Beyond Nature's Code: Governing the Frontiers of Synthetic Biology

GENEVA GRADUATE INSTITUTE

INSTITUT DE HAUTES ÉTUDES INTERNATIONALES ET DU DÉVELOPPEMENT

GRADUATE INSTITUTE OF INTERNATIONAL AND DEVELOPMENT STUDIES

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Research team:

Ahmed Shaim Mahir

Joël Goux

Josué Laos

Yue Wu

Supervising Professor:

Dr. Jérôme Duberry

Managing Director Tech Hub

Partner Organisation:

Dr. Anne Bardsley

International Science Council

Cover Photo: “Dolly the Sheep”, the first cloned mammal. Photo credit: 2002 REUTERS/Jeff J Mitchell. accessed on June 13, 2024, < https://www.reuters.com/article/idUSKCN1061Z8/>

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List of Abbreviations

AI	Artificial Intelligence
BOLD	Barcode of Life Data Systems
BWC/BTWC	Biological Weapons Convention/ Biological and Toxin Weapons Convention
CAR-T	Chimeric antigen receptor T-cell
CBD	Convention on Biological Diversity
CRISPR	Clustered, regularly interspaced, short palindromic repeats
CWC	Chemical Weapons Convention
DIY	Do-it-yourself
DNA	Deoxyribonucleic acid
EU	European Union
FDA	Food and Drug Administration
GDO	Gene Drive Organism
GMO	Genetically Modified Organism
HGT	Horizontal gene transfer
HIV	Human immunodeficiency virus
iGEM	International Genetically Engineered Machine
IGSC	International Gene Synthesis Consortium
IMF	International Monetary Fund
IP	Intellectual property
IPCC	Intergovernmental Panel for Climate Change
LATAM	Latin America
LMO	Living Modified Organism
MedTech	Medical Technology
NAS	National Academies of Sciences
NGO	Non-government organisations
R&D	Research and development
SEC	Security and Exchanges Commissions
SynBio	Synthetic Biology
USA	The United States of America
USDA	United States Department of Agriculture
WHO	World Health Organization

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1. Introduction

Synthetic Biology is bringing pivotal changes and advancements in the way we understand life (Elani, 2021). Key ethical questions are put on the table when addressing human interference with our environment. The trade-offs between promising solution-driven technologies and catastrophic consequences are key challenges in addressing the governing frameworks of SynBio (Macfarlane, et al., 2022). Following some important momentum in multilateral and democratic processes addressing this science, it becomes important to understand the overall field, its challenges, and the opportunities it brings us. Moreover, key actors in the multilateral and research systems could address some of the challenges impairing an effective and safe application of new biotechnologies.

For this reason, the following report focuses on four different fields surrounding SynBio and is framed to answer the following research questions.

1.1. Research questions

i. *What are the possible technological developments and implications of synthetic biology, specifically in the domains of food systems, biodiversity, healthcare, and international security?*

ii. *What are the current precautionary principles, legal standards, ethical guidelines, and regulatory structures that frame the development of synthetic biology?*

iii. *Which policies and frameworks could address and rectify the deficiencies identified in the current governance of synthetic biology?*

The report is structured into five sections. First, key literature on biotechnologies is presented and discussed, levelling our understanding of what is understood by "SynBio". Second, gaps associated with the framework governing SynBio are highlighted. Third, data is presented in the form of expert interviews, enriching the literature, and providing material for analysis and mitigation. Fourth, data from the interviews are superimposed with the gaps reflected in the literature. Last, a policy brief is brought forward as a potential strategy to support a multilateral and democratic approach to SynBio.

2. Methodology

The main objective of the report is to propose improvements in the already existing frameworks that govern fundamental research of SynBio by assessing the implications on the focused areas mentioned in the introduction. Furthermore, by analysing the current gaps in existing frameworks we try to bring a method in which the challenges experienced in the field can be mitigated. The following figure showcases the steps undertaken to perform the research, data collection, analysis, and policy proposal.

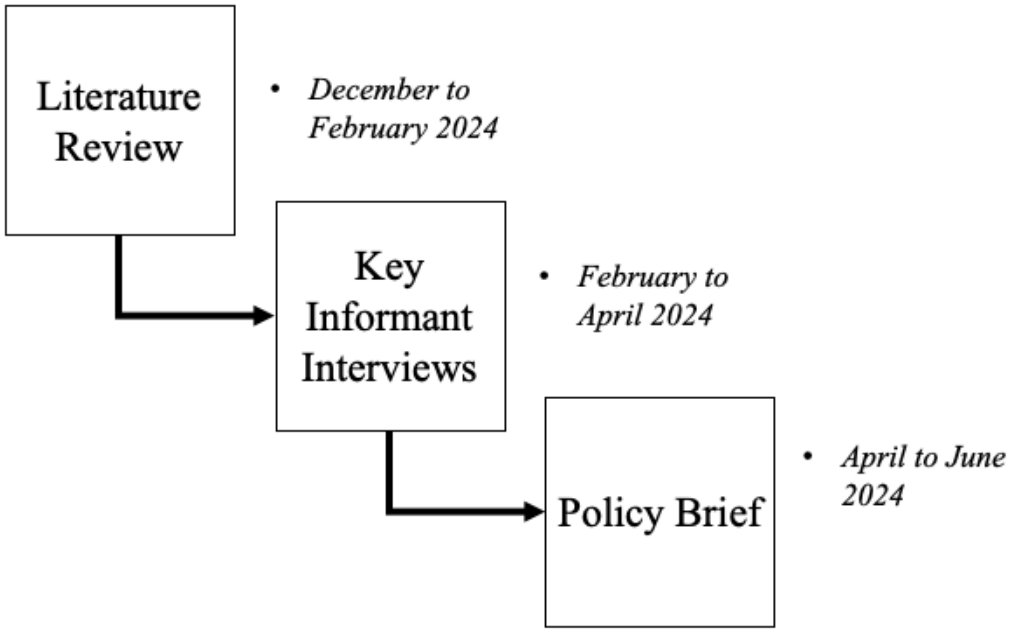

Figure 1: Processes and Timeline of Research Project

2.1. Process 1 - Literature review

Based on desk research, the literature review will be conducted from the following points for the four different themes addressed:

i. A review of existing governance of fields related to or adjacent to SynBio and benchmarking approaches to governance within those fields.
ii. An in-depth overview of major emerging technologies within the pre-defined subfields of SynBio.

iii. A mapping exercise of the main stakeholders of the subfields of SynBio in previous points, specifically focusing on the main purposes and participatory roles of
iv. A gap analysis of the reviewed frameworks highlighting the missing legal and precautionary principles for safe advancement of this key defining human advancement.

2.2. Process 2 - Key informant interviews

i. 14 interviews are conducted with experts in different fields.
ii. The interviewees were selected through expertise sampling.
iii. Interviews are semi-structured.
iv. Question templates are established following the gaps highlighted from the literature

2.3. Process 3 - Policy recommendations

i. The policy recommendations will be the analytical and concluding remarks of the research process.
ii. Informed by the literature review and the key informant interviews, the brief would include a thorough review of all the relevant governance or lack thereof within the domains and how they can be amended and/or newer forms of governance be included.
iii. The main objective is to provide concise and direct recommendations that can affect the short, medium, and long term of the industry's governance and continuing operations.

3. Definition of Synthetic Biology

There are no internationally accepted definitions of SynBio with the field associated with major new breakthroughs of biotechnology. The normative elements of SynBio are constituted in the ability of new methods and practices to modify living organisms mostly through the modification of naturally occurring genetic forms or by the creation of new genetic material (Keiper & Atanassova, 2020).

SynBio is enabled by the following six categories of technologies (Keiper & Atanassova, 2020).

i. Chemical Synthetic Biology (xenobiology) or Biorthogonal (Carpenter , Hausner, & Sutcliffe, 2011).
ii. Genetic circuit engineering (e.g., bisabolene) (Peralta-Yahya, et al., 2011).
iii. Metabolic engineering (West, Hou, & Lee, 2011) (Peralta-Yahya & Keasling, 2010).
iv. Protocell design (Xu, Xu, & Yomom, 2019).
v. Genome Synthesising (Sleator, 2010).
vi. Minimal Cell (or genome) (Hutschison III, et al., 2016).

4. Current governance of Synthetic Biology

The CBD is the main framework of governance for SynBio at a multilateral level. The main purpose of this international system is defined in Article 1 of its founding text as "[…] the conservation of biological diversity, the sustainable use of its components and the fair and equitable sharing of the benefits arising out of the utilisation of genetic resources" (CBD, 1993).

An important outcome of the CBD can be defined as the Cartagena Protocol on Biosafety which set in 2000 the precautionary principle on the safe transfer, handling, and usage of LMOs.

A second major outcome of the CBD Is the Nagoya protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefit-sharing set the mechanism for sharing genetic resources, the pillar of SynBio, emphasising on the fair and protected distribution of access to these resources amongst states (Nagoya, 2014).

The following figure taken and adapted from Keiper & Atanassova in a recent publication in 2020 showcases the current international framework under the CBD (p.3).

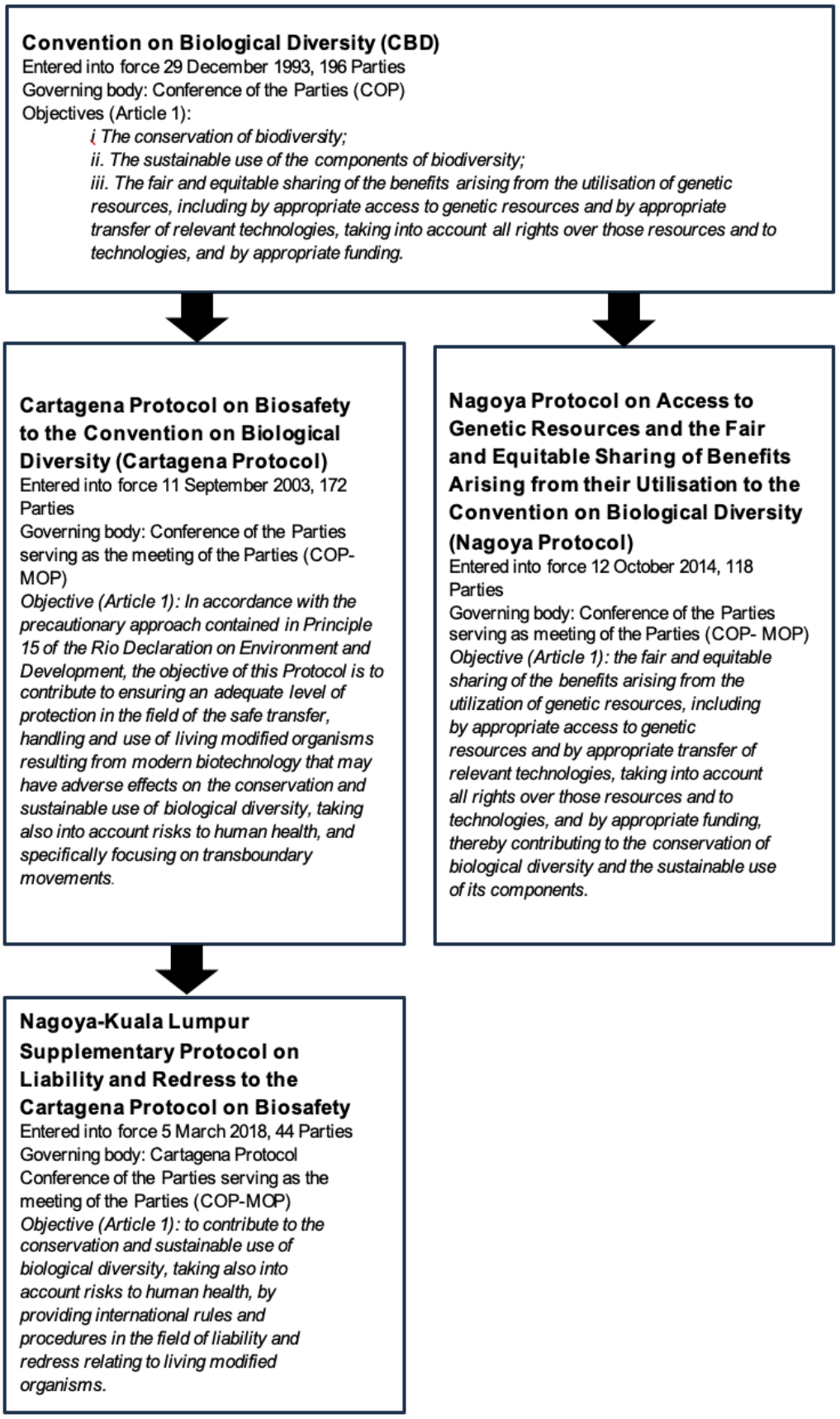

Figure 2: Overview of the governance of Synthetic Biology at the international level

5. Food systems

5.1. State of the industry

Agribusiness and the overall food systems are industries where SynBio has seen the most wide-spread applications and adoptions. GMOs have been used in the field for the past three decades and have created many ripple effects within the industry (Abdul Aziz et al., 2022; Oliver, 2014). Major breakthroughs in the field have resulted in higher crop yields and changed the way that food is produced in our world (Kumar et al., 2020; Raman, 2017).

5.2. Major use-cases

Within agriculture, the world of GMOs has expanded to include products that can be considered beyond the traditional norm. For example, a recent but significant development could be discussed through the development of meat analogues and alternatives created through novel biotechnologies. Plant-based and in-vitro cultured meat made from animal tissue, are gaining adoption (Kumar et al., 2021). Most of the research and development of these products are conducted in research labs situated in the US and Europe but expansion into other territories have been gradually growing (Kelley et al., 2014).

5.3. Major opportunities

SynBio is offering many opportunities for continuous development of the field. By perfecting the overall balance within our foods, the industry can enhance their nutritional content (Roell & Zurbriggen, 2020). Second, given the environmental issues the earth is facing, SynBio technologies could offer new frontiers for the reduction of the environmental impact of our food production processes (Coban et al., 2022). Moreover, food safety is a key topic when discussing opportunities, as the modelling and testing within SynBio can detect and neutralise any pathogens that may have contaminated the supply chains (Niehl et al., 2018). According to literature, one of the most important opportunities for the industry in the current context, is that of developing alternate proteins (Liu et al., 2021).

5.4. Major risks

Whilst offering many opportunities, major risks limit and slow the faster adoption of new technologies within food systems. First, releasing new synthesised foods into many markets constitutes a challenge and risk, with many regulatory and consumer-related issues rising when conducting R&D (Faccio, et al., 2019). More research into the impact of the new GMOs is necessary as the industry could be impacted by catastrophic spillovers when releasing newly designed crops into the environment, with the potential to disrupt entire food chains. The unintended effects paradigm should also be carefully considered, as modifications to crops or food could have unforeseen impacts on human health and result in doing more harm than good. There are also ethical questions to consider, as to what extent human intervention into the natural world can be condoned and the consequences of altering life-forms, even if they are by-products or not sentient (Rodrigues et al., 2023).

5.5. Main stakeholders

Key stakeholders can be categorised into four main groups. First, farmers and food production & processing stakeholders, can be described as the lynchpin to how novel products undergo the full cycle of research and commercialisation. Second, researchers and the institutions they are associated with drive the new fundamental developments of the field. Third, given the necessary precautionary nature of the work, regulatory agencies in food and agriculture have an important role to play in ensuring the quality and safety of the product. Last, consumers constitute the end-users of the industry, driving demand following ever-so changing lifestyles.

5.6. Frameworks of governance

The current governance for food systems within SynBio is driven by ongoing developments as well as emerging trends, although inadequate due to novel technology implementation. When addressing geographical disparities in research, three characteristics can be observed. The first concerns countries that have pro-GMO legislation, especially markets where agriculture forms a significant part of exports (He et al., 2020; Pellegrini, 2013; Uscátegui-Clavijo & Montaguth-González, 2023). Second, countries who enforced a moratorium on GMOs and SynBio influence within the food industry (Ghouri et al., 2023). The final type of frameworks is found in countries that are restricting and regulating the

influence on a case-by-case basis (Genetic Literacy Project, 2021). It is important to note here that GMO legislations have been the first commercial and research-driven regulation, often influencing and inadequately adapted to other sectors of SynBio (Sundaram et al., 2023). Broadly speaking, precautionary principles that were formed for food-related SynBio, currently apply in the EU for all synthetic biology innovation related to food systems as per Article 191 of the Treaty for the Functioning of the EU. More specifically, the "Deliberate Release Directive 90/220/EEC" allows for the regulation to distinguish between Type A (for academic research) and Type B (for commercialisation) of any SynBio product within food systems. Interestingly, the system is inherently process-based which contrasts with the product-based regulation and approval of the process of the Food and Drug Administration (FDA) in the US (Marchant & Stevens, 2015).

5.7. Highlighted gaps

When discussing the future of the industry and its governance, some prominent gaps can be highlighted. There is a need for cohesion between the industry and its consumers, as EU regulators and companies need regulations and frameworks that align with their target markets. There also seems to be a general lack of alignment between countries' roadmaps to food production within SynBio, but this is to be expected given that each country has different needs and priorities. However, some coordination has been noted as needed to ensure the industry's efficiency (Joyce et al., 2013). Moreover, there are various regulatory frameworks currently conflicting between "process-based" ones and "product-based" ones spreading throughout the world (Marchant & Stevens, 2015). Finally, there are no substantial international agreements or agency work related specifically to food products and systems within SynBio (Joyce et al., 2013). There are singular regulations such as ones around food additives allowed but none comprehensive enough to cover the emerging innovations of the industry (WHO, 2023).

6. Biodiversity

6.1. State of the industry

Whilst most research, funding, and regulation on SynBio has been directed towards food systems and healthcare, the impact of the field on biodiversity is increasingly relevant

offering many opportunities in the domain of conservation and biodiversity assessments all whilst representing an important risk to the fragile balance of ecosystems (Corlett, 2017).

Alongside climate change, biodiversity, and its conservation, throughout the world, has become a key political and research issues, tools and instrument that provide reversible solutions to this major global problem have become relevant for many sectors of industry and research (Rohregger, Sganzerla, & Simão-Silva, 2020).

The approach of SynBio on diversity can be delimited into five categories.

i. Protecting native species from alien/invading ones
ii. Adapting species to new climate conditions caused by climate change
iii. Measuring biodiversity and key metrics amongst population (e.g., hybridization, inbreeding…)
iv. Identifying sources of population
v. De-extinction

Whilst the majority efforts on SynBio regarding biodiversity focuses more on avoiding spill over effects from the release of GMO, LMOs and GDOs gene-drive organisms on local biodiversity, a nascent and promising branch of biology and conservationism is focusing on using new tools (Piaggio, et al., 2017; Gostel & Kress, 2022).

6.2. Major use-cases

The major use-cases of SynBio on biodiversity are mostly enabled via four major technologies.

i. Gene-drive organism
ii. DNA barcoding
iii. Gene editing
iv. Genetic engineering

DNA barcoding consists of sampling DNA sequences of a species or a specific population and one gene sequence using markers called barcodes which can then be used for future referencing (Redford, Brooks, Macfarlane, & Adams, 2019). Whilst DNA barcoding has

many fields of application, it can be used for discovery and monitoring of levels of biodiversity. New undiscovered species can be better recognised, and when applied at a macro level, richness of biodiversity can be assessed (Semenov, 2021).

GDOs have also showcased promising use, especially in illness prevention and biodiversity endeavours (James & Santos, 2023). Gene-driven organisms are living entities with modified genetic material (gene-drive) which has been modified to cause genetic changes in populations via reproduction (Reynolds, 2021). Gene editing, a major enabling technology, has also important applications in biodiversity, with two major components to it, namely, genetically modifying a species to adapt into a new environment. Gene engineering and sequencing are also technologies which could have an important impact on biodiversity when discussing the re-introduction of an extinct species into an environment (Shapiro, 2017).

6.3. Major opportunities

Key opportunities of SynBio technologies are often discussed within conservation efforts (Redford, Brooks, Macfarlane, & Adams, 2019). New SynBio technologies can improve the ability of the field to better assess rates of extinction, or the interaction of native species with alien ones as well better understand the adaptation of species to new environmental conditions causing this manner (Zenda, Liu, Dong, & Duan, 2021).

Important efforts are currently being pursued in research to better assess living organisms and discover species. Open-source gene barcode databases such as The Barcode of Life Data Systems (BOLD) collect millions of data points supporting biology research (van der Bank, et al., 2019). The usage of gene editing could offer a new adaptational frontier (Zenda, et al., 2021). Still very speculative, SynBio showcases itself as potentially revolutionising the way humans interact with living organisms on earth and beyond.

Gene-drive organisms could also offer a useful tool for biologists to remove invasive species and protect native systems (Veitch, et al., 2019). One could imagine the release of GDOs in an environment with the goal to completely remove an invasive species within an environment.

6.4. Major risks

SynBio represents existential threats and risks for the safeguard of entire ecosystems and species (Giese & von Gleich, 2014). The potentially unwanted spillover effects of the introduction of LMOs and GDOs within a controlled environment would have devastating effects (Courtier-Orgogozo, et al., 2020).

The highest risk highlighted in literature often refers to the uncontrolled spread of terminator genes spreading within a specific population, guiding it to mass extinction (Barron, 2008). This gene, even if applied into a specific population, could travel through crossbreeding or through HGT and introduce itself in uncontrolled zones (Wright, et al., 2013).

6.5. Main stakeholders

Key stakeholders when discussing SynBio and biotechnology are biologists (conservationists), biotechnologists, governmental agencies administering biodiversity and conservation activities, as well as international bodies focused on biodiversity. Other stakeholders of the field such as non-governmental organisations, biotechnology companies, food companies and actors focusing on sustainability also have involvements in the discussions related to SynBio's impact on biodiversity. Conservationism in most parts has their activities guided by government policies (Rands, et al., 2010).

6.6. Frameworks of governance

The CBD, and its affiliated bodies constitute the internationally accepted normative basis for activities related to SynBio biodiversity. Its key principle can be read in the preamble stating that "[…] where there is a threat of significant reduction or loss of biological diversity, lack of full scientific certainty should not be used as a reason for postponing measures to avoid or minimise such a threat" (CBD, 1993). This view, addressing the urgency of biodiversity loss, contrasts with the more prudent principles guiding biotechnologies which focus more on certainty before release (Rabitz, et al., 2020).

6.7. Highlighted gaps

The advancement of technology in the space of SynBio and biodiversity offers promising opportunities but is faced with major ethical and implementation risks. In an

already over stressed environment and changing climate with potential catastrophic consequences, risk assessments methods for this are becoming ever so stringent (Macfarlane, et al., 2022). Yet, the willingness to implement solutions to dying ecosystems is well present in all aspects of society.

The trade-off between solution-oriented risk assessment and caution-focused ones are a difficult challenge that regulators and ethical framing bodies face (Finkel, 2019). There is currently no globally accepted framework guiding the release of conservation SynBio instruments into the environment. As previously mentioned, current regulations, be it permitting the release of GMOs into the environment, were built as a response to food-system addressing technologies, which can be considered inadequate to guide conservation-focused technologies and new advancements of SynBio in general.

A key recurrent gap highlighted in literature is the inadequacy of current regulatory and precautionary principle frameworks for the research and development of innovative technology, especially when it comes to the creation or modification of life outside of GMO-foods related topics. The lack of common understanding of processes in this context seems much behind what is addressed in the field of healthcare or food systems, this potentially having negative consequences with heterogeneous application of SynBio advancements. Release risk assessments of LMOs and GDOs are also lacking a clear framework and ethical concerns as well as safety assessments which are not well adapted to current needs.

7. Healthcare

7.1. State of the industry

SynBio has many applications in the field of healthcare. The discipline is expanding opportunity frontiers especially in the enhancement of compounds directed against diseases, the treatment of infections, drug development, therapies, and vaccines all with the potential to improve quality of life. Following the COVID-19 pandemic, increased research and funding has been directed in developing new processes (Dixon & al., 2022). CRISPR-Cas9 has been

described as a pillar of SynBio and healthcare which gives researchers and experts the ability to modify the genome sequence generating a whole new set of key healthcare solutions (Dixon, Freemont, & Pretorius, 2022).

7.2. Major use-cases

The following categories can be described as the main application of SynBio technologies in healthcare (Garner, 2021).

i. Synthetic biology-based vaccines are produced by using techniques and approaches on a large-scale nucleic acid manipulation.
ii. Synthetic biology-based diagnostics are novel processes and compounds which permit physicians and researchers to diagnose not only faster but with increased specificity, sensitivity, accurate quantification, and resilience to contamination. Synthetic biology enables iterative prototype and a gene circuit that can help the improvement of diagnostics.
iii. Synthetic biology-based therapeutics often refer to cellular immunotherapies which is a relevant tool for surgical interventions and pharmaceutical industries for the treatment of diseases. This allows the dominance of individuals for a longer-term disease management such as the detection and target of cancer cells by controlling the spatiotemporal activity of therapies in drugs (Tan, et al. 2021).

SynBio is currently applied in many areas of healthcare research fields. For instance, the pathways into designer cell growth media to produce medical agents, build novel genetic circuits for diabetes and cancer targeting, fight diseases, treat complex immune diseases, metabolic disorders are all core groups of research within SynBio (Andrianantoandro, et al., 2006). Some major examples of synthetic biology are the following (Yan, et al. 2023).

i. Genetic engineering of therapeutic and medical applications
ii. Tissue engineering
iii. Cancer diagnosis and treatment
iv. Engineering cells for metabolic disorders
v. Construction of nanoparticle-mediated genetic circuits
vi. Drug delivery
vii. Developing novel vaccines

viii. Pharmaceutical synthesis

7.3. Major opportunities

SynBio offers important opportunities in the development of new medical processes, enhancing overall effectiveness of the field as well as long-term population health outcomes. Moreover, the improvement of computational processes and the recent jump in performance of machine learning is accelerating the research opportunity frontiers, offering the development of even more complex objects (Innovate UK, 2016). The development of new biomarkers, drug releasing molecules, and clinical trial processes are all important elements proving much attention to the field (Innovate UK, 2016).

7.4. Major risks

However, key fundamental risks limit the application and release of LMOs and other SynBio products, especially when discussing human interaction and impact on health. In a publication by Lux et al. (2023) five major risks regarding SynBio, and healthcare are presented.

i. Many parts are undefined: this becomes a major risk for the application of this technology in the human body. A reason why this is the first challenge, is because synthetic biology has been viewed as a lack of biomolecular and engineered genetic components.
ii. The circuitry's unpredictability: since its sophisticated functionalities and limitations are not accessible for human understanding to build genetic circuits. Instead, it has been used in an abstract way.
iii. Complexity is unwieldy, especially when working with the human body, making the research process and the long-term effects of a potential SynBio solution difficult and risky to assess.
iv. Many engineered parts are incompatible; the challenges have demonstrated the complex relationship between the engineered parts, which could potentially affect the environment of the host organism and the organism itself.

v. The variability crashes the system; researchers have known that the naturally evolved living system will operate despite the lack of some parts, which leads to a need for novel design and understanding the approaches regarding synthetic biology.

7.5. Main stakeholders

Biomedical professionals can be considered key end-users of the field. Most currently researched SynBio instruments can be discussed specifically in tackling infectious diseases such as Malaria, Tuberculosis, and HIV (Hollis, 2013). Additionally, governmental laboratories, research institutions, non-profit organisations, for-profit organisations, universities are examples of important stakeholders of the field. International organisations focusing on health and disease research, and treatment are involved in the participation on both the direct application of SynBio solutions and the cooperation between stakeholders (van Weely & Leufkens, 2004).

7.6. Frameworks of governance

Governing frameworks associated with the medical ethical guiding and international law constitute the major pillars (WHO, 2015). Ethical governance guiding the process of clinical trials, which is a key step in releasing new medical devices and pharmaceuticals, has yet to successfully process a synthetic biotic for commercial sale, as the majority of SynBio applications are still in the research phase (Brennan, 2022). Currently, smart therapeutics based genetic encoded circuits have been used for the purpose of disease treatment and prevention such as CAR-T which have entered clinical trials. However, many attempts have failed in early clinical stages due to the unanticipated side effects on humans and the low therapeutic capacities. Stability, efficacy, and safety constitute three main guiding principles in the application of synthetic biology (Xu, et al., 2023).

7.7. Highlighted gaps

The following points constitute the main gaps in the governing frameworks of SynBio. First, safety and risk assessment and testing pertaining to the application of new SynBio based compounds are difficult to monitor with clinical trial structures being

inadequate to offer the traditional testing process which diagnostics solutions, vaccines, new drugs, and other treatments typically go through.

Second, major ethical considerations limiting the application and testing of new products are an important barrier for the development of SynBio. The ethical issues of governing trials such as non-maleficence, human centeredness and risk control, consent and consequences are limited and sometimes not included in the current frameworks guiding SynBio as a whole. The recent occurrence of the first of human cloning which took place in 2018, was followed by a full review of the ethical guiding frameworks in China, showcasing the inability to prevent or apply adapted precautionary principles prior to the incident (Song & Joly, 2021). Current international medical law needs better homogenisation and adaptation to give access to safe testing of SynBio for researchers to avoid performing illegal and unethical testing on living animals.

8. International security

8.1. State of the industry

While the world has grown more interdependent due to globalising force, it has also become more susceptible to the spread of catastrophic biological events (Koblentz, 2010). Given its ability to modify or synthesise from scratch organisms that can be highly destructive to human health and the environment, SynBio adds to the uncertainty in the landscape of international security by creating a new threat space where pathogenic bioweapons have been made unprecedentedly accessible (Trump et al., 2021). There has still been severe weakness in countries and global society to prevent, detect and respond to such catastrophic biological events, as can be the consequence of misuse of SynBio (Wang, 2021).

In the meantime, SynBio has been an increasingly critical arena for global competition in the geopolitical realm (Maye et al., 2012). Although enhancing international security from potential damage of SynBio calls for further international cooperation, countries share different approaches, interests, and priorities in the agenda (Hamilton et al., 2021).

8.2. Major technologies and risks

According to the different approaches followed, SynBio can be divided into branches of bioengineering, synthetic genomics, protocells and xenobiology (Gómez-Tatay & Hernández-Andreu, 2019). The ability to modify existing organisms or create new organisms from scratch of SynBio distinguishes it from conventional biotechnologies and contributes to greater complexities and uncertainties (Zeng et al., 2022).

Major risks of use of SynBio are distinguished into biosafety and biosecurity based on different causes of risks. Biosafety refers to measures against unintentional or accidental release of specific biological agents and toxins, whereas biosecurity copes with intentional or negligent release of biological materials or the acquisition of knowledge, tools, or techniques that could be used to cause harm (Sharples et al., 2015). However, distinction between biosecurity and biosafety can be unclear across research sectors and countries (Hamilton et al., 2021).

i. Biosecurity

Similar to previous technological breakthroughs, SynBio encounters the dilemma of dual use, which can be more challenging in some cases as the effect of engineered organisms have higher uncertainty, yet conventional mechanisms of risk identification and monitoring are either insufficient or unapplicable in these situations (Wang & Zhang, 2019; Wang, 2021).

Malevolent or negligent use of SynBio techniques requires both accessibility of biological materials and availability of relevant information, techniques or know-how that could be exploited for use such knowledge for irresponsible or nefarious purpose (Sture et al., 2013; Trump et al., 2021; Trump et al., 2020).

The most immediate biosecurity risks from the dual-use nature of SynBio are biological weapons and bioterrorism (NAS et al., 2018), whereas open access of genetic sequences of pathogenic bacteria and viruses, publication of methodology in scientific journal, as well as availability of easy and low-cost CRISPR-Cas9 technology have rendered the entry barrier unprecedentedly low to any interested users (Wang & Zhang, 2019).

Digital information can be used to manipulate biological systems, increasing reliance on genome databases. Hence, cyber biosecurity constitutes another emerging concern, which

refers to the privacy, integrity, and security of public health data against cyber exploits (Adler et al., 2021).

ii. Biosafety

According to the definition of biosafety, which refers to the prevention of the risks to public health and the environment that could be produced by accidental interactions between dangerous biological agents and other organisms or the environment (Gómez-Tatay & Hernández-Andreu, 2019), main concerns relate to relevant personnel working with synthetic organisms and the potential disruption of released organisms on environment and public health (Ahteensuu, 2017).

Major risks that fall into this category include the uncontrolled diffusion of gene-edited material and the uncertain effect on the genetic structure of environment, off-target effects in human body from genome editing, or the unknown disruption of ecologies with genetically altered organisms, especially through GDOs (Scher, et al. 2016).

8.3. Main stakeholders

Biosecurity and biosafety are also becoming a global concern and require multilevel resources and international collaboration, which typically involves coordination between heterogeneous groups of stakeholders.

Traditional stakeholders include the public health and security sector of state government, and international organisations specialising in environment, public health or more generally, scientific research. Countries have incorporated the target of biosafety and biosecurity into national agenda to different extent, while governmental organisations have been actively working on the administration and regulation of science and research activities.

As far as research is concerned, R&D personnel and institute administration share different responsibilities in managing biosecurity and biosafety.

As SynBio has been attracting interdisciplinary interest and giving access to broader participation methodologically, this gives rise to a fast-growing global “do-it-yourself” (DIY) movement of “amateur/garage” biologists, some of which having little or no formal science education or research credentials (Novossiolova et al., 2021).

Last, as the primary beneficiary and bearers of consequences for the materials, products and impact generated from SynBio, the general public constitutes as another crucial group of stakeholders.

8.4. Frameworks of governance

Based on the foundation of Biological Weapons Convention (1975), Chemical Weapons Convention (1997) and Cartagena Protocol (2000), current international conventions and protocols create overlapping governance structures that cover the realms of concern (Kelley et al., 2014). Meanwhile, countries have implemented pertinent legislation as well as biosafety and biosecurity measures, but implementation varies between countries and is typically a patchwork of regulations (Hamilton et al., 2021).

Convention, Protocol and Agreement in the international level	Laws and regulation mechanism in the European Union	Laws and regulation mechanism in the United States
Geneva Protocol on banning the use of chemical and biological weapons in war (1925)	Directive 2000/54/EC (2000)	National Environmental Policy Act (1969)
Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction (1975)	Directive 2001/18/EC (2001)	Toxic Substances Control Act of 1976 (1976)
Convention on Biological Diversity (1992)	Directive 2009/41/EC (2009)	Select Agents and Toxins, Code of Federal Regulations Title 42: Public Health, Part 73 (1977)
Chemical Weapons Convention (CWC) - Organization for the Prohibition of Chemical Weapons (OPCW) (1997)		Federal Food, Drug, and Cosmetic Act (FD&C Act) (2006)
Guidelines for the Safe Transport of Infectious Substances and Diagnostic Specimens, World Health Organization (1997)		Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th Edition, Centers for Disease Control and Prevention (CDC) (2007)
The International Plant Protection Convention (IPPC) (1999)		Guide for the Care and Use of Laboratory Animals, National Research Council (2011)
United Nations Security Council Resolution 1540 (non-proliferation of weapons of mass destruction) (2004)		Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, National Institutes of Health (NIH) (2013)
Cartagena Protocol on Biosafety (2000)		
Nagoya-Kuala Lumpur Supplementary Protocol on Liability and Redress to the Cartagena Protocol on Biosafety (2010)		
Laboratory Biosafety Manual, 4th revised edition, World Health Organization (WHO) (2020)		

Figure 3: Overview of the Synthetic Biology Security Conventions and Regulations

8.5. Highlighted gaps

i. Regarding the governance framework, there has been a lack of top-down efforts that standardise global government and usage of SynBio while bottom-up efforts are not coordinated in their research or messaging (Trump et al., 2021). Meanwhile, in the major existing conventions such the BWC or the CWC, there has been a lack of measures to enforce compliance and to investigate and respond to events of noncompliance (Trump et al., 2021).

ii. Current conventions function with nations serving as the unit of action, with little supervision over research carried out by individuals and small organisations (Wang & Zhang, 2019).

iii. Domestic regulatory frameworks governing SynBio, and biosecurity are fragmented, divided across multiple pieces of legislation and tend to address single subjects indirectly, some of which may be mutually inconsistent (Hamilton et al., 2021; Zhang, 2013).

9. Gaps of Synthetic Biology frameworks

To conclude this literature review, the gaps highlighted in the literature are condensed into the following four main categories.

i. Lack of adequate international governing frameworks which adapt to the current state of SynBio technologies.
ii. Fragmentation of regulation of precautionary principles between nations leading to unbalanced research and use of SynBio.
iii. Lack of frameworks that bridge academia and fundamental research with the commercialisation and implementation of SynBio.
iv. Inadequate principles and guiding frameworks for the release of LMOs into the environment.

These four types of gaps need to be further researched and complemented to potentially address solutions through policy implementation.

10. Data Collection

Following the literature review of SynBio and its use cases in four specific industries, namely, Food, Health, Biodiversity, and Security, interviews were conducted to complement the findings. The outcome of these interviews permits us to further analyse the field by superimposing gaps in the current governing frameworks of SynBio with the input given by thoroughly selected field experts. This data collection allows us to bridge the gaps highlighted in the literature review. The interview was designed as a primarily qualitative process with the aim to gain valuable information from different experts in the field of SynBio covering four main areas, namely, the industry (private sector), academia/research, NGOs, and governments/regulatory. These areas of expertise were delimited in the interview framework as key for shaping research and development as well as precautionary principles.

10.1. Interview questions

The interview was designed and conducted around an open-ended questionnaire that followed the following base questions that were adapted to fit each background of experts:

i. *In your sector, what are the main opportunities and risks?*
ii. *What are the main international SynBio governance mechanisms you are in contact with in your own field/work or through your network/which are the frameworks you actively or passively follow?*
iii. *What makes them more important than others?*
iv. *Why are they important for your sector more or less than others?*
v. *Do you think they allow us to mitigate risks and support opportunities?*
vi. *What is missing in all of this?*
vii. *Convention on Biological Diversity/Kyoto Protocol/or other- is it sufficient - are there other conventions or precautionary principles that are of importance?*
viii. *How would you govern SynBio/your own field to make it more efficient and to drive innovation/research?*
ix. *Do you have any examples of "successful" (how do you define this term?) forms of governance that could be applied to SynBio?*
x. *Where do you see your field headed towards? What excites you more?*

Interviewees were selected in two ways. First, authors of well-cited publications were selected as potential interviewees. Some of the authors of the papers cited in the literature review of this project were invited to the interview. Second, other experts that are typically not traditional authors of peer-reviewed papers were also invited, especially in the industry and government administration. 65 experts were contacted via different channels such as email and LinkedIn, but only 14 experts accepted to participate. It is important to note that experts mostly active in the private sector were more responsive and likely to accept to be interviewed.

The following tables give an overview of the expert sample interviewed.

Table 1: Interviewee overview

	Industry	Academia/ Research	NGO	Government/ Regulatory
Health	2	1	0	0
Biodiversity	1	1	0	0
Food	1	0	0	0
Security	2	1	0	2
Other	0	1 (Ethics)	2	0

Table 2: Expert Region Overview

Europe	North America	LATAM	Asia	Africa
6	3	3	2	0

Table 3: Expert Background Overview

Interviewee No.	Background
1	Serial entrepreneur in SynBio in healthcare based in Europe
2	Employee at a European biological innovation institute
3	Researcher and professor in new technologies in a European university
4	Consultant in biodiversity based in LATAM
5	Employee of a security agency in North America

6	Researcher and academic in health security from a research institute in Asia
7	Researcher and academic in new healthcare sciences at a European university
8	Author and researcher in ethics at a North American university
9	Representative from a SynBio NGO based in LATAM
10	Representative from a SynBio NGO/lobby group based in Asia and Europe
11	Investor in new SynBio tech startups based in North America
12	Representative from a multilateral organisation based in Europe
13	Representative from an industry consortium in food and healthcare biotechnology based in Europe
14	Biotech consultant based in LATAM and North America

11. Interview Results

In the following section, the outcome of the interviews is summarised and presented. On average, each interview lasted 35 minutes. The following section is divided following the interview questionnaires, namely, Opportunities, Risks, Governance Mechanism, and Comparable Mechanism.

11.1. In your sector, what are the main opportunities and risks?

Each interview began by asking the interviewee about their perception of their industry's major opportunities and risks, leaving them the space to interpret what they understood by opportunity and risk. All interviewees were quite enthusiastic in answering this question. Most highlighted a large list of positive aspects of their respective field, expressing strong belief in SynBio's overall potential to contribute to the greater good. For example, Interviewee 1, a serial entrepreneur, mentioned the ability to easily find SynBio-based tech solutions to major problems. Others also noted the potential ability of current research and development to address and solve major crises such as global warming, human health issues, and biodiversity loss or end global hunger. One expert, for example, expressed the following remark: "The development of synthetically created animal proteins could drastically reduce the impact of water consumption that our current food system imposes" (Interviewee 13).

Moreover, 6 out of the 14 experts interviewed mentioned the potential economic benefits of SynBio with one interviewee even comparing the industry to a future “internet boom” (Interviewee 11). Two interviewees also mentioned the possible synergies between other expanding technologies, such as AI or other MedTech and robotics advancements, could have on the further development of SynBio (Interviewee 7, Interviewee 13). The spillover effects of the latter have the potential to speed the development of the SynBio opportunity frontier.

When discussing the opportunities that the current frameworks of governance such as the CBD, national GMO laws or the Nagoya Protocol bring as opportunities for the field, most interviewees seemed sceptical in the ability of this governance to foster growth in both research and commercialisation of new biotechnologies. Interviewee 10, however, mentioned the current momentum in AI governance, especially in the EU with the AI Act, as a potentially triggering element for more efforts in other adjacent fields.

When discussing risks, the focus of the interviews and their outcomes were not set on the particular and technical risks of the release of GMOs and LMOs into the environment. As presented in the literature review, multiple risks can arise when dealing with the handling of new biotechnologies.

Interviewee 6 mentioned the following element in presenting the risks associated with the current governance framework “[...] the risk appetite in biotech research is a very difficult balance between driving new frontiers like cloning like you said, and avoiding major ethical breaches, that really creates major hurdles for my team drafting the ethical framework [...] that is something we particularly see in our field compared to other types of research”.

Being able to apply foresight and mitigate such negative spillovers can be challenging. The main elements mentioned in the interviews were focused on political and regulatory risks and not technical ones. Some interviewees particularly mentioned the risks of not having safe(r) regulatory or ethical “rail guards” in place within research mentioning for example the controversial case of a gene-edited baby through CRISPR which caused a major uproar in the field and put the spotlight on the (in)adequacy of current research ethics frameworks in China (Wee, 2019).

Another major risk highlighted by several interviewees was the risk of political stalemate and regulatory fragmentations between major research drivers, especially in food systems and in the medical industry. Some experts shared their concern about the potential loss of

momentum and funding in new SynBio technologies if no commercial futures could be envisioned in Europe (Interviewee 13). Furthermore, four experts mentioned during the interview that the global race towards technology supremacy is a primary risk, especially when discussing Europe in comparison to the US or China. The risk discussed in this case is that Europe would fall behind and would need to rely on non-EU IP, which could cause serious risk in security and self-reliance, further impacting geopolitical dynamics and global security. The current governing frameworks, as understood by both Interviewee 2 and 13, seem to take their roots in the early adoptions of GMOs crops, fragmenting countries in three major types: 1) jurisdiction where the release of GMO in the environment is legal in both a commercial and research basis; 2) states where the usages of GMOs and their release are not fully possible but with exceptions; 3) jurisdictions that have fully banned the release of GMOs. This environment has been described by many interviewees as a major issue in the equal development of SynBio research and use-cases. Some interviewees shared their concern about the risk of political stalemate and an over-politicisation of the industry. Some argued that the best way to advance in the field would be to keep open structures for research and development and only regulate once products and technologies are ready to be deployed commercially. For example, an expert in food systems mentioned that their organisation could not continue developing alternative protein production methods since the EU authorities are currently reluctant to authorise this new type of food in the European market (Interviewee 13).

In connection with the risk of over politicising SynBio, the risk of growing misinformation as well as the lack of awareness with the overall fundamental principles of Biotechnology were often mentioned. This risk was brought forward by the experts interviewed for this report and seemed to be an important concern in the work of both researchers and commercial actors. The link between the overall fear of the consequences of the release of LMOs into the environment for biodiversity and human health can have a direct impact on how funding is allocated.

It is important to acknowledge that the current sample of interviewees collected for this report is skewed towards the industry and a European or Western approach to fundamental research. This might have impacted the overall understanding and results in showcasing the current opportunities and risks SynBio is faced with. Nevertheless, key common grounds such as the

overall positivism towards the future of the branch as well as the negative spillovers from fragmented jurisdictions were reflected by most interviewees.

11.2. What are the main international SynBio governance mechanisms you are in contact with in your own field/work?

The second part of the interviewing process was to ask each expert how they interacted with the current governance environment. None of the 14 experts except for one (Interviewee 12) interviewed for this project specifically mentioned or had any direct interaction with the multilateral governing structures presented in the literature review of this report as well as conventions and protocols of the CBD. Moreover, some interviewees seemed not even to be aware of these governing mechanisms.

For most interviewees, the major concern and important tools referred to were limited at national and institutional levels. For example, USDA and FDA developments in the subject were mentioned by ⅓ of interviewees, showcasing the importance of institutional decision-making in the US. Moreover, all 4 interviewees in academia mentioned study protocols and ethical principles of their respective institutions as major guiding governing mechanisms in their field. An expert in the biodiversity field also mentioned being mostly concerned with their national reviewing body for LMO release and did not seem to care much about supranational or regional structures (Interviewee 4). Standardisation of precautionary principles and study protocols within the biotechnology/SynBio fields were mentioned by researchers interviewed for this project. For example, 2 interviewees mentioned iGEM, an NGO that promotes research in SynBio and has developed a study framework template that is currently being implemented in different universities in Europe, the US as well as in LATAM (Interviewees 4 and 9).

Two governing approaches were brought forward in the interviews, namely, a top-down approach in which study standards are imposed on research and the industry at the political level (e.g., memorandums, restrictions, funding allocation). The second approach is defined as bottom-up or “grassroots” which stems from research and the industry in general. Lobby groups such as iGEM can be considered as bottom-up stakeholders in the governance frameworks of SynBio. The issue of an over politicisation of the field seems to also take a

top-down approach in which political actors established governing frameworks for researchers, oftentimes as a direct result of political pressure (Interviewee 2). Particularly, a lack of a top-down approach to funding within SynBio was highlighted by some of our interviewees too (Interviewees 5 and 11).

11.3. Do you think they allow us to mitigate risks and support opportunities?

Following an overview of the governing frameworks associated with the expert interviewees, the next questions were focused on how the current frameworks could be potentially applied as risk mitigator. In this sense, the interviews resulted with only half of the interviewees being convinced of the need for change in the current governing frameworks and structures of SynBio; this divide seemed more skewed towards experts coming from the industry, especially in Europe, discounted with the current status quo (Interviewees 1, 2 and 13). The other half of the interviewees did not really mention that they saw the need to change the current status quo. Researchers and the healthcare experts were less likely to suggest structure changes during the interview, whereas the two NGO representatives presented more arguments for further changes (Interviewees 9 & 10). Better access to data in the medical field was mentioned by Interviewees 7 and 13 and more flexible and faster regulations mentioned by 3 European-based experts (Interviewees 1, 2 & 12).

The only element that seemed to be mentioned the most by interviewees was better education and understanding of SynBio and other biotechnologies by the general population as a result of the risk of over politicised SynBio. Almost all interviewees brought this point up during this interview section. Misinterpretation and false fears were noted as harming the overall progression of the industry and research, thus, hindering funding and political support for the field at both the national and international levels. The need for educational, government sponsored schemes was brought forward for example by Interviewee 5 who compared the need for better understanding of new developments in the food industry as similar to vaccines.

Furthermore, when asking experts how they would govern SynBio, two main answer groups seemed to transpire from the interview. First, several interviewees particularly mentioned the need for more flexibility in the current frameworks, especially when discussing research. Some interviewees mentioned that current structures governing GMOs were completely

out-of-date and that more contemporary regulations that did not confine LMO release would be better overall, especially in the EU. North and South American governing frameworks were pointed out as more favourable for the commercial release of LMO compared to European counterparts.

11.4. Do you have any examples of "successful" (how do you define this term?) forms of governance that could be applied to SynBio?

All 14 of the experts interviewed for this project could not directly name a successful comparable governing or multilateral mechanism that could be used as inspiration for SynBio. 2 of the interviewees mentioned the current work pursued in the field of AI as a potential leading way for SynBio (Interviewee 1 & 13). A few experts argued that there was no need for a common SynBio framework as biotechnology applications are too wide ranged (Interviewee 14). 3 experts particularly mentioned that they did not identify with the term "Synthetic Biology" as a general industry and shared their belief in a more segmented vision of biotechnologies (Interviewee 1, 4 & 13).

The general understanding that SynBio could be a term encompassing many applications of biotechnology was not homogeneously accepted in these interviews. Many experts particularly refuted the need to have the term Synthetic Biology applied to their expertise and preferred to be referred to as "Food technologists" or "Biotechnologists" for example (Interviewee 13).

12. Analysis: Superimposing Interview Data with Gaps

After comparing the findings of the literature review and the interview data, we found that the existing gaps identified in the literature were largely reflected in the interviews, with some additional points directly brought up in interviews or implied by the experts. Interviewees seemed to agree with the gaps highlighted in our literature review, especially when discussing the current fragmented regulatory landscapes. Regulations concerning the release of GMOs, deficiencies in precautionary governance, lack of ethical guardrails, as well as across-sector communication confirmed to a certain extent the hypothesis brought forward in part 6 of this report. The consistency in the literature review findings and the interview results can be partly explained by the fact that some of the interviewees were directly sourced from the authors of the literature; however, considering that interviewees who were not

related to literature cited also directly or indirectly referred to related points, it can be argued that the gaps identified in the literature review sufficiently define the key features of the factual state of governance in SynBio.

12.1. Regulatory fragmentation

Both the literature review and interviews across all four sectors confirm in general the absence, or at least deficiencies, of adequate international governing frameworks that adapt to the current state of Synthetic Biology technologies, especially when discussing ethical governance frameworks in terms of precautionary, justice and trustworthiness. Meanwhile, interviewees from different sectors pointed out that existing international and national regulations are underperforming or responding with a lag regarding the technological advancements of SynBio, for example the latest 9th BWC review conference in 2023 failed to incorporate ethical frameworks for scientific research or any substantial science and technology review mechanism to contain biological risks (Interviewee 13). Certain spontaneous initiatives, on the other hand, have been established to fill in the gaps left by the absence of government regulations, such as the International Gene Synthesis Consortium (IGSC) established as early as 2009 stemming from private gene synthesis companies forming their own business association to monitor gene synthesis technology before the launch of the first national regulation of gene synthesis in the United States (Interviewee 14).

However, despite the emergence of various attempts at regulation in the public or private sphere, it is worth noting that most of these attempts originated in or covered developed countries, such as Western European countries, the United States, and the Western offshoots, while developing countries such as Latin American countries or large parts of Asian countries are only in the very initial stage of governance. The fragmentation of regulatory approaches across states was highlighted in both literature and interviews, as well as a consensual understanding of the situation where the fragmentation of precautionary regulations between states is derived from differences in technological development, awareness, and capacity across countries (Interviewee 6, 11), which suggests the formidable challenge to arrive at any universal, sweeping approach of precautionary regulation.

The experts interviewed also further pointed out concerns regarding such fragmentation and the trend of politicisation of national governance frameworks, as it not only hampers the equitable advancement of SynBio but also exacerbates ethical and security concerns, as divergent regulation due to unbalanced research and use of SynBio across countries can create loopholes for exploitations. This is particularly relevant when discussing the usage of personal data for research purposes as well as for commercial endeavours (Adler et al., 2021; Interviewee 13).

The fragmentation in regulation across countries derived from differentiated conditions points to the immediate need to enhance international cooperation in terms of information sharing and harmonisation of certain operative standards, both in scientific research and in the regulatory and governance fields as the fundamental step to bridge the gaps across countries. Meanwhile, difficulties in regulation in certain countries due to technological inadequacy can also provide an alternative regulatory approach, such as strengthening the use of more traditional and well-established regulatory channels such as financial disclosure or incorporating screening of biosecurity risk information in detecting suspicious transactions in reference to the attempt of combating financing of terrorism of the International Monetary Fund (IMF).

12.2. Discrepancy over forms of regulation

Whilst interviews revealed certain common understandings regarding the current regulatory landscape in general, the incommensurable discrepancies in perspectives among interviewees from different areas of expertise epitomise the compartmentalisation in the regulation across sectors, concerning the demarcation of the term “Synthetic Biology” per se, and the feasibility, necessity, and specifics of a supranational top-down regulatory framework. Such discrepancies, which interestingly evidenced the fragmentation and lack of communication, are partly attributable to varying interpretations of the term “Synthetic Biology” amongst interviewees, which directly relates to differences in opinions on the appropriate scope of regulatory approaches, such as whether regulations should target the production or research activities employing relevant technologies, the materials consumed for the relevant technologies, or the products, which underscored the conflicts among “process-based” and “product-based” regulations as found in the literature reviews.

Considering that ideas about solutions present a clear division between academia, governance, and industry, interviewees from academia generally welcomed the idea of a more universal regulatory framework, while representatives from industries and governance showed less interest in an additional overarching governance framework or body. Instead, they more frequently emphasised the need for better liaison and alignment among existing national or industry regulations. Representatives from industries, in addition, tended to advocate for less stringent oversight to foster technological innovation and entrepreneurship. Yet some interviewees with an academic background raised concerns about the fairness and effectiveness of self-regulation of the private sector due to the profit appeal and lack of external oversight (Interviewee 7).

Considering the absence of shared perspectives or common interpretation of the connotation of synthetic biology even among the stakeholders, we think that science and procedural deliberation is quite insufficient, at least at this stage, to generate substantial agreement on any overarching framework of governance in the specific realm of "Synthetic Biology". In this case, better incorporation of regulation of risks of synthetic biology into established regulatory frameworks, such as BWC and CWC in preventing the malicious application of the technology, or integration and harmonisation of existing standards in containing industry-specific risks, such as national standards of releasing GMOs, are more operational and practical regulatory directions. At the same time, cross-industry dialog and information sharing remains an area that requires sustained efforts.

12.3. Misinformation and misinterpretation

Despite the discrepancy of perspective regarding form of regulation, the consensus in terms of solutions is more at the epistemological level, including imparting basic scientific knowledge and the latest technological advances in an understandable way to the public, with academia emphasising upon translation of technical details into decision-making, and industry stressing upon public education. This evidenced the notable absence of communication bridging academia and fundamental research with the commercialisation and implementation of Synthetic Biology solutions as mentioned in the literature review. Yet, the lack of scientific understanding of non-technical experts, especially policymakers with no technical background and the general public as potential consumers, was more of concern to the experts, the ones from the private sector in particular.

Following the early controversy over genetically modified crops, public fear, largely stemmed from entrenched understanding due to misinformation and misinterpretation of synthetic biology techniques and products, has greatly hindered the potential of synthetic biology to create benefits as an innovative technology. In one sense, the public tolerance for the risks associated with synthetic biology technologies has been irrationally reduced to an extremely low level by the spreading of misleading information, causing governments and other regulatory bodies adopting evidence-based regulation to lose credibility, which led to the policymakers adopting more prudent regulatory measures that are less friendly to technological innovation in response to the public's risk tolerance and policy expectations (Leonelli, 2021). On the other hand, negative public attitudes towards the profitability of the technologies in question have affected the funding of private companies and the commercialisation of synthetic biology technologies (Marris, 2015).

Given this, promoting a proper understanding of technological basics among people lacking a professional background seems to be a commonly-agreed, indispensable step in advancing SynBio to further realise its potential, which calls for wider involvement of researchers and technologists in science popularisation and policy-making (Interviewee 7).

12.4. Permeability of current international regulatory body

Another gap, which was unexpected but implied in the interviews, is the lack of awareness of the existing international regulatory system mentioned in the literature review, as none of the interviewees referred to the protocols, which contrasts with the reiteration of BWC and CWC in interviews regarding security. This general lack of mention perhaps hints at the limitations of the CBD in the absence of measures to enforce compliance or to respond to noncompliance, or its impotence as a universal convention to bind a rather specialised area, which leads to a possible direction for further empirical research on the extent to which these conventions have trickled downwards into specific national or sector-focused regulations. It is also necessary to rethink how to extend the practical impact of the normative role of CBD and the derived Protocols.

13. Policy Recommendations for Synthetic Biology Governance

As highlighted earlier in the preceding parts of this report, SynBio has become a revolutionary frontier within science, which has promised transformative developments in

human, health, food systems, biodiversity, and international security. However, given the potential for misuse and unintended consequences, a robust policy framework is necessary for further direction. The following section outlines a policy framework with five key recommendations – all comprehensive, inter-connected, and aimed to fulfil policy disparities highlighted previously in the literature review and bridged with the data from the expert interviews.

13.1. Utilising Existing International Governance Frameworks

Our interviews have decidedly impressed upon us that the usage of already-existing international governance frameworks should be increased and adapted, with the current ones about related industries informing how to make cohesive international standards that protect research and encourage progress within the industry. Given the difficulty of reaching multilateral agreements, there is also a rationale for prioritising the modification of existing frameworks to suit the needs of SynBio instead of starting from the beginning.

One such example of an existing international agreement is the BWC whose foundations of transparency, risk assessment, and international cooperation can be used as the basis for other encompassing agreements around SynBio, especially in the global security field. However, keeping in mind the limitations of a top-down universal framework, we have to understand that these frameworks cannot be applied across the SynBio landscape and should be fine-tuned to the sectors in question.

13.2. Harmonising Standards for Genetically Modified Organisms (GMOs)

As mentioned in the analysis of our interviews and the literature review, the regulatory landscape for GMOs is quite fragmented, highlighted particularly by the division of how GMOs are approved in Europe and the US (the two biggest development regions). As noted by interviewees, this fragmentation was directly politicised and led to confusion that has hampered development and research, eroding the public's trust in these products. This inconsistency is emblematic of the regulatory failings of SynBio from its infancy and should be amended so that GMOs (and future SynBio products) are given a solid foundation to build upon.

For specific policies, the research conducted has pointed to establishing an international harmonisation process for GMO approval, resulting in cohesive safety assessments and

regularised risk assessments. This can take the form of an international agreement but could also be the result of an established centralised database of approved GMOs, which relevant national regulatory agencies would have access to, along with their risk assessments. This would enable the relevant stakeholders to share information freely, without the risk of intellectual or corporate espionage. Practically speaking, this harmonised approach would also make the introduction and development of future GMO products more streamlined and efficient. This approach can also be applied to other SynBio products, where harmonisation of standards is required.

13.3. Critically Assessing Financial Investments

Within this research, the issue of finance and funding has also come up as a key point of governance that has been ignored in any current prominent frameworks (see point 2.3 in Results). In the current market-driven landscape of SynBio, where private enterprises have taken the initiative of key research and driving the industry forward, the financials involved can be a potential alarm for ethical concerns. Transparency and stringent control/monitoring processes of the funding can be the only avenue for research that has the public trust and imperative to continue developing forward. This recommendation is also based upon the principle of inclusive governance, where countries who lack the technological capacity to monitor and control all aspects of SynBio research, could use financial assessments to prevent exploitation by private firms in these regions.

Within the field of SynBio, dual-use or risky applications such as pathogen development, bio-weapons and resilient GMO synthesis (which can affect the biodiversity of a biome) should have mandated financial disclosures as part of the research process. This disclosure should include the sources of funding, amounts invested, who the investors are, and any potential conflicts of interest. A stronger application of this could take the form of prohibiting funding from sources that haven't been vetted adequately and/or have a history of unethical practices or promoting harmful applications. This could be tied to a centralised database of known funders with ethical assessments in every state that companies and researchers have access to. One example of a finance control mechanism that can be used to govern the utilisation of public funds for SynBio research is similar to that of the SEC's financial fraud check system. This is a system where certain transactions are flagged and automatically reported to the SEC for approval and investigation of possible fraud. In the SynBio context,

this system can be used in high-risk sectors to mandate that funding used for high-risk applications is heavily scrutinised and subject to approval from an independent watchdog.

13.4. Integrating Academic Expertise into Policymaking & Public Discourse

Within the project, the academics and institutional researchers interviewed have displayed a trove of knowledge about the industry as a whole that is hugely valuable for establishing governance principles. Their expertise, valued as researchers, can be used within the policy-making process effectively. Furthermore, as noted in the interviews, academics can play a crucial role in informing the public about the advancements in Synthetic Biology - wherein they can allay doubts and misconceptions and reinforce the rationale and reasoning behind certain complex SynBio research. By connecting this key expertise with public perception, it can also build assessment competence and institutional capacity across regions - particularly where the SynBio products are being tested and made available to the public.

Therefore, it is necessary to advocate for the establishment of protocols of these academic experts' research translating into policy. For instance, the establishment of a body like the IPCC for SynBio research could work as one conduit for policy making. While the difficulty of forming these groups or accords through multilateralism is noted in Recommendation 1, we believe that this body may be easier to establish as compared to drafting and agreeing to an international convention or treaty.

This could also be done by encouraging more policy briefs to be published alongside research papers as it ensures that policymakers will always have up-to-date information on policy gaps and ethical issues in play. This incorporation of academics into actual policy making may also result in a knock-on effect in the public discourse - academics being trusted as arbiters of truth within SynBio and their research being trusted as key evidence.

13.5. Implementing Stringent Monitoring and Control Processes

In certain sectors, such as the international security and health fields, specific rail-guards need to be implemented. A rigorous monitoring and control system of measures can be used to prevent misuse as part of national and international standards, especially within applications that may have dual-use implications (such as the case of synthesis of pathogens) as mentioned previously in Recommendation 3.

To focus on the specifics, national and international guidelines for the conduct of SynBio research and development need to be implemented. This would include, for example, strict protocols for the handling, storage, and transport of biological materials. Existing guidelines such as the BWC for similar applications should be perused to establish these guidelines.

Second, an international watchdog agency will monitor particularly contentious/concerning SynBio research activities, collect and analyse relevant data, and disseminate best practices across the industry. There are already existing private enterprises that contribute similarly to the industry, such as the IGSC, but they do not have the same regulatory capacity that an international watchdog would have.

Finally, financial incentives, such as subsidies or government funding, should be provided exclusively to industry actors that have implemented a rigorous customer vetting procedure and financial due diligence to ensure that SynBio products are not misused. This is particularly important in the niche fields of bioweapons, pathogens, and gene synthesis, as their applications may have far-reaching unintended consequences if not policed correctly.

14. Conclusion

The overall process of superimposing current key literature on SynBio and its governance with the direct lived experience of experts in the field permits us to propose the policy recommendations brought forward in the previous section. Key issues such as fragmented regulatory landscapes as well as the inadequate governing frameworks of certain fields within biotechnology seem to be major hurdles that need to be addressed. Furthermore, the competitiveness surrounding GMOs can be reflected throughout research. This report first addressed the current status quo of major guiding principles in the fields of Synthetic Biology, looking into both research frameworks such as precautionary principles as well as a multilateral governance of the field. This review resulted in gaps which were then applied in interviews with experts supposed to represent the food, health, security, and biodiversity fields. The subsequent analysis of the data collected permitted us to draft policy recommendations that could be developed and driven by representative and multilateral institutions. By fostering an environment that supports collaboration and a more democratic approach to research and applications, Synthetic Biology could become a respected and driving force for a better future.

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