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ORIGINAL PAPER

Locating Responsible Research and Innovation Within Access and Benefit Sharing Spaces of the Convention on Biological Diversity: the Challenge of Emerging Technologies

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Abstract This paper reviews the location of Responsible Research and Innovation (RRI) approaches within the access and benefit sharing (ABS) policy spaces of the Convention on Biological Diversity (CBD) and Nagoya Protocol. We describe how a range of dialogues on ethical research practices found a home, almost inadvertently, within the ABS policy process. However, more recent RRI dialogues around emerging technologies have not been similarly absorbed into ABS policy, due in part to the original framing of ABS and associated definitional and scope issues. Consideration is given to the challenges posed to these policy processes by the transformative and rapid nature of scientific and technological change today, including the emerging field of synthetic biology. Drawing on experiences from regulating ABS, we emphasize that the integration of RRI into policies for new, emerging, or poorly understood activities such as synthetic biology faces deficiencies such as limits to government capacity, jurisdictional confusion, shortages in funds, and an absence of strategic approaches. We conclude that a coordinated combination of diverse policy processes within the CBD might provide an invaluable space for RRI dialogues on social justice, sustainability, biosafety, and other issues raised by emerging technologies.

Keywords Synthetic biology · Access and benefit sharing · Nagoya Protocol · Genetic resources · Scientific and technological change · Ethical research

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Introduction

A wide-ranging and impassioned dialogue and policy process has developed over the past 20 years around academic and commercial research on genetic and biological resources, and associated traditional knowledge. This has focused both on the societal desirability of such research and on approaches to reduce inequities in its practice and outcomes. This process, located within the context of the *United Nations Convention on Biological Diversity* (CBD) [1] and, more recently, its *Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity* [2], has produced literally dozens of declarations, codes of ethics, institutional policies, and national "access and benefit sharing" (ABS) measures [3]. The location of Responsible Research and Innovation (RRI)—meaning the effects and potential impacts of research and innovation on the environment and society—within the ABS process of the CBD grew from a range of policy developments. These included the Brundtland Commission, which in 1987 linked social justice and equity to conservation [4], and advances in the rights of indigenous

peoples through the 1991 International Labour Organization's Convention No. 169, the UN Declaration on the Rights on Indigenous Peoples, the World Intellectual Property Organization, and other policies and processes. Over the last few decades, RRI has found expression in a range of arenas, but ABS proved a central convening home for RRI dialogues associated with the use of genetic resources and traditional knowledge [5–9].

The range of documents growing from and informing ABS define the terms of equitable research and commercial partnerships, and the broader objectives they serve. These include research codes of ethics, institutional policies, corporate guidelines and standards for best practice, and numerous national measures that promote or require ethical and responsible research practices [3, 6–8]. Although the term "Responsible Research and Innovation" is not used within the CBD, and ABS and RRI dialogues have not overlapped to date, both address similar issues relating to ethics, inclusion, and the social desirability of innovations. Von Schomberg, for example, sees RRI as "a transparent, interactive process by which societal actors and innovators become mutually responsive to each other with a view to the (a) (ethical) acceptability, (b) sustainability and (c) societal desirability of the innovation process and its marketable products" [10]. All three of von Schomberg's "normative anchor points"—namely that research and innovation respects fundamental rights and the highest ethical standards; that it is environmentally sustainable; and that it ensures societal relevance and acceptability—are also encapsulated in the CBD. This biodiversity gold standard not only locates research, technology, and innovation within an environmental blueprint for conserving the Earth's rapidly dwindling biological diversity but also strives to do so by meeting the goals of economic development and social and economic justice.

This paper aims to review the location of RRI approaches within the CBD and Nagoya Protocol, the challenges posed to these processes by the transformative and rapid nature of scientific and technological change today, and the resulting difficulties of developing truly responsive, adaptive, and integrated RRI processes. The ABS policy process provided an excellent forum for discussions of RRI associated with genetic resources and traditional knowledge in the 1990s and early 2000s. However, as we will discuss using the example of synthetic biology, the complexity of the science, the unpredictability of effects, and the vastly different speeds and styles of policy-making and research and development (R&D) provide significant stumbling blocks to the integration of RRI into new, emerging, or poorly understood activities such as synthetic biology.

Synthetic biology is located at the interface of leading genetic and information technologies, and the juncture of a wide range of developing ethical and political concerns. As a result, it has sparked lively policy debates in recent years, but these are usually on the margins, and it is only very recently that public awareness has grown about these new technologies. Promises of healthcare, biofuel, food, industrial processing, and other advances increasingly attract attention, as do the potential dangers posed by the release of organisms, demand for biomass to feed the "biological factories", and the ethical issues arising from engineering life [11–15]. A range of laws and other instruments could potentially regulate synthetic biology, including the Cartagena Protocol for Biosafety under the CBD. This paper focuses on the interface between synthetic biology and the ABS component of the CBD policy process, which has been home to the most extensive RRI dialogues within the CBD to date and is recently the focus of government attention through development, ratification, and implementation of the Nagoya Protocol.

The first section of the paper reviews the challenges faced when an environmental treaty includes the promotion of societally beneficial research in some of the most technologically advanced industries in the world, including those using synthetic biology. The next section describes some of the basic policy challenges facing regulators of synthetic biology. These include the difficulties of reaching agreement on its definition and the spectrum of activities it involves—from basic research to commercialization; whether it is a new technology or simply an evolution of traditional genetic engineering; as well as the geopolitics of the countries doing the research. We conclude with lessons from the ABS policy process that might be instructive for emerging technologies such as synthetic biology in the coming years. These include the challenges faced by policy makers when developing new regulatory frameworks for activities that are poorly defined or understood. We also discuss the possibility that we have reached the limits of the ABS arena to address RRI for advanced

emerging technologies, but that the CBD as a whole might provide important fora for these RRI dialogues.

Responsible Research and Innovation and the Convention on Biological Diversity

A product of the 1992 UN Conference on Environment and Development, the CBD was one of three legally binding agreements arising from the so-called Earth Summit, alongside the Framework Convention on Climate Change (UNFCC) and the UN Convention to Combat Desertification. The Convention's first two objectives are centrally those of an environmental treaty—the "conservation of biological diversity" and "the sustainable use of its components" [1].

The third objective of the CBD was part of a compromise, in which the biologically diverse countries of the South sought to address centuries of inequitable exchange between the largely developed and technologically advanced countries of the North, and their former colonies in the South. It was also viewed as a possible funding mechanism for the conservation of biological diversity, providing both financial support and indirect incentives [16–18]. Emerging from this intent was a new and broad-ranging policy process known as access and benefit sharing: "the fair and equitable sharing of the benefits arising out of the utilization of genetic resources, including by appropriate access to genetic resources and by appropriate transfer of relevant technologies, taking into account all rights over those resources and to technologies, and by appropriate funding" (CBD, Article 1). Somewhat inadvertently, through its third objective, the CBD policy process has become home to a host of what outside the CBD process are referred to as RRI dialogues. These include the implications of new technologies; societal expectations for research and innovation; ownership and sovereignty over genetic and biological resources; appropriate ways to secure consent and reach agreement on terms from stakeholders; and the nature and sharing of benefits deriving from research.

Some of the most important RRI principles of the CBD embrace the need for benefit sharing, require mutually agreed terms (MAT) to be developed between those providing and those using genetic resources and traditional knowledge, and require prior informed consent (PIC) to be obtained before resources or knowledge are collected and used, including from indigenous peoples whose rights were previously unrecognized by many of the governments instituting these new laws. Such approaches are now widely embedded in the practices of companies and researchers [19, 20]. For example, the much publicized case of the Hoodia plant revealed how South African scientists had claimed the traditional knowledge and innovations of the indigenous San peoples to develop anti-obesity products, spurring a dialogue on appropriate PIC and MAT from indigenous groups and the ensuing development of benefit-sharing agreements with the San [21]. A range of subsequent benefit-sharing agreements have evolved based on San knowledge of southern African plants such as rooibos (*Aspalathus linearis*), *Sceletium tortuosum*, and buchu (*Agathosma crenulata* and *Agathosma betulina*) [22, 23]. Similarly, personal care companies like Aveda in Australia and Natura in Brazil have developed innovative partnerships with indigenous communities for the use of their knowledge in product development [24]. In Namibia, the indigenous Himba have negotiated agreements to develop perfumes based on their traditional knowledge [25]. Many comparable agreements have been negotiated throughout the world, signalling a sea change in the way biodiversity and traditional knowledge are used, studied, commercialized, and acknowledged.

Despite these agreements, experiences to date suggest that the RRI arenas of the CBD and Nagoya Protocol are focused largely on prior informed consent, bilateral agreements, and benefit sharing from research and development, rather than on attempting to shape substantively the way in which innovation is approached and designed. Inclusive innovation, the means by which new goods and services are developed for and/or by those who have been excluded from the development mainstream [26]—particularly the billions living on the lowest incomes—is also weakly addressed by the CBD. Within the framework of the CBD, innovators can thus innovate for whatever they wish so long as the basic principles of prior informed consent and mutually agreed terms are adhered to. RRI dialogues within ABS policy have tended to focus on RRI *products*, or benefits, with the broader gains of ethical research *processes* often overlooked.

There have been exceptions, however, and progress has been made since adoption of the CBD within practical partnerships to recognize the contribution of traditional knowledge to the scientific innovation processes

[27], to forge more equitable research partnerships between industrialized and developing countries, and to include in benefit-sharing arrangements a R&D focus on diseases that primarily afflict groups living in poverty [28]. In the higher-technology sectors which access genetic resources, these forms of research collaboration, capacity-building, and technology transfer are most common to government or donor-supported agencies like the US National Cancer Institute and the International Cooperative Biodiversity Groups, and their partnerships with companies (see, for example, [29–31]).

Commercial and academic ABS partnerships formed over the last few decades offer models and insights for the advancement of RRI today. However, within the ABS context, RRI dialogues on research-intensive industries have largely stalled due to insistent efforts to fit a suite of dynamic and rapidly shifting industries and technologies into an outdated and rigid framework [22–24]. At the same time, ABS policy-makers have turned their attention increasingly to biotrade, or biological resources that are part of slower-moving, lower-technology industries that operate in more familiar ways and often yield more immediate and tangible benefits for communities. This means, however, that the Nagoya Protocol and national ABS measures have not explicitly addressed new technological advances like synthetic biology that would appear to fall directly within their remit. Instead, such debates are now taken up increasingly by the CBD's Subsidiary Body on Science, Technology and Technological Advice (SBSTTA), and through the narrow risk assessment lens of the Cartagena Protocol on Biosafety [32–34]. The approach to RRI and synthetic biology within the CBD has thus been piecemeal, rather than holistic and integrated.

One of the reasons for this disjointed approach is because the CBD was drafted decades before synthetic biology and emerging technologies took shape and is understandably outdated. This is most evident with issues surrounding its scope, or "breadth of coverage", and whether or not digital genetic information is included within the definitions of genetic resources and genetic material in the Nagoya Protocol [35, 36]. Ruiz Perez Muller refers to the continued focus on physical material in the Nagoya Protocol as "literally codifying the definitional mistake" found in the CBD [37]. The definitional mistake identified by Ruiz Perez Muller and others [38, 39] is the emphasis placed by the CBD and Nagoya Protocol on the physical, rather than the informational, dimensions of genetic resources, which are then accessed from in situ and ex situ sources. Article 2 of the CBD defines genetic resources as "genetic material of actual or potential value", and genetic material is defined in turn as "any material of plant, animal, microbial or other origin containing functional units of heredity." Neither the CBD nor the Nagoya Protocol, however, defines "functional units of heredity" [32, 40]. At the time of CBD negotiations, the focus was on full sequences that coded for proteins, but today it is DNA "parts" that are of most interest to researchers and it is unclear whether a partial coding sequence or a DNA sequence that regulates gene expression constitutes a functional unit of heredity. As Bagley and Rai describe: "…as biological science, including synthetic biology, moves away from a focus on individual full gene sequences towards a focus on parts of genes as well as the full genome and proteome, it is unclear how the notion of a 'functional unit of heredity' will map onto the new science" [35].

New scientific approaches not only confuse the issue of scope, and to what material ABS laws will apply, but also the timing of when they are triggered. The ABS policy apparatus is built on a transaction—providing access to genetic resources from a particular country or collection to an identified researcher and company (often in another country) in exchange for a share of benefits. It is assumed that this transaction is central to the business practices of industrial sectors that use genetic resources, and the Nagoya Protocol has focused on mechanisms, like checkpoints, to monitor them to ensure equity. Often overlooked, however, is the fact that today, few companies require these transactions; even at the time of CBD signature in 1992, they were marginal to most company's R&D programs. Over the last few decades, large pharmaceutical companies have defunded natural product programs for a range of reasons, but these included difficulties created by the CBD for natural product research [31, 41, 42].

In recent years, there has been a resurgence of interest in genetic resources. Almost every industry in the world uses biotechnology, defined in the CBD as "…any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use" [1]. Genetic information has never been more sought after or valuable. What has changed profoundly, however, is the manner in which this material is accessed, and how it is used. These bear little resemblance to common

practice in 1992, when the CBD was adopted. To begin with, genetic information today is often transmitted digitally, and if physical material is collected, it is in tiny amounts, and frequently from a company's own collections [42, 43].

As one scientist from the SCRIPPS Institution of Oceanography, University of California, San Diego, has remarked: "We no longer have to collect large quantities of an organism and return it to a lab and work on it. We can work with much less material and often still get the same answer…. With a miniscule amount of any material, we can get the genetic material out, sequence it, and learn how those chemicals might be programmed genetically to see if we can engineer it easily in the laboratory. Genetic information is now loaded onto public websites and even if the organism was collected from a remote location, once released publicly it is out there for anyone to see and use" [42].

Such trends emphasize the decoupling of research from the original environments in which the physical material may have been collected. A chief executive of one biotechnology company has noted: "We get microorganisms by picking up some of these old collections that no one wants anymore, and now have one of the largest collections in the world. But with modern techniques, we can also scratch a little dirt off the sidewalk, and can scan out the microbial genome universe. DNA pervades the environment around us, and the code is a citizen of the world. We don't need whole organisms, just a snippet of DNA, so we don't need to sequence whole genomes. As a result, overseas collections aren't really necessary" [44].

Layers of additional problems plague the ABS formula as a result of advances in R&D strategies. For example, researchers today blend genes from many different microorganisms from around the world and access these genes digitally. As noted by a scientist from the J. Craig Venter Institute, well known for first publishing the genome of a single individual, "If people start engineering microbes with genes inserted from many different microbes, who owns it? Do the scientists need to obtain permission from all of the many countries of origin for genetic material? How would ownership be shared? This question applies equally well to both the more familiar rDNA and newer synthesized DNA. And if the genes are synthesized from sequences downloaded from a public database, how do you even identify the countries of origin?" [44].

With the coming into force of the Nagoya Protocol in 2014, member countries are now devoting significant resources to the agreement's implementation. Yet this is largely done without recognizing the profound changes in science and technology that have transformed research and innovation. With the best intentions, policymakers are creating institutional and legal structures to make 1990s R&D more equitable and are missing the opportunities and threats of 2016 R&D. Responsible research and innovation is thus stuck in a largely outdated scientific paradigm tied to the unfolding ABS framework.

Moreover, discord within the ABS policy process, something the Nagoya Protocol was developed to address, has not lessened. Industry and researchers express frustration at the growing bureaucratic and costly ABS regulatory apparatus, which they see as restricting important basic research on threatened ecosystems and species and impeding scientific and technological developments that could address the multiple crises we face in the Anthropocene [43, 45–47]. Others see misappropriation, and "biopiracy", of genetic resources and traditional knowledge as widespread [20, 29, 48].

Although the interface between synthetic biology and ABS is still poorly developed, a recent case of "synthetic biopiracy" [49] underscores the importance of embedding this fast-moving scientific and technological field into the ABS policy dialogue. In this case, a US biotech firm and a US university lodged a patent claim based on a variant of an influenza gene that was initially collected from a human victim in China, and later published, claiming these were "synthetic" but without disclosing its origin [36, 50].

Both "providers" (countries from which genetic resources are accessed) and "users" (researchers and companies that use genetic resources) find themselves caught up in an environment characterized by misunderstanding, mistrust, and regulatory confusion. The ABS policy process has catalyzed and provided an invaluable home for discussions around RRI and ethics in science, but it has yet to respond meaningfully at an institutional level to scientific and technological advances. Moreover, evidence ironically suggests the formalization of ABS may have unintended negative consequences on marginalized communities and can hamper economic development [51].

Synthetic Biology, RRI, and the CBD

It is into this arena that the already contested area of research and innovation known as synthetic biology arrived as a "new and emerging issue" [52]. Given its recent appearance, synthetic biology has not been addressed in the text of multilateral treaties such as the CBD; however, a range of laws could apply to it, including the Cartagena Protocol for Biosafety [27]. The inclusion of synthetic biology within national laws drafted to implement the Nagoya Protocol is still uncertain, depending upon how national governments define genetic resources and genetic material, the utilization of genetic resources, and derivatives [32, 36]. As we have discussed, there are many difficulties of including this technology into ABS law—with the exception of the few companies which prospect for genetic resources in a way that fits well within ABS as understood by the Nagoya Protocol. Beyond the CBD and ABS, governments have been inconsistent and slow to come to terms with this new technology, with the environmental and social concerns going unaddressed, and the harmonization of laws across countries proving challenging. For researchers, legal uncertainty often persists [36]. However, interest in synthetic biology at CBD meetings is growing, and there are calls by the CBD's scientific body for the Nagoya Protocol to explicitly take up the issues raised by this technology [33]. It is thus possible that the broader RRI issues raised by synthetic biology might find at least a temporary home within the ABS process, possibly as a side and emerging issue, rather than a central component of ABS policy-making.

Synthetic biology has come of age in the last few years, with a rapid escalation in government and private sector investment, and the commercialization of products and applications. As of late 2015, at least 116 products and applications were on the market, or close to market entry, and about 565 unique entities were conducting some type of synthetic biology work across the globe, a more than 200 % increase since 2010 [53]. However, inconsistencies and confusion remain about the most basic elements of what defines synthetic biology [40], all of which have a bearing on its interface with RRI. These include questions about whether it is still in the basic research phase or has emerged into commercial application; whether it is an evolution from traditional genetic engineering or a revolutionary leap into a new paradigm; and the geopolitics of who is doing the research. All of these issues return, fundamentally, to the social and political context in which this technology is emerging, which we discuss briefly below.

What Is Synthetic Biology?

The term synthetic biology emerged in the early 2000s to distinguish it from classic genetic engineering, but it continues to apply to a wide range of disciplines, techniques, potential applications, and end products [54, 55]. The European Commission undertook a survey of more than 30 definitions of synthetic biology and arrived at the following: "synthetic biology is the application of science, technology and engineering to facilitate and accelerate the design, manufacture, and/or modification of genetic materials in living organisms to alter living or non-living materials" [56]. The most widely cited definition of synthetic biology to date is "the design and construction of new biological parts, devices, and systems, or the re-design of existing, natural biological systems, for useful purposes" [57]. Building upon this, the National Science Foundation's Synthetic Biology Engineering Research Center (Synberc) adds: "…. The element that distinguishes synthetic biology from traditional molecular and cellular biology is the focus on the design and construction of core components (parts of enzymes, genetic circuits, metabolic pathways, etc.) that can be modelled, understood, and tuned to meet specific performance criteria…" [58].

Synthetic biology makes use of the same underlying principles of traditional biotechnology, and recombinant DNA (rDNA) techniques, but is distinguished by the scope and speed of genetic change that it can achieve [59]. Moreover, as Bergeson et al. observe, "the application of standardized engineering techniques to biology can kick-start quickly and relatively inexpensively the creation of organisms and entire biological systems with novel or specialized functionalities" [59]. Synthetic biology diverges from biology in that, while it enhances our understanding of genomes and life, the majority of research is focused on commercial and industrial applications. As synthetic biologist Drew Endy from Stanford University has remarked, "Biology is not just a science anymore, it is a material" [60].

Despite its extensive application and use, a widely agreed definition for synthetic biology remains elusive, and strongly contested. This is not only because the technologies are extraordinarily complex and changing but also because of the enormous political, social, and economic implications that would emerge from an

agreed definition. A definition makes discussions of benefits and risks, and desirable policy-making, possible [55]. This in turn would lead undoubtedly to stricter regulation, a scenario opposed by many involved in the diverse industries that synthetic biology has spawned [61].

This lack of definitional clarity has to some extent been used opportunistically. Commentators have observed, for example, that if researchers are talking to the public, they refer to synthetic biology as an incremental building upon what we have done before, and if talking to potential investors or funders, they describe it as a transformative technique that will change everything [62]. Friends of the Earth echo this: "If you were to ask a company 'is this synthetic biology?' [63], because I am from a civil society group the answer is 'no'. If I were an investor, the answer would be 'yes'" [63].

Concern about public opinion to a large extent frames the discomfort that many working within synthetic biology have with the term. Unlike nanotechnology and other emerging technologies, the term "synthetic biology"—joining *synthetic* and *biology*—triggers fears about the ability of public institutions to manage an unknown set of risks, and the moral and ethical implications of creating and engineering living organisms [64, 65]. As noted by a researcher at the UK Centre for Synthetic Biology: "Having the word 'synthetic' next to the word 'biology' does provoke a reaction in people that can be negative" or the public "may associate synthetic biology with things that are artificial, fake, or man-made" [65].

Understanding the interface between RRI and synthetic biology is all the more challenging because of its definitional confusion. If there is no agreement on the research and innovation sphere within which synthetic biology is contained, then determining the extent to which such activities comply with RRI criteria such as ethical acceptability, environmental sustainability and societal desirability becomes almost impossible. This lack of clarity further prevents us from determining even *which* activities might be relevant to assess using such criteria.

Is Synthetic Biology Evolutionary or Revolutionary?

The precise nature of synthetic biology research also has a direct bearing on RRI. Synthetic biology is considered by many to be an extension of conventional molecular biology and genetic engineering, and part of a continuum. Some groups call it "extreme genetic engineering" [66, 67]. Others see it as a potentially transformative and new science [54, 55]. The transformative and revolutionary view of synthetic biology depends upon the removal of current levels of unpredictability in biology [35, 54]. Under this scenario, there is full-scale application of engineering principles such as standardization, the decoupling of information from manufacture, and abstraction. The end result is that well-characterized DNA parts (sometimes called BioBricks) could be readily assembled in many different ways to generate predictable outputs [35]. Thomas Murray describes this as "a faith that biological systems can be brought to heel and made predictable and controllable" [54].

Even in its current form of extreme genetic engineering, synthetic biology is already revolutionary in the social, economic, ecological, and political space in which it takes place. The technology is "faster, cheaper, better" all the time, as synthetic biologists like to describe it, and as a result, it is a science available to [54] "both institutional and non-institutional stakeholders, including the citizen science community" [59] or the "hacker community" as some call it.

Other transformative aspects of the technology include the "decoupling" (a popular term in the synthetic biology world) of production from finite, non-renewable resource consumption. "With this technology we can decouple the production of oil from geography", notes the US biotechnology company Solazyme, which uses microalgae to create energy and transportation fuels [68]. Many companies argue that synthetic biology is a positive environmental development that can replace petroleum-based products and assist with environmental remediation. An alternative view is that the supply of feedstocks, raw materials used to produce sugar for the "biological factories" to make chemicals, biofuels, isoprene, and other products, is of significant concern. Feedstock crops replace food crops, and forests and other areas are cleared to grow agricultural feedstocks, in some cases through land grabbing and the violation of the rights of indigenous peoples and local communities [12, 13, 69]. The decoupling of production and nature may seem possible in the laboratory, but the technology continues to rely on natural raw material, the sourcing of which requires a critical assessment of the societal desirability of the research activities, its ethical dimensions, and the environmental and social consequences of the full lifecycle of different components of commercialization.

Is Synthetic Biology Basic Research or a Commercial Activity?

The question of whether synthetic biology is solely a field of basic research or whether it has developed into a commercial sphere has been a long-standing debate, again with profound implications for regulation and RRI [70]. In the last few years, however, this once controversial issue has been quietly resolved. The global synthetic biology market reached nearly $2.7 billion in 2013, for example, with predicted growth to $16 billion by 2018 [71]. The applications of synthetic biology are diverse and include specialty/fine chemicals, biofuels, medicine, plastics, polymers and rubbers, and plant feedstocks for microbe consumption. Examples of commercial products include foods and flavourings like vanillin, resveratrol, saffron, and stevia from the Swiss company Evolva; biofuels from Solazyme (US) and Joule (USA and Netherlands); industrial enzymes produced by Verenium (USA, now BASF, Germany) and Novozymes (Denmark); chemicals, industrial fluids, pharmaceuticals (artemisinic acid), and personal care ingredients (squalene) from Amyris (USA); and dozen more chemicals, industrial enzymes, and isoprene from DuPont and other large chemical companies [70]. With more than a billion dollars in government funding in the USA and Europe alone, and a significant jump in private sector investment, hundreds of research entities involved across the globe, and more than 100 products and applications on the market, synthetic biology is no longer a basic research enterprise [53].

More and more, therefore, there is relevance in asking questions about how research priorities are determined, whose interests the products serve, how research is funded, and the environmental and social consequences of particular research directions. With a firm link to commercialization, ABS also takes centre stage in deliberations about the source of genetic resources, the research partnerships that are developed with low and middle income countries, and the technology transfer components that are typically required in ABS agreements. While some commercial activities may indeed be "decoupled" from their biological source and transcend beyond the direct use of genetic material, this may not necessarily be sufficient to exclude them from the wider political ambit of scientific and technological equity and "fairness" required by the CBD and the Nagoya Protocol [49].

Who Is Doing the Research?

Such concerns play themselves out in the geopolitical space, with most synthetic biology research taking place in the USA and Europe [53]. However, there is an increased engagement from the BRICs. China, for example, is also considered to be invested heavily, based on the number of scientific publications and teams entered in the International Genetically Engineered Machine competition [53], and Brazil, India, Mexico, Argentina, South Africa, and Singapore are also beginning to engage strongly [53].

Globally, research investments are increasing, both within the private sector and government agencies and research centres [54]. For example, between 2008 and 2014, the US government invested approximately $820 million in synthetic biology research; in 2014, 60 % of government funding was from the Defence Department, totalling $100 million, more than three times the amount spent by the National Science Foundation [53]. The UK government is the largest supporter of synthetic biology research in Europe and has funded more than $165 million in such research since 2010, over double that funded by the European Commission [53].

Beyond the number of products and applications existing on the market, or on the horizon, data on synthetic biology research in the private sector is extremely difficult to come by [63, 72–74]. There are a number of reasons for this, including the absence of triggers that feature in other sectors such as sales, patents, public companies, and government regulation. Many synthetic biology applications are developed and used within companies, as part of industrial manufacturing and other processes, and are never sold; these applications and processes are often not patented and are better protected through secrecy; many companies are privately owned; and biotechnology in general (apart from GMO crops) is very lightly regulated by governments, with few reporting requirements or mechanisms [44]. The opacity of these activities combined with the astonishing scale and speed of these technologies and their commercial use creates concerns within the public and policy arena [40, 50]. If RRI is supposed to be "transparent and iterative", creating a climate of mutual trust and responsiveness between societal actors and innovators [10], we are very far from achieving this within the field of synthetic biology.

Emerging Technologies: Lessons from the CBD and the Nagoya Protocol

A central challenge to all emerging technologies is the slow and lumbering pace of policy development and change, which contrasts markedly with the pace of scientific and technological change today. In 1992, when the CBD entered into force, the first gene had not yet been sequenced (this happened in 1995), and while the Nagoya Protocol was under negotiation, in 2007, the second-generation sequencing platforms came on line and suddenly and profoundly reduced the cost of reading DNA [73, 75]. In 2010, when the Nagoya Protocol was signed, Craig Venter announced the creation of the first synthetic life form, and in the last few years, a host of synthetic biology products and applications has come to market. The result of the different pace of change in policy and science is that within the CBD and Nagoya Protocol, many assumptions about how genetic resources are accessed and used are years out of date. The hundreds of meetings and millions of dollars spent on ABS thus often address activities that are uncommon today and project a value for genetic resources that cannot be realized as put forth in the policy framework.

This disconnect has also created conflict and stalled research on genetic resources in high biodiversity countries. Remarked one executive at a medium-sized biotechnology company: "When you are dealing with a place that is unfamiliar with industry, and doesn't do CBD agreements often, they often don't understand that what they are asking for is outrageous. They think *we* are outrageous. During discovery, the organism from nature is so upstream and so much investment and risk has gone in before it becomes a drug, that the original organism is not that valuable – it only has value in hindsight, and without considering the tens of thousands of molecules with billions of dollars of research funds sunk into them that went nowhere." [44].

Governments and others involved in ABS can be woefully out of date on scientific, technological, and business developments, and often lack the institutional capacity and clarity to regulate advanced research, define the societal desirability of different approaches to research and regulation, or develop long-term strategies. This is not unique to the CBD policy process, however. As Bergeson et al. put it for the case of the USA and synthetic biology: "The regulatory framework that has evolved is complicated, increasingly circuitous, and not for the faint of heart. First-time and experienced innovators alike are increasingly vexed by the daunting jurisdictional divides crafted years ago based on fundamentally different kinds of products and technologies" [59]. A central governance conundrum is how policy makers can address their responsibility to prevent harmful or unethical developments in research and innovation while ensuring that such interventions are grounded in a reasonable understanding of the rapidly changing innovations that they seek to regulate.

Limits to capacity; an absence of strategy and understanding; a shortage of resources to improve capacity, develop strategies, and implement laws; and jurisdictional confusion are shared by many other areas of law in which the regulated activities are new, emerging, or poorly understood by policymakers. For example, the governance of non-timber forest products, often one of the lowest technology activities in biologically diverse countries, suffers from a strikingly similar list of ills as ABS and synthetic biology regulation [76].

While governments commonly grapple with limited capacity, researchers can follow a self-defeating pattern of ignoring or playing down the need for policy, understandably wary of uninformed interventions. A combination of approaches, expertise, and knowledge is needed, and researchers, industry, government, and civil society organizations have begun to come together to address the benefits and risks posed by synthetic biology [53, 71]. It is also the case that if scientists do not actively defend concerns about their work, in language that is accessible and believable to a sceptical public, those concerns will take a life of their own. The journal *Nature Biotechnology* lamented in October 2015, in relation to public concern about GMOs, that: "…search engines and apps that prioritize content by popularity and immediacy mean that gravity in news is superfluous. Misinformed propaganda now floats unfettered across the globe at the speed of electrons" [77]. The editors conclude, however, that funding for real public engagement and better communication is critical, and note that most UK and US funders spend less than 1 % of their budgets on outreach: "If we are to have a thriving science-based society, there is an urgent need to work on the public understanding of science" [64, 65, 77]. But such engagement also needs to be sensitive to a context where, through social media and the Internet, the public is increasingly connected to scientific outputs, is sceptical of science and "technology push", of being

"educated", and is suspicious of the intent behind science education. A government-industry funded programme in South Africa, for example, to "increase public understanding of biotechnology" has drawn considerable criticism, due to its perceived lack of credibility and impartiality [78]. Science education on synthetic biology is not only about bringing the public "on side" but, perhaps more importantly, about "equipping future researchers…with the necessary knowledge and tools to fully participate and take responsibility in the research and innovation process" [79].

Funding is also needed to study the nature and risks of new technologies. The potential impacts of synthetic biology on human health and the environment, for example, have received only a small portion of global research funds, and a lower level than other emerging technologies [53]. Of all the funds spent on synthetic biology research by the US government, support for research on risks was less than 1 % of expenditures, and another 1 % was spent addressing ethical, legal, and social issues [53]. This contrasts with the National Nanotechnology Initiative funding of risk research at around 3.5 % between 2005 and 2012, and ethical, legal, and social issues at around 2 % [53]. Without adequate understanding and information, it will be difficult for policy-makers to develop an appropriate framework for RRI on synthetic biology.

Conclusion

The CBD has provided a forum for expression of a wide range of environmental, historical, human rights, and other concerns. As a result, RRI implicitly and inadvertently has emerged as a central theme in the ABS policy process. While great strides have been made in defining broad societal goals for research and innovation, and a range of voluntary measures have emerged from this process, governments are also boxed in by ABS policy that has not kept up with changes in science and technology. Factors such as limited government capacity and expertise in regulated fields, an absence of policy strategies, jurisdictional confusion, and a lack of resources further hinder government efforts to keep policy current and meaningful.

As synthetic biology and other advanced technologies come of age, there is increased urgency to integrate RRI more explicitly and holistically into the full range of policy processes of the CBD, including those of the Nagoya Protocol and Cartagena Protocol. The CBD might serve both the product and process concerns of RRI better by institutionalising approaches of anticipation, reflection, and deliberation; framing responsibility in the context of uncertainty and on-going change; ensuring transparency; and moulding governance and policy to prevent harmful or unethical practices in research and innovation.

What is clear is that the broader umbrella of the CBD is more likely than the increasingly narrow ABS process to provide the much needed space for addressing social justice, economic, sustainability, biosafety, and other RRI issues raised by emerging technologies.

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