How will **synthetic biology and conservation** shape the future of nature?

A framing paper prepared for a meeting between synthetic biology and conservation professionals

Clare College, Cambridge, UK
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WILDLIFE CONSERVATION SOCIETY

How will **synthetic biology** and **conservation** shape the future of nature?

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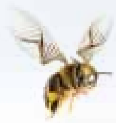
1. Purpose

This paper serves as a framing piece for the meeting "How will synthetic biology and conservation shape the future of nature?" to be held 9-11 April, 2013. The meeting is organized by the Wildlife Conservation Society (WCS – www.wcs.org), a global conservation organization with a 120-year history saving wildlife and wild places as well as operating the largest system of urban wildlife parks in the world, led by New York's flagship Bronx Zoo.

The purpose of the meeting is to bring together experts from both synthetic biology and conservation in order to learn from each other, exchange views, and explore how both disciplines might best help each other. We anticipate that the outcome will be an enhancement of the practice of conservation, more educated about synthetic biology and a concomitantly improved practice of synthetic biology, more educated about the concerns and imperatives of biodiversity conservation.

This paper is designed to provide:

- common background information for the meeting participants focusing on introducing synthetic biology to conservationists and conservation to synthetic biologists
- a framework for dialogue at the meeting
- an introduction to the logic and flow of the meeting



2. Introduction

Humans have always sought to reshape nature to meet their needs. Beginning with the control of fire and the domestication of plants and animals through to massive water diversion schemes, the development of nitrogen fertilizers, and the planting of extensive monocultures, this shaping and reshaping of nature has become an essential part of being human. Humans have now reached an apogee: we are responsible for driving species to extinction at rates that far exceed background rates in the geological past; on average humans appropriate about 25% of potential net primary terrestrial productivity, mostly from agricultural land-use and harvests[1]; we use over half of all accessible fresh water; we apply more nitrogen fertilizer than is fixed naturally in all terrestrial ecosystems; and humans are changing the atmosphere through the dramatically increased production of methane and carbon dioxide.[2]

A growing understanding of such pervasive human influence on natural systems has resulted in a proposal to name the current epoch the Anthropocene. This proposed epoch began around the year 1800 with the onset of industrialization.[3] It is suggested that since then, as a result of continual expansion and growth in human populations and their collective impact on the natural environment and living systems at all scales, there may be an impending abrupt and irreversible state shift in the Earth's biosphere.[4] Whether or not this happens, it is clear that humans have already become the dominant ecological and evolutionary force on the planet.[5]

The Anthropocene epoch is characterized not only by the extent of human alteration of nature but also by the development of concern for its conservation throughout the twentieth century, in the form of increasingly systematic attempts to protect species and ecosystems. However, despite decades of effort and hundreds of millions of dollars, the conservation community has not been successful in preventing depletion of biodiversity.[6] Much has been achieved, and there have been local successes. Well-focused projects have been successful at reversing declines of particular species and habitats. However, at a global level, governments and conservation organizations have failed to achieve internationally agreed upon goals to reduce the rate of biodiversity loss.

Much of the past human impact on the biosphere has been a result of growth in human endeavors such as commercial fishing and industrial agriculture, as well as their indirect impacts, such as growth in industrial waste and the associated release of long-lasting chemicals into the environment. Human impact on the biosphere is now realized in increasingly novel ways, with humans breaching boundaries between species, creating novel forms and functions and integrating the living and the non-living. This includes the creation of:

- cyborg insects[7]
- robotic fish that swim with real fish[8]
- artificial trees to absorb atmospheric carbon[9] and even achieve artificial photosynthesis[10]
- machines harnessed to the human brain[11]
- nanobots equipped with bacteria inserted into the human body to fight disease[12]

The development of powerful technologies has allowed humans to achieve some of these ends through the purposeful manipulation of DNA itself, giving rise to the field of synthetic biology. Though there is no agreed-upon definition of synthetic biology, three useful framing concepts are:

- "the design and construction of new biological parts, devices, and systems and the re-design of existing, natural biological systems for useful purposes"[13]
- "a scientific discipline that relies on chemically synthesized DNA, along with standardized and automatable processes, to address human needs by the creation of organisms with novel or enhanced characteristics or traits"[14]
- a scientific focus on the design and fabrication of biological components and systems that do not already exist in the natural world, and on the re-design and fabrication of existing biological systems[15]

In all these we find emphasis on scientific design or engineering, focus on putative human benefit, and a somewhat soft insistence on the creation of novel life forms. Whether or not new life forms are a necessary minimum for the field of synthetic biology seems to be part of the debate in this new field of inquiry.

The field is moving fast, with billions of dollars invested globally, and developments of novel applications or improvements of existing ones emerging weekly. In the last seven years, some 40 reports (in the English language alone) have addressed the social, ethical and legal issues raised by synthetic biology,[16] and synthetic biologists have reached out to form collaborations with researchers in the social sciences, law, arts and humanities.[17] Despite these collaborative efforts, there has been very limited consideration of the risks and benefits that synthetic organisms may pose to the biological world,[18] and the conservation and global change communities have paid virtually no attention to synthetic biology. Evidence of this lack of attention can be found in a number of recent surveys which outline many of the problems and promises that face the natural world[19] but rarely give more than passing mention of synthetic biology.[20]

The patterns and drivers of extinction change through time,[21] and the changes to which conservation has responded to date may not be accurate models for the future changing world. That world will contain synthetic biology, although the form it will take is still unclear. Some commentators depict the future of synthetic biology in glowing terms: "many of the major global problems, such as famine, disease and energy shortages, have potential solutions in the world of engineered cells."[22] Others write in deeply negative language: "The proposed use of synthetic microbes in the production of the next generation of fuels, medicines and industrial chemicals may massively increase human impact on biodiversity, while accelerating biopiracy and making a mockery of any notion of 'benefit sharing.'"[23]

As Marris and Rose[24] state as regards depictions of synthetic biology: "Utopias and dystopias seem to be the only scenarios possible," and yet the future is likely to lie in between: complex, messy and contested. Those researching and innovating in synthetic biology, and those seeking to conserve biodiversity, will need to understand each other far better than they do at present if there is to be an informed debate preceding intelligent decisions. Problems may very well be intractable, and solutions hard won.

There is much to discuss. Is synthetic biology to be feared by conservationists, interpreted as a final assault on the diversity of the natural world? Or will it provide them with solutions to known threats to biodiversity, such as the fungal diseases that threaten many amphibians and bats with extinction?[25] Are conservationists ignorant Luddites who advocate 'naturalness' for no more reason than a general feeling of comfort with the status quo? Wild species and ecosystems are a vital source of genetic raw material for synthetic biologists: does that give the industry an interest in preserving wild species and ecosystems faced with extinction? If the purpose of synthetic biology is to create intelligible and predictable living systems, then synthetic biologists might share with conservation biologists a concern for the possible consequences of unwinding natural complexity.

3. What is Synthetic Biology?[26]

Imagine planting a seed programmed to grow into a house; resurrecting a favorite extinct species to run or fly free for the first time in centuries; microbrewing gasoline as we now brew beer; or even creating de novo a branch of life independent of any extant on Earth. These examples might sound far-fetched. But they are the promise of, or at least the advertising for, the field of synthetic biology. The stated goals of synthetic biologists are varied, but they can be summarized as the modification and construction of biological systems (ranging from organisms to in vitro biochemical systems) with understandable and predictable behaviors.

Reading and writing DNA are core technological capabilities for synthetic biologists. Several decades ago, DNA sequencing employed instruments that were large, expensive boxes requiring laborious manual sample preparation; these instruments produced only short sequence reads of small amounts of DNA. The latest instruments are fully automated and can process the equivalent of several human genomes per day. The impending commercial release of nanopore sequencers, in which sequences are directly read electronically from long contiguous DNA molecules, promises to accelerate the flood of genomic information. That information can be manipulated electronically, enabling the design of new sequences, which can be physically instantiated through the chemical synthesis of DNA. Over the last several decades, the ability to stitch together synthetic DNA has improved to the point where entire microbial genomes, comprising more than a thousand genes and a million bases, can now be assembled from scratch.[27] The cost of both sequencing and synthesizing DNA has fallen dramatically over the past two decades, and the productivity of sequencing and synthesis instrumentation–that is, the number of processed bases per person per day—has improved almost as fast.[28] As a result, it is now possible to order out sequencing and synthesis via the internet, with shipping services delivering physical samples to and fro in a global marketplace.

The construction of synthetic genomes today serves to help unravel the function of genetic elements and their interactions. Synthetic genomes may also someday serve as the basis for economically important production systems, but there is presently no capability to design genetic systems containing even one hundred, let alone one thousand, components.

One state-of-the-art example of synthetic biology is the recent reconstitution of a nitrogen fixation cluster from the bacterium K. oxytoca in E. coli.[29] The native gene cluster consists of 20 genes spread across 23.5 kilobases of DNA, with a complicated structure that includes physically overlapping genes and sequences that encode more than one function. While this evolved structure is apparently optimal for regulating physiological function, such complexity confounds human attempts at both basic understanding and genetic manipulation of the pathway.

A team led by Chris Voigt at MIT has now unpacked the physical complexity of the nitrogen fixation gene cluster. The purpose of this unpacking, which draws conceptually on a procedure in software programming called refactoring, "is to reorganize the cluster, simplify its regulation, and assign a concrete function to each genetic part."[30] The refactored pathway and added regulatory elements, now genetically "wired up" to a controller circuit that enables tuning expression levels, comprises 89 defined and functionally characterized genetic parts. Unsurprisingly the refactored system does not perform as well as the evolved system. Yet these twofold feats – the construction of the functional pathway and the initial characterization of the parts – provide

valuable new scientific knowledge. This knowledge in turn provides the basis for considering design changes and for moving the pathway into new organisms, thereby potentially enabling nitrogen fixation capabilities where none currently exist. It is a certainty that this strategy will also be used to manipulate metabolic pathways that produce many different compounds and then to reconstitute those pathways in a variety of bacterial and eukaryotic hosts.

Efforts such as this are clearly described by the participants as directed toward facilitating the engineering of biological systems. Results thus far, across the field as a whole, indicate a long road ahead. There is, however, clearly a great deal of progress, and even rudimentary control over biological systems has begun to transform not just industries but entire economies.

Many analysts anticipate that synthetic biology will provide benefits to society in a range of different sectors, including human health; agriculture and food production; environmental protection and remediation; bioenergy; chemical synthesis; and biosensor development.[31] Six sectors of potential transformation have been identified:[32]

- bioenergy: synthetic fuels, biofuels, electricity, hydrogen, etc.
- agriculture and food production: engineered crops, pest control, fertilizers, etc.
- environmental protection and remediation: restoration, monitoring, detection, etc.
- consumer products: computers, sporting goods, cosmetics, etc.
- chemical production: industrial compounds, high-value compounds, plastics, chemical synthesis, etc.
- human health: medical drugs and devices, over-the-counter medicine, clinical therapies, etc.

The Early Impacts of Engineering Biological Systems

Humans have long sought to improve their control over organisms. Agriculture, including plant and animal breeding, served this end for much of human history. An understanding of physical inheritance, then genes, and eventually molecular biology has put humans on a path to set the growth and behavior of plants, animals, and microbes to serve human ends.

The effort to build biological systems has many faces in many locations around the world. Scientists are at work to expand upon biochemistry, changing not just the sequence but also the content of the genetic code beyond the four base pairs.[33] This new code offers advantages for programming new functions as well as the possibility of isolating the lineage and biochemistry of new organisms from extant life. Similarly, other efforts aim to introduce into existing genomes a range of new amino acids not found in any living organism, which could vastly expand protein function well beyond existing biochemistry.[34] Still others hope to reanimate extinct species or to create truly novel living systems, with intriguing potential consequences for ecology and biodiversity.[35] Synthetic biologists are interested in life not so much as they find it – though that is certainly fascinating – but life as they might build it. One consequence of this effort is a focus on constructing biological systems that have predictable behaviors.

Aviation provides a useful analogy. Humans have always marveled at, and sought to explain, how birds stay aloft and how they accomplish such wonderful feats of acrobatics and endurance. Yet we are not restricted to studying only evolved systems in our efforts to understand or employ the principles of flight. Indeed, humans have primarily made progress in understanding the principles of flight through constructing and testing artificial systems. Nevertheless, there is still no definitive mathematical description of how geese fly. Nor is there a goose anywhere built from aluminum or carbon fiber capable of carrying hundreds of humans over thousands of miles, powered by jet turbines with blades that move at

nearly the speed of sound. Despite our continued ignorance of the detailed mechanisms of bird flight, we quite successfully build and rely on aircraft that display behaviors we can understand and predict. This, of course, is the very definition of engineering.

In less than a century, humans progressed from vaguely controlled flight in rudimentary hang gliders to the Boeing 777. This aircraft was designed and tested entirely in silico before the first 777 airframe was, in effect, printed out via computer-aided manufacturing and then flown by a test pilot. The combination of predictive design, powerful test and measurement capabilities, and the ability to build exactly what is designed underlie many of the technologies we rely on every day. This includes not just airplanes, but computers and communications, automobiles, power generation, and, in many cases, the shoes on our feet. For the majority of its practitioners, synthetic biology is no less than the application of these same engineering principles to living systems. It may seem a distant dream indeed to build biological systems with behaviors as predictable and well-defined as a Boeing 777, but it is a dream that a great many synthetic biologists share, and there is already substantial progress towards realizing it.

To set the context for these efforts, consider that humans have been modifying biology through artificial selection for many millennia. Within the last few decades, humans have refined these skills by learning to explicitly move genes from one organism another, a technology usually referred to as recombinant DNA. This technology is a remarkable demonstration of human ingenuity, and it also has provided tangible and substantial economic benefits.

The global market for the products of biological engineering is growing rapidly. Genetically modified organisms are now used to produce drugs, food, fuels, materials, and enzymes that are used in nearly every home and business in the developed world. In 2010, U.S. revenues from genetically modified systems reached over $300 billion, or the equivalent of more than 2% of GDP. These impressive revenues are generated within three sub-sectors: genetically modified drugs (i.e., "biologics") at $75 billion; genetically modified seeds and crops at $110 billion; and industrial biotechnology (e.g., fuels, materials, and enzymes) at $115 billion.[36] U.S. biotech revenues are growing at an annual rate of approximately 15%. Global revenues are similarly growing at a rapid clip; China and Malaysia may each have biotech revenues in excess of 2.5% of GDP, and both countries plan to at least double that share by 2020.[37] These revenues are primarily generated through the application of more than three decades of experience with recombinant DNA technology. In this context, a very generous estimate of 2012 total international revenues from synthetic biology would be $1 billion,[38] primarily consisting of engineering tools and reagents, including synthetic genes. Companies founded on the promise of selling fuels, drugs, or other products made using synthetic biology have yet to generate much in the way of revenues, let alone profits. Nonetheless, the promise of developing a diverse and valuable range of products continues to generate enormous investment.

There is an explicit expectation that the economic benefits of new technologies will be even greater than those from the use of recombinant DNA. For example, over the last decade Chinese leaders have publicly announced that the country would rely heavily on genetic modification techniques to solve the impending, population-driven crises in health care and food supply.[39] As of 2008, China has dedicated approximately 30% of all new research and development funding to biotechnology, distributed both to academic institutions and to commercialization efforts.[40] Similarly, the United Kingdom is investing more than $30 million to develop and deploy new biological technologies in the economy. In the U.S., the National Science Foundation has funded the Synthetic Biology Engineering Research Consortium (SynBERC) with almost $30 million over six years, again with the expectation of eventual commercialization of industrial applications.[41] In 2012, the Office of the President published the National Bioeconomy Blueprint, outlining a long term, strategic plan for integrating new biological technologies into the economy.[42]

Prospects and Potential Concerns

The overwhelming majority of direct government investment in synthetic biology is aimed at developing organisms that provide a service or a product. The proposed applications break down synthetic organisms into two general categories, with widely divergent potential consequences for biodiversity and the environment: organisms that will be contained for their entire life cycle, and those that will be released into the environment.

A great deal of the investment into synthetic biology is aimed at producing organisms that will be grown in contained environments of one kind or another. The intent is that these organisms will never enter the environment alive. Many compounds, with uses ranging from drugs to industrial enzymes or to plastics precursors, are already made this way. Companies such as Amyris, Gevo, and Solazyme are entering the market with a variety of chemicals and fuels produced by bacteria, yeast, and algae modified with complex genetic circuits. It has been argued that the positive economic and environmental impacts of these production systems are great. But an honest appraisal of the relevant risks must acknowledge that, however such companies contain their organisms and the relevant modified genes, no containment system will be perfect. As of this writing, there appear to be no documented examples (or systematic studies) of gene leakage into the environment from the disposal of contained, genetically modified cell cultures.[43]

Even assuming that cultured cells present a low environmental risk, those organisms must eat something. Increasingly, the feedstocks for biological production systems will comprise field crops designed specifically for that purpose. The development of new feedstock plants holds the prospect of employing such traits as improved drought and salt tolerance, or programmed cellulase production that begins cellulose breakdown even before harvest. The long regulatory approval process for such crops reflects the uncertainty surrounding environmental release, and multiple cases of gene leakage from field crops have been documented over the years.[44] That said, genetically modified (GM) crops have become quite popular with farmers in many countries, reaching nearly 100% penetration in some markets.[45] Moreover, the crops can be adopted by farmers very quickly; the market penetration of GM sugar beet jumped from zero to 95% in the U.S. over the course of just 24 months, even after only provisional approval.[46] Driving such rapid adoption and high penetration are positive reviews of the environmental and economic performance of GM crops.[47] Nonetheless, uncertainty over the behavior of GM crops in the environment inevitably slows the deployment of new traits, particularly in countries such as the UK in which there is widespread distrust of corporate influence on agricultural practices.

Synthetic biology is also being used to develop algal and cyanobacterial strains that produce biofuels directly in contained environments. Such efforts are aiming very high indeed, while starting off from a difficult position. In 2012, the National Academy of Sciences concluded that, at current resource usage and fuel yield, algal biofuels are unsustainable and uneconomical at even the modest production level of five percent of U.S. fuel demand.[48] As if in response, the Department of Energy released a "Funding Opportunity" aimed at increasing average algal biofuel yields to economically competitive levels, while reducing resource usage and carbon emission, by 2022.[49] The eventual production strains may be grown either in enclosed bioreactors or in open ponds or sluiceways, again begging questions about the environmental release of genetically modified organisms. This issue is the subject of extensive consultation.[50] Only time, and a great deal of investment, will determine if photosynthetic microbes can be developed as an environmentally friendly, economically viable source of fuel, and if containment works.

"the promise of developing a diverse and valuable range of products continues to generate enormous investment"

Perhaps even more significant than economic concerns, the pace of synthetic biology is driven by international, multi-generational enthusiasm. Initially run in 2005 with a handful of students, the International Genetically Engineered Machines (iGEM) competition has now grown to have an annual participation of approximately 2000 secondary school and university students participating on more than 200 teams from around the world.[51] There are already more than 14,000 iGEM alumni. Projects are based on the creation and use of standardized biological components, which are collected in the Registry of Standard Biological Parts.[52] iGEM projects have resulted in numerous articles in top-tier journals.[53] Many of the projects now designed and implemented by undergraduates over the course of a summer would have been infeasible for a team of PhDs just a few years ago. It is indicative of the international nature of synthetic biology that the five or six finalists in each year have generally consisted of teams from Asia and Europe: a U.S. team took home the Grand Prize only once in the first seven years of iGEM.

Participation in the new field is rapidly expanding beyond universities and large companies. Community laboratories have been founded across the United States to provide both educational opportunities and lab space for start-up companies.[54] Rapidly falling costs for reagents and instrumentation have facilitated a new wave of garage biology entrepreneurs.[55]

This broad proliferation may cause security and safety concerns in some circles. In many countries it is illegal to manipulate DNA without dispensation of some kind from the government. Moreover, broad access to biological technologies is thought by some to pose a risk of bioterror or bioerror. Yet it is worth considering that producing any sort of "good" application via synthetic biology is still quite difficult; producing a "bad" application will require at least as much effort, while in all likelihood receiving less support.

As a strategic security position, the U.S government has chosen to embrace and support what might be called "garage biology". The relevant document, signed by President Obama, can be paraphrased as "garage biology is good and necessary for the future physical and economic security of the United States."[56] This position acknowledges the historical analysis that because entrepreneurs and small organizations – i.e. "garages" – have been critical drivers of diverse technological innovation in the U.S. for several centuries, so are garages likely to be critical for future innovation in biotechnology.[57]

Admittedly, such enthusiasm may be based on optimistic expectations about the time scale for economic development and job creation. Governments and private investors alike are acclimated to a relatively rapid return on capital in industries ranging from automobiles to information technology. Yet these industries are built on many decades, if not centuries, of accumulated experience.

The complexity of a new smartphone, a new internal combustion engine, or even new shoes is only possible because the relevant materials and manufacturing methods are so well-described and understood from a physical, chemical, and engineering perspective. In contrast, while we are roughly thirty years into using recombinant DNA, and while biology comprises critical components of our economy, the products resulting from biotechnology are of minimal engineering complexity. As discussed above, a Boeing 777 is built from about 130,000 different kinds of parts, with each of the total of 4 million parts described in a quantitative design model.[58] The most complex biotechnological products now on the market are derived from organisms that contain approximately 10 new genes, with a few dozen additional mutations, inside an organism with a genetic background consisting of thousands of genes that may have a name but only a minimally-described function.

Through synthetic biology and other efforts, biotechnology is being pushed very hard to achieve a great deal in a short period. But we should not expect biotechnology to replace our accumulated industrial infrastructure overnight. Aeronautical engineering advanced from Kitty Hawk to the Comet Airlines in 50 years, but it took well over a century to reach the Boeing 777. Synthetic Biology is still close to the stage of canvas and sticks. For example, even assuming all the relevant technical problems are solved, biofuels should not be considered a rapid solution to any problem, particularly

replacing the large, existing volume of petroleum production. Despite the claims of inventors and investors alike, it will be many years before the combination of feedstock, production, and distribution are mature enough to satisfy the substantial demand for biofuels.

Nonetheless, the potential of synthetic biology is so great that it is continually a source of both hope and anxiety. The announcement in 2010 of a synthetic bacterial chromosome elicited just such a wide range of reactions.[59] The achievement was initially considered so remarkable, and with such wide ramifications, that it was the proximate cause for the creation of a new Presidential Commission in the U.S. Yet however beautiful the science involved in this experiment, revisiting Genesis it was not. This fantastic technical accomplishment was more akin to photocopying an existing genome than creating new life. The Presidential Commission for the Study of Bioethical Issues consulted a variety of technical experts, bioethicists, and religious authorities about the impact of the synthetic biology. After considering the resulting testimony, in addition to comments from the public, the Commission concluded that federal support of synthetic biology should continue with minimal regulatory overhead. However, the Commission suggested a policy of "prudent vigilance" to monitor developments and recommended a set of actions to facilitate that monitoring across the relevant federal agencies.[60]

The field of synthetic biology is expanding fast, but not without engendering considerable debate.[61] Not all contributors of material considered by the U.S. Presidential Commission were sanguine about the prospects of synthetic biology. Some commentators have been quick to note that few, if any, of the Commission's recommendations for monitoring synthetic biology have been implemented.[62] And it is significant that outside the U.S., many countries are taking a slower approach to investment and commercialization. Future debate is likely to be energetic.

4. What is conservation and how is it practiced?

Conservationists seek to reduce human impacts on the diversity of the natural world. Concern for nature has a long history, but in its modern form, conservation became a recognizable movement when activists began to establish wildlife conservation organizations towards the end of the nineteenth century (for example the New York Zoological Society, now the Wildlife Conservation Society [WCS], in 1895).[63]

In the 1980s, the term "biodiversity" became the shorthand used by conservation advocates and scientists (in lieu of "nature"), and the objective of conservation became biodiversity. Conservation has as its goal the maintenance of biodiversity in all its richness both for its own sake as well as for the well-being of humans. Biodiversity is defined by the Convention on Biological Diversity as "the variability among living organisms from all sources including, inter alia, terrestrial, marine and other aquatic ecosystems and the ecological complexes of which they are part; this includes diversity within species, between species and of ecosystems."[64] It is usually seen as having three components: genes, species, and ecosystems, each of which has three attributes: composition, structure and function.[65]

Biodiversity refers to the variation found in all parts of the living, natural world, independent of their utility to humans. There is a long-standing tension in the conservation community between those who favor including or excluding from biodiversity elements of the natural world that have been strongly influenced by humans, such as forests of fruit trees planted by people or domesticated plants and animals. While the definition of 'biodiversity' emphasizes variation, common uses of the term often also imply abundance and distribution, so that, for example, the extent of unconverted tropical rainforest is an important issue for conservationists, even if new areas embrace progressively fewer species not found elsewhere. This is partly because the increased abundance and distribution of species and ecological communities will be likely to include increasing quantities of genetic variation, and thus structural, compositional and functional diversity, but also due to the fact that some of the

benefits provided to people by biodiversity are greater at larger scales, especially some ecosystem services (e.g., carbon sequestration, wetland nutrient cycling) and aesthetic and cultural values (e.g., spectacular scenery, recreation and tourism).

The driving concern for conservation is the loss of living diversity, usually expressed (inadequately) in terms of loss of species. Conservationists describe the rise of industrial society as the beginning of an "'extinction spasm": when human activity raised background rates of extinction to between 100 and 10,000 times the geological 'background' rate of one species per million species per year. Future rates are expected to be another order of magnitude higher. The earth is therefore approaching the sixth great episode of extinction in its history.[66]

The measurement of extinction rates is highly problematic. Surveys are too few, and it is difficult to rule out the possibility that individuals of rare and declining species remain. Recent assessments have used metrics based on loss of biomes; population and range extent decline; and statistics derived from threatened species lists to conclude that the rate of loss of biodiversity has not slowed and continues at accelerating rates.[67] This is not surprising given that the main impetus—the scale of the human footprint on the earth[68]—is large and increasing.

It is now recognized that biodiversity alteration (e.g. changes in abundance and community structure, range shifts) is as important as biodiversity loss (species extinction) in conservation.[69] Biodiversity alteration is reversible (at least to a degree), while biodiversity loss (with current conservation interventions at least) is not.[70]

Conservation focuses on variation and on living, functioning organisms in nature. Species taxonomy is, in theory, a "natural classification" which has the advantage that the differences between identified units is informative about the causal processes that drive those differences and can therefore be used to predict the characteristics of new units belonging to the same groups. The individuals that make up species have similar characteristics based on their evolutionary history. Species are organized into higher groupings of genera, families, orders, etc. and share characteristics in a hierarchically clustered manner. If the classification of species is not just about similar characteristics but also reflects characteristics that are shared because of common descent, then there is also an evolutionary classification that represents the historical processes that have shaped current diversity. In practice, there are conflicts between the evolutionary classification and the biological species observed in the real world, but the majority of biodiversity scientists agree that the most fundamental definition of biodiversity would be the total amount of independently evolved genetic variation – i.e., the branch lengths added up across the tree of life. This discounts species that share large amounts of their genetic variation with other species, and emphasizes species where there are few close relatives or that have long evolved independently.[71]

Conservationists often talk about the importance of conserving not only species and ecosystems but also the evolutionary processes that formed them. This objective – to retain the potential for species to respond to natural selection through evolution – is likely to become more significant in the future as environments and their pressures change at ever increasing rates and intensities. Conservation is therefore not simply aiming to retain all current species as if they were books in a library, but seeking to maintain the elements from genetics, environment and natural selection that will allow future species to persist and diversify, or (analogously) to allow for new books to be written.

"conservationists often talk about the importance of conserving not only species and ecosystems but also the evolutionary processes that formed them"

What Conservationists Do

The term conservation, as opposed to preservation, became widely used in its modern sense after World War II. Early in the twentieth century, the term was used to refer to the rational use of natural resources for human benefit, particularly as an issue of federal policy in the United States. The differences between rational use and more preservationist concerns have remained in tension ever since. There are on-going practical debates between those who argue that conservation is most effectively based on the sustainable use of resources and those who argue for preservation, and between those who argue on behalf of conservation versus those who favor rural poverty alleviation.

Biodiversity conservation is effectively a subset of environmentalism, although its core concerns (e.g., rare species and extinction) long pre-date the "new environmentalism" of the 1960s. However, conservation is somewhat detached from wider environmentalism and its focus on the relationship between human needs and the living biosphere (for example, concerns about the limits to growth in the 1970s, sustainable development in the 1990s, or anthropogenic climate change today). Biodiversity conservation has responded to these debates (for example in its concern for the links between biodiversity, ecosystem services and poverty), but has remained tightly focused on the maintenance of biodiversity. In part this reflects the powerful role of science in conservation thinking, and particularly the "mission-driven" discipline of Conservation Biology that coalesced in the 1980s. It also reflects the complex mix of values that influence conservationists, including both biocentric and anthropocentric ideas.[72]

Most efforts in conservation have been directed at species and ecosystems, although an increasing amount of effort is focused on restoration of species and ecosystems.

Protection of Species

Concern about the extinction of individual species has been an important element in conservation since the era of scientific collecting and hunting in the nineteenth century. The hunting-to-extinction of mammals like Steller's sea cow (Alaska) or the quagga (a subspecies of zebra in the South African Cape), and of birds such as the Great Auk (North Atlantic) or the passenger pigeon (United States), were important in the foundation of the conservation movement, and attempts to preserve other threatened species, such as the American bison, became legendary conservation successes of the early movement.

Though there is no single agreement on what it means to conserve a species (other than the prevention of extinction), recent work has proposed six attributes of a successfully conserved species. The species should:

1) be demographically and ecologically self-sustaining
2) be genetically robust
3) have healthy populations
4) have populations distributed over the full ecological gradient of the historical range
5) have more than one population in each of these ecological settings
6) be resilient to environmental change[73]

Protected Areas

Since the establishment of formal conservation organizations at the end of the nineteenth century, the most important conservation strategy has been the creation of protected areas to separate humans from other species.[74] The idea of controlling access to particular pieces of land for nature or for particular species (e.g., designating sacred groves, gardens, or hunting reserves) is ancient, and cuts across cultures. Internationally, this approach drew on the model of game or hunting reserves (e.g., in Europe and European colonial territories such as those in Africa); on the United States' idea of national parks as pristine or wilderness areas; and on the British notion of smaller and more managed nature reserves.

The modern idea of protected areas is often traced back to the establishment of Yellowstone National Park in the United States in 1872. Similar large protected areas were created in many colonial territories in the later nineteenth century, including in Australia, Canada and New Zealand in 1894 and in Africa a few decades later. In other countries, reserves emerged based on different models. By the start of World War II, there were protected areas in many European countries as well as in Argentina, Brazil, Mexico and the United States, and across the British Empire and the Dutch East Indies.[75]

Park and reserve creation accelerated in the decades following World War II.[76] The extent of terrestrial and aquatic protected areas more or less doubled globally over the 1970s, and the current target is at least 17% of terrestrial and inland water areas and 10% of coastal and marine areas.[77] Systems of protected areas exist in every country of the world, and currently over 177,000 individual nationally declared protected areas have been created, covering 17 million square kilometers, or 12.7% of the earth's terrestrial area outside of Antarctica.[78]

The World Commission on Protected Areas (WCPA) defines a protected area as: "a clearly defined geographical space, recognized, dedicated and managed, through legal or other effective means, to achieve the long-term conservation of nature with associated ecosystem services and cultural values."[79] Protected area systems have developed in different countries in ways that reflect national needs, priorities, and resourcing.[80] Protected areas need to be well managed in order to be effectively conserved. And in order to conserve the full range of ecosystems, protected area systems need to be distributed across all terrestrial, freshwater and marine systems.

Conservation Beyond Protected Areas

Developments in ecological science have challenged the notion that nature can be fully protected within protected areas. From the 1960s, there has been recognition of the implications of research on island biogeography for small isolated areas of habitat and nature reserves.[81] The number of species on small isolated islands tends to decline, because rates of immigration (which decrease with isolation) do not match rates of extinction (which decrease with size). Thus a protected area that becomes isolated and surrounded by other forms of land-use (a forest surrounded by agriculture, for example) must be expected to lose species. Reserves are increasingly isolated, surrounded by intensively managed lands.

Concern such as these have been matched by developments in the field of "landscape ecology"[82] and a growing literature on the possibility of creating connections between ecosystem fragments along which species might move.[83] This has given rise to the concept of linked or "meta" populations that can be managed as single units.[84] As well as the increasing interest pursuing conservation through sets of protected areas that are managed as part of "ecological networks"[85] and as part of landscape-scale conservation.[86]

These efforts to conserve species and protected areas are complemented by a great deal of work that aims to incorporate biodiversity into the economic and development sectors. This has focused on ecosystems and in particular on "ecosystem services." Ecosystem services are the benefits that humankind derives from ecosystems; these, in turn, result from ecosystem functions and the processes that are driven by the interactions between living and non-living ecosystem components. Ecosystem services include provisioning services (e.g., food and fiber production); regulating services (e.g., climate, water and disease regulation); and cultural services (aesthetic and recreational values). Since diversity, at a genetic and species level, is generally a positive factor for enhancing ecosystem services,[87] biodiversity and ecosystem services are

often discussed as one, and very often the same actions are necessary to conserve them.[88] Whether or not conserving biodiversity and conserving ecosystem services come to the same thing, however, is debated.[89]

The rise in appreciation of human dependence on ecosystem services, particularly as laid out by the Millennium Ecosystem Assessment,[90] has spawned a great deal of work on "payment for ecosystem service" schemes designed to help conserve natural ecosystems and the services they provide to people. This work includes programs such as REDD (Reduced Emissions from Deforestation and Degradation), designed to stabilize forest carbon. These programs, along with extensive work in ecological economics, are designed to make humans into better stewards and managers of biological diversity.

The Convention on Biological Diversity also recognizes the issue of ownership of biota and materials derived from what has been called nature's endowment. So, the politics of ownership extend well beyond the protected area itself to include plant and animal matter and the products that might be developed from that material through innovation. The importance of this issue is indicated by the growing literature on global patent protection for improvements on nature and the corresponding contested discussions of ownership between North and South, and between government and private agents. Accordingly, the CBD promulgated the Nagoya Protocol on Access and Benefit-Sharing in 2010, the principles of which diminish the private appropriation of biodiversity.

At heart, there are profoundly complex interrelated dependencies and conflicts between human-mediated genetic innovation and our current system of legal rights and protections concerning the private ownership of intellectual property. Biology in its entirety can be understood as one interdependent, complex, and open living system. This living system shares a common language based on the nucleic-acid base pairs that make up our DNA. Sequences of base-pairs are freely shared through a variety of channels – including sexual reproduction and inheritance, horizontal transfer, and the incorporation of environmental DNA. To date, human-engineered genetic innovations have been fully dependent upon this common, pre-existing, and open biological alphabet and language – which is our shared evolutionary legacy. Given this circumstance, the question of whether or not sequences of genetic code should be subject to private ownership and copyright or patent protections is profound, and raises fundamental issues regarding the privatization of the commons.

Conservation and Ecological Restoration

There is a much longer tradition of action to conserve species and ecosystems than of restoration, the third major conservation strategy. Formalized only in the 1980s, restoration ecology was based on efforts begun in the second half of the nineteenth century. It has focused primarily on restoring ecosystems but has also been used to restore species populations, particularly in island settings.[91] Restoration has often proven to be expensive, requiring long-term investment and obtaining uncertain success rates, especially in regards to the return of functions as well as form.[92] While it is possible to show positive return on investment from restoration, conservation will often be the better option.

5. Biodiversity Conservation and Synthetic Biology

We do not know what impacts synthetic biology will have on biodiversity conservation. There are some who are convinced that the effects will be positive and an equal number that are convinced they will be catastrophic. What follows is a discussion designed to help inform and to stimulate further discussion during the meeting.

There is a range of potential negative impacts of synthetic biology on biodiversity: land conversion for crops that were developed using synthetic biology may cause immediate, direct effects on species, ecosystems and protected areas; there may be complex secondary effects on society and economy as well (e.g., land conversion by people displaced or impoverished by first order changes). These complex interrelations are addressed in this section. But, of equal significance, synthetic biology could provide conservationists with more effective methods of conservation, including the creation of new tools that can help to gather and process field samples affordably or to monitor for the presence of particular threats – be they pathogens or chemicals. Likewise, synthetic biology could be used to reintroduce lost genetic variation into extant, but diminished and threatened populations.

Synthetic Biology and Species Conservation

Synthetic biology may directly affect species conservation in various ways. Most significantly, it may provide a mechanism for overturning one of the catch phrases of conservation: extinction is forever.[93] Synthetic biology techniques are being used or proposed for use in recreating extinct species (e.g., mammoth[94] and passenger pigeon[95]). An initiative entitled "Revive and Restore" has brought together many disciplines to assess the feasibility and advisability of such actions.[96]

These possibilities raise a set of complicated ethical questions for conservation that include:

1) If synthetically produced species can replace extinct ones, then what is lost?
2) When is a synthetically recreated species "enough" like the species it is designed to recreate?
3) Are novel species that perform vital ecological functions supporting endangered species to be embraced or eschewed?
4) Is genetic variation introduced via synthetic means any different than naturally produced variation? Would natural selection acting on these two different types yield different results?

Synthetic biology may also affect the evolutionary processes that conservationists strive to maintain. Some have maintained that synthetic biology-mediated horizontal gene transfer, common among bacteria, will replace Darwinian evolution.[97] Horizontal gene transfer is defined as "the process of an organism passing DNA to another organism that is not its descendant and that need not even be closely related."[98] Scientists are creating alternate genetic codes not based on the usual four amino acids that could be used to help make semisynthetic life forms.[99] This is called xenobiology by some[100] and is promulgated as a means of making impossible the transfer of engineered modifications out of target organisms and into other taxa.[101] That is, by creating an alternate genetic code, there would be little to no concern about movement of synthetically based traits into naturally occurring organisms. Such actions, proposed or achieved, promise the previously unimaginable fact of releasing into the world an entirely new and completely unrelated tree of life.

The creation of such novel organisms creates a challenge for conservation and raises both empirical and normative questions. How should such taxa be viewed? Are they new forms of biodiversity (and thus also the responsibility of conservation), or are they a new form of threat? Will these newly engineered taxa, with or without novel DNA, be able to exchange genetic material with non-engineered taxa? And if they can, how should the hybrids be classified? And how should we classify hybrid taxa that are partially endangered taxon and partially

unrelated, non-endangered taxon? As the creator of what he calls the first "synthetic species," a fruit fly, Moreno[102] claims that "the transition from transgenic organisms towards synthetic species could constitute a safety mechanism to avoid the hybridization of genetically modified animals with wild type populations, preserving biodiversity." Some, including Freeman Dyson[103] have even stated that "Genetic engineering, once it gets into the hands of housewives and children, will give us an explosion of diversity of new living creatures, rather than the monoculture crops that the big corporations prefer. Designing genomes will be a personal thing – a new art form, as creative as painting or sculpture."

One of the constraints that synthetic biologists face is the fact that natural selection can act on alterations they have made in the genome of an organism. Conversely, this same evolutionary action can be used to improve synthetic designs through in vitro selection.[104] As Snow and Smith[105] point out, many of the features of organisms that make them attractive for gene discovery and metabolic engineering, such as microalgae, also "complicate efforts to assess gene flow and evolutionary consequences over the long term." The action of horizontal gene transfer and other methods of increasing genetic variation have the potential to move synthetically-engineered genes out of the modified organism and into other taxa, some only remotely related to the original organism. For example, horizontal gene transfer has even been responsible for moving algal genes into animals.[106] The development of sophisticated, fast, and increasingly inexpensive ways of analyzing genomes has allowed a progression in our understanding of how genes move and can be shared between species. The advent of synthetic biology techniques puts into human hands an ability to move genes that is far in advance of our understanding of the functioning of this part of the natural world.

Synthetic biology's focus on microorganisms brings to the fore the lack of attention this very diverse and ubiquitous group of taxa has received from the conservation community. Several authors warn that our understanding of ecology has largely been derived from large organisms, and that this is not a good predictor of the ecology of the microbiota for a number of reasons.[107] The liberal exchange of genetic material through horizontal gene transfer, movement of DNA through viruses, or uptake of 'naked' DNA[108] may interact both with the genome as well as with the microbiomes of species to alter genomes, behavior and ecological functions in ways that we have yet to understand. Additionally, the cooperative behavior of some bacteria[109] which can form consortia, or "communities of multiple species that are capable of performing more varied and complicated tasks than clonal populations,"[110] makes even more difficult extrapolation from larger to smaller organisms.

Finally, natural diversity remains the most important source of genetic diversity used by synthetic biologists. High throughput machines have been used to assess millions of microbial genomes in many of the world's biomes,[111] and more targeted searching in tropical rainforests identified a microbe that may greatly improve dissolving of cellulosic biomass in biofuel production.[112] Conservation of intact ecosystems is important to maintain this diversity of taxa, and their conversion can result in substantial losses of species, including microbial taxa.[113]

Synthetic Biology and Ecosystems

Although synthetic biology is about the alteration of the genomes of organisms, recent work has shown the unexpected, and sometimes strong, interactions between the genomes of organisms and community and ecosystem level processes.[114] Genetic diversity has been shown to affect ecological processes such as primary productivity, population recovery from disturbance, interspecific competition, community structure, and the fluxes of energy and nutrients.[115] Work on a few "foundation species" has illustrated the genetic basis of ecosystem processes and how genetically modified plants may influence bacterial communities, the establishment of mycorrhizal fungi, soil respiration, and interactions with insects.[116] This work suggests that there may be ecosystemic impacts of altering the genome of novel organisms released into the wild.

Eventual release of restored or genetically modified species may pose risks to existing communities and organisms. The ecosystems that came into being after the extinction of the restored species may be changed post-reintroduction in ways that are harmful to the persistence of current species. On the other hand, restoration of important forest trees like the American chestnut may recreate ecosystems that increase the conservation value of these forests. The fate of novel genetic material in the nuts as they move through the foodchain is unknown.[117] Nonetheless, concerns continue to be raised about the potentially serious, direct and indirect impacts that escaped genetically-altered organisms might cause.[118]

Restoration of damaged or destroyed ecosystems may be expedited through use of synthetic biology. This may include recreation of previously occurring ecosystems such as chestnut forests of the northeastern US or creation of novel ecosystems in areas which have been heavily polluted or destroyed.[119]

Additionally, genetically modified organisms have been developed to help detect ecosystem-level impacts like pollution, including fish developed to detect endocrine-disrupting chemicals[120] and plants to detect soil pollution.[121]

Finally, synthetic biology organisms could directly affect existing protected ecosystems in a variety of ways:

- becoming invasive or otherwise affecting populations of protected species or disrupt protected ecosystems
- changing the economic value of land (and hence demand for land) within protected areas (e.g., making crop production possible in land currently regarded as marginal for agriculture and hence allocated as a protected area)
- changing the way land surrounding protected areas is used and hence affecting immigration and/or extinction of species inside it
- accelerating (or slowing) the rate of ecosystem conversion outside protected areas and hence the relative importance of existing protected areas (e.g., reducing pressure on habitats like tropical forests and making protected areas less necessary and therefore uneconomic to run)
- changing demand for products currently illegally harvested from protected areas (e.g., meat, timber, non-timber forest products)

Indirect Effects of Synthetic Biology on Conservation

Little is known about the possible direct effects of synthetic biology on conservation, but even less is known about the indirect effects. However, there has been greater interest in, and attention to, the indirect effects, including by environmental advocacy groups opposed to the broad-scale implementation of synthetic biology. A focus of this concern has been on production of inputs or "feedstocks" for the production of fuel using synthetic biology approaches.[122]

Synthetic biology extends existing biotechnology capabilities in several ways, and because of this it may exacerbate the potential for socio-economic and environmental impacts. The technology promises faster, cheaper and more tightly designed innovation in crop systems. It depends on sophisticated research capabilities, and new 'living systems' are therefore more likely to be developed in the industrial world, especially by private interests. Advances in crop systems through the application of synthetic biology are therefore vulnerable to exactly the same critiques as existing biotechnologies: they will offer more dramatic advances, faster, and less under the control of developing world research agencies and producers. Where the outcomes are positive, the benefits will be felt quickly and widely. If the outcomes are negative, those impacts will also be felt early and widely.

Synthetic Biology and Land-use Change

The greatest concern currently expressed about synthetic biology and land-use change arises from what might happen if production of fuels and other products (including plastics and chemicals) from biomass is made much more economical due to synthetic biology.[123] It is difficult to separate the portion of this debate that is about synthetic biology from that which is connected to biofuels in general. The expansion of biofuel production has a range of impacts on environment and society and has been extensively examined.[124] Many production pathways that deliver yield useable energy from biological feedstocks and platforms do not yet involve developments in synthetic biology, but to some other biotechnology innovation. However, the importance of synthetic biology to biofuel feedstock development is growing rapidly.

There are several possible land-use implications of the rise of synthetic biology that involve not only biomass production but also food crops. First, there are direct impacts on biodiversity where the area under biofuel crops expands at the expense of areas of biodiverse habitat and associated ecosystem services such as carbon storage (e.g., tropical forest or savanna). Where biofuels are grown intensively, pesticides and fertilizer runoff create negative externalities with the potential to have wider impacts on biodiversity across wider areas of land, and in freshwater and coastal and perhaps marine ecosystems. Additionally, the ecological characteristics that make a plant suitable for a biofuel feedstock also may increase its chance of becoming an invasive species.[125] And it may change such system characteristics as soil-atmosphere interactions at the local scale, which may accumulate globally. Large areas for production facilities based on algae may be required, putting pressure on wetlands, mangrove areas, and deserts.

Second, there are impacts on biodiversity of indirect land-use change as a result of the adoption of biofuel crops.[126] Displacements occur across national borders (e.g., the EU's importation of biofuels that it subsidizes to be grown in developing countries) and between crops. Biofuels compete with other uses of existing crops, with knock-on effects on food markets.

Third, there can be social impacts of increasing commercial demand for land suitable for biofuel cultivation. Fairhead et al.[127] argue that this contributes to the problem of "green grabbing" ("the appropriation of land and resources for environmental ends"). Their argument is that real or anticipated profits from biofuels (especially demand stimulated by government regulation, as in the United States and the EU) leads to the takeover of ownership and use-rights over land previously publicly or communally owned or land set aside for conservation.

Synthetic biology may also affect land-use for food production. It is an increasingly important technology for the creation of improved varieties of food crops. The mapping of the crop genomes (including tropical crops important to the food security of resource poor rural households, like sorghum or cassava) opens up the possibility of rapid improvements in crop performance and perhaps greater area in planting. Expansion of the agricultural frontier through the conversion of previously uncultivated lands for the use of new crop varieties (for example those adapted to salinity or poor nutrient soils) could have potentially serious impacts on biodiversity.

Synthetic biology is being applied to the production of a wide range of high-value plant metabolites such as fragrances, flavors, pigments and medicines.[128] Some non-timber forest products are also being targeted for production in microorganisms, such as natural rubber.[129] Products from other extensive tree crops, such as palm oil, are being targeted for production through synthetic organisms. Developing new modes of production through such synthetic biology techniques can shift the production and the markets for existing crops and products with corresponding impacts on land-use and rural producer livelihoods.[130]

Synthetic Biology and Rural Households

Biofuel crops will most likely compete with other crops, especially food crops. The cultivation of biofuel crops in food-deficit regions such as the Sahel is likely to have a negative impact on food availability and price: profits for the larger biofuel farmer may be accompanied by high urban food prices and hunger for households living in food poverty. The evidence for these relationships is inconclusive given the short time this has been occurring. The pass-through relationship between biofuel production and commodity prices is complicated, and the last decade has witnessed huge spikes and troughs in food prices.

The development of synthetic-biology versions of some currently collected or cultivated natural products may change local livelihoods and land-use patterns to the detriment of rural households.[131] Production of products like minor forest projects has always been subject to market fluctuations, with many producers entering and leaving the market based on price. Such synthetic biology products may exacerbate the switching of production systems.

Synthetic Biology and Human Health

There are numerous examples of the potential use of synthetic biology to contribute to human wellbeing and health, for example genetically modifying mosquitoes to fight dengue,[132] and early successes in engineering algae to produce anti-malaria vaccine[133] and cancer drugs.[134] Increasing the availability and decreasing the costs of anti-malarial drugs has the potential to significantly alter the livelihoods of rural producers in many part of the world, particularly sub-Saharan Africa. Synthetic biology strategies are also being applied to target infectious diseases and cancer, develop vaccines, engineer the human microbiome, and develop cell therapies and regenerative medicine.[135] The potential impact of such developments on continuing improvements in human health is very complicated to predict.

Improved health of rural communities is reflected in enhanced availability of agricultural and herding labor, and improved productivity. It also potentially contributes to improved school attendance and performance, and therefore potential for the development of off-farm incomes. Where women are free to control their own fertility, and family planning technologies are available, improved health can form part of reducing family size and hence stabilizing population. Population growth (and corresponding consumption) are key macro-scale drivers of biodiversity loss. It is unclear what role synthetic biology and its products will play in these relationships. Will they simply be a rate modifier, speeding up or slowing down these processes, or will they offer fundamentally different solutions than those that are currently possible, or conceived of?

Synthetic biology and novel products

Synthetic biology also enables the creation of novel uses for existing crops – for example, we have known for over a decade that genetic circuits enabling the production of pharmaceuticals and industrial compounds within cells can be successfully integrated into the germplasm of common crops, such as corn or tobacco – allowing these plants to be "appropriated" as production platforms for desired molecules.[136] Similar opportunities have proved possible using animal systems as production platforms. For example, synthetic biology tools have been used on goats so they will produce spider silk in their milk[137] and pigs so that their organs can be used for human transplants[138]; camels are expected to be used to produce drugs in their milk,[139] and an altered salmon with much higher growth rates has been approved for human consumption.[140]

6. Learning to live with synthetic biology

The future will undoubtedly feature synthetic biology, but yet to be determined is the shape and extent of its role. There is no single entity with control over the development of synthetic biology. To the contrary, there are active efforts to decentralize the technology and create a "DIY" (do it yourself) culture.[141] One of synthetic biology's pioneers, George Church, has written glowingly of the promises this new technology will bring including improving human and animal health, extending lifespan, increasing intelligence, and resurrecting extinct animals –even hominids.[142] It seems inevitable that synthetic biology will proceed in developing new products based on new or modified organisms, despite the frequent calls for more oversight of synthetic biology and the desire for governments to put in place regulations specific for this field.[143] The institutions to put such restrictions in place simply do not currently exist. Efforts to similarly influence the Cartagena Protocol on Biosafety and the Convention on Biological Diversity have not as of yet yielded results. There are very strong voices in opposition to the deployment of synthetic biology, mostly from the environmental/social advocacy community.[144] And there are disagreements on the role that synthetic biology should play both in Europe[145] and in developing countries.[146]

Conservationists may chose to ignore synthetic biology but they do so at their own risk and the risk of the biodiversity they are devoted to conserving. Synthetic biology is a fact and the fact that it is being pursued throughout the globe by governments, industries, academics, and individuals means that it will be with us for a long time. But given the early stages of its development, it is a key time for the conservation community to engage and to try to influence the practice and outcomes. It is also a key time for the synthetic biology community because, as Pauwels[147] observes, "When industry is trying to introduce a new technology, public trust has large strategic implications as the market for that technology develops. A key variable for consumers is whether companies handle this new technology in a socially and environmentally responsible manner."

Promises of a future in which synthetic biology has solved all of humanity's major problems jostle with promises of a future in which synthetic biology has exacerbated the injustices and environmental damages. In a telling comment, Marris and Rose[148] point out that "It is often left up to the most vocal critics of new technologies to articulate the complexities in public, and this is also the case for synthetic biology."

Hype and exaggerated claims are counterproductive to developing adaptive and ethically sound regulatory models responsive to stakeholder concerns.[149] In order to operate and to prosper, synthetic biology must engage with the larger society and secure societal permission from regulators and from the public.[150] This engagement with ethicists, anthropologists, the policy and advocacy communities, and the larger scientific communities has typified synthetic biology in the United States and Europe.[151] The British public is increasingly aware of synthetic biology and its potential benefits and drawbacks, and in general it shows conditional support with concerns about control, who benefits, health and environmental impacts, and misuses and governance.[152] Most Americans support moving forward with the science but are concerned about the creation of biological weapons, the moral implications of synthetic biology, and negative health implications; they are to a lesser extent concerned about environmental damage.[153] Support is highly contingent on how the public thinks the science will be used.[154]

To gain public and regulator trust and support, the synthetic biology community must respond and be seen to respond to expressed concerns. Commentators have pointed to a variety of factors that need to be seen as part of the development and application of synthetic biology, including distributive justice and fairness,[155] scientific uncertainty,[156] public beneficence, responsible stewardship, intellectual freedom and responsibility, and democratic deliberation.[157] As Sandler[158] stated about nanotechnology, what a society should want from an emerging technology is "that they contribute to human flourishing in socially just and environmentally sustainable ways."[159] Conservation practitioners need to be part of these discussions.

7. The need for a "new" conservation

Despite local successes, conservationists have not been succeeding at their objective of conserving greater biodiversity. Numerous measures have been applied to quantify this lack of success, and a general air of despair has settled over the field. In the last few years there have been strong voices demanding a new approach to conservation, called by some the "modernist movement,"[160] one that particularly incorporates human wellbeing into the goals of conservation. Debate rages around this topic and about the need to change the approach, the methods, and the values of conservation.[161]

However, little of this debate has addressed two of the most dramatic technologies that are being developed – geoengineering and synthetic biology. These two are not equivalent in the stage of their development or their discussion. Concern over the reality of climate change and its impact on humanity and the rest of the natural world are driving the discussion about climate-related geoengineering: a deliberate intervention in the planetary environment of a nature and scale intended to counteract anthropogenic climate change and its impacts.[162] Geoengineering is outside of the scope of this Framing Paper but represents a major threat and/or opportunity for conservation.

Synthetic biology is much further in its development and testing than geoengineering. Its very development raises a set of key issues for conservation (modified from Redford, Adams, Mace).[163]

- Extinction may not be forever. There are on-going attempts to recreate endangered species using the tools of synthetic biology. If successful, would such species be regarded as representatives of the species to which extinct forbears belonged? Or would they be viewed as "invasives from the past" and a threat to existing species? In accounting terms, how would extinction rates in conservation targets deal with recreated species? Currently such experiments are slow and hugely costly, but if such costs fall as some predict (by analogy with the costs and power of computing), such re-creations might become routine and affordable. How would choices be made about which species to save? More fundamentally, what conservation value would these forms have if the habitats that once supported them are gone? Might we face the moral hazard whereby confidence in our ability to recreate extinct species undermines our willingness to conserve naturally occurring biodiversity?[164]
- Synthetic life evolves. How will synthetic organisms interact with existing species and how far will such interactions be predicable from current ecological understanding of interspecific interactions? Will they become invasive and damage existing communities, or might they be safe and useful in restoring degraded or polluted ecosystems, or might they even address other ecological problems that have been intractable to date? Will the incorporation of synthetic organisms into ecosystems (e.g., through field agriculture, medical application or accidental release) be seen as adding to the living diversity of the ecosystems in which they are incorporated, and if so, will these be judged as of higher value, or will loss of authenticity mean they are judged degraded?[165] Who will regulate the release of synthetic organisms outside the contained laboratory: will the permissive regulatory environment of 'garage biology' be widely endorsed, will national governments try to establish individual regimes, and how will local and international views on the matter be taken into account?
- Our various definitions of "natural" will no longer be fit for purpose. Much of conservation is based on conserving ecosystems developed through ecological and evolutionary processes over the course of time, sometimes reflecting tight sets of inter-linkages that are hard to restore once lost. Will interactions between synthetic and natural organisms arise easily, or might the very different origins lead to largely disruptive impacts on natural communities? What would be the change to public perceptions of what is "natural" and the notion of evolution as a process beyond human construction?[166] Will these technologies challenge the ethical basis for conservation action, as they have done in other settings?[167] How will we evaluate organisms created using novel nucleic acids as part of their genetic code – products of xenobiology?[168]
- Nature's services can be synthesized. The value of an ecosystem to society is increasingly central to arguments about the importance of biodiversity.[169] One of the most common promises of synthetic biology is to engineer organisms that generate services of benefit to people (e.g., carbon sequestration, pollution control). What impact will this have on the relative value attached to natural ecosystems that already deliver these ecosystem services? Might ecosystems containing synthesized elements out-compete existing evolved ecosystems, delivering more services with less biodiversity?
- Synthetic life delivers private benefits. Many forms of life being developed by synthetic biology are being patented. The benefits provided by these organisms will reflect the economic interests of those able to invest in and develop them. This may well favor applications in existing industrial processes and commodity chains (energy, agriculture, aquaculture) and the operations of large business corporations. Impacts on the wider environment will tend to be treated as an externality. Corresponding impacts on price and other economic changes for smaller producers (e.g. smallholder farmers) will affect their decisions about land conversion and management, and hence future patterns of biodiversity loss. How will a balance be struck between private risk and gain versus public benefit and safety?

A serious need exists for wider discussion of the relationship between synthetic biology and biodiversity conservation and what choices society can and could make. But this discussion is difficult, for two reasons. First, synthetic biology is a technical field little understood by non-experts. It will be difficult to create conditions for representative groups from society to engage in a well-informed, structured and balanced discussion. Second, these discussions are hard to frame because it is difficult to identify the right counterfactuals or alternative futures to compare with those underpinned by the new technology. It seems inevitable that synthetic biology will be a major factor in affecting the future. But that future world will not be a slightly older version of the world that we currently inhabit. Rather, it will have a significantly altered climate, changed sea levels, novel pests and diseases, non-analog ecological communities, and a human population with changed priorities. The costs, benefits and risks of synthetic biology need to be considered against that backdrop, not against a projected version of the present as is the common practice, but rather through mechanisms such as scenario development.[170]

But despite these difficulties, the discussion between conservation and synthetic biology must take place. It cannot be based on alarmist or triumphalist positions but on a clear-eyed examination of the norms, oversight, and public education necessary to make decisions about the enormous power of altering life on Earth. Such a careful, respectful, public discussion must examine the continuing role of conservation values. Much of conservation as currently practiced is predicated on the core ideals of wilderness and nature, though other practices envisage a carefully managed planet with all the biological components in place – albeit carefully tended by conscientious (human) custodians. Synthetic biologists propose to further equip humans to actively and consciously engineer the living world. The transformed world of 2050 will demand new strategies and new approaches in conservation. Synthetic biology can and should be incorporated into these as a powerful new tool to face the powerful new challenges facing conservation.

As we prepare for the meeting and engage in the discussion we should be asking ourselves, and each other (at least) two questions:

1) How might the tools and capabilities of synthetic biology best be put to use in the service of the goals and objectives of conservation biology?

2) How can the practice of synthetic biology be illuminated and modified based on the values of conservation?

We look forward to your participation in the meeting and to carrying on for many years the conversations we start there.

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