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Chapter 1

New Biology and the Foundations of a Health Bioeconomy

Introduction

In 2004, scientists and entrepreneurs Craig Venter and Daniel Cohen, who together pioneered techniques to map the human genome, proclaimed that the twenty-first century would be defined by the biological sciences. They wrote: "While combustion, electricity and power defined scientific advance in the last century, the new biology of genome research . . . will define the rest" (Venter and Cohen, 2004: 73). Although reflecting a degree of hubris, the "century of biology" aphorism captures a shift in science and industrial policy and the emergence of a new zeitgeist in the latter part of the twentieth century. Biology came to replace physics as the exemplar "big science." The physical sciences had dominated science policy and political discourse for most of the century, and popular culture was defined by their perceived hazards, risks, and opportunities in finely balanced geopolitical contexts. Of course, in the context of commercial innovation, chemistry was predominant throughout the twentieth century. Furthermore, information and communication technologies (ICTs) brought major social and commercial transformations in the latter decades of the century. Nevertheless, the advent of new biology, and significant advances in life science technologies,[1] heightened expectations of a revolution in health care.

However, the transformative potential of the life sciences, and a fledgling bioeconomy, was tempered by scientific, technological, social, and commercial challenges and uncertainties. This is evident in the context of health and health systems, where molecular biology first took root in the clinic in the 1960s through developments in cytogenetic testing (Hopkins, 2006). In the United Kingdom,

cytogenetic testing built on a long and rich history of publicly funded basic research. From the 1970s to 1990s, sophisticated screening technologies and new diagnostic and therapeutic options for drug development began to emerge. The development of recombinant deoxyribonucleic acid (DNA) technologies[2] in the 1970s was a major breakthrough in biological approaches to therapy, which had been incrementally evolving throughout the second part of the twentieth century. These new, step-change innovations would eventually disrupt conventional therapeutic pathways and commercial research and development (R&D) strategies.

The array of innovative technologies and medicinal therapies that are emerging in the twenty-first century challenges our existing regulatory systems and established health-care pathways, reimbursement systems, and clinical practices. These technologies and therapies are also restructuring entire industrial sectors. In the cases of regenerative medicine (RM) and stratified medicine, for example, de novo business models and value chains[3] must be created because there is no existing route to market (Mastroeni et al., 2012; Mittra and Tait, 2012). For RM, conventional preclinical animal studies for safety and efficacy are often inadequate, and the "gold standard" of a three-stage, placebo-controlled, randomized clinical trial (RCT) system is not always appropriate (Mittra et al., 2015; Webster et al., 2011). Furthermore, contemporary health innovation demands much greater participation by patients and publics in research, which raises important issues around consent and third-party use of personal data (Haddow et al., 2007; Mittra, 2007a). The value ascribed to the patient experience and perspective, and the increasing role of politically active patient groups in therapeutic innovation, means that patients are now at the center rather than the margins of biomedical R&D and the health bioeconomy. Pricing, reimbursement, and cost-effectiveness of new medicinal therapies are also continuing challenges for institutions and organizations responsible for purchasing and delivering health-care services, with the patient again central to these concerns. It is within this context that the notion of a complex and multifaceted health bioeconomy has gained social and political traction.

It is important to recognize that the use of new technologies and therapies (in this book I use "therapy" to refer only to medicinal products) within the clinic affects early-stage innovation options and strategies. Contrary to popular representations, modern therapeutic innovation does not follow a simple, linear path (Tait and Williams, 1999).[4] Furthermore, the fact that risk and uncertainty are intrinsic features of life sciences R&D is a continuing challenge for those

responsible for foresight and policy analysis on science and technology futures (Williams, 2006). The long-term economic and noneconomic value claims underpinning new promissory technologies and therapies also appear opaque in the early stages of the innovation lifecycle, which makes identifying and exploiting sustainable routes to market difficult. The health-related life sciences, and the bioeconomy within which they are constituted and shaped, raise a number of important questions about novelty and value, organization and management of interdisciplinary R&D, and the blurring of boundaries between the laboratory and the clinic and between public and commercial spheres.

The Concept of "Innovation Ecosystem"

This book is about the evolution of new biology and the health bioeconomy in the twenty-first century. Throughout, I investigate how the institutional and organizational landscape for health R&D within Europe and the United States has been transformed, and reciprocally shaped, by new science and technology options. I critically explore this institutional and organizational change in the broader context of perceived problems facing contemporary health innovation and expectant stakeholder narratives that have coalesced around the concept of "translation." Here, translation denotes new policies and practices aimed at bridging the laboratory and the clinic to generate the promised social, clinical, and commercial benefits from significant investments in life sciences (Kraft, 2004, 2013; Mittra and Milne, 2013). More specifically, my objective is to reflect on the range of actors, institutions, and organizations that are now integral elements of a complex and distributed "innovation ecosystem" (Adner and Kapoor, 2010; Durst and Poutanen, 2013; Mastroeni et al., 2012).[5] Crucially, I address the impact of these changes on R&D practices and notional ideas of value and worth that circulate within the health bioeconomy.

The concept of innovation ecosystem highlights the interdependencies between different actors and organizations that co-produce new scientific knowledge, technologies, and therapies. It also captures the attendant social and institutional innovations that are necessary for products to reach a market and generate various types of value and benefit. The concept is much broader than many conventional theories of innovation systems, because it encapsulates the all-important social, economic, commercial, and policy/regulatory drivers. Central to the success of an innovation ecosystem is diversity, resilience, and

robustness. In terms of how I employ the concept in this book, the ecosystem comprises the basic science, the individual business models and value chains for specific technologies and therapies, regulation (including product regulation as well as health technology assessment and reimbursement), funding agencies, markets, and, of course, the patients who are the ultimate beneficiaries of new therapies. It is only by capturing all these systemic elements, and relevant stakeholder interactions, that we can begin to understand both the opportunities and the challenges facing new biology and its application to health.

Of course, as Papaioannou et al. (2009) rightly warn, the term "innovation ecosystem" should not be used uncritically. It can lead to reductionist and functionalist accounts if it is translated as a straight biological metaphor and disassociated from the concept of ecology. I hope to avoid any pitfalls in the use of the term by grounding the concept in case examples of particular innovations that have highly interdependent organizational and institutional linkages and value chains. I also avoid the tendency to present health-related innovation ecosystems as universal explanations for the evolution of knowledge and technology dynamics in the sector. The utility value of the ecosystem approach, for the purpose of this book, lies in the fact that it encourages us to broaden our analytical scope and explore the range of actors that produce knowledge, technology, and therapy for the growing health bioeconomy. Furthermore, it compels us to take seriously the notion of dynamism in the system and rethink our notions of value and waste. In presenting a broad systemic analysis of the health innovation ecosystem, I unveil some of the more substantive implications new biology has for industry, science, medicine, and society. It is at the nexus of these stakeholder communities that a diverse range of expectations and values are being negotiated and contested as new technological and scientific opportunities emerge.

A key question to explore is how different actors and organizations constituted within the health bioeconomy operate in the interdisciplinary environments required to successfully "do health R&D" in the twenty-first century. There is no simple answer, because different stakeholder communities and practitioners are driven by their own institutional logics and subjective understanding of the value and challenges of health care driven by new biology (Mittra, 2013). Throughout this book, I conceptualize the creation or enactment of value within health innovation in its broadest sense. This is to avoid reducing complex issues and health-care product development processes to the crudest of economic metrics, or alternatively to valorize only the social and ethical dimensions. The bioeconomy encapsulates

many different types of value and valuation practices, or what some usefully refer to as "orders of worth" (Stark, 2009). These shape the evolution of the science and the strategies of those responsible for its progress. However, while the benefits and impacts of new biology on therapeutic innovation are often contested, there are a number of perceived challenges and opportunities in contemporary health R&D that have inspired significant policy shifts and changes in regulatory, commercial, and broader socioeconomic norms and practices. The promissory value that is now ascribed to the concept of "translation," particularly within the science and policy communities, exemplifies the tectonic shifts that are taking place within biomedicine. Together, these have materially affected the everyday practices of R&D. They have also defined the availability and scope of new therapeutic options within the clinic.

In the remainder of this chapter, I outline what I consider to be distinctive about new biology in the context of a set of contemporary health innovation challenges that have led to significant change in how R&D is organized and practiced. The substantive chapters then provide rich illustrations of different aspects of these transformations, from the perspectives of the various organizations, institutions, and actors that comprise the innovation ecosystem. I also review some of the critical social science literature on the bioeconomy, and the expectations around future value that are being contested and debated. This clarifies the conceptual and theoretical approach that is used to frame the empirical material I present later. The key question I address in this chapter is: *What, if anything, is distinctive about new biology and the health bioeconomy, and how do they challenge conventional systems of health innovation and the enactment of value*? At the end of the chapter, I briefly explain the empirical data sources used to inform my arguments and outline the overall structure of the book.

What, If Anything, Is Distinctive about New Biology?

Since the inception of the Human Genome Project (HGP)[6] in 1990, and the announcement that the full human genome had been successfully sequenced in 2003, medical research, clinical practice, and the structure of the biopharmaceutical industries have undergone profound change. This is evident in the context of how R&D is now funded and organized. Translational Medicine (TM), as I discuss later in the book, has emerged as a powerful narrative and organizing principle for meeting the various challenges facing conventional drug development. These challenges include high failure rates for new

drugs (referred to as "attrition" by the pharmaceutical industry), low productivity, and a perceived knowledge and culture gap between the laboratory and the clinic that new molecular biology appears to throw into sharp relief (Mittra et al., 2011; Mittra and Milne, 2013).

However, what, if anything, is truly distinctive or exceptional about this new biology? Are we merely being captured by the hype and hubris of the scientists, industrialists, and those who popularize science through depictions of dystopian or utopian futures when we glibly accept the new century as one defined by advances in molecular biology? Is the science of life ontologically and epistemologically distinct from other sciences? In his book, *The Disorder of Things: Metaphysical Foundations of the Disunity of Science* (1995), John Dupré makes the important point that when we look at science through the lens of contemporary biology, it appears far more disunified than sciences such as physics and chemistry, as they were portrayed by many philosophers of science in the first half of the twentieth century. These were the emblematic "big sciences" of the nineteenth and twentieth centuries. Biology, unlike physics and chemistry, does not exhibit the methodological unity or grand theoretical narrative to link the disparate fields under its domain. It therefore lacks a sense of internal disciplinary integrity. Furthermore, as Bensaude-Vincent (2007) rightly argues, biological systems cannot simply be reduced to a central code or program, as the crude, and false, analogy of the "gene as script" implies. Reductionism also makes little sense in the context of biological taxonomy, so biology, as presented by both Dupré and Bensaude-Vincent, is highly pluralistic in character. I argue that a distinctive feature of new biology is that it is necessarily interdisciplinary in nature and pluralistic in terms of how it is organized and managed. The implication for scientific practice is that people can work in various domains of the broadly defined "life sciences" without sharing strict methodological or epistemological commitments. Furthermore, they do not need to have unified objectives, or shared values and valuation practices, in terms of how potential application areas are prioritized and routes to market or clinic managed. I would further argue that the decentralized nature of the funding streams for the new biological sciences, and highly distributed innovation ecosystem within which specific application areas are shaped, contributes to, or at least reflects, this lack of disciplinary integrity and unity in knowledge production. It also generates uncertainty about product development pathways and the realization of value.

For the purpose of this book, I refer to both new biology and the life sciences as a specific set of interdisciplinary approaches,

technologies, and scientific knowledge and expertise (tacit and codified) where "life" at the molecular level is a key component driving innovation and clinical practice. When *combined* with a particular set of organizational and institutional arrangements for "doing R&D," the novelty of the late-twentieth-century and early-twenty-first century biological sciences is illuminated. In the context of health, this structure is highly distributed, displays nonlinear attributes, and has the dynamics of an ecosystem. Of course, it is important to recognize that the foundations of new biology were being prepared long before the initiation of the HGP in the 1990s. From the 1970s, recombinant proteins were being developed for therapeutic use. Before then, in the 1950s and 1960s, there were major breakthroughs in the development of novel vaccines and genetic-based diagnostics, which at the time constituted a new biological paradigm. However, the transformation of new biology into a big science that could be developed on an industrial scale, and contribute to an expectant bioeconomy, is a much more recent phenomenon and the central focus of this book.

My primary interest in new biology, and the health-related life sciences, is in understanding how it is evolving in a very specific late-twentieth- and twenty-first-century context of a highly distributed (spatially and temporally), interdisciplinary, and cross-sectoral innovation ecosystem. Within this ecosystem, multiple actors, organizations, and institutions coproduce knowledge and products and contribute to the realization of different types of value. Importantly, the social sciences have a pivotal role within this new regime of biomedical R&D, not only as observers of knowledge production processes, but as an integral part of the innovation ecosystem itself. Indeed, science and social science have coevolved in quite new and interesting ways as new biology has taken root both culturally and institutionally (Tait, 1990; Wield, 2013).

To illustrate further in the context of health innovation, in the late 1990s and early 2000s, the multinational pharmaceutical industry, which had dominated the market for conventional drug therapy for over a century with relatively simple, small-molecule compounds, was confronted with the challenge of an emerging therapeutic paradigm built around new biology (Mittra, 2008; Wield, 2013; Wield et al., 2013). At the same time, firms were struggling to sustain growth with these conventional blockbuster drugs (Mittra et al., 2012). The so-called productivity crisis within the large multinational firms (Hara, 2003; Pammolli et al., 2011) led to incremental changes in how these companies organized and managed their internal and external R&D processes. This was because the new life sciences required a much

broader innovation system, involving different types of organizations and expertise, than that of traditional chemistry-based drug discovery (Hopkins et al., 2007; Mittra, 2007b, 2008; Nightingale, 2003; Rafols et al., 2014). All the major firms invested heavily in new biology and adopted similar strategies as they experimented with different ways of doing R&D. These large companies also began to strategize alternatives to blockbuster drug development, where sales in the billions of USD are required for sustained growth and the meeting of shareholder and market expectations. Personalized or stratified medicine and new biologics-based therapies, and more recently RM, emerged to challenge this conventional business model. These technologies and approaches required new and different strategies to identify and capture opportunities for value creation within a complex and evolving health innovation ecosystem. The crisis in the pharmaceutical industry, and the emergence of new biology as both an opportunity and a challenge, forms the basis of chapter 2.

However, for now I simply want to emphasize that the range of commercial and public sector actors and institutions that are now involved, perhaps by necessity more than design, in meeting the challenges and exploiting the opportunities presented by new biology, has led to the emergence of very different and often conflicting narratives of hope and promissory expectations (Borup et al., 2006; Brown et al., 2000; Bubela et al., 2012a). Translational policies and commercial strategies for exploiting life sciences have also threatened to disrupt prevailing professional and disciplinary boundaries, creating new and evolving relationships between industry, science, medicine, commerce, and society (Calvert, 2010; Cox and Webster, 2012; Martin et al., 2008; Mittra, 2013). Such changes are particularly resonant in the broader context of the emerging health bioeconomy, within which new path-breaking therapies are being developed and must find a way to successfully navigate precarious and uncertain routes to market.

Conceptualizing the Health Bioeconomy

Having defined and considered what might be unique about new biology that makes it an interesting and worthy object of study, it is important to then consider the nature of the broader bioeconomy. What is the health bioeconomy and how might it be best theorized and used to reflect on recent developments in health-related life science innovation?

The concept "bioeconomy" has been defined in a number of different ways for a number of different purposes (Schmid et al., 2012).

It began to gain traction in the late 1990s and early part of the twenty-first century in relation to economic activities and opportunities emerging from new biology. In its 2006 report, *The Bioeconomy to 2030: Designing a Policy Agenda,* the Organization for Economic Cooperation and Development (OECD) defined the bioeconomy as

> the aggregate set of economic operations in a society that use the latent value incumbent in biological products and processes to capture new growth and welfare benefits for citizens and nations. These benefits are manifest in product markets through productivity gains (agriculture, health), enhancement effects (health, nutrition) and substitution effects (environmental and industrial uses as well as energy); additional benefits derive more eco-efficient and sustainable uses of natural resources to provide goods and services to an ever growing population. (OECD, 2006: 1)

This is a broad definition of bioeconomy that focuses on new economic models and practices that must be nurtured to extract value from R&D investments in life sciences, and respond to various global challenges for both public benefit and, crucially, national competitiveness. This neoliberal flavor is also captured in President Obama's 2012 *National Bioeconomy Blueprint* (The White House, 2012) when it states: "Technological innovation is a significant driver of economic growth, and the U.S. bioeconomy represents a growing sector of this technology-fueled economy" (The White House, 2012: 1).

It is this supposed, underlying neoliberal philosophy that has been the central focus of many social science critiques of the bioeconomy (Hamilton, 2008; Parry, 2007) and the speculative value propositions and ideologies that underpin it. Cooper (2008), for instance, argues that the emergent biotechnology industries cannot be seen as separate from neoliberalism's rise as a dominant political philosophy:

> The biotech revolution…is the result of a whole series of legislative and regulatory measures designed to relocate economic production at the genetic, microbial, and cellular level, so that life becomes, literally, annexed within capitalist processes of accumulation. (Cooper, 2008: 19)

Similarly, Styhre and Sundgren (2011) describe the bioeconomy as the "economic regime of accumulation where technoscientific know-how developed in the life sciences is capable of making the lived body a principal surface of economic value creation" (Styhre and Sundgren, 2011: 3). From both these perspectives, biotechnology is coterminous

with the neoliberal bioeconomy—the utility (and indeed "vitality") of life itself being determined by a particular set of dominant economic practices and subject to new and emerging processes of speculative commodification (Rajan, 2006). A number of social scientists have drawn on both Marxist and Foucauldian thought to theorize and think through the social implications of new biology and these emerging economic and institutional regimes that shape it. They have coined concepts such as "biovalue" and "biocapital" to serve as both descriptive and explanatory tools (Rajan, 2006; Rose, 2001; Waldby, 2000).

Together, these concepts are used to describe the constitutive elements of the emergent bioeconomy, which have given rise to a new "biopolitics." Some authors claim that this biopolitics goes far beyond surveillance at the population level, which Foucault described, to the constituent cells, molecules, and genomes of individuals (Helmreich, 2008). Such authors emphasize the transformative effects of life sciences and its capitalist modes of production on human bodies, tissues, identities, and sociopolitical relations. These ideas are deployed as part a powerful critique of both the increasing attribution of speculative surplus value and worth to biological material in crude economic terms, and the commodification processes that drive this phenomenon (Cooper, 2008; Novas and Rose, 2000; Parry, 2006).

Taking seriously the notion of latent value in biological processes, which the OECD emphasized in its definition of bioeconomy, there is consensus among these authors that there is something unique about the biological sciences in the twenty-first century, which justifies the promiscuous use of the prefix "bio" to conventional terms such as value, capital, and politics. It is the tight coupling of new biology with traditional capitalist modes of production and organizational processes that generate novel types of biovalue and a related biopolitics. For some, the speculative and often contradictory nature of the bioeconomy has led to an exploration of the emerging politics and sociology of hope, hype, and expectations (Borup et al., 2006; Brown, 2013; Novas 2006). I draw on aspects of this rich body of work later in the book to explore value and expectations in TM initiatives. In particular, I show how organizations in the bioeconomy display the attributes of anticipatory and promissory organizations (Pollock and Williams, 2012), which not only build expectations about the future of medicine, but also actively shape technological options and therapeutic value chains.

This particular approach to life sciences and the bioeconomy has not gone uncriticized. For example, Birch and Tyfield (2012) have critiqued many science and technology studies (STS) approaches for

both fetishizing the biological sciences, and conceptualizing an ever growing number of ambiguous bioconcepts that lack any meaningful explanatory power. Furthermore, they suggest that STS theorists have, due to their focus on technoscientific features of the bioeconomy, given too little attention to the transformations of the underlying economic and financial process of contemporary capitalism (Birch and Tyfield, 2012: 301). The essence of Birch and Tyfield's critique is captured in the following statement:

> We highlight the problematic adoption of Marxist language in these bio-concepts without the necessary adoption of Marx's theoretical formulation of the labor theory of value (LTV) underpinning key terms like value, capital, and surplus value. In adopting Marxian concepts, the fetishization of the "bio" has meant that – to different degrees – STS scholars like Waldby, Rose, Rajan, and Cooper have missed an opportunity to update the understanding of the bioeconomy in light of the financial and economic restructuring of the economy. (Birch and Tyfield, 2012: 301)

The authors go on to argue that it is important to consider "asset-based" economic processes as an integral part of the bioeconomy, rather than the "commodity-based" processes that STS scholars tend to prioritize and which are captured in, for instance, the rhetoric of "life as surplus" (Cooper, 2008). The former, according to Birch and Tyfield, is a tangible or intangible resource that both produces value and entails value as property, while the latter is simply an object produced for exchange. Furthermore, terms like "latent value" and "surplus value" imply that there already exists intrinsic, but yet untapped, value and vitality in biological material and processes. This neglects the fact that such things accrue value over time through the immaterial labor of commercial and public institutions.

Birch and Tyfield's work, captured in the quotations above, not only subjects the narrow, commodity-based approach to critical analysis, and questions the newness of concepts such as biovalue and biocapital, but does so in the context of what the authors consider to be real changes in economic processes that shape the bioeconomy. In particular, they identify a "…shift in value creation from productive to immaterial labor…a financialized-rentier regime of accumulation; and…the shift from commodity-based to an asset-based market exchange" (Birch and Tyfield, 2012: 301) as three key transformative processes underpinning the neoliberal bioeconomy.

Birch (2006) has also suggested that policy discourses centered on national competitiveness, and the economic representations and

practices underpinning the bioeconomy, have naturalized and served to justify policies, institutions, and governance regimes that have shaped the current innovation system for biotechnology. Hilgartner (2007) shares this sentiment when he suggests that organizations such as the OECD are ambitious "anticipatory enterprises" that both predict and shape the emergent bioeconomy, such that the economic representations serve an important performative function. Birch (2007) has also described the bioeconomy as a "virtual abstraction" of economic practices in which benefit and potential "…are intertwined concepts…repeated numerous times throughout this policy literature, which essentialises and naturalises the claims made about its innovative potential" (Birch, 2007: 89). Other authors have been even more explicit in describing the bioeconomy as a political project and promissory construct to support neoliberal capitalism, rather than a strictly scientific, technological, or economic endeavor (Goven and Pavone, 2015).

I do not wish to discuss in-depth the subtle nuances and minutiae of these particular debates about the nature of the bioeconomy. I simply want to emphasize that the policy assumptions and political traction that has driven a global bioeconomy agenda in the twenty-first century have been questioned by a number of social scientists, and particularly STS scholars. It has also encouraged a range of new approaches for studying the evolution of life science industries and the socioeconomic values underpinning them. The approaches so far outlined highlight the gap between speculative and actual economic value. They also raise serious questions about transformative expectations and the performativity of market-based policies and understandings, particularly their impact on science and society. For some, the negative implications of the current regime tend to be emphasized or implied, but it is not always clear where this should lead in terms of normative policy change. Much of this work has provided valuable conceptual and theoretical tools for understanding various components of the bioeconomy, and the foundations on which it has been constructed. However, we must go further to better understand the dynamics of the innovation ecosystem and its different stakeholder interactions and expectations of value.

It is my aim in this book to consider more pragmatically what the key challenges are to the success of a vibrant health bioeconomy, notwithstanding the validity of some of the critiques concerning its purported neoliberal assumptions and modus operendi. I also want to think through how the challenges and limitations to exploiting new biology for both therapeutic and economic benefit might

be overcome. In so doing, I consider if new conceptual approaches to value and valuation practices in health innovation might enable a more sophisticated analysis of the innovation ecosystem for the health-related life sciences and its nascent bioeconomy.

Value in the Health Bioeconomy

There are a number of challenges facing the health bioeconomy and the transformation of life science knowledge and expertise into a viable biobusiness. Gary Pisano's 2006 book, *Science Business: The Promise, the Reality, and the Future of Biotech*, was an important and at the time well-received account of some of the structural problems and challenges facing the life science sector, which were preventing it from making the anticipated contributions to the bioeconomy and public health. Pisano's great insight was in revealing some of the reasons why the biotechnology sector was not thriving and successfully turning what was believed to be revolutionary science into commercially viable and high-value products. On the one hand, Pisano highlighted some of the distinctive features of the biotechnology industry, particularly the high risk and uncertainty of R&D. Drug innovation is expensive, time consuming, and highly risky. It can take up to 20 years to take a new therapy from discovery to the clinic, and at various stages along that development pathway the therapy is liable to fail. This is an industry unlike any other. On the other hand, and perhaps more interestingly, Pisano pointed to the fundamental clash of values, norms, and practices between the worlds of science and business. The challenges of funding R&D and successfully integrating different knowledges and practices were highlighted by Pisano as key reasons for the gap between the promise and the reality of contemporary biotechnology.

However, Pisano's analysis was quite narrowly focused on intellectual property regimes (particularly patents) and finance/funding models for the biotechnology sector. It lacked a more systemic understanding of the broader innovation ecosystem and the full range of enablers and constraints that shape its evolution. Although intellectual property regimes constitute an important element in the innovation process, and play a strong role in shaping the innovation ecosystem and the locus of value within it, they are not the central focus of this book. Much has been written about how patents in biotechnology enable or restrict innovation, determine the value of new therapies and the viability of different business models, and in a sense govern the innovation process (Gold et al., 2007). I do not wish to downplay

their importance, but I contend that they are just one part of the innovation story. I discuss patents and intellectual property only insofar as they help inform and illustrate particular case examples (such as business models and reimbursement systems for stratified medicine or RM). In this book, I want to take some of Pisano's key insights, particularly in the context of how different values and norms emerge in health innovation, to a different level by exploring the innovation ecosystem in a much broader sense. This requires consideration of how regulations and policies, in the context of changing social and clinical expectations and constraints, shape innovation and R&D practices and create new organizational principles. In this context, we need a way of better conceptualizing the role of value and values, which will be a prevailing theme throughout the book.

All the different accounts of the bioeconomy so far discussed rest on a particular understanding of value and/or values. The two concepts have, for historical reasons, been treated as separate within the social sciences. Stark (2009) traces this demarcation to what he calls "Parsons Pact," when the American sociologist Talcott Parsons attempted to delineate the boundaries of sociology so as to placate the economists who felt their territory was under threat. Parsons suggested that sociology would study *values* while economists would be left alone to study *value*. The economic and social facets of "value" were now decoupled and have largely been treated as distinct domains ever since. Put simply, and perhaps crudely, sociologists study the subjective social relations underpinning the economy, while economists, and the calculative sciences, study "objective" economic value, reflected, for instance, in the market price. However, there is now a growing network of social scientists trying to rejoin value and values to develop more pragmatic studies of "valuation as a social practice," which tries to capture both the objective and subjective elements of value (Beckert and Aspers, 2011; Dussuage et al., 2015; Helgesson and Muniesa, 2013; Lamont, 2012). Indeed, the very definition of value has always had both an economic and noneconomic component, but in common parlance value does tend to evoke the former rather than the latter. Furthermore, this emerging body of work emphasizes that there is no real intrinsic value to any object (value is not an attribute), nor transcendental values that exist outside of social norms and practices. Some go further by arguing that value emerges from firms and entrepreneurs' ability, through business models (which are essentially constructed narratives of how things can be made to work), to build networks and system structures that will permit the realization of value (Perkmann and Spicer, 2010). These perspectives

enable us to think about value in a much broader, interdisciplinary sense, rooted in the complexity of social practices and institutional assemblages where valuation and worth are constantly negotiated and established through a variety of tools and technologies (Helgesson and Kjellberg, 2013).

In this book, I use the terms value and values to capture both the economic and noneconomic processes of evaluation and different accounts of benefit or worth in the context of the health innovation ecosystem and its bioeconomy. This, I argue, allows us to avoid overemphasizing the pecuniary aspects of value, and reducing innovation systems and the bioeconomy in health to the crudest of economic metrics. As Beckert and Aspers rightly note, value and valuation are matters of concern even in the absence of money (Beckers and Aspers, 2011: 3). Fourcade (2011a) suggests that money actually tends to conceal the "real" essence of things because it simply conflates economic value with market price. Indeed, some argue that there are different "regimes of value" (Appadurai, 1986), but no single scale under which different types of value may be subsumed (Beckers and Aspers, 2011: 6), despite the common tendency to reduce value simply to matters of finance. So value and price are far from synonymous, and nowhere is this clearer than in the case of pharmaceuticals, as we shall see later in the book.

Helgesson and Muniesa nicely capture the multiplicity of value when they write:

> What things are worth can be manifold and change—and these values can be conflicting or not, overlapping or not, combine with each other, contradict each other. All, or almost all, depends on the situation of valuation, its purpose, and its means. Broad segmentations such as the distinction between "economic" and "non-economic" value can make sense at some level, only the devil is in the detail. Something valued as a financial asset, for example, can be valued differently by different accountants or different investors. And then this thing can be valued in an entirely different way in other circumstances (i.e., not as financial asset, but as a political project, as personal property, you name it). (Helgesson and Muniesa, 2013: 7)

This broad and more inclusive approach to value and valuation, which encourages us to unpack the different ways in which value is enacted or performed in specific professional domains and social contexts, opens up new avenues for studying things like the bioeconomy and the organizational practices of new biology and clinical medicine. Stark (2009) argues that the plurality of principles of evaluation that

operate within society suggests that any social order (such as a modern economy) contains multiple "orders of worth," which determine value and form the very basis of calculation and rationality (Stark, 2009: 11). Kelly and Geissler (2011) have applied this concept to the realm of modern clinical trials, describing them as generative of many different orders of value and intersecting the worlds of both commodities and public goods, which problematizes the conventional distinction between fiscal and moral virtues (Kelly and Geissler, 2011: 3). Mol's (2003) study of the multiplicity of meanings, practices, and, I would suggest, the different orders of worth within a hospital ward for the treatment of atherosclerosis is also within the spirit of this plural approach to value and valuation practices, as is Fourcade's (2011b) analysis of the different ways in which economic value is ascribed to intangible things such as "nature" when calculating liabilities from oil disasters. In the latter example, Fourcade revealed how political and cultural specificities led France and the United States to develop very different methods, metrics, and evaluative criteria to determine the appropriate fiscal penalties associated with the destruction of valuable biomass.

Espeland and Stevens (1998) have looked at the related problem posed by the need for "commensuration," which is the ability to compare different entities by a common metric. This is particularly pertinent to many innovation ecosystems in health R&D where there are multiple, overlapping value chains and systems, including public and commercial organizations subject to very different metrics of evaluation and criteria for success. Commensuration is also relevant to the "abstract value" of commodities, which is nicely captured in Brown's (2013) study of use and exchange value in the cord blood economy. In this case, it is not always useful to strictly delineate "use value" and "exchange value" on the grounds that the former provides public incentives for the bioeconomy (contribution to public health and a broader moral order of worth) and the latter provides incentives for commercial organizations (producing objects with proprietary rights for exchange in markets).

However, there is a danger in conceptualizing this multilayered approach to value and valuation practices as simply a conflation of the economic and the ethical/moral, where the latter and perhaps more subjective judgment of moral value and worth is given undue priority. In the social sciences, this can easily manifest as a mechanism to permit values-based arguments (in the transcendental sense) against various technologies to be prioritized. Taken to an extreme, it can ultimately threaten at a very early stage of development, under the auspice of

upstream engagement and more recently responsible research and innovation (RRI), potentially beneficial innovations (Tait, 2009). It can also lead to the marginalization of commercialization processes and economic value as an important facet of innovation ecosystems and therapeutic product pathways, which is damaging if ethical and moral judgments, and the often overused trope of "societal concern," take precedence and are subsequently valorized in academic and policy discourse. In this book, my interest in adopting a broader and more inclusive definition of value (which takes seriously the notion that economic value emerges from multiple types of other values and valuation practices) is to allow for a more sophisticated description and analysis of how health innovation systems are made to work in practice. I want to unpack how different R&D options, knowledge, and expertise; and the more tangible benefits of innovation are valued (or not) by different stakeholder communities who must nevertheless work together to develop new therapies. In a sense, actors and institutions in the contemporary health-related biosciences, each with their own expectations of value and benefit, must "muddle through," to borrow a concept from Lindblom's (1959) seminal essay on scientific administration and decision making.

So value and values, in the context of how I use the terms throughout this book, do not relate strictly to pecuniary matters on the one hand, and intrinsic ideologies and belief systems on the other. The latter would simply reify the notion of transcendental values, which I think is important to avoid in this context. Nevertheless, I do want to capture the nuances and differences of multivalent institutional values and valuation practices (scientific, clinical, commercial, and political), which determine how objects (in this case novel technologies, therapeutic products, and the processes that produce them) are valued on the basis of both economic and noneconomic criteria. Even if crude economic value (established by market price) is the ultimate driver of some aspects of the health bioeconomy, and the basis on which it is deemed a success or failure, this broader approach to value and its underlying practices is required to fully understand the nature of health innovation ecosystems and how they can deliver the benefits promised to various stakeholders. Crucially, the relevant stakeholders now include patients and publics. For example, Mazanderani et al. (2013) highlight the important role of patients in producing "biographical value" through "illness narratives." They talk about the commodification of illness experiences in terms of the "rise of different and overlapping markets in which illness narratives are produced, circulated, used and exchanged, generating value in different ways for

different people" (Mazanderani et al., 2013: 891). These narratives, which may be published through various social media, have value for other patients, health charities, and patient groups; as well as those who may want to measure the quality of health care. This is a nice example of how value should be seen in its broadest sense, encompassing both economic and noneconomic elements and implications. I discuss this in more detail in chapter 6.

This idea of broadening our idea of value is being debated not only by social scientists, but also by the science, industry, and policy communities responsible for advancing new biology. A series of articles published in the Lancet in 2014, for example, came with the tagline "Increasing Value, Reducing Waste." Each article considered how the value of medical research could be increased by reducing known sources of waste. Examples included a more robust and transparent process for setting research priorities (Chalmers et al., 2014), increasing access to all research to minimize bias and improve data sharing (Chan et al., 2014), and reducing burdens of regulation and management (Salman et al., 1014). Value in this context refers to not only conventional economic value that drives the bioeconomy, but also value in terms of specific patient and societal benefit. It also encompasses benefit to science and clinical practice more generally, particularly in terms of improving the quality of research and health care and achieving greater efficiency with existing resources.

However, Cutler and McClellan (2001) caution that while reduction of waste might be considered a valuable endeavor, it must be balanced against the potential for less rapid innovation. Indeed, I would argue that some waste is a natural part of any ecosystem, even an innovation one (there is no real waste in a natural ecosystem). Furthermore, who ultimately defines what is wasteful? Much of the recent interest in capitalizing on "big data" initiatives and opportunities (ABPI, 2013; Kayyali et al., 2013) is centered on this supposed need to minimize waste and increase the efficiency and value of health research. However, as I explain later in the book, the wealth of new information made available by advancements in new biology may problematize our notions of waste and efficiency. Furthermore, efficiency drives rarely prove to be a panacea for innovation challenges, as we shall see in chapter 2 in the context of multinational pharmaceutical companies and their investment in life science technologies for drug discovery.

Nevertheless, questions are now being asked by policymakers, industrialists, scientists, health-care providers, patients, and taxpayers about the value and worth of medical research and life science

innovation. Such questions operate with an ever more broad and sophisticated concept of value. For example, recent developments in "value-based pricing" for medicines, which I discuss in chapter 5, entail a much broader notion of long-term benefit and patient value, specific to particular therapy areas, than conventional reimbursement systems (BMJ, 2013). Narayan et al. (2013) claim that

> in major depression, value may be defined as the ability to rapidly resume social and work responsibilities; for pain, it may be defined as the ability to quickly resume physical activities of choice; and for Alzheimer's disease, it may be defined in terms of benefits that allow patients to remain independent for longer . . . in such an environment, the main driver of improved outcomes and meaningful benefits may not be innovative therapeutics alone but an ecosystem comprising the therapeutic and wrap-around tools and services. (Narayan et al., 2013: 85, 86)

From this perspective, integrated solutions for health care are needed. This compels us to recalibrate our notional ideas of value as high-tech life science approaches must coevolve with other organizational innovations in the broader ecosystem to deliver longer-term value in terms of both patient benefit and sustainable commercial revenue. The authors proceed to argue that there are continuing challenges for these new integrative solutions in health care, particularly in terms of regulatory pathways and business models. Porter (2010), looking at the issue from a US perspective, points to the organizational and information systems of health care that make it difficult to measure and provide value:

> Providers tend to measure only what they can directly control in a particular intervention and what is easily measured, rather than what matters for outcomes. For example, current measures cover a single department (too narrow to be relevant to patients) or outcomes for a whole hospital, such as infection rates (too broad to be relevant to patients). Or they measure what is billed, even though current reimbursement practices are misaligned with value. Similarly, costs are measured for departments or billing units rather than for the full care cycle over which value is determined. (Porter, 2010: 2478)

This is a continuing challenge for the successful management of health-care systems and the sustainability and resilience of a health bioeconomy. My colleagues and I at the Innogen Institute have responded to these challenges in recent years by developing a unique

approach to innovation ecosystem analysis for new and complex therapies that challenge existing product development pathways and value chains (Mastroeni et al., 2012; Mittra and Tait, 2012; Mittra et al., 2015). Case examples and relevant vignettes from this body of work is illustrated later in the book. But these challenges of determining the value and benefit of new life science therapies, which depend largely on the level of unit analysis, the calculative practices used, and the discrete parts of the innovation system that are ascribed value and considered to be "of worth," can be better unpacked and understood within this broader definition of value.

Another illustrative example comes from the Dutch innovation context, where the concept of "valorization" has been used to denote this conjunction of the economic and noneconomic aspects of value. Stemerding and Nahuis (2014) talk about the challenge of the "valorization of knowledge" and describe how valorization was used by Dutch policymakers toward the end of the 1990s to define and direct "…the process to create value from knowledge by making it available for economic and/or societal use and by translating it into competitive products, services and new business" (Stemerding and Nahuis, 2014: 80). This approach has become institutionalized within the Dutch innovation system and has led, according to supporters of valorization, to the use of indicators and evaluative practices that go beyond crude, instrumental economic metrics as the basis for value. The valorization concept is particularly pertinent to collaborative public-private partnerships, which I discuss in detail in chapter 4.

So, the conflation of economic and noneconomic value should not necessarily lead to an anything goes approach to the study and critique of innovation ecosystems and/or a prioritization of the more difficult to quantify ethical and subjective social values. However, understanding how different actors involved in innovation processes generate, negotiate, and integrate different notions of value and orders of worth to make R&D work in practice is an important and much needed contribution social science can make to the biomedical innovation process. Frow (2008) talks about her interest, in the context of synthetic biology, in understanding what practitioners count as worth knowing and to what ultimate end. She has explored how the field is being shaped by different valuation practices. In this book, I am interested in exploring this in the context of a broad range of active therapeutic R&D processes for novel therapies based on new biology that is driving, but also challenging, specific enactments of the health bioeconomy.

Overarching Aim of the Book

My broad aim in this book is to problematize those accounts that simply dismiss new biology as hype, or see its impact on organizational norms and practices as marginal, or perhaps even negative. I also want to explore the transformative effects of new biology and the growing bioeconomy on the structure and organization of R&D within health innovation ecosystems, rather than the more vague and ambiguous realm of biopolitics and social relations. I do not begin with a strong normative view about the neoliberal aspects of the bioeconomy. Neoliberalism, which is quite a vague and ill-defined term, is often used pejoratively when talking about emergent biotechnologies and the institutional and organizational relationships that nurture them. Indeed, I suggest that the very nature of new biology, and the diverse and complex value chains underpinning its different application areas, means that it is perhaps inevitable that a broadly neoliberal framework has so far guided its development and continues to shape its R&D pathways. The key is to better understand these new R&D processes and practices, and the multiple values and valuation practices that are being performed by different actors within the health innovation ecosystem.

In building the argument, I reflect on those insightful accounts and conceptual approaches that have explored how different promissory visions and expectations in science and technology shape R&D policy and practices (Borup et al., 2006), and engender new communities of promise and organizational principles in translational life sciences (Martin et al., 2008). I draw on work that has discussed how diverse and often contested notions of value in the bioeconomy drive science and technology options, and often create new "bio-objects" that challenge conventional boundaries and the status quo of public and commercial research (Webster, 2013). I argue that the perception that there is a problem of "translation" in health R&D, and the subsequent changes in policy, funding, and strategic behavior of commercial and public sector innovators, has had a material effect on the "doing" of R&D and the way it is valued by different professionals and experts that are embedded in the innovation ecosystem. In this context, the concept of novel experimentation applies not only to the basic research underpinning new biology, but also to the organizational structures, management strategies, and policies that are being implemented to capitalize on new biology. Just like basic research, there are successes and failures in these organizational and policy experiments. This notion of "trial and error" is an inevitable

feature that drives progress, as is the building of future expectations and visions. If we accept this notion, we need not fall into the trap of judging any policy or organizational experiment that does not meet its initial objectives or expectations as a failure, or as having no value in the broader context of the evolving innovation ecosystem.

A key argument I make in this book is that the emergence of TM, as both a general philosophy and set of specific industry and policy-driven initiatives to ensure novel therapeutic products make it to the clinic, must be seen in the much broader context of the systemic challenges facing multinational commercial drug development, the changing relationship between basic and clinical research, the emergence of new organizational relationships and interdisciplinary ways of "doing" R&D, and regulatory/policy challenges of assessing risk and benefit of new types of therapies. The concept of a health bioeconomy is central to this, as it represents a vast range of economic and noneconomic activities and valuation practices. As Wield (2013) usefully points out, health brings together two important but often separate aspects of the bioeconomy: innovation in new therapies (with very long lead times) and health policy and services, which are driven by issues of treatment cost and access to health systems. There is often little integration of the policy and innovation perspectives, so it is important to provide a more systemic and integrated account.

Empirical Data and Case Studies

The data informing the arguments made in this book emerged from a range of projects I have conducted either solo, or in collaboration with colleagues within the Innogen Institute at the University of Edinburgh. Together, the complete dataset includes 15 interviews I conducted with senior R&D managers and scientists within big multinational pharmaceutical firms and small and medium-sized biotechnology companies in Europe and the United States (conducted in 2004 and 2005); 35 interviews and a workshop I organized with key practitioners involved in various translational initiatives, including senior academic scientists, clinicians, health-care service managers, policymakers, and regulators (conducted between 2010–2013); 15 interviews with investors, scientists, and academics in the field of RM (conducted with colleagues in 2013); data from three workshops and a small number of interviews on product development strategies for an ESRC/TSB RM project (2010–2011); and field notes from attendance at various industry and stakeholder conferences and workshops over the past 12 years. Most of the data derives from qualitative

research interviews (which are fully anonymized throughout) and workshop data, but also includes significant secondary gray literature and policy document analysis.

Throughout the book, rich case study examples are used to tease out key themes, such as the organizational restructuring of the pharmaceutical industry and its attempt to integrate new biology, challenges and opportunities of personalized and stratified medicine, and the associated development of new diagnostic biomarkers and related devices to better target therapies to specific patient subpopulations, and RM, which promises more fundamental changes to the nature of therapy and translation to the clinic. My aim is to integrate microlevel critical analyses of institutional and organizational norms, disciplinary practices, and relationships in emerging technology areas that challenge the status quo, with more systemic macrolevel analysis and evaluation of how regulation, policy, and markets shape technology pathways and options within complex innovation ecosystems. Further information about specific datasets used in this book and reference to projects within which data were collected are described in more detail in the notes within individual chapters.

Outline and Structure of the Book

The book comprises seven chapters. In the following chapter, I address the question: *What impact does the life sciences have on the organizational structure, commercial strategies, and R&D practices of the pharmaceutical industry?* Looking back to the late 1990s and early 2000s, I draw on interview data to critically explore the strategies developed within the largest multinational pharmaceutical companies as they tried to respond to a so-called productivity crisis, and exploit the emerging opportunities presented by new molecular biology. After providing a brief history of pharmaceutical innovation, I reveal how companies began to experiment with new ways of organizing and managing R&D, strategically using mergers and acquisitions, and alliances with smaller biotechnology companies, to appropriate external knowledge, skills, and expertise and build new capabilities in life sciences. I also address the pharmaceutical industry's struggle to identify new sources of value for life science-based therapies, and think through potential future routes to market—a market begrudgingly accepted by large companies to be unlikely built on blockbuster small-molecule drugs.

In chapter 3, I address the notion of a "broken middle" in the health innovation pathway, which led to the emergence and prioritization of

translational medicine/research as a powerful commercial and public policy strategy embraced by industry, government, and the scientific and clinical communities. The key question to be addressed in this chapter is: *What perceived challenges, opportunities, and practitioner values in health innovation have driven a new translational policy agenda, and with what consequences for the bioeconomy?* In this chapter, I explore diverse practitioner definitions and multiple meanings ascribed to translation, as well as the nature and underlying realities of the problem it seeks to address. I then think through some of the practical implications and effects this has had on health policy and innovation, and indeed the very relationship between the public and commercial sectors in health research. A particular focus in this chapter is the strategies of organizations such as the National Institutes of Health (NIH) in the United States, and major funding bodies in Europe and the United Kingdom (Technology Strategy Board and Medical Research Council), to capitalize on new biology and generate long-term scientific, commercial, and clinical value and, ultimately, patient benefit.

In chapter 4, I move from a broader macrolevel analysis to look at changes in R&D practices. The question to be addressed in this chapter is: *In what ways has the "doing" of R&D been reshaped by the institutional and organizational restructuring precipitated by translational policies and how are stakeholder expectations and values recognized and managed?* In this chapter, I address the crucial organizational and institutional impact of the translational policy agenda. I do this in terms of how interdisciplinary and cross-sectoral collaborations are having a material effect on what it means to do R&D in the laboratory and the clinic, and are determining what is ultimately valued. If interdisciplinarity disrupts conventional professional and sectoral boundaries, it may also reveal tensions around different notions of value and benefit. Translational R&D structured around new biology may bring many new opportunities for therapy development, but it must also deal with institutional constraints and manage different expectations about scientific, clinical, economic, and social values and benefit. In this chapter, I critically explore some of the salient organizational and institutional changes that are being precipitated by this public and commercial interest in new ways of doing life sciences. Three rich case studies of public-private partnerships are used to illustrate the key arguments, alongside interview data from key practitioners.

Chapter 5 is driven by the question: *How has new biology both challenged and transformed conventional regulatory systems and the*

resilience and adaptive capabilities of health-care systems to innovative therapies? The central focus here is on the broader regulatory and policy challenges of developing radically new approaches to therapy that do not have established routes to market and conventional business models, value chains, and regulatory precedents to take them from the laboratory to the clinic. Many of these technologies, if they are to be successful, must find a way to fit into, or transform, existing health-care pathways and navigate complex and often sclerotic regulatory and reimbursement systems. In this chapter, I reflect on some of the key regulatory developments and strategies in the United States and Europe before exploring path-breaking technologies and approaches (using the case examples of RM and stratified medicine) that challenge our conventional regulatory systems. I also explore the implications of new therapies for health technology assessment and reimbursement systems, particularly in the context of new approaches to value-based pricing. This chapter deals with the problem of how new technology can break through existing institutional logics and rationalities built into an already well-established system of institutions and organizations that may have a vested interest in maintaining the status quo. I also highlight the direct impact that regulation and policy can have on the trajectory of new technology and therapeutic innovations, and the ability of researchers, particularly in the public sector, to deliver viable health solutions to the clinic.

In chapter 6, I address the question: *What are the implications of the changing role of patients and publics in the new health bioeconomy, and how can their expectations and values be better understood and managed?* Here, my focus shifts to the increasing role patients and publics are expected to play in health innovation and research. I consider the broader and long-term implications of this for the development of new therapies. The success of new biology and the health bioeconomy requires a far greater and more active role for the public and patients in health and clinical research, in addition to the collaboration of diverse institutional actors with very different notions of the value of the science for commerce, medicine, and society. These issues are becoming increasingly salient and powerful as patients actively lobby for better access to innovative therapies, and policymakers strive to increase value and minimize "waste" to meet these growing expectations and societal needs. The issue of "big data," and how this may be used to improve innovation, is a crucial factor to take account of in the context of the health innovation ecosystem. This chapter tries to capture and critique the different ways in which the patient and broader publics have become valued participants in the R&D process.

In the final concluding chapter, the key themes addressed in the substantive chapters are summarized and I return to the core notion of value in the emergent health bioeconomy. The question to be addressed in this chapter is: *What is the future for therapy in light of the many experiments in translational medicine; the nature of the evolving bioeconomy and the constellation of value therein?* Here, I consider the long-term consequences—for industry, science, medicine, and broader society—of the current and largely experimental policy initiatives and strategies that are arguably precipitating change in the nature and organization of R&D, and the various interdisciplinary and cross-sectoral practices that have been engendered.

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