ETHICAL ISSUES IN SYNTHETIC BIOLOGY: A COMMENTARY

WENDY ROGERS*

This paper provides a brief overview of ethical issues associated with synthetic biology and identifies three ethical challenges to consider in the development and management of synthetic biology. First, the injunction to use synthetic biology for the good of humankind raises questions about who should determine the direction and uses of synthetic biology. This issue is discussed in terms of setting the research agenda. Second, there are questions about the extent to which bioethics is, and ought to be, a 'critical companion' for novel and emerging technologies. This question is stimulated by the observation that some of the most cogent criticisms of synthetic biology have come from within the field, rather than from external bioethical critiques. Finally, there are calls for professionalisation as a mechanism for self-regulation regarding ethical behaviour. However, as there are diverse disciplines engaged in synthetic biology, it may be difficult to settle on a single set of agreed professional norms.

I CONTEXTUALISING SYNTHETIC BIOLOGY

Debates about the ethics of synthetic biology tend to focus on a small number of what are seen as key issues, and to take a broadly consequentialist approach.[1] The potential benefits of synthetic biology are characterised as advancing knowledge and understanding, and creating useful practical applications.[2] Potential advances in knowledge relate to increasing our understanding of complex biological processes such as the functioning of DNA or the chemical processes necessary for life to exist. Prospective practical benefits include: the creation of 'biofactories' for manufacturing cheap medicinal products; new energy sources and biofuels; organisms engineered to clean up environmental degradation; and new materials for a range of applications.[3]

Despite the significance of these potential benefits, there are a number of serious ethical concerns about synthetic biology, regarding both physical and non-physical harms. Physical harms relate principally to safety and security. Given the novel nature of synthetic biology creations, the accidental or intentional release of engineered organisms may lead to extensive and unpredictable environmental damage, or damage to the health of human and non-human animals. This potential for harm leads directly to concern about biosecurity, and raises questions about the most appropriate ways to safeguard both knowledge and physical products.[4] Alongside these physical harms, concerns about broader issues of wellbeing have led to various normative and existential questions.

* BM.BS (Flinders University of South Australia [FUSA]), BA (Hons) (FUSA), PhD (FUSA), Dip RACOG, MRCGP (UK), FRACGP, Professor of Clinical Ethics in the Department of Philosophy and the Department of Clinical Medicine at Macquarie University, Sydney, Australia.

1 Ainsley Newson, 'Current Ethical Issues in Synthetic Biology: Where Should We Go From Here?' (2011) 18 *Accountability in Research* 181, 185.

2 Eric Parens, Josephine Johnston and Jacob Moses, *Ethical Issues in Synthetic Biology: An Overview of the Debates* (Woodrow Wilson International Centre for Scholars, 2009), 14.

3 Ibid 14.

4 Ibid 17.

These include concerns about the fair distribution of benefits and harms from synthetic biology; the implications of 'playing god' through the creation of artificial life; and the potential impact of synthetic biology upon deeply held beliefs about the appropriate relationship between humans and the natural world.[5]

II COMMENTARY

There is unresolved debate in the literature as to whether synthetic biology raises unique ethical issues.[6] Whether or not the issues are ethically unique, there is some agreement that the ethical management of synthetic biology requires a multidisciplinary response, a focus upon professional duties and responsibilities, and a commitment to transparency and public debate.[7] To this end, there has been discussion amongst synthetic biologists about their own roles and responsibilities, leading in some cases to formal commitments. The Synthetic Yeast 2.0 project ('Sc2.0'), for example, has its own statement of governance and ethics, which is binding upon all researchers involved with the multi-national collaboration to synthesise a yeast genome.[8] The statement enjoins researchers to work for the benefit of humankind; be open and transparent; comply with relevant national and local regulations; avoid providing materials to those with nefarious intent; embrace an ethos of personal and environmental safety; undertake ethics training; and have a commitment to open sharing of intellectual property. This statement identifies concerns about biosafety and bioterrorism, commits to only beneficent uses of synthetic biology, and seeks to guarantee ethical practice through strategies including legal and regulatory compliance as well as mandatory ethics training.

In what follows, I briefly explore three issues raised in this statement and elsewhere in the literature. In so doing, I hope to identify some of the complexities underlying what may be presented as relatively straightforward ethical issues raised by synthetic biology, and to question the role of bioethics in engaging with the ethical challenges of synthetic biology. The first is the injunction to use synthetic biology for the good of humankind, which I call the agenda setting question. The second concerns the role of bioethics in synthetic biology, and to what extent bioethics is and ought to be a 'critical companion' for novel and emerging technologies. Finally, I touch upon the subject of professionalisation, as many in the field consider that whether or not synthetic biology turns out to be a force for good in the world will depend upon the behaviours of those working in the field. Whilst none of these issues is unique to bioethics, familiar issues can play out in unfamiliar ways in this new field.

A *Agenda Setting*

Agenda setting is one of the most critical, and most neglected, issues in research ethics. Most of the information we have about agenda setting in research comes from the medical arena. There are plausible claims that medical research has, to a significant extent, been diverted away from the ideal aim of knowledge generation in the service of healthcare, and instead is subject to the commercial aims of the pharmaceutical and biomedical industry.[9] That is, the agenda is not set by aims to do with improving human health, but rather is the result of

---

5 Ibid 18; Markus Schmidt et al, 'A Priority Paper for the Societal and Ethical Aspects of Synthetic Biology' (2009) 3 *Systems Synthetic Biology* 3, 5.

6 David Heyd, 'Is There Anything Unique in the Ethics of Synthetic Biology?' (2012) 55 *Perspectives in Biology and Medicine* 581, 584; Newson, above n 1, 189.

7 Newson, above n 1, 190; Schmidt et al, above n 5, 5.

8 Synthetic Yeast 2.0, *Statement of Ethics and Governance* (24 Nov 2013) syntheticyeast.org <http://syntheticyeast.org/wp-content/uploads/2014/04/Sc2_EthicsAndGovernanceAgreement_131124final.pdf>.

9 Wendy Rogers and Angela Ballantyne, 'Justice in Health Research: What is the Role of Evidence-based Medicine?' (2009) 52 *Perspectives in Biology and Medicine* 188.

commercial interests. The evidence for this claim is increasingly persuasive, to the point that there are credible estimates that 85 per cent of medical research is wasted, usually because it asks the wrong questions, is badly designed, remains unpublished or is poorly reported.[10]

These failures in medical research provide salutary lessons about the perils of allowing research agendas to evolve unprotected from market forces. This is an opportunity for the synthetic biology community to take stock, consider the forces at work on current research agendas in synthetic biology, and act together to shape these agendas. First, we need to ask what it might mean to have a research agenda in synthetic biology. Who would propose the agenda, and what values would it be based upon? Debate about medical research, although stopping short of suggesting some kind of overarching agenda, has led to various recommendations about prioritising research.[11] These include strategies for increasing the yield of basic research; increasing transparency about which projects are funded and why; taking account of the needs of end-users; building upon existing research; and increasing communication about what research is in progress.[12] These strategies are consistent with the focus in synthetic biology on transparency and open communication of results, but it is not clear who are the 'end users' and whose needs should be prioritised. Are they governments who want weapons, the private sector who seek profitable products, or the public? And if the latter, the public is clearly not homogenous in its attitudes towards synthetic biology, which would make development of a research agenda based upon public views difficult.[13] The Sc2.0 Statement refers to 'the good of humankind' but this does not translate easily into a consultation or prioritisation strategy, especially where funding comes from commercial sources. Taking agenda setting seriously will make decisions about which projects to pursue or abandon easier, by providing transparency about the grounds to justify such decisions.

B *Bioethics as a Critical Companion for Synthetic Biology*

French philosopher Bernadette Bensaude-Vincent proposes that bioethics should be a critical companion for synthetic biology.[14] Bensaude-Vincent argues that bioethicists and critical activists have largely taken the claims of synthetic biologists at face value, that is, they have concurred with what she calls the 'visions of incredible futures'.[15] In so doing, programs aimed at identifying ethical, legal and social issues (ELSI programs) tend to reinforce rather than challenge the credibility of the promises made by synthetic biologists. She notes that, somewhat ironically, the most serious challenges to some of the more utopian promises of synthetic biology come from within the field rather than from either ethicists or critical activists.[16] Three of these challenges revolve around theoretical assumptions, experimental aspects and economic considerations, which are considered in this commentary.

---

10 John PA Ioannidis, 'How to Make More Published Research True' (2014) 11 (10) *Public Library of Science Medicine* <http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001747>.

11 Iain Chalmers et al, 'How to increase value and reduce waste when research priorities are set' (2014) 383 *Lancet* 156.

12 Ibid.

13 Hart Research Associates, *Awareness & Impressions Of Synthetic Biology: A Report Of Findings* (Hart Research Associates, 2010) 6, 7.

14 Bernadette Bensaude-Vincent, 'Between the Possible and the Actual: Philosophical Perspectives on the Design of Synthetic Organisms' (2013) 48 *Futures* 23.

15 Ibid 23.

16 Ibid 24, 26.

1 *Theoretical Assumptions*

First, there is concern that some of the foundational theoretical assumptions underpinning synthetic biology may be flawed. For example, synthetic biology draws heavily on the analogy between cells and computers, where genetic expression is seen as the program/software, and the cell machinery or chassis taken to be the equivalent of computer hardware. However, although software may be self-replicating, the hardware is not and so the analogy between cells and computers is flawed. Computers do not replicate themselves.[17] Given the ubiquity of this metaphor, it is perhaps surprising that this criticism is not widely aired, because the way that we conceptualise objects such as cells has significant implications for the ways that research about them will develop. In addition, many of the imagined futures of synthetic biology assume that recipient cells will be receptive to the introduction of new genomic material and that the resulting organisms will be permanently reliable.[18] This assumption is questionable given the tensions between evolution and preservation in naturally occurring cells.

2 *Experimental Challenges*

Second, there are experimental challenges in applying the engineering principles of standardisation, decoupling and abstraction to biology. Bensaude-Vincent notes that 'unlike the parts assembled in mechanical engineering, the building blocks of synthesis inevitably interact'.[19] These interactions, which may be more or less unpredictable, affect the identity and behaviour of the ensuing organisms. That is, the rational principles of engineering come unstuck in the chaotically interactive world of biology. For example, there are claims that the majority of the parts in the international Registry of Standard Biological Parts (an open access repository of synthetic biology 'snippets') do not function as advertised.[20] Furthermore, engineering metabolic pathways is messy and painstaking work. It is notable that the successes of synthetic biology, such as the development of Artemisinin, have been plagued by unexpected interactions between parts, and proceeded by trial and error rather than by applying rational engineering principles.[21] The proclaimed principles of synthetic biology do not always, and perhaps only rarely, correspond with practice. It will be important for bioethicists who wish to engage, critically or otherwise, with synthetic biology, to understand experimental issues as well as to question dominant assumptions.

3 *Economic Assumptions*

Third, it is unclear whether the predicted bioeconomy is sustainable. Rob Carlson has noted that given current costs, the finances needed to upscale synthetic biology far exceeds plausible investment capacities.[22] The promise of course is that as critical mass builds, costs will fall, but it is unclear whether in fact this is the case. It is also unclear as to whether an open source system, such as is currently endorsed by many of the scientists, will encourage the investments thought to be necessary to create commercially viable synthetic biology. At least one economic analysis suggests that some kind of hybrid system that incorporates

---

17 Antoine Danchin, 'Bacteria as Computers making Computers' (2008) 33 *FEMS Microbiology Reviews* <http://dx.doi.org/10.1111/j.1574-6976.2008.00137>.

18 Bensaude-Vincent, above n 14, 27.

19 Ibid 27.

20 Sam Kean 'A Lab of their Own' (2011) 333 *Science* 1240, 1241.

21 Bensaude-Vincent, above n 14, 27.

22 Rob Carlson, *Biology is Technology: The Promise, Peril, and New Business of Engineering Life* (Harvard University Press, 2010) 104–5, cited in Bensaude-Vincent, above n 14, 27.

limited proprietary protections may lead to greater rates of innovation than a completely open source system.[23]

Bensaude-Vincent's examples argue for bioethicists to engage deeply and critically with specific scientific claims and individual projects, as the issues that arise are complex and particular. Crucially, ELSI contributions can help to ask the hard questions, such as what would count as failure in particular avenues of investigation. Without such engagement, the humanities and social sciences will contribute little to shaping and enriching the field, but instead will be left to react to the promises made by perennially, and sometimes wildly, optimistic synthetic biologists.

C *Professionalisation*

My final point concerns the behaviours that we might want synthetic biologists to engage in, and how to encourage these behaviours. Professionalisation has been suggested as a potential option for supporting high ethical and governance standards in synthetic biology.[24] Professionalisation has the flexibility of self-governance whilst incorporating elements of legal regulation, and mandating accountability for individuals and for a profession as a whole.[25] Another potential advantage of professionalisation is that members of a profession are seen as responsible, with clearly defined fiduciary duties and various standards that can be enforced.[26] Obviously there is a gap between being seen as, and actually being, responsible that cannot be bridged by membership of a profession alone, but membership may help to support an ethos of professional responsibility and accustom synthetic biologists to recognising and responding to the ethical dimensions of their work.[27] Fostering an ethic of responsibility and accountability through professionalisation may bridge the gap between engineers and molecular biologists, and encourage the latter to link their expert knowledge more explicitly with moral obligation.[28] Leadership is essential to building professional ethos, otherwise it is very difficult to instil ethical ideals and promote ethical practice, especially where members of the (new) profession come from different training backgrounds and cultures. Such fertile ground will be necessary for codes of ethical conduct, such as that in the Sc2.0 statement, to flourish. This will entail normalising practices, such as discussion of the implications of the work at hand, and having a constant willingness to ask questions about who may be harmed or benefited, and what values are at play in particular projects. Without deep and meaningful engagement at all levels, professionalisation is unlikely to achieve its intended goals. And of course, professionalisation will not stop those with truly nefarious intent, although an ethos of ethical practice may render those who pose a risk to biosafety and biosecurity easier to identify.

III CONCLUSION

In summary, synthetic biology does hold the promise of new and exciting technologies, but as with any new field, there are challenges in shaping and directing the field and minimising the risk of harm. Some of the emerging ethical norms, such as the injunction to use synthetic biology only for the benefit of humankind, may prove difficult to implement unless care is taken with setting the research agenda. Bioethical engagement will hinge, to some extent,

---

23 Joachim Henkel and Stephen Maurer, 'The Economics of Synthetic Biology' (2007) 3 *Molecular Systems Biology* 117.

24 Lorna Weir and Michael J Selgelid, 'Professionalisation as a Governance Strategy for Synthetic Biology' (2009) 3 *Systems and Synthetic Biology* 92.

25 Ibid 95.

26 Ibid.

27 Ibid.

28 Ibid 92.

upon bioethicists having a critical stance as well as an intimate knowledge of the science. Otherwise, they risk irrelevance. Finally, professionalism is touted as a potential ethical regulatory mechanism for synthetic biology but the success of this will depend upon strong and ethically sophisticated leadership.

***