considerations herein are a result of my personal experience and observation of UAEM's work through the years. I was the first executive director of UAEM in Brazil from 2010 to 2012 and continue to collaborate with this institution in Brazil and abroad.

universities and research institutions in access to health technologies while setting their IP practices and policies.[509]

The joint law student and MSF campaign and subsequent negotiations with Yale and BMS led to two major results. First, BMS authorized a generic company in Sub-Saharan Africa to produce D4T. This authorization led to an overall reduction in the price of not only D4T but other HIV medicines controlled by a variety of pharmaceutical companies in the international market, especially in developing and least-developed countries. Pharmaceutical companies started to differentially price medicines based on individual countries' economic power and needs.[510] Second, in 2001, the students founded an organization to critically discuss the role of universities in access to medicines: UAEM.[511]

UAEM's activism and campaigns and its criticism around publicly funded research and the IP practices and policies in universities and research institutions—especially licensing practices—have led to change. Three main pillars guide UAEM's activities: access, innovation, and empowerment (student activism). Its vision comes from the belief that "[u]niversities and publicly funded research institutions will be part of the solution to the access to medicines crisis by promoting medical innovation in the public interest and ensuring that all people regardless of income have access to medicines and other health-related technologies."[512]

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[509] See, initially: Universities Allied for Essential Medicines, "UAEM History", online: *Univ Allied Essent Med* <https://www.uaem.org/who-we-are/history/>; Donald G McNeil Jr, "Yale Pressed to Help Cut Drug Costs in Africa", *N Y Times* (12 March 2001), online: <https://www.nytimes.com/2001/03/12/world/yale-pressed-to-help-cut-drug-costs-in-africa.html>; Rai & Eisenberg, *supra* note 363; Piper, *supra* note 37.

[510] For initial discussions about differential prices of medicines and monopoly power and the distortions and impacts of differential prices on access to health technologies in the short and long term, see: Polido, Salomão Filho & Basso, "Propriedade intelectual e preços diferenciados de medicamentos essenciais", *supra* note 35; Scherer, *supra* note 399.

[511] "Since this initial victory, UAEM has grown into a worldwide student organization with chapters at over 100 research universities in more than 20 countries, and a membership which includes students of medicine, science, public health, economics, and many other areas. The focus of the organization has expanded from only asking how universities can best license their innovations to promote global access, to also asking how universities can best direct and measure their research to have the greatest social impact worldwide, and promoting these ideals at the national and international levels. We work continuously to raise general awareness of these issues, and conduct independent research about them to empower our fellow students to tackle these challenges." Universities Allied for Essential Medicines, *supra* note 509.

[512] Universities Allied for Essential Medicines, "UAEM-Who We Are", online: *Univ Allied Essent Med* <https://www.uaem.org/who-we-are/>.

UAEM projects and activism have attracted students and partners worldwide to a critical debate about access to health technologies, student activism, innovation, empowerment, and the role of universities and research centres in publicly funded research. Among several proposals, UAEM suggested a global access license framework (GALF) for health technologies developed by research institutions using public funds.[513]

In its nineteen years, UAEM has become an example of knowledge translation and collaboration among different agents, mostly academic and research communities and civil society. The engagement of UAEM members and their dialogue with TTOs in various institutions also show how new communication forms arise in CAS. In training and empowering students from multiple institutions and countries, UAEM is developing numerous niches within the biomedical innovation ecosystems that may influence CAS design and reform.

Considering the above, the organizational framework of UAEM relates to several points previously raised about CAS and the interaction and coevolution of IP and biomedical innovation systems. The high degree of diversity and mobility of agents in UAEM's framework allows for setting strategies in the short and long terms. A student who was once a rule-follower or influencer may become during her/his career a decision-maker.[514] This variety of roles and areas of specialization and institutional richness at UAEM increase diversity within the systems and the likelihood of agents' emergent behaviours. The organizational framework of UAEM and the absence of central control further lead to coordination

[513] In Canada, three universities had adopted UAEM's Global Access Licensing Principles to guide their research activities; the most recent case was McGill University in May 2019. Universities Allied for Essential Medicines, "UAEM-Global Access Licensing Framework", online: *Univ Allied Essent Med* <https://www.uaem.org/our-work/global-access-licensing-framework/>; Meaghan Thurston, "Affordable, life-saving medicines for all: McGill adopts Global Access Licensing Principles for research conducted on campus", (23 May 2019), online: *McGill Newsroom-Media Relat Off* <https://www.mcgill.ca/newsroom/channels/news/affordable-life-saving-medicines-all-mcgill-adopts-global-access-licensing-principles-research-297381>.

[514] An example of this mobility is Amy Kapczynski who was in 2001 one of the student leaders at the D4T case and now is a Professor at Yale Law School. Previously, she taught at University of California Berkeley School of Law.

between the students and increase the impact of their actions. UAEM is, in this sense, an example of a bottom-up, decentralized, and coordinated approach to systems' design and reform.[515]

6.3.1.2. Expert Communities' Declarations related to Openness and Collaboration

One can identify coordination of actions among expert communities when analyzing the declarations and principles that guide their R&D activities. Groups of academics and researchers mainly issue these documents, sometimes supported by their affiliated institutions. All these documents highlight the importance of openness and collaboration for science. Although most of the documents are soft law, they work as communication tools informing agent expectations and behaviours and assisting in coordinating efforts that might lead to CAS reform.

Several declarations, statements, and sets of principles demonstrate a trend towards openness in how agents engage in biomedical R&D, as these instruments promote public awareness of the importance of sharing data, information, and knowledge. They also point to the need for and importance of creating infrastructures and procedures that guarantee access, sharing, and dissemination of the fruits of the scientific endeavour and the importance of preserving the public domain. One example is the 'Bermuda Principles' (1996) which states the fast release of primary genomic sequences in the public domain, considering the completion of the Human Genome Project (HGP). These principles call for the coordination of the global scientific community's activities in large-scale sequencing centres.[516] A second

[515] In the past few years, there has been an increasing participation of UAEM in several international debates (new R&D models, transparency, and de-linkage), forums (WHO) and collaboration with other institutions (MSF, KEI, and DNDi). This may show a tendency to a combined strategy towards bottom-up and top-down approaches.

[516] The Principles were signed by 50 scientists from all around the globe in the *First International Strategy Meeting on Human Genome Sequencing* (Bermuda, 25-28 February 1996) it. In 1997, during the *Second International Strategy Meeting on Human Genome Sequencing* (Bermuda, 27th February-March 2nd, 1997), the scientists reaffirmed the Principles and further elaborated in sequence quality standards, submissions, and annotations. For more information about them, see: "Bermuda Sequence Policies Archive", online: *Hum Genome Proj Inf Arch 1990-2003* <https://web.ornl.gov/sci/techresources/Human_Genome/research/bermuda.shtml>; "The Bermuda Principles", online: *Bermuda Princ* <https://www.bermudaprinciples.org>.

example is the 'Durham Statement on Open Access to Legal Scholarship' (2009) from several US university librarians and legal scholars[517] about open access to legal scholarship and information.

A third example is that the National Institutes of Health (NIH) Public Access Policy (2004) established that all manuscripts published by NIH-funded investigators must be made publicly available no later than 12 months after the official publication date.[518] These are three examples of concerted actions within expert communities that support cooperation and openness. One can view these statements as science informing legal agents about science's working premises. They may further inspire law and policymaking processes and universities' and research centres' IP practices, policies, and strategies and influence other agents' behaviours towards openness and collaboration—including within the private sector.[519]

[517] The USA universities that signed the "Durham Statement on Open Access to Legal Scholarship" are University of Chicago, Columbia University, Cornell University, Duke University, Georgetown University, Harvard University, New York University, Northwestern University, the University of Pennsylvania, Stanford University, the University of Texas, and Yale University.
[518] National Institutes of Health (NIH), "NIH Public Access Policy Details", online: <https://publicaccess.nih.gov/policy.htm>.
[519] Other examples of coordination among agents and bottom-up approaches that have influenced, and reshaped complex adaptive IP and biomedical innovation systems are open and new biomedical RD&I models emerging from universities and research institutes, as well as collaborative networks within these institutions. Chapter Seven briefly presents some of these initiatives while theoretically discussing the emergence of openness in law and science.

6.4. Regulating Knowledge at the Bottom-Layers of the Biomedical Innovation System: The Brazilian Case[520]

This section provides an overview of the complexity of law, public policies, and institutions applied to the regulation of intangible assets generated by biomedical R&D in one jurisdiction: Brazil.[521] It generally describes the state of biomedical R&D and gives some examples of the Brazilian leading public university's IP internal regulation and organizational framework: the University of Sao Paulo (USP).[522] The goal in doing so is twofold. First, I aim to illustrate the quantity of information and knowledge that agents within this system need to navigate through legal, policy, and institutional environments. Second, I will reflect on how the diversity of agents, regulations, and biomedical R&D models may enable

[520] Brazil has encountered significant problems in the past few years (especially, from 2015 to now), mainly related with the diminishment of investments in S&T, education, and public health, as well as the dismantling of the infrastructure of that support these systems. For brief information about it, see: Elida Oliveira, "Panorama da ciência no Brasil é 'assustador, ameaçador e pode se tornar irreversível', diz cientista", *G1 Ciênc E Saúde* (11 February 2020), online: <https://g1.globo.com/ciencia-e-saude/noticia/2020/02/11/panorama-da-ciencia-no-brasil-e-assustador-ameacador-e-pode-se-tornar-irreversivel-diz-cientista.ghtml>; Agência FAPESP, "Crise na ciência não se deve apenas à falta de recursos, avaliam cientistas" *Agência FAPESP* (7 February 2018), online: <https://agencia.fapesp.br/crise-na-ciencia-nao-se-deve-apenas-a-falta-de-recursos-avaliam-cientistas/27103/>; Vivian Costa, "Pandemia ressalta necessidade de investimento em educação, saúde e CT&I – SBPC", (11 May 2020), online: *J Ciênc* <http://portal.sbpcnet.org.br/noticias/pandemia-ressalta-necessidade-de-investimento-em-educacao-saude-e-cti/>; Estado de Minas, "Bolsonaro aumenta gastos com Defesa e diminui com Saúde e Educação", *Estado Minas Econ* (31 January 2020), online: <https://www.em.com.br/app/noticia/economia/2020/01/31/internas_economia,1118536/bolsonaro-aumenta-gastos-com-defesa-e-diminui-com-saude-e-educacao.shtml>.

[521] Brazil is the 5th most populous country in the world with 209.5 million people (2018). It is the largest country in Latin America in terms of geography and demography, with a highly miscegenated population (the three main ethnicities are white European, black African, and local indigenous population). It is made up of five regions that encompass twenty-six Provinces and one Federal District. Economically speaking, it is an emerging economy and one of the BRICS countries (Brazil, Russia, India, China, and South Africa). Brazil is also a part of Mercosul (Mercado Comum do Sul / Southern Common Market/ Brazil, Argentina, Uruguay, Paraguay, and Venezuela are Member-States and Bolivia, Chile, Peru, Colombia, and Ecuador are Associated Member-States) and the 58th largest economy in terms of global economic competitiveness. It is classified as an upper-middle-income economy (World Bank) or a developing economy (UN). República Federativa do Brasil, "Página Inicial — Governo do Brasil", online: *Gov Bras* <http://www.brasil.gov.br/>; República Federativa do Brasil, "Página brasileira do MERCOSUL", online: *MERCOSUL* <http://www.mercosul.gov.br/>; The World Bank, "World Bank Country and Lending Groups – World Bank Data Help Desk", online: *World Bank* <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519>; "United Nations Statistics Division- Standard Country and Area Codes Classifications (M49)", online: <http://unstats.un.org/unsd/methods/m49/m49regin.htm#developed>.

[522] Universidade de São Paulo (USP), "Institutional – USP – Universidade de São Paulo", online: <https://www6.usp.br/english/institutional/>.

universities and research centres to fulfill their missions.[523] This diversity creates multiple niches and, therefore, possibilities for action in law, organization, and behaviour.[524]

In evaluating opportunities for change within the biomedical innovation system, we must consider several elements: the institutional culture and beliefs about IP protection; the idea that pursuing these rights is a synonym for academic and research success; the rules imposed by funding agencies; and the metrics that used to evaluate results.[525]

[523] Renato Dagnino and Rogério Bezerra specifically inquired if Brazilian public universities' practices and policies have helped them accomplish their institutional missions and positively affected access to knowledge and promoted social and economic development. In their opinion, directing these institutions' activities to respond to social and economic needs would undermine in part the marketing and profits desires that put pressure on academics and researchers and diminish the importance of IP protection in their activities. Therefore, these agents' knowledge and inventions should be directed to answer society's needs and address market failures—like neglected diseases R&D—rather than promote market needs. See: Dagnino & Silva, *supra* note 476; Silva & Dagnino, "Universidades públicas brasileiras produzem mais patentes que empresas", *supra* note 476.

[524] The description herein is not exhaustive considering the scope of this section is illustrative. Additionally, depending on the objectives and characteristics of different biomedical R&D projects taking place in universities and research centres and the agents participating on them, specific regulations related to governmental programs and areas might apply.

[525] Even though evaluating the state is not the focus of this dissertation, it is important to recall its role in CAS design and reform. As an agent, the State plays multiple roles. It (i) coordinates legislative and policymaking processes and maintains institutional, legal, public policy, and governance schemes that enable CAS operation; (ii) engages in R&D through public research institutions and universities alongside different partners; and (iii) funds R&D to the public and private sectors. How the state has facilitated or prevented the expert communities' experimentation, assisted them to promote institutional reforms and develop their IP policies, and created the infrastructure that allows them to engage effectively in R&D are some of the important questions to improve the relationship between law and science. At least two theories provide insights into the role of developing countries in these systems: (i) the redefinition of the role of the state in the knowledge society and economy through the idea of the 'Entrepreneur State' and the adoption of an approach that facilitates the pursuit of agents' goals within innovation systems; and (ii) the emergence of the 'New Developmental States' (NDS). For initial considerations, see: Mariana Mazzucato, *The Entrepreneurial State: Debunking Public vs. Private Sector Myths*, 1 edition ed (London ; New York: Anthem Press, 2013); David M Trubek, "Developmental States and the Legal Order: Towards a New Political Economy of Development and Law" (2008) SSRN Electron J 35; Peter Evans, "The Capability Enhancing Developmental State: Concepts and National Trajectories" (2011) Discussion Paper No. 63 Cent Stud Inequal Dev CEDE 32; Peter Evans, "In Search of the 21st Century Developmental State" (2008) The Centre for Global Political Economy, Working Paper" (2008) Working Paper n.4 Cent Glob Polit Econ 22.

6.4.1. Overview and Key Discussion Points about Brazil

Brazil ranked 62nd in the Global Innovation Index (GII) among the 135 evaluated countries in 2020.[526] It has a vast potential in biomedical RD&I and has produced substantial knowledge in the biomedical field. Cutting-edge fields include genomics and personalized medicine that are linked to international collaborations.[527] Brazil is also an innovative developing country[528] and has in-place health, educational, and manufacturing capacity enabled by laws, institutions, and human resources that allow for high-quality research and collaboration nationally and internationally.[529]

Brazil has a strong higher education system, with 302 public and 2,306 private institutions in 2019. Among the public institutions, 43.7% (132 institutions) are provincial, 36.4% (110) are federal, and 19.9% (60) are municipal.[530] Public universities and research centres are responsible for 95% of the country's entire scientific production (publications and R&D).[531] These institutions are also among the country's top

[526] The GII-2020 specifically highlighted the role of Brazilian public institutions in the health sector: "During the last few decades, Brazil has built a relatively broad system of support for innovation. Policies implemented in the country range from direct support to scientific research—carried out mainly by universities and public research institutes—to tax incentives and subsidized credit for innovative companies. In health, for instance, Brazil has built a wide system of public research laboratories, such as the Oswaldo Cruz Foundation (Fiocruz), the Adolfo Lutz Institute, and the Butantan Institute, among others. This system has made Brazil an important center for epidemiological research, which has been critical in tackling the COVID-19 crisis."(p.149). *Global Innovation Index 2020. Who Will Finance Innovation?* (Geneva, Switzerland, 2020) at xiii, 149–155.

[527] For some examples of Brazilian research on genomics and cutting-edge fields, see: Cláudia Izique, "Research at the cutting edge of knowledge | AGÊNCIA FAPESP", (May 2013), online: *Agência FAPESP* <http://agencia.fapesp.br/research_at_the_cutting_edge_of_knowledge/17297/>; Agência FAPESP, "Novo portal reunirá bancos de dados genômicos da América Latina", online: *AGÊNCIA FAPESP* <http://agencia.fapesp.br/novo_portal_reunira_bancos_de_dados_genomicos_da_america_latina/26716/>.

[528] See: Morel et al, *supra* note 23 at 401.

[529] Cross, Thompson & Sinclair, *supra* note 287; "Research, Innovation and Dissemination Centers (RIDCs) (11-year grants) - Research Grants - FAPESP Virtual Library", online: <http://www.bv.fapesp.br/en/8/research-innovation-and-dissemination-centers-ridcs-11-year-grants/>; *A Pesquisa no Brasil: Promovendo a excelência*. *Análise preparada para a CAPES pelo Grupo Web of Science*, by Grupo Web of Science (Clarivate Analytics, 2019); "Relatório bibliométrico revela desempenho e tendências da pesquisa brasileira", (13 September 2019), online: *Portal Period CAPES - Produção Científica* <http://www.periodicos.capes.gov.br/?option=com_pnews&component=NewsShow&view=pnewsnewsshow&cid=774&mn=71>.

[530] *Censo de Educação Superior. Notas Estatísticas de 2019*, by Instituto Nacional de Estudos e Pesquisas & Ministério da Educação (Brasília: Instituto Nacional de Estudos e Pesquisas Educacionais Anísio Teixeira (Inep), 2019).

[531] Maurilice Moura, "Universidades públicas respondem por mais de 95% da produção científica do Brasil | Ciência na Rua", (11 April 2019), online: *Política Científica E Tecnológica* <https://ciencianarua.net/universidades-publicas-respondem-por-mais-de-95-da-producao-cientifica-do-brasil/>; Grupo Web of Science, *supra* note 529; note 529.

national patent fillers and patent holders.[532] These facts and numbers must be considered by agents (not only those interacting in those institutions) when co-designing and reforming IP and biomedical innovation systems and evaluating the value and effects of institutional IP practices, policies, and strategies for Brazil's social and economic development.

Traditional and static views of IP systems remain the principal guide to debates about how to regulate biomedical R&D in Brazilian universities and research centres. These discussions lack diverse agents' participation and experimentation with new regulatory strategies and R&D models, especially on aspects related to openness in science and law.[533] There are, however, a few examples of innovative IP strategies, practices, and policies at the institutional level, and some agents have started contesting old assumptions and models.[534]

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[532] "Unicamp lidera ranking de maiores depositantes de patente nacionais", online: *Inst Nac Propr Ind* <http://www.inpi.gov.br/noticias/unicamp-lidera-ranking-de-maiores-depositantes-de-patente-nacionais>.

[533] In Brazil, most of the debates about openness and IPRs are highly concentrated on issues related to copyrights and data protection and the creation of infrastructures that allow FAIR principles. Some institutions like Fiocruz Foundation have initiated discussions about open science, as presented in Chapter Seven. These debates are also mainly concentrated in academic and research institutions and their traditional discussion forums and associations (for instance, the National Forum of Innovation and Technology Transfer Managers ("Fórum Nacional de Gestores de Inovação e Transferência de Tecnologia—FORTEC"). The participation of patients and civil society in these forums is still incipient. See, initially: Sarita Albagli, Maria Lucia Maciel & Alexandre Hannud Abdo, *Ciência aberta, questões abertas* (IBICT, 2015); Paula Xavier Santos et al, *Livro Verde - Ciência aberta e dados abertos: mapeamento e análise de políticas, infraestruturas e estratégias em perspectiva nacional e internacional* (Fiocruz, 2017); Milton Shintaku & Luana Sales, eds, *Ciência Aberta para Editores Científicos*, 1st ed (Botucatu, Brazil: ABEC, 2019); Paula Xavier Santos, "Ciência Aberta Gestão e abertura de dados para pesquisa: o que é, para que e como?" (2018), online: <https://www.arca.fiocruz.br/handle/icict/28706>; *Relatório anual da Pesquisa FORTEC de Inovação –Ano Base 2017. Políticas e Atividades de Propriedade Intelectual e Tranferência de Tecnologia* (Rio de Janeiro, Brasil: Fórum Nacional de Gestores de Inovação e Transferência de Tecnologia (FORTEC), 2018); "FORTEC – Fórum Nacional de Gestores de Inovação e Transferência de Tecnologia", online: *Fórum Nac Gestores Inov E Transferência Tecnol FORTEC* <http://fortec.org.br/>.

[534] The debate taking place at Fiocruz about open science (that includes patents) and diverse partnerships like the one between SGC-Unicamp, FAPESP, DND*i*, and Brazilian pharmaceutical generic industries (Aché and Eurofarma) are examples of this mindset change and experimentation. For more details, see: Paula Xavier Santos & Anne Clinio, "Gestão e abertura de dados para pesquisa: implicações para a pesquisa e a inserção da Fiocruz neste cenário [Debate Fiocruz MG]" (2018), online: <https://www.arca.fiocruz.br/handle/icict/28697>; Maria Baracho, "GT de Ciência Aberta representa Fiocruz em iniciativa da Universidade de McGill | Observatório em CT&I", *Obs Fiocruz-Portal Obs* (cecember 2018), online: </noticias/gt-de-ciencia-aberta-representa-fiocruz-em-iniciativa-da-universidade-de-mcgill>; Gabriela Villen, "Parceria com indústria farmacêutica permitirá pesquisa básica em inovação aberta | Unicamp" *Notícias Unicamp* (29 January 2018), online: <https://www.unicamp.br/unicamp/noticias/2018/01/31/parceria-com-industria-farmaceutica-permitira-pesquisa-basica-em-inovacao>; "SGC | SGC Unicamp", online: <http://www.thesgc.org/scientists/groups/unicamp>.

While not a magic bullet, greater openness in biomedical RD&I offers Brazil the potential of increasing the country's capacity and delivery of services to the country's citizens. A shift toward openness can redefine how agents conduct science through increased participation by expert communities (including legal professionals). These debates need to occur in the early stages of the scientific endeavour as part of IP literacy practices and agents' empowerment. Therefore, legal infrastructure is a condition to facilitate agents' interaction and to inform their behaviour within CAS. Chapter Seven discusses these issues better.

In Brazil, 2,361 professionals from different fields carry out several other functions at the Clusters of Technological Innovation (Núcleos de Inovação Tecnológica—NITs) that are similar to TTOs.[535] This number is insufficient to ensure that biomedical RD&I is carried out in a manner that ensures access, innovation, and social and economic development.[536] More pointedly, it is insufficient to allow professionals the time (even if they had the necessary training) to experiment and innovate how they obtain and licence IP protection or to engage with new and open R&D models.[537] This situation is more likely to lead to the adoption of practices that appear successful in developed countries but are ill-adapted to the needs of Brazil. On the other hand, some international actors who engage with Brazilian researchers—

[535] *Relatório FORMICT. Ano-Base 2018. Política de Propriedade Intelectual das Instituições Científicas e Tecnológicas e de Inovação do Brasil*, by Ministério da Ciência, Tecnologia, Inovações e Comunicações (MCTIC) & Secretaria de Desenvolvimento Tecnológico e Inovação (Brasília: Ministério da Ciência, Tecnologia, Inovações e Comunicações (MCTIC), 2019) at 21.

[536] "The number of professionals working at the NITs varies according to the institution's technology transfer structure, with 17 NIT having only 1 professional, 206 NITs having 2 to 10 professionals, 29 NITs having 11 to 20 professionals, 8 NITs have 21 to 30 professionals, 6 NITs have 31 to 50 professionals and 4 NITs have more than 50 professionals. Regarding the training of professionals working at these NITs, it was found that engineers, chemists and physicists represent 25.2%, administrators and economists represent 18%, professionals with legal training they represent 10%, biologists represent 7.2%, media professionals represent 4.2% and other training represent 35.5%." *Author's free translation*. *Ibid* at 22.

[537] In Brazil, there is a discussion forum, the National Forum of Innovation and Technology Transfer Managers (Fórum Nacional de Gestores de Inovação e Transferência de Tecnologia—FORTEC), that congregates all NITs, monitors of their activities, and provides human resources training and IP literacy. For instance, FORTEC has a Graduate Program in Intellectual Property and Technology Transfer for Innovation directed to NITs' staff. note 533; note 533; Fórum Nacional de Gestores de Inovação e Transferência de Tecnologia (FORTEC), "PROFNIT | Mestrado Profissional", online: *PROFNIT-Programa Pós-grad Em Propr Intelect E Transferência Tecnol Para Inov* <http://www.profnit.org.br/pt/sample-page/>.

such as multinational pharmaceutical firms—have access to highly trained IP legal advisors, leading to results that may not be in the Brazilian national interest.[538]

There is little empirical evidence about the interaction of Brazil's IP and biomedical RD&I systems, let alone any study applying CAS theory.[539] Similarly, there is few studies on institutional IP policies, practices, and strategies but none on empirically testing whether the tragedy of anticommons hypothesis happens in Brazil.[540] On the other hand, some studies report the effects of IPRs on access to knowledge and health technologies in Brazil and other developing countries, mainly from academics and NGOs.[541] The gap in information and knowledge needed to inform law and policymaking processes and institutional IP strategies, policies, and practices in different levels and universities and research centres is large. In the longer term, legal analysts embedded in multidisciplinary analysis can fill this empirical gap; for the present, we are left with significant uncertainty.

The Brazilian government initiated public consultations in 2020 to inform its development of a Brazilian National IP Strategy (Estratégia Nacional de Propriedade Intelectual—ENPI).[542] The

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[538] For an overview of the main Brazilian IP law firms and considerations about the profitability of the pharmaceutical industry, see: The Legal 500, "Intellectual property in Brazil | Law firm and lawyer rankings from The Legal 500 Latin America guide", online: *Leg 500* <https://www.legal500.com/c/brazil/intellectual-property/>; Brickwood, *supra* note 389; Ledley et al, *supra* note 388.

[539] There is one study sponsored by IPEA about the value of CAS to public policies. However, there is no empirical analysis applying those reflections to IP and biomedical innovation systems in Brazil. Furtado, Sakowski & Tóvolli, *supra* note 359.

[540] The fact that public universities are the ones that most file patents in Brazil also stands when comparing them to the Brazilian private sector. It leads to questioning whether this practice is advancing these institutions' mission. However, in total the majority of patent files and granting in Brazil are for foreign nationals/firms. Moura, *supra* note 531; Silva & Dagnino, "Universidades públicas brasileiras produzem mais patentes que empresas", *supra* note 476; Jornal Primeira Página, "99% das pesquisas são feitas pelas universidades públicas - InvesteSP", (20 February 2018), online: *Investe SP* <http://www.investe.sp.gov.br/noticia/99-das-pesquisas-sao-feitas-pelas-universidades-publicas/>; Silva & Dagnino, "Universidades públicas brasileiras produzem mais patentes que empresas", *supra* note 476; note 532; note 533.

[541] Chaves et al, *supra* note 7; César, Rosina & Polido, *supra* note 259; *ibid*; Grupo Web of Science, *supra* note 529; Silva & Dagnino, "Universidades públicas brasileiras produzem mais patentes que empresas", *supra* note 476; Moura, *supra* note 531; Buss, Carvalheiro & Casas, *supra* note 259; Jordão Horácio da Silva Lima, *Os desafios da implementação da Estratégia Global sobre Saúde Pública, Inovação e Propriedade Intelectual no Brasil* (text, Universidade de São Paulo, 2019) [unpublished]; Stiglitz et al, *supra* note 5; Isabela Soares Santos et al, "The Right to healthcare and fiscal austerity: the Brazilian case from an international perspective" (2018) 23:7 Ciênc Amp Saúde Coletiva 2303–2314; Stiglitz, *supra* note 15; Cross, Thompson & Sinclair, *supra* note 287.

[542] *Texto Base para Consulta Pública para Construção da Estratégia Nacional de Propriedade Intelectual (ENPI)*, by Grupo Interministerial de Propriedade Intelectual et al, Construção da Estratégia Nacional de Propriedade Intelectual (Brasília: Governo Federal, 2020).

consultations have, so far, identified nine macro causes for the low effectiveness of Brazil's current IP system. These are as follows: (i) imbalances in the uses (underuse or overuse) of IPRs by national and international agents; (ii) the lack of any strategic IP vision in national companies and other agents in the domestic innovation and creative ecosystem; (iii) the insufficient number and competence of IP professionals; (iv) the difficulty of obtaining various IP rights; (v) the lack of expertise by judges on IP matters; (vi) the violation of IPRs; (vii) the predominance of isolated, short-term, and discontinuous government actions in the IP area; (viii) the absence of a comprehensive approach to IP issues at the international level; and (ix) the need to modernize IP legal frameworks.[543] While all of these issues are important, I focus on those issues related to experts within the domestic IP system here.

6.4.2. Brazilian Legislation, Policies, and Institutions

Federal, provincial, municipal, and institutional laws and policies regulate biomedical R&D activities in Brazil. This legal and policy framework allows universities and research centres to set specific provisions at the institutional level. This logic enables institutions to apply different regulatory strategies for particular projects and set specific goals, as long as they respect higher-level policy and legislation.[544]

[543] *Ibid* at 39–40.
[544] Balmes Vega Garcia, *Direito e Tecnologia. Regime Jurídico da Ciência, Tecnologia e Inovação* (Sao Paulo: LTr, 2008); Abraham Benzaquen Sicsú & Mariana Silveira, "Avanços e retrocessos no marco legal da ciência, tecnologia e inovação: mudanças necessárias" (2016) 68:2 Ciênc E Cult 04–05; César, Rosina & Polido, *supra* note 259.

Brazil has a well-established and robust national IP system[545] and is a signatory to all major international agreements on IPRs and related areas.[546] When adapting its legislation and following the minimum standards of protection, Brazil has incorporated most of the flexibilities permitted under the TRIPS agreement,[547] such as exceptions and limitations to IPRs, compulsory licenses, and parallel importation.[548]

At least two aspects of the Brazilian Federal Constitution of 1988 are worth highlighting. First, the Constitution explicitly mentions IPRs, science and technology, and culture in its text. Second, it connects these topics to the country's social and economic development.[549] These provisions provide the foundation

[545] For a comprehensive list of the IP Brazilian legislation (IP Laws, IP-related Laws, IP regulations (executive orders), Treaty approvals, and Memberships) which includes Law 13.123 of May 20, 2015 (Access and Benefits Sharing of Genetic Resources and Associated Traditional Knowledge); Law 9.610 of February 19, 1998 (Law on Copyright and Neighboring Rights, as amended by Law 12.853 of August 14, 2013); Law 11.484 of May 31, 2007 (Integrated Circuit Topographies); Law 9.279 of May 14, 1996 (Law on Industrial Property, as amended up to Law 10.196 of February 14, 2001); Law 5.648 of December 11, 1970 (National Institute of Industrial Property (INPI)); Law 9.609 of February 19, 1998, on Protection of Intellectual Property of Software, its Commercialization in the Country, and Other Provisions; Law 9.456 of April 28, 1997 (Plant Variety Protection Law),and; Law 10.973 of December 2, 2004 (Innovation and Research in Science and Technology), see: World Intellectual Property Organization, "Brazil - WIPOLex", online: <https://wipolex.wipo.int/en/legislation/profile/BR>.

[546] More information about the Brazilian IP system and related legislation, see: Maristela Basso & Rodrigues Edson Beas, *Intellectual Property Law in Brazil* (Alphen aan den Rijn, The Netherlands : Frederick, MD: Kluwer Law International, 2010); César et al, *supra* note 7; César, *supra* note 260; Newton Silveira, *Propriedade intelectual: propriedade industrial, direito de autor, software, cultivares, nome empresarial, abuso de patentes* (Sao Paulo: Editora Manole, 2014) Google-Books-ID: akVnCgAAQBAJ; World Intellectual Property Organization, *supra* note 545.

[547] For the official text of the TRIPS agreement, related Amendments and Declarations, and an overview about it specially on issues about the TRIPS Agreement and public health, see: *TRIPS Agreement*, *supra* note 249; *Doha Declaration on the TRIPS Agreement and Public Health -*, *supra* note 268; *Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and public health*, *supra* note 268; *Amendment of the TRIPS Agreement*, *supra* note 268; World Trade Organization, "WTO | Intellectual Property - Overview of TRIPS Agreement", online: <https://www.wto.org/english/tratop_e/trips_e/intel2_e.htm>; World Trade Organization (WTO), *supra* note 268.

[548] Brazil is also a member of the Convention on Biological Diversity (CBD), the primary international document about biodiversity and environmental protection and international legislation related to food and agriculture which have IP dispositions on their text and are important and complementary areas dialoguing with biomedical R&D. For more details, see: Convention on Biological Diversity, "CBD - History of the Convention", (12 June 2019), online: *Conv Biol Divers* <https://www.cbd.int/history/>; Conference of the Parties, *Convention on Biological Diversity (CBD)*, (5 January 1992); "International Union for the Protection of New Varieties of Plants (UPOV)", online: *Int Union Prot New Var Plants UPOV* <https://www.upov.int/portal/index.html.en>.

[549] Article 5, XXIX sets out the rights of authors and inventors and emphasizes that such rights must be guided by social interest and the technological and economic development of the country. Articles 215 and 216 ('Culture') define Brazilian cultural rights and heritage and establish the State's obligation to protect them. Articles 218 and 219 ('Science and Technology') set out the State's responsibility to promote and encourage scientific development, research, and technological expertise. Article 219 establishes the protection of the national market "as part of the national patrimony" to promote socio-economic and cultural development. Assembléia Nacional Constituinte, *Constituição Federal Brasileira*, (10 May 1988); Chamber of Deputies Directing Board, *Constitution of the Federative Republic of Brazil, 1988 (English, non-official version, 2010)*, (10 May 1988).

for a favourable policy environment for biomedical R&D activities and align with local values that protect the health, social and economic development, and industrial progress in Brazil. They further promote public interest, cooperation, and openness.

The Brazilian Industrial Property Law (Lei de Propriedade Industrial—LPI / Law 9,279 of March 14, 1996)[550] regulates rights and obligations related to industrial property, including invention and utility model patents, industrial designs, geographical indications, trademarks, trade secrets, and unfair competition. The governmental body that administers, grants, and regulates the protection of industrial property rights in Brazil is the National Institute for Industrial Property (Instituto Nacional de Propriedade Industrial—INPI), a federal agency responsible to the Ministry of Economy.[551]

Among its institutional duties, INPI sets general guidelines for patent applications and examination and guidelines for the pharmaceutical and biotechnological fields.[552] INPI has differential deadlines and procedures for patent examination to support social and economic development and local institutions.[553] The agency also has a role in IP literacy and education. For example, its Academy of IP (Academia do INPI) "is responsible for carrying out activities to disseminate the culture of IP and innovation, and has

[550] Congresso Nacional, *Lei de Propriedade Industrial (alterada pela Lei n° 10.196, de 14 de fevereiro de 2001)*, 9,279 (14 May 1996).

[551] Previously, the INPI was under the umbrella of the Ministry of Industry, Foreign Trade, and Services (Ministério da Indústria, Comércio Exterior e Serviços—MICS) instead of the Ministry of Economy (Ministério da Economia). MICS is also in the process of being entirely incorporated by the Ministry of Economy. This is one of the major institutional changes that happened in Bolsonaro's government, as well as the failed attempt to privatize INPI. More information available at Instituto Nacional de Propriedade Industrial & Ministério da Econômia, "INPI-Instituto Nacional de Propriedade Industrial", online: *Inst Nac Propr Ind* <http://www.inpi.gov.br/home>.

[552] See: Instituto Nacional de Propriedade Industrial (INPI), *supra* note 417; Instituto Nacional de Propriedade Industrial (INPI), *supra* note 417; Instituto Nacional de Propriedade Industrial (INPI), *Brazil: Guidelines for Examination of Patent Applications - Block II - Patentability (established by INPI Resolution No. 169/2016)*; Instituto Nacional de Propriedade Industrial (INPI), *Brazil: Guidelines for Examination of Patent Applications - Block I - Content of Patent Applications (established by INPI Resolution No. 124/2013)*.

[553] For instance, INPI has priority examination of patent applications for small enterprises, ICTs, and start-ups and for public interest technologies (green technologies and specific diseases). "Modalidades de trâmite prioritário", online: *Inst Nac Propr Ind* <https://www.gov.br/inpi/pt-br/servicos/patentes/tramite-prioritario/modalidades-de-tramite-prioritario-de-patentes>.

worked in the areas of teaching, research and extension" and collaborates with other governments and other institutions such as the World Intellectual Property Organization.[554]

The IP laws incorporate several limitations and exceptions to IP protection.[555] As noted earlier, these include compulsory licenses, parallel importation, and research exceptions. Beyond these exceptions, the law also prohibits the patenting of higher life forms and genes in Brazil, although it creates an exception for genetically modified microorganisms.[556] It similarly bans on patents over genetic resources. Nonetheless, the process of isolating the genetic information related to biodiversity is patentable—as are the products derived from this biodiversity—if they otherwise respect the standard criteria for patentability.[557]

Additionally, a distinctive feature of Brazil's patent law that was revoked recently—the Previous Consent of Anvisa (Anuência Prévia) predicted in article 229-C of LPI—deserves attention. Anvisa Previous Consent established that, regarding any invention with a potential impact on public health, both INPI and the National Health Surveillance Agency (Agência Nacional de Vigilância Sanitária—Anvisa) should approve it. In most countries, only the intellectual property office—INPI's counterparts—needs to approve the application. After years of debate about the legality of Previous Consent, Anvisa and INPI established a formal collaborative procedure for joint patent evaluation of health-related technologies.[558]

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[554] Instituto Nacional da Propriedade Industrial (INPI), "Academia do INPI", online: *Inst Nac Propr Ind INPI* <https://www.gov.br/inpi/pt-br/servicos/academia/academia>.

[555] For detailed assessment on the protection of biotechnology and pharmaceutical patents in Brazil, see: César, *supra* note 260; Zucoloto & Freitas, *supra* note 258; Basso & Beas, *supra* note 546; Santos & Clinio, "Gestão e abertura de dados para pesquisa", *supra* note 534.

[556] "Article 10: The following are not considered to be inventions or utility models: (…) IX - natural living beings, in whole or in part, and biological material**,** including the genome or germ plasma of any natural living being, when found in nature or isolated there from, and natural biological processes". Information available at: *Lei de Propriedade Industrial (alterada pela Lei n° 10.196, de 14 de fevereiro de 2001)*, *supra* note 550.

[557] See: Instituto Nacional de Propriedade Industrial (INPI), *supra* note 417; Instituto Nacional de Propriedade Industrial (INPI), *supra* note 417; Instituto Nacional de Propriedade Industrial (INPI), *supra* note 552; Instituto Nacional de Propriedade Industrial (INPI), *supra* note 552.

[558] One side defends the importance of Previous Consent for public health and the other its illegality because it would establish a fourth patentability criteria not applied to other fields. If an invention affects public health, Anvisa will participate in the patent application review after INPI's evaluation on the patentability criteria and formal requirements. In early years of the Previous Consent, Anvisa could reject the patent, regardless of INPI's determination on patentability. Anvisa has commonly

In August 2021, Anvisa Previous Consent was revoked by a legislation aiming to reduce bureaucracy and improve the economy functioning, specially considering private sector's activities.[559]

Brazil protects copyrights and related rights[560] under Law 9,610 of February 19, 1998.[561] Unlike patents, copyrights do not require formal registration to be protected and are effective immediately upon publication.[562] Databases are not subject to specific protection as in the European Union but, as in Canada, can be protected under copyright law in Brazil. The latter protection applies only to a database's organizational components (the original form in which the information is organized or compiled) and does include the database's content.[563] There is also a *sui generis* regime for software protection (Law 9,609 of February 19, 1998)[564] instead of copyright or patents. Not specifically in the realm of IPRs, but critical to biomedical R&D activities, is data protection. In Brazil, the General Law for Data Protection (Lei Geral

rejected second-use and polymorph patents. Anvisa is also responsible for the market and commercialization approval of any health technologies (regulatory approvals) which is independent of patent evaluation or granting. Biological products have a specific registry process and other requirements to fulfill such as the deposit of microorganisms and biological samples in specific institutions. For more information, see: Agência Nacional de Vigilância Sanitária, "Página Inicial da Anvisa - Anvisa", online: *Anvisa- Agência Nac Vigilância Sanitária* <http://portal.anvisa.gov.br/>; *Lei de Propriedade Industrial (alterada pela Lei n° 10.196, de 14 de fevereiro de 2001)*, *supra* note 550; Agência Nacional de Vigilância Sanitária, "Regularização de Produtos - Medicamentos: Prévia Anuência", online: *Agência Nac Vigilância Sanitária-ANVISA* <http://portal.anvisa.gov.br/registros-e-autorizacoes/medicamentos/produtos/propriedade-intelectual/previa-anuencia>; Lima et al, *supra* note 259 at 151–162; Agência Nacional de Vigilância Sanitária, "Anvisa e INPI: acordo acelera análise de patentes - cosmetovigilancia - Anvisa", (12 April 2017), online: <http://antigo.anvisa.gov.br/resultado-de-busca?p_p_id=101&p_p_lifecycle=0&p_p_state=maximized&p_p_mode=view&p_p_col_id=column-1&p_p_col_count=1&_101_struts_action=%2Fasset_publisher%2Fview_content&_101_assetEntryId=3365956&_101_type=content&_101_groupId=219201&_101_urlTitle=anvisa-e-inpi-acordo-acelera-analise-de-patentes&inheritRedirect=true>.

[559] Congresso Nacional, *Decreto Regulamentador, Lei de Federal Inovação*, 5,563 (10 November 2005) at 195.

[560] See: World Intellectual Property Organization (WIPO), "Brazil - Copyright and Related Rights (Neighboring Rights)", online: *WIPO-Lex* <http://www.wipo.int/wipolex/en/results.jsp>.

[561] Brazilian Copyright Act / Law on Copyrights and Neighboring Rights was amended by the Law 12,853 of August 14, 2013. Congresso Nacional, *Lei dos Direitos Autorais e dos Direitos Conexos (alterada pela Lei n.° 12.853, de 14 de agosto de 2013)*, 9,610 (19 February 1998).

[562] However, to guarantee the optimal protection of authorship recognition and moral and patrimonial rights delimitations, in Brazil published works can be registered with the National Library Foundation (Fundação Biblioteca Nacional) in its Copyrights Office (Escritório de Direitos Autorais—EDA). Biblioteca Nacional, "Escritório de Direitos Autorais", online: *Bibl Nac* <https://www.bn.gov.br/servicos/direitos-autorais>.

[563] See, especially, article 87. *Brazil*, *supra* note 561.

[564] World Intellectual Property Organization (WIPO), "Brazil: Law No. 9.609 of February 19, 1998 (Law on Protection of Intellectual Property of Software, its Commercialization in the Country, and Other Provisions)", online: *WIPO-Lex* <http://www.wipo.int/wipolex/en/details.jsp>.

de Proteção de Dados—LGPD / Law 13,709 of August 14, 2018) regulates personal data and privacy protection.[565]

Brazil has several platforms that organize, monitor, enable, and facilitate R&D and collaboration.[566] The National Council of Scientific and Technological Development (Conselho Nacional de Desenvolvimento Científico e Tecnológico—CNPq) developed two platforms to promote and manage science, technology and innovation (ST&I) in the country: the Integrated Carlos Chagas Platform[567] and the Lattes Platform.[568] The data that is publicly available at these platforms includes, for instance, information about research and academic activities and the output of Brazilian researchers and institutions. The Lattes Platform has two directories. One registers the curriculum (Curriculum Lattes) of academics and researchers, and the other the activities of research groups in different institutions.[569] The Carlos Chagas Platform facilitates research activities (for instance, gathering data on scholarships, grants, forwarding projects and scholarship requests, the progress of processes, issuing opinions, signing of concession terms, and issuing technical and accountability reports for Brazilian and foreign researchers).[570] These platforms are part of the government's planning and strategy for ST&I and guide Brazilian academics and researchers' behaviours and expectations. Moreover, to enhance scientific communication

[565] Congresso Nacional, *Lei Geral de Proteção de Dados Pessoais (LGPD). Redação dada pela Lei nº 13.853, de 2019*, 13,709 (14 August 2018).
[566] IT has a critical role in organizational aspects of biomedical R&D, as it enables the creation of an infrastructure that allows science to work on its best and promote the flow and sharing of data and information. There is criticism about several aspects of these platforms (their layout, content, easiness to upload and update, and their usability considering the diversity of agents using them, including people with disabilities) but their value and contribution remain. How to use them to better integrate and coordinate actions among researchers and institutions, and strategize are issues that remain open to debate.
[567] Conselho Nacional de Desenvolvimento Científico e Tecnológico—CNPq, "Plataforma Integrada Carlos Chagas", online: *Plataforma Integrada Carlos Chagas* <http://carloschagas.cnpq.br/>.
[568] Conselho Nacional de Desenvolvimento Científico e Tecnológico—CNPq, "Plataforma Lattes", online: *Plataforma Lattes* <http://lattes.cnpq.br/>.
[569] *Ibid*.
[570] Conselho Nacional de Desenvolvimento Científico e Tecnológico—CNPq, *supra* note 567.

and strengthen its research capacity, Brazil created, in 1998, the Scientific Electronic Library Online (SciELO) that works under open access principles and provides access to several journals.[571]

As Brazil is the most biodiverse country on the planet, it possesses an unlimited and underexplored asset to advance biomedical RD&I. Brazil enacted the Law 13,123 of May 20, 2015, that sets out the rules for accessing genetic resources and associated traditional knowledge (TK) and benefit-sharing.[572] Any R&D that involves biodiversity assets and related TK must follow its specific rules and authorizations.[573]

Zucoloto and Freitas provide a detailed evaluation of Brazil's IP system and regulatory aspects of health biotechnology. They conclude that Brazil has not achieved its full potential even though several policies, laws, and new funding sources have been created to regulate biotechnology activities. Thus, it is necessary to review and improve the current laws and regulations to facilitate RD&I.[574] For example, Zucoloto and Freitas mention the difficulty of understanding the process to patent inventions related to the Brazilian biodiversity given the number of agents, steps, legislation, and authorizations involved.[575] They also describe research and academic communities' behaviour as relevant to the country's innovative capacity. For instance, it is common for a substantial part of intangible assets produced by academic and research communities in Brazil to be transformed into publications rather than into patents. This epitomizes a culture that prioritizes publications over innovation, behaviour that may cause a lack of

[571] Scientific Electronic Library Online (SciELO), "SciELO.org", online: *Sci Electron Libr Online SciELO* <https://scielo.org/>; Cross, Thompson & Sinclair, *supra* note 287.
[572] Congresso Nacional, *Lei de Acesso e Repartição de Benefícios de Recursos Genéticos e Conhecimento Tradicional Associado (Access and Benefits Sharing of Genetic Resources and Associated Traditional Knowledge Law, Brazil)*, 13,123 (20 May 2015).
[573] The Council of Management of Genetic Heritage (Conselho de Gestão do Patrimônio Genético—CGEN) is the governmental body responsible for issues related to access and benefits sharing of genetic resources and associated TK Governo do Brasil, "Ministério do Meio Ambiente", online: *Minist Meio Ambiente* <https://www.gov.br/mma/pt-br/pagina-inicial>.
[574] For specific debates about the review of Brazilian patent legislation, see also: Lima et al, *supra* note 259; Paranaguá, *supra* note 259.
[575] Zucoloto & Freitas, *supra* note 258 at 153–188.

novelty and impede patent grants. This practice might also benefit foreign agents that acquire information about Brazil's research and turn it into patented inventions.[576]

6.4.3. Regulating the Relationship Between Universities, Research Centres, and the Private Sector in Brazil

The 'Innovation Laws' regulate the relationship between public universities, research centres, and the private sector. Brazil enacted its Federal Innovation Law in 2004 (Law 10,973 of December 02, 2004) that it amended (Law 13,243 of January 11, 2016) to adjust to the country's ST&I Code. The Code's framework especially includes incentives for scientific development, research, scientific and technological capacity building. It further provides public institutions with greater autonomy to engage in public-private partnerships (PPPs), license, and sell technologies.[577] Brazilian provinces and municipalities also have specific 'Innovation Laws.'[578] Completing this regulation, the 'Law of Goods' (Lei do Bem / Brazilian R&D Tax Credit Law, Law 11,196 of November 21, 2005) establishes tax incentives for technological innovation, especially for the national private sector and its interaction with the public institutions.[579]

The Federal Innovation Law has an organizational function as it creates the institutions by which the innovation system operates and agents interact.[580] More specifically, it creates the Clusters of Technological Innovation (Núcleos de Inovação Tecnológica—NITs), which are similar to TTOs.[581] The

[576] *Ibid*.
[577] For a timeline and evolution of law and policy related to the university industry relationship in Brazil and the mechanisms created to fund the NITs, see: Julia Paranhos et al, "Criação, Institucionalização e Funcionamento dos Núcleos de Inovação Tecnológica no Brasil: Características e Desafios" (2018) 24:2 REAd Rev Eletrônica Adm Porto Alegre 253–280.
[578] See: Congresso Nacional, *Lei Federal de Inovação*, 10,973 (12 February 2004); Congresso Nacional, *Código Federal de Inovação*, 13,243 (11 January 2016); *Decreto Regulamentador, Lei de Federal Inovação*, *supra* note 559; *ibid*; Paranhos et al, *supra* note 577; Marli Elizabeth Ritter dos Santos, Patricia Tavares Magalhães de Toledo & Roberto Alencar Lotufo, *Transferência de Tecnologia: estratégias para a estruturação e gestão de núcleos de inovação tecnológica* (Campinas, SP: Komedi, 2009).
[579] Congresso Nacional, *Lei do Bem*, 11,196 (21 November 2005).
[580] See: *Lei Federal de Inovação*, *supra* note 578; *Código Federal de Inovação*, *supra* note 578; *Decreto Regulamentador, Lei de Federal Inovação*, *supra* note 559; *ibid*.
[581] See, initially: Paranhos et al, *supra* note 577; Ministério da Ciência, Tecnologia, Inovações e Comunicações (MCTIC) & Secretaria de Desenvolvimento Tecnológico e Inovação, *supra* note 535; Ritter dos Santos, Magalhães de Toledo & Lotufo, *supra* note 578; *Código Federal de Inovação*, *supra* note 578; *Lei Federal de Inovação*, *supra* note 578.

main task of the NITs is to coordinate the IP policies and practices in public universities and research centres (referred to by the Federal Innovation Law as Scientific and Technological Institutions / Instituições Científicas e Tecnológicas—ICTs).[582] Each ICT can create its own NIT or create one in collaboration with other ICTs. In this way, NITs and ICTs work as niches that enable experimentation regarding the regulation by IPRs of biomedical R&D. Thus, there is a considerable diversity of organizational frameworks and legal and policy arrangements that these institutions can create to regulate their activities.[583]

Each Brazilian public university and research centre must respect the general regulations described above. Nevertheless, they also have the freedom to draft internal rules that specifically apply to their IP strategies, policies, and practices in light of their institutional visions and missions and R&D activities. Most of (if not all) Brazilian universities and research centres have these regulations already in place.[584]

Paranhos et al. explain that Brazil was late in legislating about university-industry relationships. This regulation was also broadly reliant on the then-existing Brazilian public Science and Technology (S&T) system built over the years to respond to local social and economic issues and the fact that the Brazilian private sector did not have a history of R&D investments. Consequently, this regulation and the

[582] Article 16 of the Federal Innovation Law details the function of ICTs that include development of IP practices and strategies. Other goals of the Federal Innovation Law include encouraging cooperation among the ICTs and promoting small enterprises (start-ups). For more details about ICTs' function, see: Ministério da Ciência, Tecnologia, Inovações e Comunicações (MCTIC) & Secretaria de Desenvolvimento Tecnológico e Inovação, *supra* note 535; *Código Federal de Inovação*, *supra* note 578; *Lei Federal de Inovação*, *supra* note 578.

[583] For detailed information about the Brazilian Federal Innovation Law, see: Priscilla M D G César, Monica S. Guise Rosina & Fabricio Polido, "Propriedade Intelectual: Potencialidades e fragilidades do ambiente jurídico-institucional brasileiro para a inovação" in *Direito E Desenvolv Um Diálogo Entre Os BRICS*, Coleção Direito, Desenvolvimento e Justiça: Direito em Debate - (Sao Paulo: Editora Saraiva, 2012) 137; Dênis Borges Barbosa, *Direito da Inovação*, 2nd ed (Rio de Janeiro, Brasil: Lumen Juris, 2011); Balmes Vega Garcia, *Direito e Tecnologia. Regime Jurídico da Ciência, Tecnologia e Inovação* (Sao Paulo: LTr, 2008); Marli Elizabeth Ritter dos Santos, Patricia Tavares Magalhães de Toledo & Roberto alencar Lotufo, *Transferência de Tecnologia: estratégias para a estruturação e gestão de núcleos de Innovação technológica* (Campinas, SP: Komedi, 2009).

[584] Ministério da Ciência, Tecnologia, Inovações e Comunicações (MCTIC) & Secretaria de Desenvolvimento Tecnológico e Inovação, *supra* note 535; Ministério da Ciência, Tecnologias e Inovações (MCTIC), "Propriedade Intelectual e Transferência de Tecnologia. Relatórios Consolidados FORMICT (2006-2018)", online: *Minist Ciênc Tecnol E Inovações* <http://antigo.mctic.gov.br/mctic/opencms/tecnologia/propriedade_intelectual/formict_propriedade_intelectual.html>.

establishment of the NITs helped increase the Brazilian private sector's view of IP protection and strategies. However, several complications emerged from this relationship as divergences about IP protection and ownership, the difficulty of communication between agents, bureaucracy, lack of specialized R&D professionals and investments, and the different views of ICTs and industry started to appear. As the importance of ICTs and NITs increases, Paranhos et al. highlight the need to consider public institutions' mission in this relationship and prioritize knowledge and technology transfer.[585]

To provide an example of how these laws and policies come together, I use its leading public university (USP) as an example to make three points. First, I briefly present USP's internal IP regulation to show how this adds another layer of complexity to interactions and coevolution of CAS. Second, I present part of USP's organizational framework to exemplify possibilities to enhance interactions among agents (and the adoption by them of new R&D models). Third, I present examples of groups at USP that critically discuss the interaction between IP and innovation systems and the university's role in access to knowledge and health technologies.

6.4.3.1. University of Sao Paulo: Overview

USP is the top-ranked and most prominent university in Brazil and Latin America and is internationally recognized for its academic and research expertise.[586] USP is located in Sao Paulo province—the wealthiest province and Brazil's business centre. Given this, its IP policies and practices need to respect

[585] Paranhos et al, *supra* note 577 at 257–258.

[586] USP was opened in 1934 and is ranked as the best academic and research institution in Brazil and Latin America. In 2019, it had 59,097 undergraduate students enrolled in the first semester, 14.047 master students, and 15,248 doctorate students. For more information, see: Universidade de São Paulo (USP), "Anuário Estatístico da USP", online: <https://uspdigital.usp.br/anuario/AnuarioControle>; Universidade de São Paulo (USP), *supra* note 522; Yamamoto Erika, "Ranking de países emergentes classifica a USP como melhor da América Latina", *J USP* (15 January 2019), online: <https://jornal.usp.br/institucional/ranking-de-paises-emergentes-classifica-a-usp-como-melhor-da-america-latina/>;
Yamamoto Erika, "USP mantém liderança entre universidades latino-americanas", *J USP* (28 September 2018), online: <https://jornal.usp.br/institucional/usp-mantem-lideranca-entre-universidades-latino-americanas/>.

both federal law and the Sao Paulo Provincial Innovation Law.[587] This Provincial Innovation Law provides that transfer of technology or licensing of inventions related to the public interest cannot be done on an exclusive basis.[588] Being located within Sao Paulo province also connects USP to the Sao Paulo Research Foundation (Fundação de Amparo à Pesquisa do Estado de São Paulo—FAPESP). FAPESP has funded programs on IP training and capacity building of NITs and imposes specific IP protection and licensing rules on the R&D projects it supports while considering the public interest.[589]

In 2019, USP filed 63 patents (50 in Brazil and 13 internationally) and was granted 74 patents in Brazil.[590] In the same year, USP entered into nine technology transfer contracts and received R$3,44 million[591] in royalties.[592] The management of IP policies and practices in USP falls to its Innovation

[587] Sao Paulo Provincial Innovation Law (Complementary Law 1,049 of June 19, 2008) was regulated by the Decree 54,690 of August 18, 2009. See: Assembléia Legislativa do Estado de Sao Paulo, *Lei Paulista de Inovação (Lei Complementar)*, 1049 (19 June 2008); Assembléia Legislativa do Estado de São Paulo, *Decreto nº 54.690, de 18 de agosto de 2009*, 54690 (18 August 2009).

[588] According to Article 8: "The ICTESPs are allowed to conclude technology transfer and licensing agreements for the granting of rights of use or exploitation of protected creation/invention that they have developed, upon previous manifestation of the Clusters of Technological Innovation. (...) Paragraph 4 - The transfer of technology and the licensing for the granting of the right of use or exploration of creation/invention, recognized in an act of the Executive Power as of relevant public interest, may only be carried out in a non-exclusive capacity." *Author's free translation.* Article 8, Paragraph 2, also specifies that the company that owns an exclusive license must lose it if it does not commercialize the invention accordingly to the license agreement's terms and timeline. See: *Lei Paulista de Inovação (Lei Complementar)*, *supra* note 587.

[589] For more details, see: Fundação de Amparo à Pesquisa (FAPESP), *Política para Propriedade Intelectual da FAPESP - Portaria PR n. 04/2011* (Diário Oficial do Estado de São Paulo, 2011); "Novo Marco Legal da Ciência, Tecnologia e Inovação é sancionado | AGÊNCIA FAPESP", *FAPESP*, online: <http://agencia.fapesp.br/novo_marco_legal_da_ciencia_tecnologia_e_inovacao_e_sancionado/22521/>; Paranhos et al, *supra* note 577.

[590] There is a delay of several years between the filing of an application and its grant, so the 74 granted applications were in respect of previously applied for patents.

[591] R$3,44 million equals CAD$820,168.49 (currency exchange rate: R$1.00=CAD$0.2384 on August 14, 2021).

[592] Agência USP de Inovação, "Patentes - Agência USP de Inovação", online: *Agência USP Inov - AUSPIN* <http://www.inovacao.usp.br/en/patentes/>; Agência USP de Inovação, "Inovação em Números - Agência USP de Inovação", online: *Agência USP Inov - AUSPIN* <http://www.inovacao.usp.br/en/numeros/>.

Agency (Agência USP de Inovação—AUSPIN).[593] AUSPIN is a NIT institutionally connected to the Provost's Office for Research (Pro-Reitoria de Pesquisa).[594] Resolution USP 7,035/14 establishes internal IP policy and practices, regulates technological innovation, and establishes procedures to ensure IPRs protection, technology transfer, and licensing at the university. It further determines AUSPIN's role in IP management, IP support, literacy, training activities, the distribution of research results (royalties), the support for technology-based start-up companies, and programs to incentivize the USP community's entrepreneurship.[595] Since 2019, the Provost's Office for Research, to which AUSPIN is connected, has promoted discussions about open science within the USP community.[596]

6.4.3.2. University of Sao Paulo Organizational Framework

USP has 49 schools and specialized institutes that support a diverse set of research groups (1,682 research groups certified in the CNPq Research Groups Directory and Lattes Platform).[597] It has 13 Research, Innovation, and Diffusion Centres (Centros de Pesquisa, Inovação e Difusão—CEPIDs) with the mission of developing basic and applied research in specific areas and contributing to innovation by promoting

[593] AUSPIN's mission, vision and values are: "Mission: To promote the use of scientific, technological and cultural knowledge produced at the University of São Paulo for the socioeconomic development of the State of São Paulo and the country. View: To make innovation and entrepreneurship a constant practice at the University of São Paulo, creating a robust interface between USP and the productive sector through incubators, technology parks, company accelerators and cooperation projects. Values: Seeks excellence in innovation and entrepreneurship through quality, agility, social responsibility, commitment and sustainability. Additionally, the USP Statute determines in article 2: "The purposes of the USP are: I. to promote and develop all the forms of knowledge through teaching and research; II. to provide higher education for the training of skilled people to the exercise of research and teaching in all areas of knowledge, as well as the qualification for professional activities; III. to extend services to the society that are inseparable from teaching and research activities." *Author's free translation*. Information available at: Agência USP de Inovação, "A Agência - Agência USP de Inovação", online: *Agência USP Inov - AUSPIN* <http://www.inovacao.usp.br/agencia/>; Reitoria da Universidade de São Paulo, *Resolução n. 5175* (Diário Oficial do Estado de São Paulo, 2005); Reitoria da Universidade de São Paulo, *Resolução (Consolidada) n. 3461* (Diário Oficial do Estado de São Paulo, 1988).

[594] Universidade de São Paulo (USP), "PRP USP – Pró-Reitoria de Pesquisa da Universidade de São Paulo", online: *PRP USP – Pró-Reitoria Pesqui Universidade São Paulo* <http://prp.usp.br/>.

[595] Reitoria da Universidade de São Paulo, *Resolução n. 7035* (Diário Oficial do Estado de São Paulo, 2014); Agência USP de Inovação, *supra* note 593.

[596] Chapter Seven discusses more details about it. See, initialy: Pró Reitoria de Pesquisa, *USP Ciência Aberta* (University of Sao Paulo, 2020).

[597] Universidade de São Paulo (USP), *supra* note 522; Pró Reitoria de Pesquisa & Universidade de São Paulo (USP), "Grupos de Pesquisa CNPq - Pró Reitoria de Pesquisa", online: <https://prp.usp.br/grupos-de-pesquisa-cnpq/>.

technology transfer and capacity building activities to elementary and high school students and the general public.[598] USP also has academic and research units that develop activities within the Brazilian Agency for Industrial Research and Innovation (Empresa Brasileira de Pesquisa e Inovação Industrial—Embrapii), aiming to improve industry and public and private universities and research centre cooperation.[599]

USP is home of the National Institutes of Science and Technology (Institutos Nacionais de Ciência e Tecnologia—INCTs) that aims at promoting specific actions in different fields.[600] In this complex institutional organization, all projects are niches that can be exponentially combined to increase diversity and enhance R&D results. Rethinking USP's organizational framework through the concepts of niches and agents' interactions can also lead to experimentation with different R&D arrangements and IP regulation. However, a more profound evaluation of this organizational framework, tools to monitor and connect it, and interaction of its diverse agents are still needed.

Some groups within USP's organizational framework openly debate access to knowledge, information, and health technologies, and broader issues related to ST&I. These groups' critical views are drivers for the design and reform of IP strategies, practices, and policies, promote capacity building and IP literacy, and create accountability inside USP. They also work on articulating these issues in conjunction with other Brazilian institutions and engage experts communities on emerging issues such as

[598] The CEPIDs are funded by the São Paulo Research Foundation (Fundação de Amparo à Pesquisa do Estado de São Paulo—FAPESP). The CEPIDs that direcly related to biomedical RD&I (considering one may never know which area may add to another in innovation) are: the Research Centre in Inflamatory Diseases (Centro de Pesquisa em Doenças Inflamatórias—CRID), the Cell Therapy Centre (Centro de Terapia Celular—CTC), the Research Centre on Human Genome and Stem Cells (Centro de Pesquisa sobre o Genoma Humano e Células-Tronco—HUG-CELL); the Research and Innovation Centre on Biodiversity and Drugs (Centro de Pesquisa e Inovação em Biodiversidade e Fármacos—CIBFar); the Research Centre on Redox Processes in Biomedicine (Centro de Pesquisa em Processos Redox em Biomedicina—REDOXOMA); and the Research Centre on Well-Being and Human Behaviour (Centro de Pesquisa em Bem-Estar e Comportamento Humano—CPBEC). Agência USP de Inovação, "CEPID – Centros de Pesquisa, Inovação e Difusão – Agência USP de Inovação", online: <http://www.inovacao.usp.br/cepids/>.

[599] Agência USP de Inovação, "EMBRAPII (Associação Brasileira de Pesquisa e Inovação Industrial) – Agência USP de Inovação", online: <http://www.inovacao.usp.br/embrapii/>; Empresa Brasileira de Pesquisa e Inovação Industrial, "Embrapii - About us", online: *Embrapii* <https://www.embrapii.org.br/en>.

[600] The INCTs are funded by the National Council of Scientific and Technological Development (Conselho Nacional de Desenvolvimento Científico e Tecnológico—CNPq). Agência USP de Inovação, "INCT – Institutos Nacionais de Ciência e Tecnologia – Agência USP de Inovação", online: <http://www.inovacao.usp.br/incts/>.

openness in science. Some examples of these groups are the Research Group on Public Policies to Access to Information (Grupo de Pesquisa em Políticas Públicas para o Acesso à Informação—GPOPAI)[601] and the Observatorium for Innovation and Competitiveness (Observatório da Inovação e Competitividade—NAP).[602]

Additionally, from 2010 to 2012, UAEM-Brazil had active chapters in the USP Faculty of Law and Public Health School.[603] These chapters worked on a range of strategic priorities, including establishing a network within the USP community and targeting capacity-building projects and research groups to increase awareness inside the university about access to knowledge and health technologies and innovation. UAEM-Brazil also initiated contact with AUSPIN to clarify the university's IP practices and policies and examined the possibility of proposing a humanitarian license clause in USP's license practices. However, these discussions did not prosper. Currently, UAEM no longer has any student representatives at USP and is therefore dormant.

6.4.3.3. The Need for Empirical Evidence

Even knowing USP's organizational framework, IP regulation, and the make-up of its community, with empirical evidence, it is not possible to draw any detailed conclusions about the interaction of IP and biomedical innovation systems in this setting. A substantial bureaucracy makes it more difficult to collect data but with USP expert community's participation, it would still be possible. Specifically, there is a need to assess the knowledge of expert communities within the USP community about the IP regulation and of

[601] Grupo de Pesquisa em Políticas Públicas para o Acesso à Informação (Gpopai), "Manual de Ciência Aberta/Casos/GPOPAI - Wikiversidade", online: *Wikiversidade* <https://pt.wikiversity.org/wiki/Manual_de_Ci%C3%AAncia_Aberta/Casos/GPOPAI>.
[602] Instituto de Estudos Avançados (IEA) da Universidade de São Paulo, "Núcleo de Apoio à Pesquisa Observatório da Inovação e Competitividade (NAP-OIC)", online: *Inst Estud Av IEA USP* <http://www.iea.usp.br/pesquisa/nucleos-de-apoio-a-pesquisa/observatorio-inovacao-competitividade>.
[603] Centro de Estudos e Pesquisas de Direito Sanitário – CEPEDISA, "CEPEDISA", online: <http://cepedisa.org.br/pt/home-3/>.

their practices, as well as their views about openness and willingness to implement new R&D models. Such an assessment largely relies on qualitative empirical research that evaluates the behaviours of agents interacting within the lower layers of IP and biomedical innovation systems.

6.4.4. Multisystemic Interactions

As previously mentioned, access to knowledge and innovation occurs within the interaction and coevolution of multiple CAS, not only IP and biomedical innovation systems. Analyzing all these systems in depth is outside the scope of this dissertation. We can limit our analysis, especially given the Brazilian context, by considering the influence of at least two other CAS: public health and industrial policy.

First, Brazil has a public and universal health system called the Unified Health System (Sistema Único de Saúde—SUS).[604] The principles guiding SUS operations are free and universal access, decentralized governance at different levels of government, and community participation in health-related executive actions and programs. The Organic Health Law (Lei Orgânica da Saúde / Federal Law 8,080 of September 19, 1990) that creates SUS[605] establishes that all health technologies must be available to all

[604] The Brazilian Federal Constitution of 1988 also recognizes (Article 196) the right to health as a universal right and establishes the responsibility of the Brazilian state in its different levels of administration to engage in coordinated action to achieve it. The *Constitution of the Federative Republic of Brazil, 1988 (English, non-official version, 2010)*, *supra* note 549; *Constituição Federal Brasileira*, *supra* note 549.
[605] See, specifically Article 6: Congresso Nacional, *Lei Orgânica da Saúde*, 8,080 (19 September 1990).

people (not only citizens) living in Brazil as part of their right to health. In this sense, access to health technologies is a right of SUS users and an obligation of the Brazilian government.[606]

Second, Brazil has an Industrial Complex of Health (Complexo Industrial da Saúde—CIS) coordinated by the Science, Technology and Strategic Inputs Secretary (Secretaria de Ciência, Tecnologia e Insumos Estratégico—DECIIS/SCTIE/MS) of the Ministry of Health. CIS is responsible for coordinating actions within several governmental bodies and between three systems (ST&I, Health, and Industrial). The activities developed under the CIS are not only RD&I but also manufacturing, sales, and the purchase of health technologies, health inputs, and services that directly relate to public procurement and specific programs.[607]

Coordinating the above two systems and guiding their interaction and activities is the Ministry of Health Research Priority Agenda (Agenda de Prioridades de Pesquisa do Ministério da Saúde—APPMS). APPMS is a document issued by the DECIIS/SCTIE/MS that aligns Brazil's health priorities with scientific research, technology and innovation activities and directs resources for SUS strategic research topics. It contains 172 lines of research tracks distributed into 14 themes. All planned funding and R&D activities in Brazil fall within the ambit of APPMS. The APPMS is the result of discussions between the

[606] Within the framework of SUS, the Brazilian Ministry of Health also coordinates several programs that aim to provide the highest standards of health to the population and tackle specific problems. Among them is the National Program on Sexually Transmitted Infections (STIs), HIV, and Hepatitis C. This program has been internationally recognized for providing free, public, and universal access to antiretroviral (ARV) therapies and for becoming a leading case of policy implementation to achieve the right to health and access to medicines. However, it also has encountered serious problems related to its financial sustainability because of the high prices of ARV therapies that are protected by patents. For detailed information about the SUS, the regulatory, institutional framework for drugs in Brazil, and the Brazilian National HIV/DST Program, see: Sueli Dallari, Fernando Mussa Abujamra Aith & Felipe Angel Bocchi Castellaro, "Drugs regulation in Brazil: challenges in the context of a globalized world" in *Drugs Regul Glob World* (Sao Paulo, 2014) 31; "Departamento de Vigilância, Prevenção e Controle das IST, HIV/Aids e Hepatites Virais", online: *Dep Vigilância Prev E Controle IST HIVAids E Hepatites Virais* <http://www.aids.gov.br/pt-br>; Chaves et al, *supra* note 7; César et al, *supra* note 7; Chaves, Vieira & Reis, "Access to medicines and intelectual property in Brazil", *supra* note 7; Maria Auxiliadora Oliveira, Jorge Antonio Zepeda Bermudez & Claudia Osório-de-Castro, *Assistência Farmacêutica e Acesso a Medicamentos* (Rio de Janeiro, Brasil: Editora Fiocruz, 2007).
[607] Carlos Augusto Grabois Gadelha, "O complexo industrial da saúde e a necessidade de um enfoque dinâmico na economia da saúde" (2003) 8 Ciênc Saúde Coletiva 521–535; Ministério da Saúde, Secretaria de Ciência, Tecnologia e Insumos Estratégicos & Departamento do Complexo Industrial e Inovação em Saúde, *Avanços, Desafios e Oportunidades no Complexo Industrial da Saúde em Serviços Tecnológicos* (Brasilia: Ministério da Saúde (MS), 2018).

DECIIS/SCTIE/MS, health researchers and managers, and civil society.[608] One of the objectives behind the APPMS is to connect health R&D themes to the priorities listed in the National Health Policy (Política Nacional de Promoção da Saúde—PNPS) to respond to local needs.[609]

The organization of biomedical RD&I is, *per se*, a multidisciplinary, multi-agent, and multisystemic activity that depends on coordinated and consistent interaction of agents to enable biomedical R&D. As the above discussion describes Brazil has a robust and complex set of legislation, policies, institutions, and infrastructure governing biomedical RD&I. The success of these legal and policy instruments in attaining Brazil's biomedical innovation goals depends not only on knowing the details, but in understanding the interplay of these instruments within multiple systems' organizational frameworks, contexts, and agents' interactions. Combining content, strategy, and form are contributions that CAS analysis and agent-centred approaches can provide and are still missing in Brazil.

6.5. Filling the Gaps: Promoting Coordination, Diversity, and Experimentation among Expert Communities and Creating Infrastructures for Action

At least two questions remain from the Brazilian case. First, are the integration and coordination of legislation, policy, institutions, and infrastructure and their governance optimal and participatory or are they confusing and incoherent? Second, is the existing infrastructure sufficient to integrate and coordinate agents? Some of these uses might include IP literacy and training programs, promotion of discussions about openness in science among expert communities, and empirical research (qualitative and quantitative) to help understand agent behaviour and expectations.

[608] Secretaria de Ciência, Tecnologia e Insumos Estratégicos & Ministério da Saúde, *Agenda de Prioridades de Pesquisa do Ministério da Saúde - APPMS* (Brasília: Ministério da Saúde, 2018).
[609] Ministério da Saúde, Secretaria de Vigilância em Saúde & Secretaria de Atenção à Saúde, *Política Nacional de Promoção da Saúde: PNPS: Anexo I da Portaria de Consolidação nº 2, de 28 de setembro de 2017, que consolida as normas sobre as políticas nacionais de saúde do SUS* (Ministério da Saúde, 2018).

CHAPTER SEVEN—BUILDING BRIDGES BETWEEN COMPLEX ADAPTIVE INTELLECTUAL PROPERTY AND BIOMEDICAL INNOVATION SYSTEMS: THE IDEA OF OPENNESS IN LAW AND SCIENCE

7.1. Identifying Commonalities and Promoting Experimentation in the Design and Reform of Complex Adaptive Intellectual Property and Biomedical Innovation Systems

Previous chapters recounted pieces of the interactional and coevolutionary story of IP and biomedical innovation systems and how agents' behaviours continuously redefine the balance between these CAS. They presented the relationship between the public domain, openness, and IP and how together, they can advance discussions about access to knowledge and innovation. They further highlighted the need for studies centred on observing agents' interactions and behaviours. I noted the bounded rationality of legal and non-legal agents who create and participate in CAS and how uncertainty plays a central role in these systems.

In examining behaviours and interaction patterns between agents, one needs to recall that CAS—and, consequently, law and science—are open systems by nature. Their boundaries are open to allow interactions and exchanges with other systems, among agents, and the external environment.

The present chapter is my contribution toward understanding the interaction and coevolution of IP and biomedical innovation systems as CAS. It focuses on how agent interactions and behaviours lead these systems to learn, change, adapt, and evolve. In particular, I question how shared norms that guide these systems develop, how new interactions emerge and how, through iteration, they transform these systems. I previously identified openness as an emergent phenomenon within these two CAS. As I described, openness is not a static concept and relates to transparency and cooperation in opposition to closedness, secrecy, and competition. Between these opposite concepts, diverse organizational frameworks may take place while agent behaviours and interactions allow CAS to operate and thrive.

The idea of openness in law and science emerged, intensified its presence, and gained momentum in discussions about IP and biomedical innovation systems among some agents over time within both individual countries and internationally. This idea appears in multiple and varied academic papers, reports, biomedical RD&I models, international and national legislation and policy documents, agent advocacy campaigns, and negotiations and debates. Thus, the emergence of openness can be evaluated historically while studying the interaction and coevolution of IP and biomedical innovation systems. This historical evaluation shows the justifications and influences that shifted agents' behaviours from closedness towards openness.[610] How, by what means, and induced by which agents' behaviours, the emergence of openness happens and intensifies are points discussed in this chapter.

The importance of investigating openness relates to its immediate connection to the intrinsic characteristics of law and science and to the behaviours of agents in these CAS. Unless agents engage in critical assessment of this phenomenon, their ability to experiment with new solutions to address complex problems will be compromised. Consequently, this chapter explains how the idea of openness manifests in law and science by presenting some biomedical RD&I models and initiatives, international legislation, and specific legislation in developing countries (mainly Brazil). This research is not exhaustive and does not advocate for any particular model that encompasses the idea of openness. As the devil is in the details and agents may never know all of them, I align my evaluation of the interaction and coevolution of IP and biomedical innovation systems to the need to observe and gather information on a case-by-case basis. Otherwise, there are risks of evaluating problems superficially and misevaluating them as occurred in respect of the tragedy of the anticommons hypothesis.

[610] For initial thoughts on this discussion, see: Paul A David, "Understanding the emergence of 'open science' institutions: functionalist economics in historical context" (2004) 13:4 Ind Corp Change 571–589; David, *supra* note 295.

7.1.1. The Idea of Openness in Law and Science: Initial Thoughts, Theories, and Conceptualizations

One can think about openness as (i) a component or characteristic of the innovation ecosystem; (ii) a guiding principle of RD&I activities and, consequently, of various CAS that participate in and enable those activities or; (iii) an emergent phenomenon within different CAS that reflects agent behaviours and patterns of interaction. Below I argue that openness reflects all of these three conceptualizations, as it has the potential to transform these systems and address complex problems arising in them. Additionally, in presenting itself as a characteristic, a component, or a principle in different CAS, openness becomes a commonality among them and, therefore, a bridge enabling agents' and systems' communication. Most of my analysis in this chapter relates to the emergence of openness, considering its connections to CAS theory and concepts and the possibility of tracking evolutionary processes taking place in IP and biomedical innovation systems.

First, in looking at openness as a component or characteristic of the innovation ecosystem, it is essential to connect it with the scientific enterprise. At the core of science is the production of data, information, and knowledge, giving rise to agents' capacity to advance the scientific inquiry and validate or refute other agents' findings and claims.[611] Information is the fuel of CAS, as it is essential to its performance and to harnessing complexity within coevolving CAS. As a component of the innovation ecosystem, openness becomes an enabler of the scientific endeavour and a requirement for effective communication within CAS. Since communication mediates agent behaviours, information must be accessible, reliable, intelligible, (re)usable (and reproducible), and quickly exchangeable. Otherwise, the

[611] In this sense: "Not only is open science often effective in stimulating scientific discovery, it may also help to deter, detect and stamp out bad science. Openness facilitates a systemic integrity that is conducive to early identification of error, malpractice, and fraud, and therefore deters them. But this kind of transparency only works when openness meets standards of intelligibility and accessibility—where there is intelligent openness." *Science as an open enterprise*, by The Royal Society Science Policy Centre (London: The Royal Society, 2012) at 08.

decision-making processes of agents and, consequently, of law and policy-making processes are compromised.

Second, in looking at openness as a guiding principle of RD&I activities and different CAS, Merton's normative structure of science specifically includes openness. He noted the critical role that sharing—under the Communism characteristic—plays in science's proper functioning.[612]

Third, evaluating openness as an emergent phenomenon enables us to see these CAS as dynamic entities. I deepen this assessment in the sections below, where I present different RD&I models, initiatives and legislation. Emergence occurs through interactions among agents and results from the combination of agent behaviours and their iteration. Emergence may lead to change and adaptation, which might occur on different scales.[613] As previously mentioned, diverse RD&I models and initiatives are niches within CAS where agents are freer to experiment. Successful experimentation in specific niches may inspire and influence agents in other niches to test different organizational frameworks and regulations. Broadly, the emergent character of openness places it as a systemic response to problems and an instrument for gradual and informed systemic learning, reform, and design. A historical uptake of openness in law and science is helpful to understand this phenomenon better, independently of how one perceives it and its emergence in and within CAS.[614]

The idea of openness also relates to cooperation, but neither is a necessary condition of the other. Cooperation is opposed to competition, while openness is opposed to closedness. Both concepts affect agent choices, and strategies in respect of the products of their research, and both mediate the flow and sharing of information and intangible assets. Cooperation does this regardless of IPRs – for example, through licensing or sharing of IPRs—while openness does this through the absence of IPRs. Even though

[612] See Chapter Four and more specifically: Merton, *supra* note 330.
[613] For discussions definitions and concepts related to emergence please refer to Chapters One and Two.
[614] See: David, "Understanding the emergence of 'open science' institutions", *supra* note 610; David, *supra* note 295.

openness and cooperation are not dependent, it is more likely to see the joint application of these ideas, considering they may share similar goals, such as enabling information flow.

Last, a more complete conceptualization and practice of openness in diverse CAS relates to setting up requirements that improve how science is done and regulated by law. It further indicates how science can more effectively generate progress and change in society. A significant contribution of openness in law and science is its potential to benefit different agents, either public or private and society as a whole. As the Royal Society states:

> Open inquiry is at the heart of the scientific enterprise. Publication of scientific theories—and of the experimental and observational data on which they are based—permits others to identify errors, to support, reject or refine theories and to reuse data for further understanding and knowledge. Science's powerful capacity for self-correction comes from this openness to scrutiny and challenge.[615]

7.1.2. Categories and Concepts

Openness manifests itself to different degrees in varied biomedical RD&I models in light of the agent goals and strategies. Open-source, open data, open science, open innovation, open drug discovery, and open-source biotechnology are some of the terms that have arisen, drawing on the concept of openness in relation to the regulation of knowledge by IPRs. The characteristics that describe (or define) each of these terms vary significantly, and I briefly explain some below. It is notable, however, that different agents may employ the term 'open' to explain their activities but employ entirely different IP and regulatory strategies and organizational frameworks to achieve this openness. Trying to capture these different meanings, in this thesis, openness indicates a paradigm in which different agents interact, perceive their reality and problems, and engage in the regulation of biomedical RD&I through the use or absence of IPRs. The goal is to maximize access and innovation by behaving openly towards knowledge regulation and sharing.

[615] The Royal Society Science Policy Centre, *supra* note 611 at 07.

Exemplifying the connection of different models and definitions, the Royal Society discussion of *open data* provides a starting point. It highlights the importance of adopting new approaches to enable change, solve problems, operationalize, and create an infrastructure to allow these approaches to fulfill their potential. The Royal Society states:

> Successful exploitation of these powerful new approaches will come from six changes: (1) a shift away from a research culture where data is viewed as a private preserve; (2) expanding the criteria used to evaluate research to give credit for useful data communication and novel ways of collaborating; (3) the development of common standards for communicating data; (4) mandating intelligent openness for data relevant to published scientific papers; (5) strengthening the cohort of data scientists needed to manage and support the use of digital data (which will also be crucial to the success of private sector data analysis and the government's Open Data strategy); and (6) the development and use of new software tools to automate and simplify the creation and exploitation of datasets. The means to make these changes are available. But their realisation needs an effective commitment to their use from scientists, their institutions and those who fund and support science.[616]

Open-source means open access to the 'source code,' which grounds much of software development. Access to the source code is guaranteed through licenses to use the software. This access puts others in a position to modify and improve the source code, creating new and derivative works.[617] In the open-source software movement, developers generally permit the free use, modification, and improvement of the software source code. However, in exchange, they require that all resulting changes and improvements in the source code remain in the public domain or a restricted common pool. Subsequent licensees must adopt the same non-proprietary idea.[618] Examples of open-source projects are the tools underlying the Internet and Wikipedia. As Matthew Todd explains:

> In open source the community participates in peer-reviewed public work. Depending on the exact licence of the project, one will have high levels of freedom to act. Crucially, one may act while the work is happening, rather than merely after it is complete. You are a player, not an observer. There is cooperation towards goals that operates alongside an open competition in how work is done, i.e., collaboration within a rather brutal, open arena of expertise.[619]

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[616] *Ibid* at 08.
[617] More information is available at "The Open Source Definition | Open Source Initiative", online: <https://opensource.org/osd>.
[618] More information is available at *Ibid*.
[619] M H Todd, "Six Laws of Open Source Drug Discovery" (2019) ChemMedChem, online: <https://doi.org/10.1002/cmdc.201900565> at 7.

The term *open science* has at least two meanings. The first definition relates to basic research, meaning access to data and scientific information. The OECD provides a definition of open science that relies on the following pillars: (i) open access, (ii) open data, (iii) open collaboration, and (iv) the use of information and communication technologies (ICT) tools and platforms for its operationalization.[620] Second, open science can also be defined as a new manner of regulating R&D by ensuring that all activities performed by the scientific and research communities—and the results of these activities—are freely accessible to all.[621] In this second conceptualization of open science, patent protection is not pursued, and knowledge is broadly available through databases that require the creation of an infrastructure to standardize and share different intangible assets. It also requires a sophisticated IP strategy because there is a risk of third parties patenting inventions if disclosing the information related to the invention is not thoroughly done and documented.[622] In the field of biomedical research, this definition of open science may translate into open drug development. Either approach to open science (and the general idea of openness) may also include other elements such as open access, open data, open-source, open educational

[620] To detailed definition of each one of this concept, see section "Open Science: Policy Challenges and Opportunities" at: OECD, *OECD Science, Technology and Industry Outlook 2012*, OECD Science, Technology and Industry Outlook (OECD Publishing, 2012) at 189.

[621] In this sense, see, especially: The Royal Society Science Policy Centre, *supra* note 611; Gold, "Accelerating Translational Research through Open Science", *supra* note 442; Gold et al, *supra* note 424; Caulfield, Harmon & Joly, "Open science versus commercialization", *supra* note 37; United Nations Educational, Scientific and Cultural Organization (UNESCO), *supra* note 272; United Nations Educational, Scientific and Cultural Organization (UNESCO), *Draft Recommendation on Open Science-41 C/22* (UNESCO Digital Library, 2021).

[622] For details, see: "A bold experiment in open science : McGill News", online: <http://publications.mcgill.ca/mcgillnews/2016/05/24/a-bold-experiment-in-open-science/>; E Richard Gold, "Accelerating Translational Research through Open Science: The Neuro Experiment" (2016) 14:12 PLoS Biol, online: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5147793/>.

resources (OER), open notebooks, open peer review, scientific and social networks, equity, diversity and inclusion, and citizen science.[623]

Paul David was the first to coin the term 'open science.' He argued for the open sharing of data and publication and that IPRs should not prevent that sharing and subsequent use. David explains that cumulative processes and interactions enable scientific progress and generate societal benefits by promoting cooperation and information sharing.[624] These processes ensure that reliable information informs science through peer review and constant dynamic collaboration, feedback, and criticism among agents.[625] David examines the dynamic relationship between openness and IPRs and how agents' behaviours and expectations led to different ways of organizing science. He recalls the shifts in the late sixteenth and early seventeenth centuries, leading to the emergence of openness as a force opposing the prevailing models based on secrecy. David explains how patronage and the asymmetry of information during the Renaissance gave place to the practices of the modern scientific community that pursues and

[623] The European Commission have defined open science as "a fast evolving, multidimensional phenomenon" (*Study on Open Science*, p.05) and followed in part the OECD (2015) definition that is centred in open research data, open access to publication, open collaboration, and the infrastructure and practices enabling them. In this context, they have created an Open Science Policy Platform, the European Open Science Cloud, and an Open Science Monitor. This last initiative tracks trends and policies in open science in their 28 Member States (MS) and G8 countries. The goal is to identify policies, drivers, barriers, and the impacts of open science in society. In this sense, see: European Commission, "Open Science Monitor", online: *Eur Comm* <https://ec.europa.eu/info/research-and-innovation/strategy/goals-research-and-innovation-policy/open-science/open-science-monitor_en>; European Commission, "Open Science Policy Platform", online: *Eur Comm* <https://ec.europa.eu/info/research-and-innovation/strategy/goals-research-and-innovation-policy/open-science_en>; European Commission, "European Open Science Cloud (EOSC)", online: *Eur Comm* <https://ec.europa.eu/info/research-and-innovation/strategy/goals-research-and-innovation-policy/open-science/eosc_en>; *Study on Open Science: Monitoring trends and divers. Reference: PP-05622-2017*, D.2.4 Final Report (Bruxelles: European Commission, 2019); *Open Science Monitor: Updated Methodological Note* (Bruxelles: European Commission, 2019).

[624] See, generally: David, *supra* note 295.

[625] Paul David further explains: "The core of this rationale is the greater efficacy of open inquiry and complete disclosure as a basis for the cooperative, cumulative generation of predictably reliable additions to the stock of knowledge. In brief, openness abets rapid validation of findings, and reduces excess duplication of research efforts. Wide sharing of information puts knowledge into the hands of those who can put it to uses requiring expertise, imagination, and material facilities not possessed by the original discoverers and inventors. This enlarges the domain of complementarity among additions to the stock of reliable knowledge, and promotes beneficial spill-overs among distinct research programs." *Ibid* at 22.

shares knowledge in the Mertonian sense.[626] For David, open science is, historically, a "comparatively recent organizational innovation."[627]

There exist some examples of the second form of open science. Most are research projects or initiatives (not necessarily entire institutions) working in niches to tackle specific problems and to coordinate the expert communities' and their partners' efforts, as explained later in this chapter. Observing the place in which these initiatives emerged, the reasons, circumstances, and agents involved in them allow agents to evaluate the emergence of open science models (and broadly, openness in science) and their subsequent influence in shaping and reforming the innovation ecosystem as a whole.

The open science model can be envisioned as a necessary part of innovation frameworks rather than as a challenge to commercialization.[628] Agents need to improve their knowledge of IP and biomedical innovation systems to better strategize and engage in complex decisions about when and how to compete and cooperate, as well as promote openness or closedness (and the numerous behaviours in between). Some agents might be more inclined to adopt open science models once they understand their benefits, and we demystify preconceptions about IPRs and openness in science. They may also spread this model's

[626] For specific assessment about the emergence of open science and detailed description of the historical origins and evolution of it, see: David, "Understanding the emergence of 'open science' institutions", *supra* note 610; *The Historical Origins of "Open Science": An Essay on Patronage, Reputation and Common Agency Contracting in the Scientific Revolution*, SSRN Scholarly Paper, by Paul A David, papers.ssrn.com, SSRN Scholarly Paper ID 2209188 (Rochester, NY: Social Science Research Network, 2013).

[627] "Judged by the historical standards, 'open science' is a comparatively recent organizational innovation. Accompanying the profound epistemological transformations effected by the fusion of 'experimentalism' with Renaissance mathematics, the cultural ethos and social organization of western Europe scientific activities during the late sixteenth and seventeenth centuries underwent a significant reorganization—departing from the previously dominant regime of secrecy in the pursuit of 'Nature's secrets.' This development should be seen as a distinctive and vital aspect of the Scientific Revolution, from which their crystallized a new set of social conventions, incentive structures and institutional mechanisms that reinforced scientific researchers' commitments to rapid disclosure and wider dissemination of their new discoveries and inventions. Yet, the puzzle of why and how this came about has not received the notice it deserves, especially in view of the complementarities and tensions that are recognized to be presented today in relations between the regimes of 'open' and 'proprietary' science." David, "Understanding the emergence of 'open science' institutions", *supra* note 610 at 574.

[628] In this sense: "Commercialization and open science are not necessarily irreconcilable and could instead be envisioned as complementary elements of a more holistic innovation framework. The idea of optimally sharing and maximally utilizing scientific knowledge is fraught with complexity, confusion, and policies at seemingly stark cross-purposes. The matter is further complicated by the fact that research is becoming more expensive, research structures are growing more complex and fractured, and innovation levels, at least in the pharmaceutical setting, are not increasing." Caulfield, Harmon & Joly, "Open science versus commercialization", *supra* note 37 at 1–3.

advantages and influence other agents while engaging in their dynamic relationships.[629] Richard Gold explains the benefits for universities adhering to this model:

> Open science models of collaboration reduce the tax imposed by university patenting to zero. Because the university holds and enforces no patents, the most difficult issues in negotiations—IP and revenue sharing—evaporate, rendering it feasible to develop standard-form contracts that firms and universities can sign in weeks rather than months or years. Beyond this, open science collaborations facilitate the sharing of tacit knowledge by making it easy for a diverse set of public and private actors to participate. Armed with this knowledge, partners can quickly develop products, services and public interventions years ahead of when they otherwise would have been able.[630]

Open innovation represents a model that seeks to maximize returns on existing proprietary inventions and renders the process of obtaining and using them by private actors more efficient. Henry Chesbrough coined the concept of open innovation, which reveals a change in the behaviour and interaction patterns between agents in the RD&I framework. The idea is to substitute the early 20th century vertical R&D model—in which R&D was performed inside and exclusively by a single firm—with a more horizontal, diversified, and dynamic model. This new model uses the idea of outsourcing R&D to different actors by promoting partnerships and/or licensing and purchasing technologies developed by others. Open innovation relies on the argument that prospecting ideas outside the institution and interacting with different actors is less costly and risky in terms of money, time and human resources. Thus, it can be an efficient tool to maximize profits. From this perspective, open innovation can be seen as a business model where universities, research institutes, and small and mid-sized enterprises are the new 'old' partners for the private sector to engage in joint R&D or to achieve a diversified R&D portfolio.[631]

Both open science and open innovation assume that isolation does not maximize innovation. Based on this idea, the infrastructure devoted to R&D within industries has become smaller. However, in open

[629] Henry Etzkowitz, "Innovation Lodestar: The entrepreneurial university in a stellar knowledge firmament" (2017) 123 Technol Forecast Soc Change 122–129.
[630] Gold, *supra* note 410 at 8.
[631] For initial thought on it, see: Henry W Chesbrough, "The Era of Open Innovation" (2003) 44:3 MIT Sloan Manag Rev Camb 35–41; Henry William Chesbrough, *Open innovation : researching a new paradigm* (Oxford : Oxford University Press, 2006).

innovation models, the level and terms of interaction between partners are still controlled by industry, or whoever is prospecting different intangible assets. Open innovation increases the exchange of knowledge, but this does not necessarily mean that knowledge will be available broadly or freely to all those who need it. In sum, open innovation is simply better management of IP assets (under a proprietary view) to increase rents.

Open drug discovery (or open drug development) uses notions of cooperation and openness to developing health technologies through different organizational and regulatory frameworks. Matthew Todd highlights the need to think outside the box while engaging in R&D activities and solving problems while explaining *open-source drug discovery*. He questions how 'open' is open innovation since IP assets, data, information, and knowledge are kept to a limited group. He notes that the central feature of open innovation is that companies reorient their approach to solve problems in the public domain and enlarge the network of experts participating in an endeavour. This reorientation means that the problem is 'open' to a solution, but the group working on it is still closed and subject to central control. The same happens for the knowledge acquired through open innovation initiatives, and that secrecy still exists, as well as limitations as to who has access to the solutions. He explains how "nebulous" the term open innovation is and that there are various initiatives under this definition that vastly differ from one another.[632]

Balasegaram et al. evaluate open-source as an underused model that can advance innovation while addressing health needs. The authors highlight indirect benefits related to open-source that translate into putting information and data into the public domain, independently of whether a project successfully develops a health technology. In this way, open-source principles applied to drug development improve CAS operation because it increases the amount of information circulating within these systems.[633]

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[632] Todd, *supra* note 619.

[633] The authors clarify: "OS ultimately fosters an R&D system that is less wasteful: in the event a project is halted, all data (including negative findings) remain in the public domain, allowing similarly informed decisions by other parties in the future. It is estimated that 85% of the US$200 billion/year spent globally on health and medical research is wasted, primarily because

O*pen-source biotechnology (open-source biotech)* has been one of the most controversial models relating to IP protection in the biotechnology field.[634] This model has similar goals to the second definition of open science provided above. It draws on the *open-source software* concepts explained above into the biotechnology field and applies a framework of licenses and collaborative behaviours to advance science. In this sense, *open-source biotech* is a collaborative, dynamic, and open model of R&D applied to the biotechnology field. In this model, not only all outcomes of R&D and follow-on innovation remain in the public domain or are regulated as 'commons,' but so do the entirety of the processes that generated them.[635] The participants in the R&D network pursue IPRs not to extract rents but to ensure that nobody can obtain exclusivity on their inventions and intangible assets. They accomplish openness by applying viral licences to their patents and requiring users to patent and license on the same terms. The result of this approach is a network of producers and users of intangible assets, all of whom have agreed (through a contract) not to limit the use of knowledge related to an invention. In other words, in an *open-source biotech* model, IPRs are pursued defensively and to guarantee complete control of R&D outcomes. Later, knowledge is set free by licensing practices and frameworks. However, the pursuit of IP protection implies paying the costs of acquiring and maintaining them, which is not necessarily affordable to most agents.[636]

In a comprehensive assessment of the above model, Janet Hope notes that no existing open-source initiative "constitutes a mature working example of an open-source biotechnology project."[637] At the time

information is not shared (~50% of registered clinical trials are never published in full, and ~50% of those published are not sufficiently complete for others to interpret, use, or replicate the research correctly), meaning that new studies cannot take advantage of previous research and patients are exposed to undue risk." Manica Balasegaram et al, "An open source pharma roadmap" (2017) 14:4 PLOS Med e1002276 at 04.

[634] See generally: Janet Hope, "Chapter 7. An Introduction to Open Source Biotechnology" in Christopher Arup & William Van Caenegem, eds, *Intellect Prop Policy Reform Foster Innov Dev* (Cheltenham, UK: Edward Elgar, 2009) 129; Hope, *supra* note 384; Joly, "Open biotechnology", *supra* note 237.

[635] Janet Hope affirms about open source biotechnology (OSB): "(…) OSB represents one of a number of proposed strategies for pre-empting or counteracting some of the adverse effects of increasing proprietary control over this broad enabling technology". (…) At a practical level, OSB is a novel approach to managing research collaborations, licensing IP and commercializing or otherwise exploiting new technologies" Janet Hope, "An Introduction to Open Source Biotechnology." Hope, *supra* note 634 at 130.

[636] See: Joly, "Open biotechnology", *supra* note 237.

[637] Hope, *supra* note 384 at 21.

of Hope's analysis, she noted the lack of empirical studies that evaluate whether agents in the biotechnology industry would be willing to adopt a model similar to the open-source software and the difficulties of collecting data in such a diverse sector. She also highlighted the need to compare proprietary and non-proprietary strategies used by biotechnology companies to evaluate the trade-offs involved in adopting this new model.[638]

The ideas presented above materialize into models and initiatives that I classify as niches. These niches are conceived and persist within different CAS as strategies that agents pursue to achieve their goals. The diversity of approaches, the bounded rationality of agents, including the tendency to transpose laws from other jurisdictions without understanding of context, intensifies the difficulty of finding a path forward. This highlights the need to study openness and related models and strategies, to better educate agents on their use, and to develop consistent and transparent monitoring and evaluation of these models.

The lack of uniformity in the meaning of 'open' within these models will complicate the process. The broad definition of openness I propose helps to address confusion.

7.2. Openness as an Emergent Phenomenon

Recalling that *emergent phenomena* arise from the interactions among agents who generate new behaviours and outcomes is critical to understanding CAS. It results in new expectations of what agents hope to achieve in developing new biomedical RD&I models. These new expectations, behaviours, and interactions generate new regulations to govern these models or result in the current IP regulation being applied differently. It is possible to identify catalysts—at the national and international level—for new

[638] Hope states about the feasibility of adopting this model: "A detailed, realistic model of open source biotechnology can only be developed by tapping into the ideas and experience not only of those who are already engaged in this field of research and development, but also of those who are not. Clarifying the relationship between generic open source principles and the realities of biotechnology research and development will also help debunk a number of common objections to the feasibility of open source biotechnology that are based on either factual misconceptions or faulty logic." Hope, *supra* note 384.

approaches to knowledge regulation in biomedical R&D and to relate these approaches to analysing whether IP systems hinder or incentivize innovation and access to knowledge in particular fields, such as areas of market failure to develop treatments for neglected diseases or rare diseases. However, the number of factors and agents influencing emergent phenomena and new RD&I models and initiatives are too complex and numerous to be simply defined by cause and consequence evaluations. Further, tracking down all factors that lead agents to behave differently (and to reiterate those behaviours) is impossible. This is because of agents' bounded rationality, imperfect information that flows through these systems, and power relations and politics affecting agents' behaviours and interactions.

Below, I illustrate how openness is an emergent phenomenon within biomedical RD&I as it responds to internal and external pressures such as the cost of conducting science, declining productivity of science and the desire to increase diversity.

7.2.1. Translating Ideas into Initiatives to Advance Science and Promote Access to Knowledge and Innovation

In 2016, the RE: Route mapping of UAEM identified 130 existing and proposed initiatives and analyzed 81 that promote R&D for the public good within universities and other settings. Several of these explicitly promoted the idea of openness.[639]

While discussions about open RD&I models are not new and have been mobilizing agents at different levels of the innovation ecosystem, as the failure of IP and biomedical innovation systems to generate results becomes more explicit, agents more actively engaged in debates about access and

[639] The UAEM project RE: Route is an important source about the variety and number of new biomedical RD&I models that have emerged and the need for consistently monitoring them. However, the RE: Route does not seek to be a comprehensive mapping nor engage in in-depth qualitative research. It also determines as criteria to classify R&D initiatives as alternative models the fact that they are driven by the needs of patients globally. Considering these points, both the RE: Route and the examples in this section are just partial pictures of the reality of new and alternative biomedical RD&I models and the emergence of openness. See: *UAEM RE:ROUTE. A map of the alternative biomedical R&D landscape*, by Rachel Kiddell-Monroe, Alexandra Greenberg & Merith Basey (Washington, D.C.: Universities Allied for Essential Medicines, 2016) at 05–08.

innovation and the number and diversity of initiatives that propose new RD&I models to tackle problems. These debates moved from just seeking a fair share and flow of scientific data and information and creating sustainable R&D infrastructures to reflections on whether it is possible to develop entirely patent-free models.[640]

The examples below illustrate the emergence of openness as a solution to failures in the biomedical RD&I system. These examples are not exhaustive but rather, give a glimpse of some of the shifts in agent behaviours within these systems. While these initiatives often arise in a complementary fashion, they also show the multitude of components and gaps to be addressed in creating a robust and resilient global health innovation ecosystem.[641]

In 2001, MSF and the Pasteur Institute created the Drugs for Neglected Diseases initiative (DND*i*). DND*i* is an entity that coordinates initiatives and advances biomedical RD&I in the field of neglected diseases. It works as a virtual R&D collaboration that brings together different agents, such as pharmaceutical industries, research centres and universities, and patients through the entire drug development pipeline.[642] Over the years, DND*i* has contributed to delivering, recommending, and implementing seven new treatments for neglected diseases and aims to deliver 16 to 18 new treatments by 2023.[643] DND*i*'s IP strategy was drafted to "ensure that treatments are ultimately affordable to patients who need them and that access to these treatments is equitable." This strategy also aims "to develop drugs as public goods when possible (although DND*i* will not necessarily be able to control all IP for short-and

[640] World Health Organization (WHO), *supra* note 63; World Health Organization, World Trade Organization & World Intellectual Property Organization, *supra* note 22; World Health Organization, World Intellectual Property Organization & World Trade Organization, *supra* note 17.
[641] To discussions about the need to coordinate efforts and address gaps on the global health innovation ecosystem, see: Keusch & Lurie, *supra* note 33; Lurie, Keusch & Dzau, "Urgent lessons from COVID 19", *supra* note 24.
[642] There is room for some criticism and improvement of DND*i*'s model considering its contracts with different partners are not available for public consultation. For more information, see: Drugs for Neglected Diseases (DNDi), "Open Innovation | DNDi", (18 November 2011), online: *Drugs Neglected Dis Initiat DNDi* <https://www.dndi.org/diseases-projects/open-innovation/>.
[643] DND*i*'s R&D projects portfolio is available at: Drugs for Neglected Diseases (DNDi), "Portfolio | DNDi", online: *Drugs Neglected Dis Initiat DNDi* <https://www.dndi.org/diseases-projects/portfolio/>.

mid-term projects)."[644] In this sense, DND*i* decides its IP strategy on a case-by-case basis and whether or not to pursue IPRs in each project.[645] DND*i* tackles problems that mainly affect developing and least-developed countries, builds on the current R&D infrastructure, and leverages local human resources. Its main activities and projects take place in those countries and prioritize local answers to problems and capacity building. DND*i*'s RD&I model pushes forward public health debates, promotes a needs-driven and access model, and engages diverse agents in these activities and partnerships.[646]

In 2003, the Human Genome Project (HGP) was concluded with complete disclosure of its findings (including human genome sequences) into the public domain.[647] The HGP was a public consortium established between scientists from different parts of the globe as a collaborative network to decode the human genome. The value of the information produced by projects such as the HGP is immeasurable. As basic research and applied technology in the biotechnology field do not have precise limits, these projects' applications and impacts cannot necessarily be evaluated when they occur; instead, they require long-term monitoring. Recognizing this fact may have influenced the decision of scientists that participated in the HGP to stress the importance of keeping this information in the public domain to advance science.[648]

In 2004, private and public sector agents created the Structural Genomics Consortium (SGC) as "a not-for-profit, public-private partnership (PPP) with the directive to carry out the basic science of

[644] Drugs for Neglected Diseases Initiative (DNDi), *DNDi's Policies – Intellectual Property Policy*.
[645] Drugs for Neglected Diseases Initiative (DNDi), *DNDi's Policies – Intellectual Property Policy*.
[646] Benjamin Coriat et al, "DNDi, a Distinctive Illustration of Commons in the Area of Public Health" (2019) 2019–93 Agence Fr Devéloppement (AFD Research Papers Series) , online: <https://www.afd.fr/en/ressources/dndi-distinctive-illustration-commons-area-public-health>; Drugs for Neglected Diseases (DNDi), *supra* note 27.
[647] Detailed information about the HGP is available at: "An Overview of the Human Genome Project", online: *Natl Hum Genome Res Inst NHGRI* <https://www.genome.gov/12011238/an-overview-of-the-human-genome-project/>; Genome: Unlocking Life's Code, "Timeline- A Brief Story", online: *Genome Unlocking Lifes Code* <https://unlockinglifescode.org/timeline>.
[648] For a critical and chronological view on the manner the HGP had influenced the role of public and private agents and how they switched positions and or took turns in the defense or not of the public domain, see: Eisenberg & Nelson, "Public vs. proprietary science", *supra* note 329 at 94–97.

relevance to drug discovery."[649] In particular, it aimed at decoding the three-dimensional structures of human proteins to support the development of new health technologies, a much-needed scientific advancement after the HGP. The mission of SGC is to make research outputs broadly available to scientific and research communities and advance research in areas such as human biology and drug discovery. SGC works under an open science collaborative network of academic and research institutions and pharmaceutical industries that runs its projects and does not protect its research outputs by restrictive IPRs. There is also an evolution of the SGC's model, considering it initially contemplated protecting IPRs (but never did) and after shifted to an open science model to accelerate and facilitate collaboration and science.[650] Additionally, SGC's organizational model is decentralized and counts on the participation of different institutions worldwide. For instance, the University of Campinas (Unicamp) in Brazil is a member of SGC's network, illustrating its global dimension, the collaborative feature of biomedical R&D, and the presence and importance of developing countries in advancing science.[651]

In January 2016, the Neuro (McGill University's Montreal Neurological Institute-Hospital) announced the adoption of open science principles to regulate its R&D activities as a strategy to increase innovation and translate more research into treatments. Part of the justification for adopting this new model was the cost (time and money) associated with pursuing IP protection and the failure of the biomedical RD&I system to have developed new treatments for neurodegenerative diseases over several decades. Over the coming years, the Neuro plans to test its open science model by making available its research

[649]Additionally: "The core mandate of the SGC is to determine 3D structures on a large scale and cost-effectively - targeting human proteins of biomedical importance and proteins from human parasites that represent potential drug targets. In these two areas respectively, the SGC is now responsible for >25% and >50% of all structures deposited into the Protein Data Bank each year; to date (Sep. 2011) the SGC has released the structures of over 1200 proteins with implications to the development of new therapies for cancer, diabetes, obesity, and psychiatric disorders." Structural Genomics Consortium (SGC), "SGC | FAQ for Non-Scientists", online: <http://www.thesgc.org/about/mini_faq#faq_1>.

[650] "SGC | Structural Genomics Consortium", online: <http://www.thesgc.org/>; Molly Morgan Jones et al, "The Structural Genomics Consortium: A Knowledge Platform for Drug Discovery: A Summary" (2014) 4:3 Rand Health Q, online: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5396214/>.

[651] note 534.

outcomes. The most significant assets of the Neuro are the knowledge it generates and the high-quality researchers who enrich this dynamic and innovative place. With its adoption of open science principles, the Neuro hopes to obtain a competitive advantage, as it will be very challenging for any other institution to create something as specialized.[652]

In 2018, several participants in the SGC network launched M4K Pharma. M4K Pharma is an initiative that uses "open science to revolutionize how affordable new treatments are discovered and developed. Through our Medicines4Kids program, we will aggregate and align the work of global academics, foundations and industry researchers to advance new cures for childhood diseases not well-served by current business models."[653] M4K Pharma is an open science drug discovery initiative, and its IP strategy does not rely on patent protection but rather on regulatory exclusivity.[654]

7.2.2. Openness in the Institutional Level: The Brazilian Case

Law and policy not only can enable the adoption of the idea of openness but can support agents in changing their behaviours towards more open practices in biomedical R&D. As presented in Chapter Six, Brazil has the necessary foundation—in its laws, policies, and institutions, such as USP – to engage more actively in openness in law and science. What it needs, however, is a more focused set of regulatory and organizational changes to catalyze that foundation into openness in IP policies and practices. These include creating incentives for academic and research communities to behave more cooperatively and experiment with new biomedical RD&I models. Discussions concerning the implementation of initiatives leaning towards openness are still incipient in Brazil.

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[652] note 622; Gold, "Accelerating Translational Research through Open Science", *supra* note 622; Knox, *supra* note 279.
[653] M4K Pharma - Medicines4Kids, "About – M4K Pharma", online: <https://m4kpharma.com/about/>; Maxwell Robert Morgan, Owen Gwilym Roberts & Aled Morgan Edwards, "Ideation and implementation of an open science drug discovery business model – M4K Pharma" (2018) 3 Wellcome Open Res (154) 154–163.
[654] M4K Pharma - Medicines4Kids, *supra* note 653; Morgan, Roberts & Edwards, *supra* note 653.

As noted in Chapter Three, Brazil has taken advantage of most of the TRIPS flexibilities in its IP legislation. While this establishes a legislative base through which to develop more open models, the problem appears to be more political than legal in Brazil, considering how power relations and politics influence governmental decisions. For instance, while Brazilian law explicitly permits the issue of compulsory licenses and parallel importation,[655] the country does not use them to address domestic needs due to political considerations.

Provincial, municipal, and institutional regulations in Brazil are more likely to be flexible in creating an environment in which experimentation with openness and cooperation can develop. Some public research institutions with missions related to public health are more likely to adopt institutional policies and practices that promote openness across several—if not all—of their projects and research initiatives. Additionally, institutions such as Fiocruz, with missions and goals connected to the public interest and public health in support of SUS and the CIS, are more likely to adopt open practices. Other public institutions also have the potential to implement open and collaborative policies and practices and experiment with new and open biomedical R&D models given that they are publicly funded and directed to promote the public interest. However, as these later institutions were not created uniquely to address public health-related needs as is the case with Fiocruz, their expert communities may be subject to more power relations and political constraints in their relationship with other agents (public and private).

The current set of metrics used to evaluate the above-mentioned institutions' successes and their projects—such as the number of patents they hold—do not incentivize cooperation and openness. So while USP has the mission of enabling the public interest, its counting of patents does nothing to encourage cooperation and coordination of actions across its units, activities, and projects. In terms of strategy,

[655] César et al, *supra* note 7; Chaves et al, *supra* note 7; Stiglitz et al, *supra* note 5.

certain institutions may be more likely to experiment with openness in law and science and collaboration due to their mandates, such as the CEPIDs and INCTs and their different projects.[656]

As previously mentioned, the private sector has also shown a willingness to engage in more open and collaborative practices and open science endeavours with different partners.[657] A recent example of collaboration between a pharmaceutical industry and a public university in an open science project is that between the Medicinal Chemistry Centre of Open Innovation (Centro de Química Medicinal de Inovação Aberta—CQMED) of the University of Campinas (Universidade de Campinas—Unicamp) and the Brazilian pharmaceutical firms Aché e Eurofarma at the beginning of 2018. The partnership aims to develop new molecules that the partners hope will lead to new medicines against cancer and infectious diseases. Embrapii and pharmaceutical industries fund this project, while SGC participates through is laboratory at UNICAMP.[658]

Fiocruz has an Open Science Policy regarding copyrights and related rights and the infrastructure in place to share its scientific production, the Arca Repository (Repositário Arca).[659] However, it is now taking steps to implement actions that enable more significant cooperation and sharing of data, information, and knowledge and the adoption of new and open biomedical RD&I models. Among these steps, Fiocruz has launched a publication that maps open science (open access, copyrights and related rights) policies, infrastructure and strategies in Brazil and internationally.[660] It has established the Fiocruz Working Group on Open Science (Grupo de Trabalho em Ciência Aberta da Fiocruz—GTCA) to evaluate

[656] See Chapter Six for considerations about Brazil and specifically about USP and Fiocruz.
[657] Elizabeth Dougherty, "Open science demystified", (6 January 2018), online: *Novartis* <https://www.novartis.com/stories/discovery/open-science-demystified>; Matthew Warren, "Big pharma is embracing open-access publishing like never before" (2019) Nature, online: <http://www.nature.com/articles/d41586-019-00610-2>.
[658] Villen, *supra* note 534; note 534.
[659] See: Instituto de Comunicação e Informação Científica e Tecnológica em Saúde (Icict/Fiocruz), "Repositório Institucional - Arca", online: *Fiocruz* <https://portal.fiocruz.br/repositorio-institucional-arca>; Fiocruz Foundation & President of the Oswaldo Cruz Foundation, *Policy on Open Access to Knowledge. Number 329/2014-PR retificada por 382/2014-PR* (Fundação Oswaldo Cruz (Fiocruz), 2014).
[660] Santos & Clinio, "Gestão e abertura de dados para pesquisa", *supra* note 534.

its efforts and to coordinate broader institutional actions related to open science. Fiocruz has also promoted training about open science by offering several courses through its Virtual Campus.[661]

The above suggests that Fiocruz is leaning towards implementing a more extensive version of open science that encompasses no patenting (or limited filling) and even more open practices.[662] In analyzing Fiocruz, it is possible to identify similarities to the Neuro's open science model. Interestingly, these two institutions have established an informal dialogue about these matters through expert networks. This later fact highlights the importance of the role of interaction among agents in shaping CAS and the tendency of agents to look for inspiration that they consider to be successful.[663] Fiocruz has also offered expertise and advice to USP as it starts to deepen discussions about open science and ways to improve its open science practices and policies.[664]

Funding agencies can play a critical role in influencing the adoption of more open and collaborative IP practices and policies in universities and research centres. In this regard, the FAPESP Intellectual Property Policy stands out. Specifically, its article 7 provides that in inventions that have been licensed with exclusivity to third parties that were funded by FAPESP, the agency can ask that the license become non-exclusive in cases where there is a strong public interest.[665] This disposition is similar to the one found at Sao Paulo Provincial Innovation Law previously mentioned in Chapter Six.

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[661] Among the courses related to open science offered by Fiocruz are "What is Open Science", "Historical Overview of Open Science", "Intellectual Property Applied to Open Science", "Access to Information Right and Protection of Personal Data", "Open Access", and "Open Data." For more information, see: Fundação Oswaldo Cruz (Fiocruz), "Ciência Aberta", online: *Campus Virtual Fiocruz Ciênc Aberta* <https://campusvirtual.fiocruz.br/portal/?q=formacao-modular/ciencia-aberta>.

[662] Santos & Clinio, "Gestão e abertura de dados para pesquisa", *supra* note 534; Fiocruz Foundation & President of the Oswaldo Cruz Foundation, *supra* note 659; Fundação Oswaldo Cruz Grupo de Trabalho em Ciência, *Termo de referência: gestão e abertura de dados para pesquisa na Fiocruz* (Fundação Oswaldo Cruz, 2018); Instituto de Comunicação e Informação Científica e Tecnológica em Saúde (Icict/Fiocruz), *supra* note 659.

[663] Baracho, *supra* note 534.

[664] See: Pró Reitoria de Pesquisa-Universidade de São Paulo, "Ciência Aberta", online: <https://prp.usp.br/ciencia-aberta/>.

[665] Article 7 determines: "7) General provisions: a) In any case, for all Intellectual Property resulting from projects financed by FAPESP, the Foundation may require, in the public interest, that: a.1) Patents owners license them to third parties; and a.2) The eventual production is made in São Paulo, in case of exclusive licensing." *Author's free translation*. Fundação de Amparo à Pesquisa (FAPESP), *supra* note 589.

Beyond policies and funding, there is a need to create an infrastructure that enables the flow and sharing of data, information, and knowledge. Alongside creating this infrastructure, capacity-building projects may increase the knowledge and awareness of expert communities about openness in science and the different models available to implement this idea.[666] Especially in developing countries, this open infrastructure not only enables sharing but works as an instrument of control, public awareness, and agency in the fight against systemic problems like corruption. Examples of this infrastructure are Lattes and Carlos Chagas Platforms mentioned in Chapter Six.[667]

The above discussion and examples are not exhaustive. They serve only to illustrate the different facets of Brazilian legislation, policies, and practices that embrace the idea of openness in law and science. However, as already noted, a comprehensive national mapping is needed to fully document the emergence of openness in law and science in Brazil. This mapping would also help uncover IP strategies and biomedical RD&I models that have either not been used or have been underused by different agents, work as a guide to legal and policy experts at TTOs to better design IP strategies, and as a path toward communication between agents.

7.2.3. Challenges and Opportunities in Implementing the Idea of Openness

The initiatives presented in this chapter and the projects taking place at the institutional level are not simple to analyze or compare. For instance, one can question whether convincing agents to engage in open drug discovery models for neglected diseases requires the same arguments and incentives to make them venture to develop new cancer treatments. Another question is whether agents should replicate and

[666] Ali-Khan et al, *supra* note 398; Sarah E Ali-Khan, Liam W Harris & E Richard Gold, "Point of view: Motivating participation in open science by examining researcher incentives" (2017) 6 eLife e29319.
[667] See Chapter Six for further details and specifically: Conselho Nacional de Desenvolvimento Científico e Tecnológico—CNPq, *supra* note 567; Conselho Nacional de Desenvolvimento Científico e Tecnológico—CNPq, *supra* note 568.

transpose successful legal and regulatory frameworks created elsewhere or, instead, should they try to innovate and implement new models?

The drive toward openness in biomedical research derives from the concern among many agents—patients, researchers, and firms—that the current system suffers from market failure, particularly in respect of neglected, rare, or public health fields.[668] Thus, each Neuro, SGC, and HGP address science failures while DND*i* and M4K Pharma address market failures. Even though there is diversity between these initiatives, they share a common aim of developing new and innovative models to tackle real-world problems. A network of like-minded agents is easily detected in these initiatives—therefore, the examples I selected are not random.[669]

The propagation of these new R&D models through expert networks illustrates at least three aspects of emergent behaviours. First, agents observe other agents' behaviours and may replicate the ones considered successful. Second, the system's organizational framework will determine the information to which agents have access and the agents with whom they will interact. Third, strategies to increase and amplify agent interactions and the information about these models influence the likelihood that other agents will implement similar initiatives. These aspects determine the possibility of an isolated behaviour turning into an emergent phenomenon. Therefore, keeping in mind the diversity of agents' roles and interactions while monitoring, evaluating, and coordinating these initiatives is essential to effective global health response and CAS design and reform.

Likewise, assessing open initiatives encompasses monitoring and evaluating the effects of their legal, policy, and regulatory frameworks on access to knowledge and innovation in all dimensions (from

[668] Richard T Mahoney & Carlos Medicis Morel, "A Global Health Innovation System (GHIS)" (2006), online: <https://www.arca.fiocruz.br/handle/icict/16466> Accepted: 2016-12-07T16:00:07Z; Yamey & Morel, "Investing in Health Innovation", *supra* note 28.

[669] For instance, Aled Edwards a renewed scientist and founder of SGC and M4K Pharma, has actively participated and collaborated with the Neuro open science initiative. SGC-Unicamp has also collaborated with DND*i*.

access to products and services to research tools, materials, and databases). To date, the policy environment has used linear models to regulate R&D activities that are inherently dynamic and nonlinear. Consequently, the outcomes of existing legal regulation of these activities are often not those most desired. Depending on their framework and strategy, IPRs can enable a variety of proprietary or non-proprietary models. These same rights have the power to influence how agents pursue biomedical R&D activities, whether towards cooperation or competition. These are some of the reasons why promoting a debate on IPRs as instruments to jointly enhance innovation and access is urgently needed.[670]

As discussed in previous chapters, IPRs have an intrinsic duality in which they simultaneously incentivize and jeopardize innovation and access to knowledge. When looking at new models, there is a need to break down the myth that openness is necessarily opposed to IP protection and has the effect of harming commercialization and innovation. It is also necessary to contest the assumption that these models bring a disadvantage to the agents that invested time and resources in biomedical RD&I. Rather, there is a need to promote the strategic use of IPRs to achieve innovation and access to knowledge goals. It is true that some open models of innovation are viewed with caution by some agents who engage in biomedical R&D activities due to their traditional views on how to use IPRs to 'protect' and 'advance' science.[671] However, it is possible to promote IP literacy on these matters and engage these agents in innovative proposals and informed, transparent, and participatory dialogue, just as the Neuro's open science initiative did during its implementation phase.[672]

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[670] Bountra, Lee & Lezaun, *supra* note 22; Gold et al, "Needed", *supra* note 364; Frederick M Abbott, "Science, Scarcity and Public Health: The Search for New Pharma Models" (2013) Scarcity Public Health Search New Pharma Models May 20 2013, online: <http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2505427>; OECD, *supra* note 63; Diana Rhoten & Walter W Powell, "The Frontiers of Intellectual Property: Expanded Protection versus New Models of Open Science" (2007) 3:1 Annu Rev Law Soc Sci 345–373.

[671] Gold et al, "Needed", *supra* note 364; Gold et al, *supra* note 254; Kiddell-Monroe, Greenberg & Basey, *supra* note 639; Abbott, "Science, Scarcity and Public Health", *supra* note 670; Bountra, Lee & Lezaun, *supra* note 22; OECD, *supra* note 63; Røttingen et al, *supra* note 15; Røttingen & Chamas, *supra* note 263.

[672] Consultations (interviews) took place with the Neuro's staff to assess their understanding about IP, open science and different RD&I models, and barriers to knowledge dissemination and innovation. For more details about this process, see: Ali-Khan et al, *supra* note 398; Ali-Khan, Harris & Gold, "Point of view", *supra* note 666.

The current lack or diminutive market interest in developing health technologies for neglected diseases today might not stand tomorrow. The question that at least remains is how agents can identify, compare, and monitor initiatives while accounting for the uncertainty that emerges from CAS and other agents' interactions. One first step is to observe and understand emergence.

Moreover, different agents will have different views and goals regarding the implementation of biomedical RD&I models. The level at which agents experiment with new models relates to their level of satisfaction with existing models and their observation of the behaviour and success of other agents using different models. As previously discussed, the interaction and coevolution of IP and biomedical innovation systems have reached a critical moment in which problems arising in those systems lead to the emergence of new patterns of interaction among agents searching for solutions. In this sense, the emergence of openness in law and science does not refer only to the models themselves but to a behavioural shift. Consequently, the world is witnessing the intensification of many debates on better ways to regulate biomedical RD&I related to the idea of openness.[673] One example of this is within the pharmaceutical industry itself—known for its protective and aggressive business model and IP strategy—that has acknowledged the value of open science models and engaged in initiatives that express the idea of openness.[674]

Despite the rise of open models, we must acknowledge that IP strategies, practices, and policies in developing countries tend towards more proprietary and closed knowledge regulation approaches than non-proprietary and open approaches. This is because agents tend to copy other agents' behaviours that they assume are successful. Nowadays, the majority of behaviours in the IP and biomedical innovation

[673] In May 2019, during the Seventy-Second WHA, member states have approved a Resolution that addresses their concerns and the need to promote transparency in the current pharmaceutical market and related RD&I models. Even though there are criticisms related to the Resolution on Transparency and some points were left out of the final draft, it is an important step towards better practices in this field. For the Resolution and comments about it, see: Seventy-Second World Health Assembly, *supra* note 270; Médecins Sans Frontières (MSF), *supra* note 270.
[674] Dougherty, *supra* note 657; Warren, *supra* note 657.

systems is still proprietary and closed. In this sense, there is a need to promote education, IP literacy, and awareness of different agents about openness, collaboration, and new biomedical RD&I models. It is necessary to overcome assumptions that agents have about these ideas and practices and increase the incentives they have to experiment with models that would best fit their reality and suit their goals.

Brazil faces an underexplored path regarding the potential to adopt open and collaborative models to regulate biomedical RD&I. It is more likely that these models will succeed in institutions such as Fiocruz (which is already putting this model into action) or in specific institutes or projects in public universities and research centres (such as SGC-Unicamp). However, the IP strategy must be evaluated on a case-by-case and project-by-project basis to carefully explore which options would lead the Brazilian IP and biomedical innovation systems to enhance access to knowledge and innovation. Each of the various Brazilian research and academic institutions will have to weigh the costs and benefits of building a robust IP portfolio to achieve its development goals. Considering the public interest that underpins not only the Brazilian IP and biomedical innovation systems but its public health system (SUS), openness and collaboration are sound principles and ideas to be pursued by the Brazilian expert communities and state alike.

There are costs and constraints to implement, operationalize, and sustain the idea of openness in any system and, hence, create reliable and open infrastructures while promoting standardization and quality in the pursuit of openness. There is also the need to inform agents about open models and develop mechanisms for their implementation. The same system that measures and rewards scientific activities incentivizes competition over cooperation. Thus, there is a need to diversify metrics and incentives for the behaviour of scientific communities.

This section gives a glimpse of shifts in agents' behaviours happening within biomedical RD&I systems. The question remains as to how much of a challenge it will be to replicate open and collaborative

initiatives in other areas where financial interests play a substantial role and that have a solid presence and influence from the pharmaceutical industries. The emergence of openness and the increasing number of initiatives that implement it will influence and is already influencing different agents' behaviours what may lead to substantial shifts in the biomedical innovation ecosystem.

7.3. Observing Emergence to Enhance Complex Adaptive Intellectual Property and Biomedical Innovation Systems' Reform and Design

Openness occurs when both IP and biomedical innovation systems develop a common language, relate to each other, and converge their signal-boundary arrangements towards common goals. This dissertation identified the existence and emergence of openness in law and science by evaluating legal instruments and projects that use the idea of openness as a guiding principle to induce open agent behaviours. The distinction between an emergent phenomenon and the existence of practices that may lead to it is very subtle. Determining how much the idea of openness in law and science has influenced or determines the shape of IP and biomedical innovation systems—especially IP strategies, policies, and practices in universities and research centres—requires further investigation. A more comprehensive mapping of how the idea of openness is expressed in legal dispositions, norms, and biomedical RD&I models is necessary.

In this dissertation, I argued that openness is more than a commonality enabling the communication and construction of new signal-boundary arrangements between IP and biomedical systems. Openness is a common underlining principle of these systems and guides their interactions and existence—in its absence CAS do not strive or are unable to harness their own complexity while addressing problems. It is possible to argue that closedness and competition might also be seen as guiding principles and opposed to ideas of openness and collaboration. Nevertheless, by asserting that IP and biomedical innovation systems are CAS—and considering their characteristics and the role of information in them—it is more likely that their operation leans more effectively towards openness and cooperation than closedness and competition.

To better function, harness its complexity, and avoid imbalance, the framework of CAS behaves organically and is driven by interaction patterns. Despite agents being boundedly rational, law is a powerful force in changing behaviours to achieve the ideal of 'what behaviour should be.' This ability is essential to guide society towards goals and enhance the operation of other CAS that interact with legal systems. However, as I have presented in previous chapters, legal reforms do not always work, and legal agents do not possess a complete understanding of the system. Only by trial and error, and by feedback and iteration, can the system improve.

One could point to the difficulty of drawing definitive conclusions about openness in law and science and that it is premature to classify it as an emergent phenomenon, given the need for further empirical research and long-term monitoring. However, based on CAS theory's perspective, in my point of view, openness in law and science is a guiding principle of complex adaptive IP and biomedical innovation systems. Openness in CAS has deep roots in these systems' organizational and intrinsic characteristics and their own existence. This leads to the conclusion that for their survival and optimal functionality complex adaptive IP and biomedical innovation systems will find their way back to openness if they are artificially closed by agent behaviours. Systemic failures may appear as a result of this dysfunctionality and work as evidence to agents to rethink their behaviour towards these CAS.

Moreover, the practices, policies, and models related to this openness in law and science have the potential to become an emergent phenomenon. How fast this emergence may happen depends on the number of incentives and efforts agents set in place for their realization. Emergent phenomena can (over the longer term) transform systems through a bottom-up approach while enabling CAS to maintain their overall coherence, robustness, and resilience and leading to change and evolution.

Expert communities have a strategic role in these systems, and their commitment to engage in informed, participatory, and transparent processes about the regulation of these systems will determine

the probability of them being implemented and successful. In developing countries such as Brazil, considering the social and economic problems already mentioned, these communities' role is even more pressing as they hold the knowledge that may empower change. Some level of competition and closedness will always exist, but availability and flow of knowledge, information, and data are essential for society to thrive.

CONCLUSION

This dissertation has shown a need to innovate how agents understand, co-design, and reform complex adaptive IP and biomedical innovation systems. Theoretical, methodological, and practical aspects underline this innovation. It is no longer enough to investigate what happens in the legal system in isolation or simply define law as a static institutional regime with predictable outcomes derived from the mechanical application of legal rules. Otherwise, the same results and problems resulting from the legal system's operation and its interaction with other systems will keep occurring. Agents need to understand the factors that influence their behaviours as well as the processes shaping their interactions with other agents, which ultimately leads to systemic change and coevolution. Systems' organizational features matter to the same degree as the systems' content. Indeed, organizational aspects can determine and influence content because they relate to the manner in which information flows and how agents can minimize uncertainty and the effects of their bounded rationality to harness complexity. For this reason, the diversity of agents, the emergence of their behaviours, and uncertainty were critical aspects of this dissertation's development.

In originally applying CAS theory and agent-centred approaches to system understanding and reform, this dissertation aimed to promote a shift in how agents understand IP and biomedical innovation systems, contributing to the debate regarding access to knowledge and innovation, especially in developing countries. Such an alternative understanding of the interaction and coevolution of IP and biomedical innovation systems is necessary because it changes how one strategizes toward reform. Another significant shift in understanding concerns the impact of bottom-up approaches, instead of top-down ones, on IP and biomedical innovation systems' structure and reform and the specific consequences for developing countries.

Accordingly, this dissertation classified and studied IP and biomedical innovation systems as CAS, focusing on their main constituents: agents. In applying an agent-centred evaluation, this dissertation proposed a new way to think about system co-design and reform processes. As argued, several problems in systems' interactions and coevolution—including the promotion of access to knowledge and follow-on innovation—relate to a dysfunctional relationship between those systems and their agents. To overcome this dysfunctionality, it was necessary, first, to clarify the relationship between law and science as a precondition to effective law and policy design and reform. As such, this dissertation examined how multiple CAS communicate, organize common places for interaction, and jointly pursue their goals, identifying the main principles guiding these processes. By unveiling organizational features of CAS, this dissertation added missing elements to legal analysis, mainly the importance of acknowledging uncertainty and the value of diversity and observing emergence in the co-design and reform of complex adaptive IP and biomedical innovation systems.

Due to the need to clarify the relationship between law and science, this dissertation recounted pieces of the coevolutionary story of IP and biomedical innovation systems, focusing on the role of agents within these systems. Specifically, it evaluated the role of expert communities that are at the bottom of the organizational layers of these systems. These agents are the most equipped to clarify how IP and biomedical innovation systems interact and coevolve and to propose bottom-up reforms to these systems. The primary examples, debates, and facts discussed assumed the perspective of developing countries, mainly Brazil. Recounting pieces of this story through the lenses of CAS and an agent-centred approach was important to show the need for shifting perspectives and adding elements that can provide dynamic legal and policy analysis.

Since legal innovation relies on a multidisciplinary dialogue between legal and non-legal agents, this dissertation had to consider behavioural insights as integral to legal analysis. Monitoring systems to

identify emergent behaviours and obtain feedback on the application of legal rules is something that, despite not being routine, is essential for informed and dynamic law and policy understanding and analysis. If agents are to promote sophisticated co-design and reform of the different systems that affect their lives, bounded rationality and uncertainty must be considered.

In addition, this dissertation assessed the tragedy of the anticommons hypothesis in biomedical research and problems related to legal transplantation and agent's assumptions that IPRs are similarly beneficial to developed and developing countries. These assessments showed that scholars were too quick in assuming what happens in complex adaptive IP and biomedical innovation systems. They further reinforced that there is no 'one size fits all' approach in CAS design and reform. Therefore, emergent patterns of interaction give rise to new agent behaviours and changes that lead to reforms and the evolution of systems. If we want to promote law and policy that respond to challenges arising in these systems, we need first to observe and evaluate what is happening instead of supposing what is happening or might happen.

This dissertation also identified the idea of openness in law and science as a guiding principle within IP and biomedical innovation systems. Openness can be seen as both a principle and commonality (common feature) of those systems and an emergent phenomenon of agent behaviour that is reflected in the international debate via legislation or new biomedical R&D models at the level of universities, research centres, and other initiatives. Thus, openness manifests itself as a catalytic instrument for system reform.

Each chapter gradually addressed critical points of how IP and biomedical innovation function, interact, and coevolve and clarified connections between CAS theory and legal theory. These chapters set the ground to classify these systems as CAS. They also built up the main arguments of my dissertation that affirm the importance of agents (and observing their behaviour) in complex analysis and legal design and reform. The interaction of agents within CAS was not only a common thread throughout this

dissertation's chapters but also a critical component to uncover the human element in system analysis that is key in driving change. In proposing agent-centred evaluations of ecosystems and summarizing it as a methodological tool to better co-design and reform CAS, it is possible to tackle problems that are not exclusive to complex adaptive IP and biomedical innovation systems. In this sense, this dissertation's general debates and methodology can inspire the joint study of other CAS and uncover patterns of interaction between agents and within systems that were not so evident. Given the increasing challenge faced by law in regulating other CAS, it is critical to observe agents, their behaviours and interactions, and emergence within different systems, informing and empowering agents in the constant and dynamic process of understanding and reforming systems.

The level of complexity and technicalities that legal systems face while regulating and interacting with other CAS has increased and will most likely increase alongside the arrival of even newer and emerging technologies. In the same way, the environment and conditions of these interactions within today's network societies and knowledge economies contribute to the increase of complexity. This complexity challenges agents to create better coordination mechanisms to govern behaviours and interactions in multisystemic settings. It is unlikely that legal innovation will arise if law is kept in isolation and exclusive to legal agents. The place where ideas about how to better regulate science emerge has shifted from isolated and exclusive sites where legal agents think about law to shared and multidisciplinary sites where legal and non-legal agents dialogue. To harness complexity in these CAS and address these challenges, legal and non-legal agents must work together. Agents need to build bridges between disciplines and systems, identify commonalities, experiment in niches, set up innovative methodologies and strategies to face old and new problems, and assume that nothing is definitive—apart from their role as system participants. In this learning process, agents can reaffirm the human characteristics of systems as a guiding point of their analysis while empowering other agents as co-designers.

By placing agents at the centre of the analysis, this dissertation intended to demonstrate their significance, as they are the 'masters' who build and monitor systems. At the same time, this dissertation emphasized agents' importance, qualities, and flaws, highlighting the need for transparent and participatory processes in the understanding and reform of CAS. The idea is to educate agents about system operation, interaction, and coevolution in light of the goal of developing legal expert navigational knowledge and judgment and diminishing the knowledge and resource gaps among different countries in legal design and reform.

Especially in developing and least-developed countries, creating and maintaining robust platforms that inform and enable the legal and policy infrastructures is critical. Without quality, transparent, participatory, and reliable infrastructures that assist legal experts in their evaluations, overcoming social and economic problems will remain a far-off goal for these countries. The level of sophistication in which agents engage to solve problems is directly related to the information they have about the systems they operate, other agents with whom those other agents interact, and their consciousness of their bounded rationality. The same applies to how they choose to see and approach problems. These problems include addressing access to knowledge and innovation, realizing countries' and agents' potential to promote change, and empowering developing country agents to become informed citizens of the global economy.

To identify and articulate complexity in the interaction and coevolution of IP and biomedical innovation systems, this dissertation assessed several debates, facts, topics, concepts and theories related to law (IP systems) and science (biomedical R&D) within a CAS framework. These elements provided the building blocks for a new way of thinking about systems and agents, where legal agents evaluate different CAS interactions and recognize the importance of working on niches. Using Brazil as a case study, this dissertation engaged in a preliminary assessment of the Brazilian IP and biomedical innovation systems to understand new routes to their co-design and reform, allowing for some suggestions.

This dissertation aimed to clarify concepts and theories, develop methodologies, and build bridges between legal and CAS theory while inspiring readers about the value CAS theory can add to legal theory and practice, especially in the IP field. The goal was to demonstrate the potential of CAS theory and concepts and its different methodologies in providing detailed and dynamic pictures of different CAS and their interaction. CAS theory also elucidates and contextualizes agents' assumptions of what happens in the complex world while modelling strategic thinking. For developing countries, the CAS perspective also enables agents at the bottom of systems' organizational layers (expert communities) to increase their importance in shaping and reforming those systems. A CAS analysis may also assist in simplifying/withdrawing hierarchical constraints upon the processes by which these systems are designed and reformed and balance influences such as power relations and politics at different levels. Considering the problems encountered by developing countries concerning corruption, transparency, and accountability, CAS thinking may genuinely be a transformative instrument.

Looking into the Future of CAS and Legal Theory

There is still a long way to go until CAS theory and its methods achieve their full potential in legal theory. Therefore, there is a need to advance theoretical debates and translate concepts between CAS and legal theories, acknowledging that agents are dealing with a system of systems and diverse multi-agent niches. In the extensive agenda for CAS legal research, initiatives that engage in modelling and computer simulation of complex adaptive legal systems and their multiple regulatory targets are already being constructed but can be improved and generate new approaches. New methodologies can also enhance agents' ability to access problems from several angles.

As explained, CAS theory and concepts position agents of elements that are generally not accounted for in legal theory. Concepts from CAS theory are also not easily translated to legal theory or make immediate sense to legal scholars, considering the specific language, terms, and notions that touch

many disciplines. Some theoretical discussions related to CAS are still under development in various fields. To better operationalize the use of CAS methods in legal systems, concepts, and theories need to be better translated into legal scholarship. There is also space for legal scholars to contribute to theoretical inquiries that would further benefit other fields that use CAS theory. Reinventing the storytelling of interacting and coevolving CAS through agent-centred evaluations is a new methodology, as well as developing frameworks of thinking to guide agents' assessment of problems. This dissertation has contributed one piece of scholarly reflection towards that end. More debate is needed if agents want to harness complexity to answer the challenges of their complex world.

CAS theory has the potential to bring disciplines together in order to create dynamic common languages or signal boundary arrangements that enable communication between agents and build bridges between them. Since legal systems do not concern only legal agents, there is a need to find the commonalities between legal systems and their different regulatory targets and promote a dialogue between agents operating within diverse systems. This highlights the importance of the relationship between law and science as a connecting concept or idea between systems.

Building and clarifying the multiple connections between legal systems and other regulated systems may assist in creating systems of systems that appropriately address selected goals. Identifying various points of contact also allows agents to choose from multiple strategies to achieve their goals. Thinking further, the search for commonalities between different CAS is a central piece of complexity's puzzle. This dissertation opted to evaluate IP and biomedical innovation systems. However, other CAS, such as health and industrial systems, also interact in this context and influence the problems and opportunities arising in and within systems.

Suggestions to Understanding and Reforming Complex Adaptive IP and Biomedical Innovation Systems in Brazil

Moving forward, I suggest some actions that can assist in understanding and reforming complex adaptive IP and biomedical innovation systems. The suggestions below are tailored to specifically inform the interaction and coevolution of the Brazilian IP and biomedical innovation systems instead of providing a 'one size fits all approach.' However, they may still inspire other countries. These recommendations speak directly to expert communities as well as law- and policymakers. As information and knowledge builders and diffusers, these communities are well-positioned to improve the operation of those systems. Yet this is only possible if they promote information and knowledge flow—since information feeds CAS—while contesting their assumptions about how intangible assets are regulated. Unless openness is critically assessed and experimented with, multisystemic malfunction will continue and endanger access to knowledge and innovation.

Specifically for legal agents at the bottom of the IP and biomedical innovation systems, they need to diversify their sources of inspiration to design and reform these systems, collaborating with non-legal agents to improve the relationship between law and science in order to promote real change. As strategy matters, working in niches and understanding the processes that lead to changes in CAS can minimize uncertainty and unwanted consequences. It also facilitates receiving feedback on the impact of IP law and policy on biomedical R&D. Reducing the place of agent interaction to niches further assists in identifying and observing patterns of interaction and increasing agent understanding of IP and biomedical innovation systems.

Based on the analysis carried out in this dissertation, there are four main points for attention and action. These points converge and intersect while promoting dynamic CAS thinking:

(i) *Consistently mapping, understanding, and monitoring complex adaptive IP and biomedical innovation systems. The creation of a multisystemic memory that can guide agents' actions and inform CAS design and reform. This requires empirical research and the creation of an infrastructure that enables coordinated efforts among agents*.

Brazil has a robust and complex legal system, consolidated institutions and policies, as well as academic and research institutions and infrastructure already in place. It also possesses reputable and knowledgeable expert communities and research leadership in several fields. Organizing these elements and their embedded knowledge into innovative and accessible platforms is the first element to systemic and informed understanding and reform. This is not to suggest reinventing the wheel but to use and expand the already existing personnel and infrastructure (for instance, Lattes and Carlos Chagas Platforms) to monitor and connect overlooked points of system interactions. Having memory that can be accessed to create reliable pictures of these dynamic systems is the first step to CAS design and reform.

(ii) Enhancing agent (legal and non-legal) understanding and critical evaluations of IP and biomedical innovation systems through multidisciplinary research, IP as a source of information, IP literacy, and multi-agent discussion forums.

The Brazilian IP system and its regulatory targets are extraordinarily complex and challenging to navigate. This level of challenge will increase with the introduction of emerging technologies, business and R&D models, and as agents create new ways to interact. Therefore, equipping agents with the ability to understand and harness the complexity of IP systems is one of the main challenges in system understanding and reform. Even legal agents may encounter hurdles in drawing complete pictures while diving into details that will make a difference in the systems' operation. The specialization and technical knowledge that some fields require have created a knowledge gap and difficulty in tailoring legal advice. Additionally, academic and research institutions' organizational, personnel, and financial resources have

limitations that place them in a disadvantageous position to propose legal innovation compared to other agents that influence their behaviour, like the private sector. This without counting power relations and politics, imperfect information, and an academic and research culture that tends to see IPRs as proprietary rights to knowledge regulation, promoting competition rather than instruments of social and economic development.

Major steps to drive change include organizing expert communities within existing forums (for instance, discussion groups in universities and research centres and forums like the FORTEC) and proposing new places in which to promote discussion, IP literacy, and the use of IP as a source of information, as well as exposing these communities to the most diverse approaches and opinions applied to the interaction of IP and biomedical innovation systems. The same platforms mentioned above can be leveraged as places for further IP training and literacy and encourage debates about CAS guiding principles. Without a more sophisticated assessment of these systems, the same patterns that created problems will keep arising. Therefore, it is time for agents to be mindful of these systems' organization and content and combine these aspects while setting up their IP policies, practices, and strategies.

(iii) Promoting experimentation and agent interactions through niches to uncover the potential of cooperation and openness and to more easily identify emergent behaviours that lead to CAS change and evolution.

There is a clear advantage in evaluating multisystemic interactions and monitoring behaviours of agents through niches, as doing so diminishes risk and enlarges the possibility of success. Hence, experimentation in CAS design and reform can happen initially in these contained places and expand to other initiatives later. In Brazil, the organizational framework of universities and research institutions allows for a high degree of experimentation in different biomedical R&D projects. Seeing IPRs through the spectrum of openness and closedness and not necessarily as proprietary rights is the first step of doing

so. Knowledge dissemination and IP literacy are essential to promote more sophisticated assessments of IPRs and IP policies, practices, and strategies.

Additionally, innovative legal reform may not come exclusively from legal agents but from their ability to recreate their role and articulate with other agents to identify and promote new ideas, especially in technical fields like IP and biomedical R&D.

(iv) Promoting Coordination

None of the above-suggested points is doable or sustainable without coordination. Coordination is essential to maximize resources and the value of information in CAS while harnessing these systems' complexity. One of the main challenges encountered during the development of this dissertation was consistently monitoring and mapping initiatives to inform the research's findings thoroughly. This is due to the fragmentation of initiatives, the number of biomedical R&D projects, and the insufficient public information about the approach agents use to regulate these projects and initiatives through IPRs. The gap (or lack of information) is even bigger if one wishes to assess these systems from the behaviours of agents and their impressions of these systems' interactions. The amount of information produced by today's knowledge economies and networked societies can be overwhelming, demanding the establishment of forums to coordinate and enable the comparison of initiatives and projects. Although coordination is crucial, no central governing body is actually required. Leadership can take place at the bottom layers of these systems as expert communities leave their 'Ivory Tower' and become innovators to facilitate the interaction of IP and biomedical innovation systems.

This dissertation has argued that, independently of the number of roles an agent assumes or how many times the agent changes his or her role, the agent will always remain a system participant. It has also been argued that, for too long, agents have overlooked and disregarded the human element in systems. Yet, no matter how agents design systems, they will always be led by people and for people. Therefore,

the constant technological advances that affect people's daily lives will not achieve their full potential if agents—especially law and policymakers—do not connect them effectively to human needs and processes.

Finally, the Covid-19 pandemic brought to light several problems related to the interaction of IP and biomedical innovation systems and the ability of agents in those systems to organize, coordinate efforts, and collaborate to promote innovation. It showed how interconnected, resilient, and uncertain these systems are and the importance and leadership of expert communities. However, systemic problems arose mainly related to access to knowledge and health technologies, highlighting the inequality between developed, developing, and least-developed countries, as well as their ability to respond to health issues. The current moment builds on long-term lessons about the interaction and coevolution of complex adaptive IP and biomedical innovation systems, showing that it is time for expert communities to redefine their roles to promote a more balanced biomedical innovation ecosystem. They can do so by rethinking these problems through CAS lenses and agent-centred approaches.

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