Synthetics: the ethics of Synthetic Biology

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Essential Readings [see also literature list below]

De Vriend, H. (2006). Constructing Life; Early social reflections on the emerging field of synthetic biology. The Hague: Rathenau Institute; Working Document 97.

Miller S. and Selgelid, M., (2006), *Ethical and philosophical consideration of the Dual-use dilemma in the biological sciences*. Centre for Applied Philosophy and Public Ethics, Australian National University and Charles Sturt University, Canberra, Australia.

Background

Synthetic Biology is a promising new field of research whose state-of-the-art and prospects are already discussed under ethical perspectives. Synthetic biology contains huge promises for society, but also large potential perils. For example, it could provide us with large quantities of biofuels without using land that can also be used to produce food. It could also provide large quantities of cheap anti-malaria medicine. Conversely, synthetic biology could lead to the creation of more lethal and virulent pathogens, which might be used in a terrorist attack. Moreover, synthetic biology will make discussions necessary about fundamental concepts like nature and life.

The field has been defined as "the engineering of biological components and systems that do not exist in nature and the re-engineering of existing biological elements; it determined on the intentional design of artificial biological systems, rather than on the understanding of natural biology." (Synbiology 2005). Synthetic biology emerged from biotechnological research and the life sciences. It is at the intersection of biology, chemistry and physics, overlapping and cross-fertilising with a range of other fields of research and technology development. An important characteristic of synthetic biology is the wedding of biology with engineering approaches. We are at the very early stages of synthetic biology. It remains difficult to synthesise anything but the smallest of organisms, most of which will be viruses. Much of the work relates to identifying the minimum set of elements within 'artificial' bacteria that could result in a living system capable of replication. That which is most likely to be possible is to identify elements of organisms that have specific functions and, having identified those desired in a synthetic virus (for example), put the elements together to provide for these functions. Bioterrorism is therefore a real issue in synthetic biology, and perhaps the most important other than pure research to identify the elements of driving living systems.

It is at this stage in the development of synthetic biology that ethical and legal analysis should be attempted, based on interdisciplinary research which includes expertise in ethics, law, science and technology foresight. It is also arguable that it is at this stage that the public needs to be made aware of the implications of this new approach to biology, and to be able to have an input into the manner in which it is regulated. Several individuals and organizations have already identified ethical issues of synthetic biology (Church 2005) (De Vriend, 2006), (European Commission 2005) (ETC Group, 2007), (Bhuktar, 2005), (Maurer et al., 2006). The most frequently cited ethical issues are biosecurity and biosafety.

Biosecurity

Reserachers have shown that it is possible to create or recreate deadly viruses such as polio and the Spanish flue. The polio virus was made using mail-ordered oligonucleotides (Cello et al. 2002). The Spanish flue was recreated using samples from victims buried in permafrost. The production of oligos is becoming less expensive as is the purchase of lab equipment. The knowledge and skills necessary to use the oligos to produce viruses is available all over the world. Nevertheless, Tucker and Zilinkas argue that in order to produce an effective biological weapon a infectious virus is only one step: "(C)ontrary to popular belief, however, a biological weapon is not merely an infectious agent but a complex system consisting of (1) a supply of pathogen […]; (2) a complex "formulation" of chemical additives that is mixed to stabilize it and preserve its infectivity and virulence during storage; (3) a container to store and transport the formulated agent and (4) an efficient dispersal mechanism. (Tucker and Zilinkas, 2006)" Tucker and Zilinkas therefore conclude that it not very likely that synthetic biology will lead to an increase in bioterrorism. However, they identify two scenarios that according to them are likely. They call the scenarios "lone operator" and "biohacker". The lone operator is a highly trained synthetic biologist with a grudge against someone or an organisation, just like the "Unabomber". For intelligence services it is very difficult to find such a lone operator, because as a professional researcher he or she has access to lab equipment without that causing any concern and because he or she is working alone there is no communication between people that might trigger the interest of intelligence services. According to Tucker and Zilinkas a lone operator could plan and execute an attack with a biological weapon. The other scenario that Tucker and Zilinkas have formulated is the "biohacker". The biohacker could like the computer hacker try to create a virus "out of curiosity or to show his technical prowess (Tucker and Zilinkas, 2006)". If indeed a hacking culture would develop in synthetic biology this could increase the risks due to reckless behaviour or hackers wanting to inflict harm.

Biosecurity has caught quite some attention in relation to synthetic biology. However, most approaches focus on how to prevent biosecurity threats. While this is of course useful, it underestimates the moral dilemma inherent in synthetic biology. This dilemma is that we do not want to impede research and beneficial technological developments while at the same time the very same research and technology may be used for terrorist purposes. Adequately dealing with this requires not simply preventive measures, but it requires addressing the dual use moral dilemma both by researchers themselves and by the government (Miller and Selgelid, 2007).

Miller and Selgelid have introduced three axes in relation to the goals of the research: good/ evil; military and non-military and military for offensive and defensive purposes. Research can be categorised on these axes. The problem with dual use technology is that although research results were obtained in research with a good purpose these results can be used in research with a bad purpose (Miller and Selgelid, 2007).

Actually it is even more complex than this suggests. Some research is intended for dual uses, that is, it has dual purposes. This is a common use of "dual use" in the US. Other research has only one intended use but another unintended use. Here it is related to the doctrine of double effect. The unintended use could be either foreseen or unforeseen. And if there is an unforeseen use there is a distinction between what could not reasonably have been foreseen, at least by the researchers, and what should have been foreseen by a careful researcher. All of these issues have a bearing on both regulation and policy and on responsibility.

There is obviously a need for a thorough analysis of synthetic biology within the dual-use context and for the integration of relevant expertise in the discourse on this field. Integrating the relevant scientific and political expertise, the project will contribute to a safe and secure development of synthetic biology, by assessing possible security challenges raised by synthetic biology and the various claims made with regard to this issue.

Biosafety

The ethical issues related to biosafety are according to some scientists of a comparable size or smaller than to those of genetic engineering while others claim that the risks are larger. Recently, an EU high-level expert group came to the conclusion that there are no qualitatively safety implications of synthetic biology, aside from the far greater capacity for manipulation and control that it will afford (EU Commission 2005).

Bhutkar has defined the following three biosafety risks of synthetic biology:

1. Risk of negative environmental impact: Synthetically created organisms can have unintended side effects. Some scientists claim that synthetic organisms could help to solve environmental problems like contamination of soil. This means that synthetic organisms should be released into the contaminated soil. However, the artificial organism could have negative side-effects.

2. Risk of natural genome pool contamination: Synthetic organisms could transfer genes to natural organisms.

3. Run-off risk: This problem is comparable to the highly visionary grey goo and green goo scenarios that have been discussed in the debate on nanotechnology: Artificial organisms that can replicate or can evolve into organisms that replicate could turn into grey or, in the instance of synthetic biology, green goo.

As mentioned above, it is noteworthy that such risks have also been discussed with respect to other fields such as biotechnology and nanotechnology.

Some claim that using bases that do not occur in nature or using a backbone of peptides instead of sugar-phosphate will lead to lower risks in synthetic biology than in genetic engineering (see for example Packard, 2005).

It is an open question whether the biosafety risks are different in synthetic biology than in genetic engineering and other related fields. Accordingly, the EU project Synbiosafe focuses on safety issues related to synthetic biology (http://www.synbiosafe.eu/).

Notions of life and other broader aspects

Several philosophical questions are raised by synthetic biology, some of which highly relevant for ethical reflection and societal debate. Some of such questions have already been analysed and discussed, broadly and in detail, with regard to related fields of R&D, others are specific to synthetic biology.

There is, for example, obviously a huge gap between common sense understandings of life and nature and the various contemporary scientific and philosophical notions of life and nature. This gap has been identified as a challenge for EU policy with regard to the societal debate on synthetic biology (European Commission 2005). Another important question is the boundary between "natural" and "artificial", "the grown" and "the made" (Habermas 2001), a prominent topic also in the debates on other fields (bio- and nanotechnology). Such notions are important categories in understanding our world and in deciding how to act, but their boundaries have become increasingly blurred. Accordingly, numerous re-conceptualisations of the relationships between nature, life and technology have taken place. One example is the concept "biofact" (a neologism comprised of, greek, *.bios*. and artefact) which refers to a being that is both natural and artificial (Karafyllis 2007). If a naturally occurring organism is recreated with synthetic elements what is its status: Should it be regarded as natural or as artificial? What about a naturally existing organism that is recreated with a minimal genome?

Research on the "ontology of emerging objects" in synthetic biology is funded by the US National Science Foundation, as one element of the flagship multi-institution research project "Synthetic Biology Engineering Research Center (SynBERC)". Intended are new forms of collaboration among ethics, anthropology, and biology.

Synthetic biology is also, in large parts, another example of the outstanding innovative potentials of genetic and informational reductionism and their usefulness as methods. It even appears to be a radicalisation and extension of older reductionist approaches such as bio-info-convergences. However, if these reductionisms are not seen as methods, but as philosophical positions, they can hamper a rational ethical and societal debate on S&T. This danger is even graver, when scientists themselves, science popularisers, business representatives or policy actors turn such reductionist approaches into a world-view that is highly objectionable to various stakeholders (such as the Christian churches). Such attempts have been made in debates that are closely related to the discussion on synthetic biology, such as the debates on nanotechnology and converging technologies (cf. Coenen 2007).

In various publications on synthetic biology, challenges of our notions of life and other broader philosophical and ethical aspects are mentioned as important ethical issues, which have not yet been systematically investigated (e.g. De Vriend 2006), and there is a need to develop "a conceptual ethical framework" for the debate on synthetic biology and "a more sophisticated appreciation of what is meant by 'life'" (European Commission 2005).

An EU High-Level Experts Group (HLEG) on synthetic biology stated in its 2005 report that "it seems likely that the notion of creating entirely new life forms will also stimulate debates about the proper ethical boundaries of science" and that to some, "this is sure to seem like 'playing God'." (European Commission 2005). The HLEG warned that "it seems likely that we do not as yet possess a conceptual ethical framework that can provide a common context for such debates" and cautioned that such a debate "will be productive only if we can develop a more sophisticated appreciation of what is meant by 'life' than is current in popular discourse."

In the case of notions of life and the blurring of the line between natural and artificial, ethical issues have to be analysed against the background of widely differing opinions within society and conflicting views of the morally legitimate goals and boundaries of S&T. While there have been numerous endeavours to tackle such questions with regard to bio and nanotechnology at EU level and in EU-funded research, there is a need for a systematic account of the pertinent research and debates and to focus on synthetic biology in this context. Even if potential ethical and societal concerns about the dangers of "Playing God" and "Tampering with Nature" are pointless or misled with regard to synthetic biology, it appears indicated to take them into account in the emerging European discourse on the field. Moreover, the promises of synthetic biology need to be proactively discussed against the background of overarching questions such as the ones what constitutes life and how informational reductionism relates to our diverse views of nature. The situation here is still favourable: Civil society stakeholders in the debate on the governance of synthetic biology have largely refrained from using "Playing God" or "Tampering with Nature" objections against the field. Moreover, topics (such as "human enhancement" and reproductive technologies) that are highly contended issues in the discussions on related fields of S&T are less relevant or irrelevant to synthetic biology. There is a good chance for a rational, scholarly and scientifically informed deliberation on highly relevant overarching issues of recent developments in S&T and for building an atmosphere of public trust for the European synthetic biology community.

International justice

One of the claimed benefits of synthetic biology, labelled polemically by the ETC Group (2007) as the field's "poster boy", is that it can help make malaria medicine cheaper, which would benefit the world poorest people that suffer from malaria (Ro, 2006). The Bill and Melinda Gates Foundation has substantially funded an ongoing R&D project on this topic.

Although a cheap drug against malaria would indeed save a lot of lives especially in poor Southern countries, it is the question whether the money invested in synthetic biology to create yeast strain to produce artemisinic acid (a precursor for a malaria drug that is a this moment scarce) is the best and most efficient way of combating mortality of malaria. Farmers in East Asia and in some parts in Africa are growing wormwood or artemisia annua for medicine production. If synthetic biology would come up with a cheap way of producing artemisinin then it could indeed cure people with malaria but it would make these people dependent on drug production in developed countries and the farmers of wormwood would be out of business (Heemskerk et al., 2006). There might be alternative ways of preventing people from dying from malaria, for example ways to prevent people from being bitten by malaria carrying mosquitoes.

Intellectual property rights protecting synthetic biology developments that are intended to help poor people could lead to an increased dependence on rich countries and companies. Poor countries cannot copy the developed technology to create artemisinin themselves because of intellectual property rights (IPR). Examples of intellectual property right issues can be seen in the discussion about generic drugs for example for the treatment of HIV/AIDS. The IPR system makes it very difficult for developing countries to import generic (cheaper) medicines. In the WTO Doha agreement developing countries are allowed to import generic medicine: "if they can provide evidence of the public health concern, demonstrate the inability of the domestic pharmaceutical industry to produce the drug itself, and prove that it will only use the drug for public, non-commercial purposes. (Centre for international development at Harvard University, 2004) " NGOs such as Oxfam have written a critical joint statement about the Doha agreement (Joint NGO statement, 2003). They state that the agreement requires a layer of bureaucracy to provide the proof that countries meet these criteria. In developing countries the money is better spend on healthcare itself than on a bureaucratic layer. Moreover, the criteria are vague, especially the one relating to the domestic pharmaceutical industry. According to the NGOs there is a probability that this will be interpreted in a way in which only countries with no pharmaceutical industry at all satisfy this claim. Besides these issues, which companies will provide the generic drugs, is there economic incentive enough? With regard to synthetic biology products and technologies developed to help the world poorest, for example by developing malaria medicine, these same issues might become relevant. Even though proponents of the malaria medicine research claim that the artimisin will be cheap, it is only one component of the two component medicine and it is not at all certain how expensive the complete medicine will be and which companies are going to produce it. So although a cheap malaria medicine could help people who are suffering from malaria there are other ways of reducing malaria mortality that would not make people in developing countries dependent on companies in rich countries using synthetic biology to create artemisinin.

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