Synthetic Biology and the Conservation of Biodiversity

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Abstract: Synthetic biology is a broad and fast-moving field of innovation involving the design and construction of new biological parts, and the re-design of existing, natural biological systems in an endeavor to generate products of usefulness to humans. It has many potential applications that may change human relations to the natural world. Synthetic biology is virtually unknown to the conservation community. Based on a meeting bringing together these two communities we consider first the differences between the two fields, and second the kinds of opportunities and risks that arise.

Keywords: conservation, synthetic biology

The advent of synthetic biology presents an interesting conundrum for biodiversity conservation (Redford *et al.* 2013). Is the new technology to be welcomed because it holds out the possibility of novel and radical solutions to global challenges such as the perfect storm of shortages in food, water and energy resources (Beddington 2010)? Or is it to be feared, for the impact of novel organisms and associated new economic arrangements on ecosystems and rural societies (e.g. ETC Group 2010)?

Synthetic biology is a broad and fast-moving field of research and innovation, inspired by the distributed development and exponential rates of innovation and growth in computing throughout the last three decades (Carlson 2010, Church and Regis 2012). It is a hybrid of engineering and biology, and definitions of synthetic biology are broad and open-ended with many, though not all, explicitly directed at real world uses. Key elements in the field are 1) its engineering approach to natural systems (designing and fabricating ‘components’ and ‘systems’ using standardized and automatable processes; 2) an emphasis on novelty: fabricating parts and systems that do not exist in the natural world (or re-designing and fabricating those that do); 3) doing so, most frequently, to address real world problems (ECNH 2010, Presidential Commission 2010). Thus a typical definition of synthetic biology is "the design and construction of new biological parts, devices and systems and the re-design of existing, natural biological systems for useful purposes" [www.syntheticbiology.org accessed 9 July, 2013]. Practically, this "design and construction" generally currently means modifying single-celled organisms by inserting up to 15 genes in the form of pathways designed to accomplish specific tasks. The range of fields where synthetic biology may be applied is wide, but incudes food production, new materials and manufacturing, waste processing and water purification, ecological restoration, health (http://www.parliament.uk/mps-lords-and-offices/offices/bicameral/post/post-events/future-environmental-impacts-of-synthetic-biology/).

Almost all new technologies and industrial sectors have implications for biodiversity conservation, as markets and human consumption drive change in the biosphere, and synthetic biology is no exception. The question of the relationship between synthetic biology and conservation was addressed at a conference organized by the Wildlife Conservation Society in April 2013 (http://www.wcs.org/news-and-features-main/synthetic-conservation-biology-conference.aspx). That meeting, that included 19 people speaking from the conservation perspective and 21 speaking from the perspective of synthetic biology in addition to speakers with expertise in journalism, psychology and advertising took the approach of exploring ideas and practices in synthetic biology and conservation, before considering areas of difference and common ground. This paper reflects on our experiences with that process. We consider first the differences between the two fields, and second the kinds of opportunities and risks that arise. This paper does not report the findings of the meeting, but summarizes our personal reflections.

Thinking in the two Fields

The first observation to be made is that there are differences in the way conservationists and synthetic biologists approach their respective subjects. Any attempt to describe such differences runs the risk of caricature, but any attempt to understand where common ground may or may not lie demands an understanding of narratives and ways of thinking. We attempt this here.

First, there is a difference in academic training, and there are gaps between the disciplines. Participants at the 2013 meeting came more or less equally from both synthetic biology and conservation, with some other experts (for example environmental and human rights activists, and sociologists of science). While many of the synthetic biologists and many conservationists were trained in biology, their shared biological knowledge was limited. Conservationists trained in biology had restricted, and frequently dated, knowledge of genetics and molecular biology. One conservationist trained as a biologist commented of their university training in genetics and molecular biology 'those were the courses we flunked'. The same may well be true in reverse for synthetic biologists trained in biology, who may not have detailed knowledge of biological structure, function, diversity or management at ecosystem or even organism levels. Furthermore, some synthetic biologists come primarily from an engineering background, and work in synthetic biology without much formal training in biology at all. Only systems biology is included in the 'foundational science for synthetic biology' by Kitney and Freemont (2012): no ecology, let alone conservation biology, is mentioned; conservation science is necessarily multi-disciplinary (Meine *et al.* 2006), but its engagement with engineering is slight.

Second, with differences in knowledge come differences in experience of scientific practice. Synthetic biologists work in a world of controlled environment laboratories, where living systems are thought of deliberately in reductionist terms: as components and parts, designed and assembled to form functioning systems. Conservationists work in and for a world of complex natural systems, often poorly defined and rarely with the level of detail of even taxonomy and ecology they would like. They encounter social, economic and political factors that demand insights well beyond their biological training. Ecologists have thought of nature like a machine since the 1960s, borrowing words from cybernetics to describe equilibrium and control (Botkin 1990), but for conservationists this metaphor has had limited relevance for the way they understand nature or human interactions with it.

Third, there are also differences in the relationship between each field of practice and its underpinning science. Conservation is informed by several research disciplines, notably conservation biology and ecology. Conservation biology is a mission-driven discipline, but conservation itself is a professional practice undertaken by people trained to protect existing wildlife and nature. Synthetic biology, at this early stage in its development, is more tightly linked to applied research. It is more entrepreneurial, its practitioners are people motivated to discover new facts and to build new devices and some to make money doing so. Synthetic biology is often described as an endeavour bringing engineering principles to biology and, as a result, many projects are conceived as potentially providing solutions to problems in areas such as agriculture, healthcare, and energy.

Fourth, the differences between synthetic biologists and conservationists, as exhibited at the meeting, are as much cultural as scientific. Conservationists and synthetic biologists seem to think differently about the future, and their role within it. At first sight it seems easy to characterise the two communities as being on opposite ends of a variety of spectra. Synthetic biologists at the meeting (along with some of the conservationists themselves) appeared to find conservationists negative about the future, even depressed. It emerged several times in debate that conservationists tended to look back and mourn the past and the biodiversity that is or may be lost. Conservationists may be *against extinction*, but are less good at saying what they are *for* (Adams 2004). On the other hand, synthetic biologists are upbeat and optimistic, seeing exciting research and beneficial applications.

Fifth, conservation practice tends to be reactive to change driven by other fields of human endeavour. The techniques and approaches used have been honed by decades of experience, both trials and tribulations, and are well-defined with established practices and procedures. Synthetic biology on the other hand is extremely proactive, developing novel techniques that could solve not only the problems of today, but also others that have not yet even been identified. Much of the science is still about the development of techniques, and so it is an emerging, rapidly growing and vibrant community. To some synthetic biologists, the primary aim of the field of synthetic biology is 'industrialisation - i.e. applications leading to products' (Kitney and Freemont 2012 p. 1034). That focus on industrialised manufacture is very different from conservation's arcadian and protectionist traditions (Adams 2004).

Sixth, attitudes to innovation are closely linked to attitudes towards risk. Conservationists tend to be risk-averse in their practice of conservation. The stakes are high, the fear of failure constantly reinforced, and the priority is generally to minimise risks of irreversible consequence of their interventions, especially given many practitioners' experiences of the outcomes from experiments in conservation. This culture of caution is critical to conservation's future engagement with synthetic biology, and it underpins specific debates about the use or release of organisms (e.g. conservationists' fear of invasive synthetic organisms, ISOs). Synthetic biologists have little to lose and much to gain from experimentation; theirs is a new science operating on a potentially very wide front.

Seventh, the beneficiaries of the work of the two fields are different. Though changing, conservation's tradition has been of state action for the public good (for example in declaring national parks or passing laws to protect wildlife). The benefits of conservation are mainly seen as public goods and services. Synthetic biology is much more closely engaged with business. Many of the benefits of synthetic biology, and much of the excitement, is evident because of the prospect of private benefits to individuals and corporations. That is creating intense investment interest. Synthetic biology is lining itself up to be an enterprise and thus wealth generating (an extension of the bio-economy), whereas conservation does not align itself that way.

2. Risks and Opportunities

Characterisations are easy to draw, and exceptions (particularly in individual thoughtful people) are quickly found. Despite this limitation, the oversimplification presented above has some explanatory power and important implications.

Differences between conservationists and synthetic biologists can be a barrier to communication and collaboration, but individuals fromboth groups appear interested in working together on problems of mutual interest. While there are likely to be sceptics in any community of thoughtful science-trained people, the April 2013 meeting certainly suggested a common understanding of the global challenge of the Anthropocene: that, for example, human influences on global climate are significant, and human action is reducing global biodiversity. This creates common ground for the formation of a loose consortium that could work together. Both communities would both wish to solve major environmental problems, safely and permanently. The community of synthetic biologists have welcomed discussion with conservation biologists as well as others in the environmental community. iGEM, (International Genetically Engineered Machines; http://igem.org/Main_Page), a competition for undergraduate students to “build biological systems and operate them in living cells” has reportedly incorporated the themes of protecting the environment, and some of its approximately 15,000 alumni have worked on projects that incorporate environmental benefits.

It is not difficult to imagine many potential risks to conservation in the application of the techniques of synthetic biology. These include the escape of novel organisms from containment into open ecosystems. Such ‘species’ – whether produced by more traditional recombinant DNA techniques, synthetic biology, or sophisticated breeding – will by their presence change existing ecosystems, (perhaps radically and detrimentally) and if they exchange genetic material with wild relatives they will change existing biodiversity, potentially reducing viability. There is also a risk that these novel organisms may become invasive, out-competing or displacing existing species (a particular risk to species that are endemic or already rare), (Jeschke *et al.*

2013). Genetic transfer between novel organisms and wild relatives might lead to hybrids that could out-compete transgenic and wild varieties, (e.g GM Atlantic salmon; Oke et al. 2013). Such risks also attend use of novel organisms for direct conservation purposes (e.g. to help restore polluted or degraded ecosystems) and these situations will require careful research and analysis, and careful balancing of potential risks versus rewards.

Biodiversity conservation would also be affected by broader environmental, social and economic impacts of novel organisms. Human rights and environmental organizations have already begun to develop a vocal and focused anti-synthetic biology movement that might affect the ways in which synthetic biology will develop (c.f. ETC 2010). The potential impacts of synthetic biology that concern this community include effects on biodiversity, but there is particular concern about the impacts that novel organisms might have on the rural economy and society in the developing world. Thus ETC (2010) presses issues of safety and threats to livelihoods linked to the application of the field of synthetic biology, making reference to previous debates about land acquisition to grow biofuels, the production of biologically-based chemicals and plastics, and the industrial burning of biomass. Yet not all technologies are the same, nor are the people who use them. In contrast to the monopolistic manner in which some genetically modified crops have been developed and deployed, many synthetic biologists view their efforts as democratizing technology, with hopes to enable individuals around the world to better participate in the discussion about, and use of, biological technologies.

Distinctions between synthetic biology and biotechnology more generally, between technologies and the issue of how they are controlled and who profits from their use (e.g. corporate or public ownership), and the question of whether biological innovation entrenches or reduces existing social inequalities, are all critically important. It is quite possible that the interests of biodiversity conservation specifically may lead conservationists and synthetic biologists alike to share a position on some risks with human rights and environmental campaigners, but differ on others. There is currently a great deal of rhetoric surrounding this topic and disagreement between those seeking common ground and there were marked disagreements expressed at the meeting. Consideration of possible risks needs to be open, broad and based on evidence across a broad range of studies and geographies if they are to be useful.

Conservation may be affected both positively and negatively by land use changes associated with the adoption of production systems using organisms developed from synthetic biology techniques. Many of these kinds of impacts already occur, sometimes increased by existing GM (genetically modified) technologies, and it is not clear what additional impact (if any) synthetic biology will have on these processes. Though often framed only in terms of negative consequences involving conversion of land under natural cover and loss of livelihoods, some genetically modified crops (and perhaps future crops modified by synthetic biology) have been shown to provide conservation and livelihood benefits (NAS 2010; Kathage and Qaim 2012). This area of indirect impact of synthetic biology and GM on conservation and livelihoods is arguably the most contested of the topics raised by at the meeting and in subsequent conversations.

As discussed at the meeting, there is the potential for synthetic biology to be used to reduce the impact of human land use on biodiversity and support ecosystem services. New technologies based on synthetic biology may be able to reduce the ultimate driver of most conservation problems by mitigating the impact of human activities.

For example, land and sea habitats that are currently unavailable to wildlife as a result of energy installations could be freed up with new methods of energy production, and the effects of climate change on conservation reduced through large scale deployments of carbon consuming algae (though these might produce their own effects). There is also an enticing prospect that synthetic biology approaches might restore degraded lands and waters for either conservation of for increased food production – potentially sparing wildlands. Finally, honeybee populations are economically important for the pollination services they provide. In some countries populations have declined in association with the colony collapse disorder. Synthetic biology techniques could be applied to develop bees that are resistant to pesticides and to mites that prey on bees and that transmit viruses. Such applications of synthetic biology may have great promise, but evaluating their utility is difficult because the problems are complex and inadequately understood.

3 Potential applications of Synthetic Biology to Conservation

Participants at the meeting expressed both concern and excitement about the potential applications of synthetic biology to conservation. Accepting that there is a need for engagement of both communities as well as the general public to consider possible risks to biodiversity from synthetic biology, what might be the possible benefits from the application of the technology? We offer a short indicative list of five.

i) Revive and restore extinct species: De-extinction, using synthetic biology tools to recreate extinct species, is a fascinating idea, and has caught the public imagination through high-profile events and publications (e.g. TEDx, *National Geographic)* strongly-supported projects such as the passenger pigeon project (*Revive and*

Restore - *http://longnow.org/revive/*), and media interest in bringing back mammoths. It is highly likely that some such projects will be pursued to completion, because the work will attract funding, inform science, help develop techniques useful in other fields, and provide an example of synthetic organisms that has public appeal. It is quite conceivable that a market will develop around the public display of de-extinct species, whether in private sector facilities ("Jurassic Parks"), or as commercial attractions in zoos. The allure of de-extinction for conservation may be obvious, although there are also good reasons to fear that in creating the ultimate 'diva species' (Sandbrook 2012), de-extinction will draw money away from other, legitimate conservation concerns in addition to other unknown longer term risks. There is a related discussion about restoring lost genetic diversity to species whose populations have been severely depleted, using museum specimens as new sources of genetic diversity. Certainly in conservation terms, de-extinction is far from the center of the debate and has unclear long-term benefits.

ii) Tackle persistent threats: Synthetic biology may conceivably provide options for engineering resistance to fungal diseases now emerging as a major threat to a range of wildlife (Fisher et al. 2012). For example, bats in North America are being decimated by white nose syndrome (see http://whitenosesyndrome.org). The syndrome, caused by a fungus apparently imported from Europe, has already killed so many insectivorous bats that we may soon see an impact on agriculture. European bats are resistant to the fungus, so one option would be to try to introduce the appropriate genes into North American bats via breeding programmes. However, bats breed very slowly, usually having only one pup a year, and only 5 or so pups in a lifetime. Given the mortality rate due to white nose syndrome, this suggests breeding is probably too slow to be useful in conservation efforts. What if synthetic biology could be used to intervene in some way, either to directly attack the non-native fungus or to interfere with its attack on bats? Bats contribute an estimated $23 billion annually to U.S. farmers by eating insects and pollinating various plants (Gruner Buckley 2013). Both biodiversity and human welfare would be improved by reducing, or even eliminating, the effects of white nose syndrome.

iii) Enhance capacity to restore degraded (and particularly highly polluted) ecosystems. Synthetic biology could conceivably contribute directly to habitat restoration, especially in remediating pollutants, eradicating invasive pathogens or competitor species, or enhancing decomposition rates. The idea of restoration needs careful management so that it does not reduce willingness to conserve intact ecosystems (Caro et al. 2012). Biological remediation of the 2010 oil spill in the Gulf of Mexico was faster than expected, and yet the massive deep water spill caused great and on-going damage. It is possible to conceive of using synthetic biology to create and modify micro-organisms with enhanced ability to consume spilled hydrocarbons to help manage such disasters. Or perhaps synthetic biology approaches could be used to eliminate or reduce the persistent and growing impact of pharmaceuticals in the environment on wild species and ecosystems (Arnold et al. 2013).

iv) Address problems arising from detrimental patterns of human of production and consumption (e.g. the consequences of greenhouse gas accumulation and anthropogenic climate change). Thus, could the physiological adaptation to relatively acidic ocean waters that is known to have evolved in some species be used to support adaptation in sensitive species that are now facing the threats posed by ocean acidification? Ocean temperature and acidity are set on long-term changes that are already affecting coral health around the globe. Steve Palumbi has shown in the lab that some South Pacific corals can handle remarkably difficult environmental conditions (pers. comm.). Many species of coral appear to possess the relevant genetic pathway within their genomes, but it is not yet clear why some corals have the pathway turned on and some do not. What if we could isolate these pathways and transplant them into other species, or turn them on in the genome if they are already there (e.g. constructing a coral or other species that is resilient to temperature and acidity changes)? So, to begin, the two fields can collaborate on genetics, molecular biology, and field biology to figure out why the corals do what they do. After that, if necessary, it seems that it would be worth exploring whether other coral species can be modified to use the relevant pathways. Corals are immensely important for the health of both natural ecosystems and human economies.

v) Control invasive species. Invasive and alien species are recognised as significant threats to biodiversity in many contexts, particularly in their impacts on biogeographically isolated fauna and flora (e.g. on isolated islands, such as Guam, invaded by the brown tree snake (*Boiga irregularis*), or New Zealand or Hawaii, where many endemic bird species are affected by rats). Attempts at control using chemical (poison) or physical methods (traps) are expensive and often ineffective. Synthetic biology might offer the possibility of species-specific biological control for invasive species, although risks clearly attach to such an approach, and past attempts at biological control have often created new invasive species problems.

3. Strategies for Finding Common Ground

There is a great need for more careful and inclusive thought about the implications of synthetic biology for biodiversity conservation. There has been a significant effort on the part of the synthetic biology community to explore ethical and philosophical dimensions of synthetic biology, and to address some of the issues of civic and environmental responsibility and biosecurity. The foundations of the field are built on the economic, design, and social infrastructure of engineering developed over the last 150 years. As examples of this commitment, the Sloan Foundation, the U.S. National Academy of Sciences, the Royal Society in the U.K., EMBO (European Molecular Biology Organization) and the BBSRC (U.K. Biotechnology and Biological Sciences Research Council) have funded research and researchers, and run meetings at the intersection of basic science, engineering, and the social sciences, often instigated by participants in synthetic biology. Institutions such as the Woodrow Wilson Center, International Risk Governance Council and the Hastings Center have devoted considerable time and resources to bringing together scientists, engineers, anthropologists, lawyers, civil society activists, ethicists, philosophers, public policy experts, and other stakeholders to consider the implications of the new field. An extension of this process is needed to more actively include the conservation community. The conservation community has an obligation to work to try to create and promote such a process. Conservation's struggles to understand and incorporate issues like human rights, livelihoods and politics into its own thinking might be useful as a model in thinking about how to address incorporation of synthetic biology.

Practical discussions between the two communities are likely to be more productive than abstract discussions; real problems can be presented and then the alternative approaches to dealing with them through traditional and synthetic biology can be evaluated. Here we recommend some approaches and topics to ensure a full and through appraisal of the alternatives.

i) The problem of containment of modified organisms is a critical one for biodiversity conservation (although it is also relevant in other fields). Existing categories of 'laboratory' and 'field' are vague, and may not enable safe use of novel organisms. There is experience in invasive species that is relevant to novel organisms (Jeschke *et al.* 2013). It may be possible to develop genetic technologies to prevent the inadvertent escape of synthetic organisms.

At the same time, some applications, such as in the case of white nose syndrome, or pollution remediation (see above), require spread, rather than containment of novel organisms. How should safety considerations be incorporated in cases like this (see Marris and Jefferson 2013)?

ii) Research on synthetic biology is already transdisciplinary. Conservation biology and (especially) ecology have important additional contributions to make, but so too do the social sciences and those who work on economies and societies. Debates about marginalisation and the 'end of pipe' position of social enquiry, leading to poor outcomes) are critically important here. Work on values held by civil society across groups and nations needs to be a particular focus (Dietz 2012). The synthetic biology community may have learned some lessons from fields such as nanotechnology and genomics in being open to public debate and bringing in social science analyses.

iii) Applications of synthetic biology to conservation need to be compared on a range of metrics, at the very least including monetary costs of making the intervention, biodiversity benefits, readiness (is the approach or technique ready, tested and validated), and risks (what might be the unintended consequences). Each of these questions may have further nuances. For example, when considering the costs and benefits, who pays and who gains? Who or what is at risk, and what is the risk of not doing anything: inaction may be a risk greater than that of taking action without full knowledge of the consequences.

When considering the risks of applying synthetic biology approaches to conservation problems it is important to incorporate counterfactual thinking. Use of counterfactuals requires knowing what outcomes would have looked like in the absence of the intervention and allows assessment of the degree to which changes in an outcome can be attributed to the intervention rather than other factors (Ferraro 2009). So in the case of deciding whether or not to apply synthetic biology approaches to conservation problems we must incorporate into our risk calculus the existing threats and trajectory if such solutions are not applied.

iv) The importance of public understanding and perceptions cannot be underestimated. Indeed, the level of public acceptance of synthetic biology solutions to conservation will inform policy, funding, and regulatory frameworks. We must give careful thought to how the issues, including risks and benefits, are framed in the media and should consider collaborating with seasoned communications experts and social scientists to listen and learn form other perspectives and to help craft effective narratives. Today, the major media coverage of synthetic biology and biodiversity is dominated by sensationalist stories of de-extinction, missing the more nuanced, positive applications that synthetic biology could offer to conservation challenges, while largely overlooking the complex governance, ethical and societal issues that need debate.

Public opinion research in the U.S. has shown a mixed reaction to the promise of synthetic biology (Pauwels 2013). While there is guarded optimism for applications developed to address medical and environmental needs, survey participants were sceptical about over-hyped futuristic visions. This research, coupled with findings from the WWViews on Biodiversity project (http://biodiversity.wwviews.org/) that 75% of global survey participants are "very concerned" about biodiversity loss, suggests a public appetite for a rigorously tested synthetic biology solution to a singularly well-suited conservation challenge.

Inclusiveness will be vital as synthetic biology applications to conservation are seriously considered. Experience with other novel technologies has shown the advantage of strategic engagement of many elements of society to gauge interest and concern and to adapt accordingly. Conservation outcomes are usually social goods and as such need to be understood and valued by society.

v) The international regulation of the development and release of modified organisms needs considerable development that will require much wider competence in understanding both synthetic biology and ecology on the part of diplomats and lawyers.

The time is now for a targeted, strategic, respectful engagement between conservationists and synthetic biologists. There is even greater need to have this discussion given the Subsidiary Body of Scientific, Technical and Technological Assessment's release for comment of a draft paper looking at the potential positive and negative impacts on biodiversity of organisms modified by synthetic biology (https://www.cbd.int/emerging/; accessed August 19, 2013). There is a need for new research, and new collaborations between researchers, civil society and other sectors of society to address both information gaps and the profound differences in the way practitioners in the two fields currently think (discussed above). Perhaps modelling and carefully limited experimental work can point the way toward a better understanding of how to apply synthetic biology to conservation more broadly. Such experiments could serve to develop personal and disciplinary ties, and if properly designed could serve as a source of inspiration for adapting to a changing climate. One idea would be for young practitioners from both fields to be brought together, perhaps as members of interdisciplinary iGEM teams, to consider novel approaches and to understand the dimensions of each other's fields. Greater outreach and information sharing is also needed to inform and influence both fields, and the publics among whom scientists work. The alternative to greater engagement between synthetic biology and conservation is ignorance, missed opportunities and unrecognised and unaddressed risks. In such a scenario, biodiversity will only be the loser.

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