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INTRODUCTION

# Philosophy and Synthetic Biology: the BrisSynBio Experiment

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The affinity or attraction of philosophy to "synthetic biology" starts already with the difficulty in defining synthetic biology or identifying clearly its origins (see [1] for a discussion of this from a molecular biology standpoint). While "synthetic biology" in its current incarnation is generally understood to have coalesced as an umbrella term around the beginning of the current century, usage of the term in the same sense that it is used today dates back to the beginning of the twentieth century—in 1912, Stephane Leduc published a book titled *La Biologie Synthétique* crediting Moritz Traube with the creation of the first artificial cell.[1] This definitional problem, including the sub-question of what techniques and applications do or do not fall under the umbrella of synthetic biology, takes on historical, epistemological and even ontological significance. However, adding to the philosophical intrigue of synthetic biology is that historical and epistemological questions in the field are closely intertwined not only with ethical and even ontological issues but also with the perceived economic and subsequent political potentials of synthetic biology. For example, the "8 great technologies" programme, through which the BrisSynBio Synthetic Biology Research Centre[2] was funded,[3] was explicitly conceived to "accelerate commercialisation of technologies where the UK is set to be a global leader".[4] The

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[1] This point is credited to Massimiliano Simons. It was made during a presentation on the history of synthetic biology at the Oxford-Bristol-Warwick Synthetic Biology Doctoral Training Centre in March 2019.

[2] BrisSynBio, a BBSRC/EPSRC-funded Synthetic Biology Research Centre (http://www.bristol.ac.uk/brissynbio/) (last accessed 7 April 2020)

[3] Of the contributors to this special section, Darian Meacham, Miguel Prado and Michael Reinsborough were partially (Meacham) or completely (Reinsborough) funded by or affiliated (Prado) with BrisSynBio. Massimiliano Simons visited BrisSynBio for a research stay in 2018.

definition and scope of synthetic biology thus acquires a political, economic and ethical significance as well as an epistemological one. This is also clear in how the European Commission has defined the term. In the EC's 2005 report on "Synthetic Biology Applying Engineering to Biology":

> Synthetic biology is the engineering of biology: the synthesis of complex, biologically based (or inspired) systems, which display functions that do not exist in nature. This engineering perspective may be applied at all levels of the hierarchy of biological structures—from individual molecules to whole cells, tissues and organisms. In essence, synthetic biology will enable the design of 'biological systems' in a rational and systematic way [2]

A 2016 opinion offered a slightly pared down but similar definition highlighting the economic and industrial dimensions:

> SynBio is the application of science, technology and engineering to facilitate and accelerate the design, manufacture and/or modification of genetic materials in living organisms. [3]

These definitions foreground the inter-disciplinary, design and commercial orientation dimensions of synthetic biology's role as a "techno-science", i.e. a scientific enterprise whose object of study is a "human construction rather than a given object in nature" [5] and necessitates a large-scale societal enterprise entailing public funding, regulation and interests. Simons also points out that in bringing the technoscientific character (its material, technological and political-economic) of science to the fore synthetic biology qua science takes on something of a "post-modern" character as explained by J.F. Lyotard in his famous *Post-Modern Condition: A Report on Knowledge* (1979): the legitimation of technoscientific knowledge is not justified only by its truth content but also "based on optimizing the system's performance-efficiency" ( [4], p. XIV; cited in, [5], p. 185). Synthetic biology thus presents philosophers with a fertile testing ground and field of experimental phenomena, bringing together epistemological, historical, ontological, ethical and political considerations.

The concrete institutional and political context of synthetic biology in the UK and the European Union has undoubtedly also contributed to its affinity and interaction with philosophical, ethical and political investigations. The top-down scientific mandate of industrial strategy programmes like the UK's "8 great technologies" included significant consideration and planning in relation to ethical, social, political and economic issues surrounding synthetic biology. Cognizant of the political and subsequent economic fallout of debates and controversies about the risks of genetically modified organisms (GMOs) in the 1990s, funding for the Synthetic Biology Research Centres financed through the "8 great technologies" programme mandated including "Responsible Research and Innovation" in the work programmes of the centres. This brought ethical and social considerations as well as a deliberative model of public engagement from the periphery to nearer the core of the scientific activities of these technoscientific enterprises (at least this was the case at BrisSynBio).[5] To this context can be added the fact that synthetic biology encompasses practices and areas of investigation, including computational and systems biology, as well as minimal biology and proto-life research wherein genuinely philosophical questions about chemical cognition, the possibility of providing a list of characteristics that could "define" life, the origins of terrestrial life, and the political economy of biomaterials (e.g. blood products, see [7]) entered into the consideration and discussion of the activities (and funding) of synthetic biology laboratories themselves.

One question that presents itself concerns the novelty of synthetic biology, or how far back that novelty extends, and the epistemological and ontological significance of said novelty or lack thereof. While synthetic biology undoubtedly utilizes novel techniques, including gene editing techniques such as CRISPR-cas9, base editing and gene drives, some have argued that it does

[0] https://www.gov.uk/government/publications/eight-great-technologies-infographics (last accessed 5 April 2020)

[5] For a more extensive critical analysis of the institutional and political context of responsible innovation practices at BrisSynBio and more broadly in relation to synthetic biology, see [6].

not present a novel epistemological or ontological framework.[6] Preston [9], for example, argues: "Synthetic biology crosses no ontological lines that were not crossed already in the Neolithic. […] [S]ynthetic biology as biological engineering represents no cognitive advance over what was required for domestication and the new agricultural subsistence pattern it grounds". The further question at stake in the novelty discussion is if the novelty (or not) of synthetic biology impacts ethical, societal and political considerations on the field's development and application?[7]

This is significant because it introduces questions about to what extent the "new" synthetic biology (gene editing and gene drives included) entails a tinkering or tampering with the fundamental aspects of life itself (whatever those may be) that introduces novel considerations, questions and problems for value theory. This is not to say that considerations must be novel in order to be significant, or that new technologies must introduce qualitatively new philosophical, political, economic, or social challenges in order to merit being examined through these lenses. This is nothing new is not an argument for saying "nothing to see here, please move along".

Another synthesis where the question of quantitative or qualitative transformation is being introduced concerns the proliferation of data-driven automation, artificial intelligence, machine learning and "deep learning" technologies in synthetic biology qua bio-design, for example the use of machine learning algorithms to explore the potential protein design space in view of de novo protein design [11]. We think that the synthesis of data-driven technologies and bio-design is now one of the most pressing and interesting areas of philosophical investigation into "synthetic biology".

The articles and the "Art-Science Dossier" in this special section stem from the workshop, "Synthetic Biology, Politics, and Philosophy", held at BrisSynBio in collaboration with the Social Science Research Group at UWE, Bristol, in June 2017. The workshop brought together social scientists, philosophers, computational biologists, genetic engineers and artists working on synthetic biology to stimulate multidisciplinary deliberation and insights into the political challenges and philosophical ideas emerging at the cutting edge of innovation in synthetic biology. The event was coordinated by Darian Meacham (Maastricht University and BrisSynBio) and Miguel Prado Casanova (UWE, Bristol).

The "Art-Science Dossier" provides an account of and critical (self-)reflection on Katy Connor's artist residency in Ash Toye's blood culture lab at University of Bristol, UK (part of BrisSynBio). Connor's descriptions and reflections appear alongside images of her work. Her textual and visual interventions are surrounded by reflections on the role of art-science collaborations in the responsible innovation programme at BrisSynBio (Meacham); the challenges of inter-disciplinary collaboration and integrating the analytic capacities of the arts into scientific research (Fannin); and an explorative text traversing the border between philosophy and theory fiction (Roden).

Lewis Coyne's contribution makes a case against the dominant mechanistic understanding of organisms by contemporary biologists and philosophers. He argues that organisms and machines share analogous features but differ in terms of their respective teleologies. Coyne uses Aristotle as a jumping-off point in a quite unprecedented manner by bringing his account of immanent teleology together with Hans Jonas' account of the living organism [12] as performative metabolic self-organization with an immanent teleological principle.

Nora Vaage's article explores what she calls the "living machines metaphor". Making use of examples extracted from the artworld, Vaage argues against the

[6] Some definitions of synthetic biology explicitly exclude gene editing technologies. We would contend that this is a good example of an attempt at the political as well as scientific-methodological delineation of the field. Likewise, to label the use of CRISPR-cas9 and other "new breeding techniques" in agriculture as *not* genetic modification—as the mutations caused by these techniques could potentially occur in nature and did not entail the introduction of exogenous genetic code (and hence not falling under existing EU GMO regulation)—reflects a political-economic attempt at delineation of techniques and fields. The European Court of Justice (ECJ) ruled in 2018 that new gene editing techniques in agriculture did fall under existing EU GMO regulation [8].

[7] Braun et al. [10] have provided a helpful literature overview and outlook on the ethical and societal challenges in synthetic biology. The lack of novelty argument was also used to justify the use of "new breeding techniques" as not falling under existing GMO regulation in the ECJ case referred to above. The ECJ's ruling indicates some of the political and epistemic messiness of the example: "Organisms obtained by mutagenesis are GMOs and are, in principle, subject to the obligations laid down by the GMO Directive. However, organisms obtained by mutagenesis techniques which have conventionally been used in a number of applications and have a long safety record are exempt from those obligations, on the understanding that the Member States are free to subject them, in compliance with EU law, to the obligations laid down by the directive or to other obligations" [8].

prevailing narrative in biotechnology which favours the mechanistic attitude. Referring to Lakoff and Johnson's seminal thesis in *Metaphors We Live By* [13], Vaage emphasizes the way in which language mechanisms partake in our *weltanschauung*. Given the unprecedented "revolutionary" scope of technology and science within our society, incomparable with any other social sphere, she advocates for a "more embodied and holistic approach to biotechnology as embedded in a natural and cultural context".

Massimiliano Simons dissects the framework of what he calls "black-box of engineering" in relation to synthetic biology and "bio-design". These disciplines (if it is correct to call them that) are evolving so fast that no widely accepted definitions exist. Common across many explanations is the idea of synthetic biology as the application of engineering principles to the fundamental components of biology. Simons presents five different candidates for interpreting what engineering is in the plurality of its conceptions and the role they play in synthetic biology.

Michael Reinsborough presents and critically examines a specific case of collaboration between artists and scientists in the context of Responsible Research and Innovation (RRI). He argues that art-science collaborations should not be limited to public engagement, or to "promote a 'science agenda'", but rather encourage a more reflective processes of agency in which we become aware of the "mutual responsiveness" [14] shared between institutional actors, publics, researchers and diverse stakeholders.

In the final article, Miguel Prado presents a critique of the concept of noise in bioinformatics frameworks for synthetic biology where the biological system is often addressed in terms of mathematical theories of information that differ radically from the continuous dynamics that characterize the morphological constitution of biological organisms. Prado's aim is to develop an understanding of the theoretical and practical role of "noise" in biological organization and evolution within the context of synthetic biology as a form of randomness. This is particularly relevant for living systems, where randomness has a functional role that contributes, in an essential way, to the structural stability of system dynamics.

The five contributions (together with an Art-Science Dossier) that comprise this special section foreground a critical approach to the mechanistic paradigm in philosophy of biology and re-enforce the "positive feedback loop" between the arts and the sciences (natural and social) and philosophy as pivotal points for thinking about the future of synthetic biology.

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