



Genetic frontiers for conservation

An assessment of synthetic biology and biodiversity conservation

Synthesis and key messages



INTERNATIONAL UNION FOR CONSERVATION OF NATURE

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About the IUCN Task Force on Synthetic Biology and Biodiversity Conservation

The IUCN Task Force on Synthetic Biology and Biodiversity Conservation and its accompanying Technical Subgroup were put together to accomplish the tasks laid out in Resolution WCC-2016-Res-086 from the 2016 World Conservation Congress. This Resolution (in part) called on the Director General and Commissions to undertake an assessment to:

examine the organisms, components and products resulting from synthetic biology techniques and the impacts of their production and use, which may be beneficial or detrimental to the conservation and sustainable use of biological diversity and associated social, economic, cultural and ethical considerations...

In addition, it called upon the Director General and Commissions with urgency to:

assess the implications of Gene Drives and related techniques and their potential impacts on the conservation and sustainable use of biological diversity as well as equitable sharing of benefits arising from genetic resources...

This assessment is the result of the work of the Technical Subgroup managed by the Task Force. Both the Task Force and the Technical Subgroup were established in January 2018.

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The views expressed in this publication do not necessarily reflect those of IUCN.

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Many thanks to the other members of the IUCN Task Force on Synthetic Biology and Biodiversity Conservation and its Technical Sub-Group: Drew Endy, Sonia Peña Moreno, Gernot Segelbacher, Cyriaque Sendashonga, Risa Smith, Simon Stuart, Wei Wei, and Anne Gabrielle Wüst Saucy. We are also most grateful for help from Carolyn Pereira Force, Roisin Gorman, Sarah McKain, Deborah Murith, Leonor Ridgway, Melanie Ryan, and Victoria Romero. Many thanks to Owain Edwards, Kate Jones, Alfred Oteng-Yeboah, and all expert peer reviewers of the manuscript, and to the Luc Hoffmann Institute for accelerating this work.

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Cover illustration: Working with the tools of synthetic biology will present conservation with a number of challenges and opportunities that will ripple across the natural world, impacting species and ecosystems discussed as case studies in the full assessment “Genetic frontiers for conservation” – island endemic birds (top left), island invasive rodents (bottom left), black-footed ferrets (bottom right), honeybees (left), horseshoe crabs (top right) – and many more.

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Foreword

The explosion of knowledge that research on DNA has brought has been extraordinary. The recent, rapid development of gene sequencing and editing technologies has led to the creation of a new generation of tools. The technologies that allow humans to alter the genes of organisms to make them do things that humans want and that those organisms would not normally do—for example, creating yeast that can make plastic or human medicine—is called synthetic biology. There is an active international discussion on how best to define the field.

Scientists now have tools available that in principle may allow them to make changes to the genetic makeup of nearly every species, including, but also extending well beyond, single gene manipulation. DNA can be copied into digital form, rearranged, turned back into organic form, then inserted back into living cells in an attempt to strengthen or create desirable characteristics or eliminate problematic ones. These new and rapidly evolving technologies create exciting opportunities in many fields, including new kinds of conservation, but they also raise serious questions and complex challenges.

It was both deep concern and qualified excitement that led IUCN to commission a broad assessment of the current state of science and policy around synthetic biology techniques as they relate to biodiversity. The goal of this assessment is therefore to provide a clear understanding, based on the best available evidence, of the issues regarding synthetic biology that are relevant to and may have an impact – positive or negative – on the conservation and sustainable use of biological diversity. Produced by a global team of practitioners and researchers, this assessment responds in part

to an IUCN Resolution adopted at the IUCN World Conservation Congress in 2016: “Development of IUCN policy on biodiversity conservation and synthetic biology” (WCC-2016-Res-086).

Application of synthetic biology to conservation is in its earliest stage. That makes the requirement that this assessment use an evidence-based approach more challenging but even more vital. While policy debates necessarily engage values and preferences, claims in support of, or in opposition to, synthetic biology that draw primarily from these need to be distinguished from those grounded in evidence. This assessment thus aims to shed light on the state of the field, with the potential benefits and harms discernible to date. It cannot be, and does not aim to be, a comprehensive risk assessment. Rather, the goal of this assessment is to inform future deliberations and increase the understanding of the different ways that evidence regarding the potential impact of synthetic biology on conservation is generated, used, and interpreted.

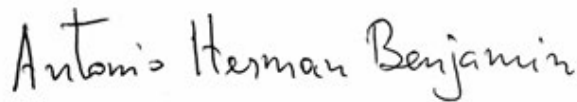
This assessment is the beginning of a process that will lead to the development of an IUCN policy to guide the Union’s Director General, Commissions, and Members. The draft policy will be discussed in many fora before it is brought to vote at the World Conservation Congress in 2020. Far greater public attention to the topic of synthetic biology and biodiversity conservation is essential, given the potential impact of scientific discoveries and policy decisions that may be just over the horizon, and also given the need for broad partnerships to address the challenges that the conservation and synthetic biology communities will inevitably face.



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Statement of principles of the IUCN Task Force on synthetic biology and biodiversity conservation

Recognising the complexity and large positive and negative potential impacts of the subject, both on and beyond the global conservation community, this assessment will draw on the values and proven processes of IUCN to provide a shared and trusted resource for subsequent deliberations.

In preparing the assessment on behalf of the IUCN membership, the Technical Subgroup has striven to adhere to the principles of:

Objectivity – assessing evidence and working to minimise and balance subjective bias;

Inclusivity – recognising and being considerate of the full diversity of views and interests;

Robustness – ensuring that all conclusions drawn are based on clear reasoning;

Humanity – interacting with all interested parties in a respectful and honest manner;

Transparency – ensuring that the process applied and all final outputs arising from it will be open access;

Consultation – giving meaningful opportunities for all interested parties to engage with the process, and responding to all formal submissions.

The work is all conducted under the umbrella of the IUCN Commission Code of Conduct and the IUCN Secretariat Code of Conduct.

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Synthesis

The American chestnut once dominated the forests of eastern North America, stretching the length of the Appalachian Mountains from Maine to Alabama and overlapping with historic territories of many Native American tribes. Legend had it that a squirrel could travel from the Atlantic Ocean to the Mississippi River without setting foot on the ground, just moving from one chestnut tree to the next. The fast-growing, majestic tree provided shelter and habitat for countless species, as well as wood, food and medicine to many generations of Native and European-American communities. An Iroquois legend, “Hodadenon: The Last One Left and the Chestnut Tree,” celebrates the chestnut as a life-giving food that, “like all the other good things given to us by Hawenio, our Creator, no longer belong to just one family, no matter how powerful they are, but are shared by all” (Freinkel 2009).

Then, in less than half a century, nearly all the chestnuts disappeared. A fungus native to East Asia arrived around the turn of the 20th century and spread quickly, killing billions of trees. Almost no adult chestnut trees remain; the tree exists now largely as a small, rare shrub that grows only a few feet tall before being killed by the blight.

Efforts to restore the chestnut to its historic range began decades ago. The initial approach was classic selective breeding: cross American chestnuts with the Asian species that is naturally resistant to the fungus, then back-cross the offspring over and over again in order to create a hybrid that is nearly all American chestnut, but with the resistance genes from its Asian cousin added. That method holds promise, but limitations

as well. Among the challenges, for example, several genes control resistance, so inheritance can never be certain, and the hybrid likely will never be as resistant as the Asian species.

There is another approach. Many other plant species contain genes for an enzyme that breaks down the compound the fungus produces that kills chestnuts. Using *agrobacterium*, a first-generation biotechnology for gene transfer, researchers have transplanted a gene for that enzyme from wheat into American chestnuts, creating a genetically engineered tree that resists the blight. These trees have already been planted in experimental forest trials, and once the formal regulatory approval process is complete, they may be planted in forests that have not held chestnuts for decades.

The genetically engineered American chestnut is based on a long-established technology but its use in American chestnut is an entirely new application that raises important scientific, legal, ethical and policy issues. What are the implications for the ecological communities that have developed since the chestnut disappeared? Is restoration of the pre-fungus natural communities even feasible now, with predictions of climate change? Are there health concerns for humans or animals who consume chestnuts from genetically engineered trees? What do Native American communities, who once depended heavily on chestnuts, say about the prospect of restoration, and what can we learn from the ongoing efforts to engage those and other communities with historic relationships with the forest? Considering these questions, might continued selective breeding be a better option?

Some concerned stakeholders object to the proposed release of the engineered American chestnut, on the basis that if approved, it would be the first genetically engineered forest tree to be legalised in the United States and would be the first approved for release into the wild with the

intention of restoring an ecologically significant tree to the forest. Some observers argue that the necessary long-term studies have not been done and thus the ways in which these potentially long-lived trees will interact with the forests of the eastern United States remains unknown.

These are the kinds of challenges and opportunities that led the International Union for Conservation of Nature (IUCN) to commission a broad assessment of the current state of science and policy around synthetic biology techniques as they relate to biodiversity. The goal of the assessment is therefore to identify the kinds of synthetic biology applications and products that might impact the conservation and sustainable use of biological diversity, both negatively and positively. Produced by a global team of practitioners and researchers, the assessment addresses the terms of an IUCN Resolution adopted at the IUCN World Conservation Congress in 2016: “Development of IUCN policy on biodiversity conservation and synthetic biology” (WCC-2016-Res-086). Among other things, that Resolution calls on the Director General and IUCN Commissions to:

- *examine the organisms, components and products resulting from synthetic biology techniques and the impacts of their production and use, which may be beneficial or detrimental to the conservation and sustainable use of biological diversity and associated social, economic, cultural and ethical considerations;*
- *assess the implications of gene drives and related techniques and their potential impacts on the conservation and sustainable use of biological diversity as well as equitable sharing of benefits arising from genetic resources;*

This assessment seeks to deliver these two mandates by taking as its starting point the approach used by the Intergovernmental Platform on Biodiversity and Ecosystem Services (IPBES). IPBES assessments “synthesize and critically evaluate peer-reviewed scientific literature, grey literature and other available knowledge, such as indigenous and local knowledge. The assessments include a review and synthesis,

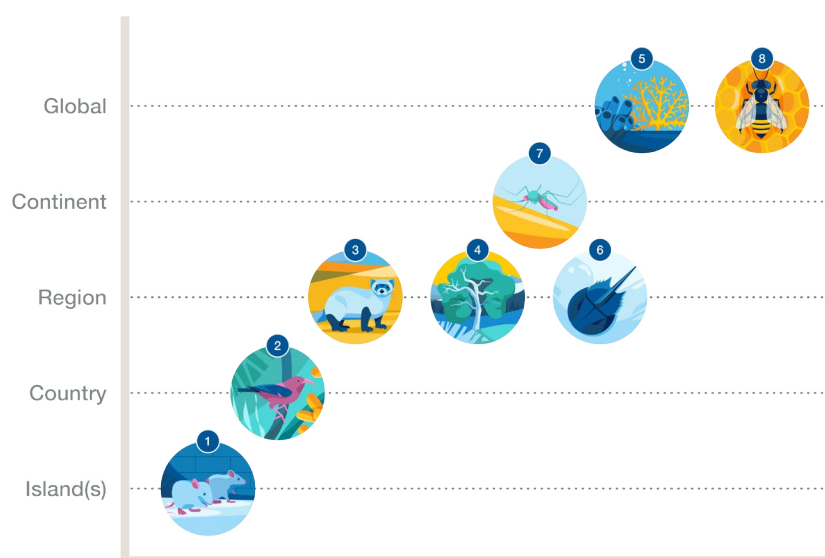
as well as an analysis and an expert judgement of available knowledge” (Scholes et al., 2018).

Many of the applications of synthetic biology and engineered gene drive systems, both those intended to have direct effects on biodiversity and those intended for other purposes, are in their early stages of development. This poses several challenges to the present assessment. First, it means that the purpose of the assessment is not to test existing hypotheses, but to gather information that may help lead to new hypotheses. That tends to move the assessment toward a narrative rather than a systematic review (Cook et al., 2017). Each of those approaches has strengths and weaknesses, but systematic reviews can be challenging to apply to complex or open questions like the application of synthetic biology to biodiversity conservation (Westgate & Lindenmayer, 2017).

The second challenge for the assessment has to do with the source of information and evidence regarding new and emerging applications of synthetic biology. Given that most of these applications are in conceptual or early developmental stages, the Technical Subgroup chose to solicit case studies as adjuncts to the main narrative review. The authors of the case studies were chosen on the basis of their detailed knowledge about those particular applications, most of which are in the early stages of development. That expertise adds depth to the analysis but by its very nature means that the input is shaped by a commitment to and a passion for addressing significant conservation challenges, for which they are currently exploring the feasibility of particular technologies. To some of these case studies the editors of the assessment added further details regarding potential negative impacts and broader socioeconomic considerations.

This assessment is not, and could not be, a risk assessment, but is part of the process by which IUCN will come to a policy approved by the membership regarding synthetic biology and conservation. Further, this assessment may help chart a way forward to decisions informed by empirical studies examining the efficacy, potential benefits and risks of synthetic biology. The IUCN Synthetic Biology and Biodiversity Conservation Task Force

Case studies of proposed synthetic biology by scale of application



- 1 Eradicating invasive rodents from islands.
- 2 Controlling invasive mosquitoes to prevent bird extinctions in Hawaii.
- 3 Synthetic biology to address conservation threats to black-footed ferrets.
- 4 Transgenic American chestnut for potential forest restoration.
- 5 Corals and adaptation to climate change/acidification.
- 6 Horseshoe crab replacement for *Limulus* ameocyte lysate test.
- 7 Gene drive approach for malaria vector suppression in Africa.
- 8 Addressing honey bee colony collapse.

Figure 1 Case studies of proposed synthetic biology by scale of application

and the IUCN Council look forward to continued engagement from across the conservation and synthetic biology communities on the results of this assessment and the ways it affects the draft policy.¹

By definition there is uncertainty regarding any conclusions about the potential impact of synthetic biology on biodiversity conservation. As a result, the Convention on Biological Diversity (CBD) explicitly applies a precautionary approach to synthetic biology (see Chapter 2). Nothing in this assessment should be seen as in conflict with that approach.

This assessment was completed in early December 2018, but the discussion on synthetic biology and the conservation and sustainable use of biological diversity continues globally, nationally and in communities around

the world. At the CBD's Conference of the Parties (COP) in November 2018, the topic was one of the central questions being debated. The COP reached two decisions of relevance to this assessment:

1. Parties recognised that synthetic biology has potential benefits and potential adverse effects on biological diversity, extended work of the Ad Hoc Technical Expert Group, and called upon Parties, other governments and relevant organisations to continue to share information on these positive and negative impacts. In the same decision, Parties also called for a precautionary approach in regards to engineered gene drive and agreed that Parties and other governments should only consider introducing engineered gene drives into the environment when case-by-case risk assessments have been carried

¹ The cut-off date for inclusion of in-press literature and unpublished evidence in this assessment was 16 November 2018.

out, risk management measures are in place, and when appropriate, the “prior and informed consent,” the “free, prior and informed consent,” or “approval and involvement” of potentially affected indigenous people and local communities is sought or obtained, where applicable in accordance with national circumstances and legislation.

2. Parties noted the divergence of views regarding digital sequence information and biological diversity and established a process to clarify the concept and consider benefit-sharing arrangements.

Two other important contextual factors surrounding this report need to be noted and addressed. First, the polarisation that surrounds debate over what can be called “first generation” genetically modified organisms (mainly insect resistant and herbicide tolerant traits engineered in agricultural crops) informs the context of new applications of synthetic biology

and this report. The polarisation around genetically modified organisms – i.e. all GMOs are either safe and beneficial or not safe and detrimental – makes it difficult to have a nuanced discussion about the conditions that lead to beneficial or detrimental use (e.g. How is the technology designed and tested? What is the social, economic, political and ecological context? Who is involved in the decision making?).

Second, one of the main concerns articulated by groups that have been critical of the conservation application of synthetic biology is that it may serve as a “Trojan horse” for other applications of synthetic biology. That is, applications of synthetic biology that seem beneficial for the environment will lead societal actors, government regulators and the public, more broadly, to turn an uncritical eye towards more questionable synthetic biology applications such as for military ends or to further consolidate control over agricultural systems.

Examples of the anticipated costs and benefits of conservation applications of synthetic biology

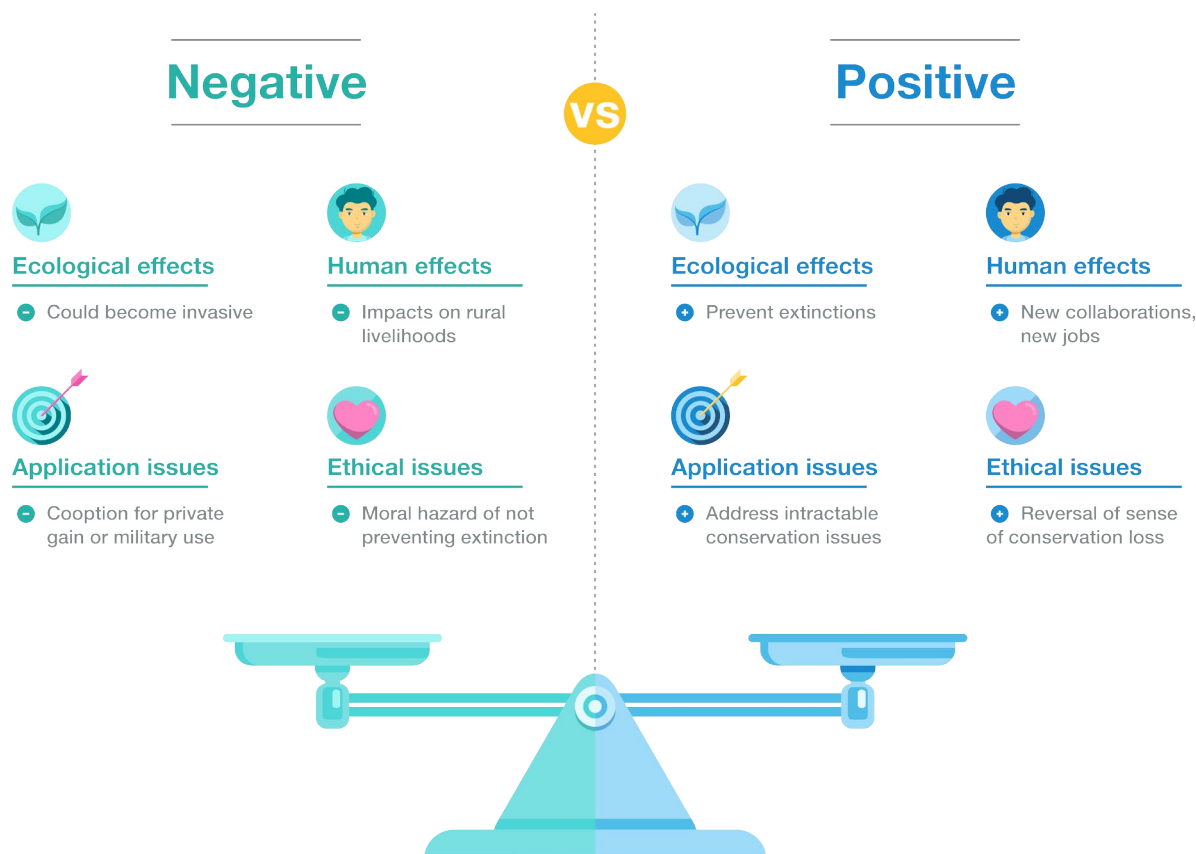


Figure 2 Examples of the anticipated costs and benefits of conservation applications of synthetic biology

This report seeks to inform nuanced discussions surrounding the future of synthetic biology for conservation. To accomplish this and to address the two points above, this report is built on the assumption that potential uses of synthetic biology need to be considered on a case-by-case basis. The fact that one application may be beneficial in a certain social, political, economic and ecological context should not imply that it would be beneficial in another context or that a completely different synthetic biology application is more likely to be beneficial. Different applications cannot be conflated and polarised thinking that bundles all applications together for summary judgement should be avoided. We elaborate upon the tensions and challenges facing this approach in Chapters 2 and 3. Our discussions in Chapters 5 and 6 of the ways that different applications of synthetic biology could be beneficial and detrimental should not, therefore, be seen as evidence for summary judgement of all of synthetic biology. Rather, this assessment is the beginning of the conversation, not the entirety of it, and hence seeks to raise the points that need to be discussed.

— What is synthetic biology?

Human beings learned long ago how to alter nature to our own ends, with implications for everything from genes to ecosystems. People in what is now southern Mexico bred maize from wild grass. At about the same time, some 10,000 years ago, people in China's Pearl River Valley bred rice from another type of grass, while in the Near East they transformed aurochs into domestic cattle. These breeding activities, which altered the traits of wild species so that they became more beneficial to humans, took place in the ecological and social settings of early domestication.

The intentional modification of genomes has been accelerating as science develops a deeper understanding of fundamental genetic processes and has moved the experiments from the fields to the laboratory. Gregor Mendel's experimental work with peas in 1856 is considered to be the beginning of modern genetics, but for the most part his work remained unnoticed by the scientific community. It was not until the mid-20th century, when James Watson, Francis Crick, and Rosalind

Franklin launched the revolution in molecular biology by identifying the structure of DNA, that science began to actively experiment with explicitly altering the biological basis of inheritance.

The explosion of knowledge that the study of DNA has brought has been extraordinary, possibly unmatched in its breadth, depth and pace in the history of science. The recent, rapid development of sequencing and editing technologies has led to the creation of a new generation of tools. The technologies that allow humans to alter the genes of organisms to make them do things that humans want and that those organisms would not normally do – for example, creating yeast to make plastic or human medicine – is called synthetic biology. It includes the broad redefinition and expansion of biotechnology (Chopra and Kamma, 2006). There is an active international discussion on how best to define the field of synthetic biology with some significance regarding legislation and treaties riding on exactly which wording is used. For this assessment we have chosen to use the definition supplied by the Convention on Biological Diversity as this is most closely related to the mission of IUCN:

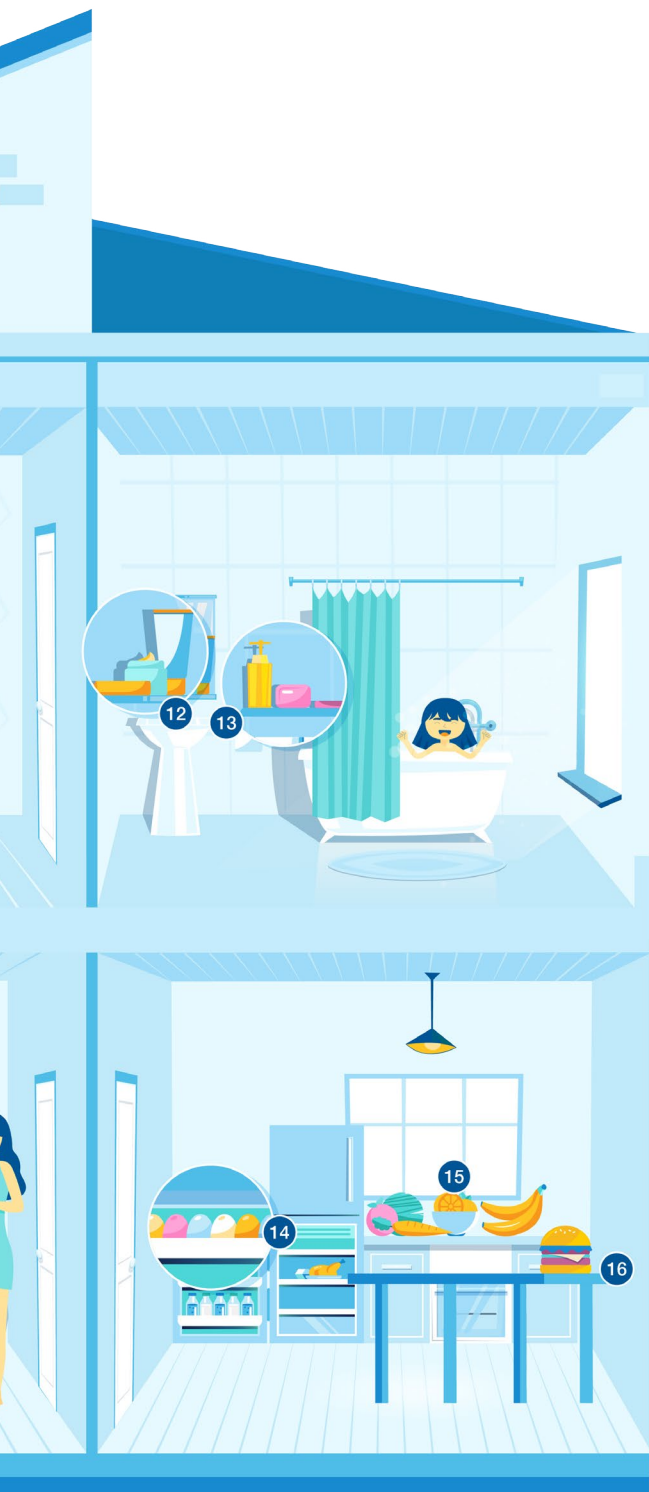
Synthetic biology is a further development and new dimension of modern biotechnology that combines science, technology and engineering to facilitate and accelerate the understanding, design, redesign, manufacture and/or modification of genetic materials, living organisms and biological systems.

It is important to consider, however, that synthetic biology and engineered gene drive systems are not discrete technologies but are among a set of tools that can be applied to various ends. The precise definition of whether a particular tool falls under the heading of genetic engineering or synthetic biology or some other field – as in the case of the American chestnut – is less significant than the way the tool is applied and for what purpose. Further, research into synthetic biology is progressing so rapidly that there may be revolutionary new approaches on the horizon before the IUCN policy-making process is even complete.

Scientists now have tools available that in principle may allow them to make changes to the genetic

A colorful illustration of a house with numbered labels 1 through 11, showing various parts of the house and its surroundings. The house is a two-story structure with a blue roof and light blue walls. The front yard features a large green tree (1) and a yellow car (4) parked in a garage. A man (2) is running towards the car, and a yellow bag (3) is on the ground. The house has a chimney (5) on the roof. Inside, the first floor shows a living room with a television (6) on a stand, a clock (7) on the wall, a sofa, and a woman holding a cup. The second floor shows a bedroom with a bed (8), a bookshelf (10), a dresser (11), and a pair of orange boots (9). The roof is labeled with the number 5.

6



- 1 **American chestnut tree**
Early versions of synthetic biology allowed scientists to engineer an American chestnut tree that is resistant to the deadly fungal disease that removed the trees from across the eastern U.S.
- 2 **Athletic gear**
Synthetic biology was used to engineer PDO, an essential component in high-performance textiles like running and outdoor gear.
- 3 **Fuel**
Synthetic amylases and other enzymes lower the cost of producing ethanol from grain.
- 4 **Technical fibers**
Spider silk is both stronger and lighter than steel. Silkworms engineered to produce this spider silk may one day be used to produce safer and more efficient cars.
- 5 **Bricks**
Biotechnology-based bricks are made with sand and bacteria fed with calcium carbonate, a key structural component of shells and coral reefs.
- 6 **Furniture**
Silk proteins produced by engineered yeast are woven into fabrics and garments like clothing or sofas.
- 7 **Medicine**
Synthetic biology technologies have been used to engineer immune cells to treat blood cancer.
- 8 **Wood products**
Synthetic biology helped create an alternative to the milk-based casein protein for use in imitation wood décor and flooring.
- 9 **Synthetic leather**
Microbes modified using synthetic biology approaches produce collagen that is formed into leather products.
- 10 **Paper**
Microbes and enzymes modified by synthetic biology can increase the efficiency of paper production and decrease the effects of paper manufacturing.
- 11 **Perfume**
Engineered yeast is now producing nootkatone, a food-safe product with many applications such as beverages and perfumes.
- 12 **Skin care and cosmetics**
Oils and moisturizers for make-up and other personal care products are being produced through synthetic biology, rather than being harvested from natural sources.
- 13 **Soap**
Soap made with oils extracted from synthetic algae instead of palm oil.
- 14 **Eggs**
Synthetic biology created phytase for chicken and pig feed, which helps the animals absorb more nutrients from their food and reduces phosphorous waste.
- 15 **Fruit**
Synthetic engineering helps prevent the browning process and reduces food waste.
- 16 **Meat**
Yeast altered with synthetic biology produce large quantities of heme – one of the key components for making lab-produced beef taste like real beef.

makeup of nearly every species including, but also extending well beyond, single gene manipulation. DNA can be copied into digital form, rearranged, turned back into organic form, then inserted back into living cells in an attempt to strengthen or create desirable characteristics or eliminate problematic ones. These new and rapidly evolving *synthetic biology* technologies create exciting opportunities in many fields, including new kinds of conservation, but they also raise questions and complex challenges.

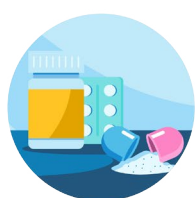
The promise of synthetic biology has attracted growing interest among researchers, developers, companies and the public. That interest has in turn led to new discoveries that have significantly broadened the application of the tools and approaches, with the potential for far broader change with direct, indirect and unanticipated consequences. The field is new and the tools are evolving very rapidly. At the forefront, there are strong proponents who think that synthetic biology is capable of solving many of humanity's problems and equally strong voices that argue that the technologies are dangerous and their potential application unproven and highly problematic.

One application of synthetic biology that has attracted particular effort and attention is the concept of gene drive. Under usual circumstances, if an organism, say a fruit fly carrying one copy of a modified gene, mates with another fruit fly, there is only a 50-50 chance that the offspring will inherit the modified gene. After

further mating with more unmodified flies, there is a smaller chance in turn that each of the offspring's offspring will carry it, just 50 per cent of 50 per cent, i.e. 1 in 4. Gene drive systems, which can occur naturally, change the rules so that a particular gene gets passed down with a higher probability than the usual 50 per cent. Using advanced genetic editing tools, scientists are working to harness the phenomenon and hope eventually to develop engineered gene drive systems in which there is a high likelihood that a target gene gets passed down and so can spread rapidly through wild populations. This assessment therefore uses the term "engineered gene drive systems" to distinguish between the naturally-occurring phenomenon and the product of human intervention through synthetic biology, the potential applications of which may be relevant to biodiversity conservation.

Human manipulation of the DNA code is now possible at a speed, specificity and scale unimagined just a few years ago, thanks to gene-splicing tools, a public repository of bioparts, sophisticated computer modelling software and supercomputers, and other advances that make up the field of synthetic biology. Application of these tools is also revealing some of their limitations. These tools and knowledge bring with them not just profound opportunities but also moral, ethical, legal, cultural, spiritual and scientific questions that will challenge our imaginations and our institutions for the foreseeable future and beyond.

Examples of proposed uses of synthetic biology technologies



Medicine

- i. Cancer treatment
- ii. Better and cheaper vaccines
- iii. Zika virus treatment
- iv. Health monitoring



Consumer Products

- i. Bioacrylics
- ii. Green chemicals
- iii. Synthetic leather
- iv. Data storage
- v. Spider silk garments



Agriculture

- i. More productive crops
- ii. More nutritious crops
- iii. Climate resistant crops
- iv. Removal of food allergens
- v. Lab-produced meat

Figure 4 Examples of proposed uses of synthetic biology technologies

Potential applications of synthetic biology to biodiversity conservation

The potential uses of new DNA technologies are vast, from new approaches to treating human disease, to improving crops to be more productive, nutritious or resistant to pests and blights, to biomanufacturing and even to application in fashion and information technology. Major investments are being made in the field with expectations of billions of dollars in markets in the coming years. The majority of investment as well as the focus of most concern to date has been in agriculture and human medicine.

Discussions and early laboratory work have begun on possible conservation biology applications to help in efforts to protect or restore biodiversity. It is clear to many observers that the potential direct

impacts of synthetic biology on nature could be profound and either positive or negative, and that the unanticipated indirect consequences of their use in other sectors, particularly agriculture, perhaps even more far-reaching. There are thus two major categories of potential impacts, positive or negative, of synthetic biology on conservation: those applications specifically intended for conservation benefit, and those that are not intended to have a conservation benefit but could have an indirect impact.

Applications in the first category of intended conservation benefit fall into two major groups: those that reduce threats (also known as mitigation) and those that increase resilience to those threats (also known as adaptation). An example of mitigation that is being explored is to use gene drive to eradicate invasive rodents on islands, one of the main causes of animal extinctions in those ecosystems. An

Ways that synthetic biology can affect conservation

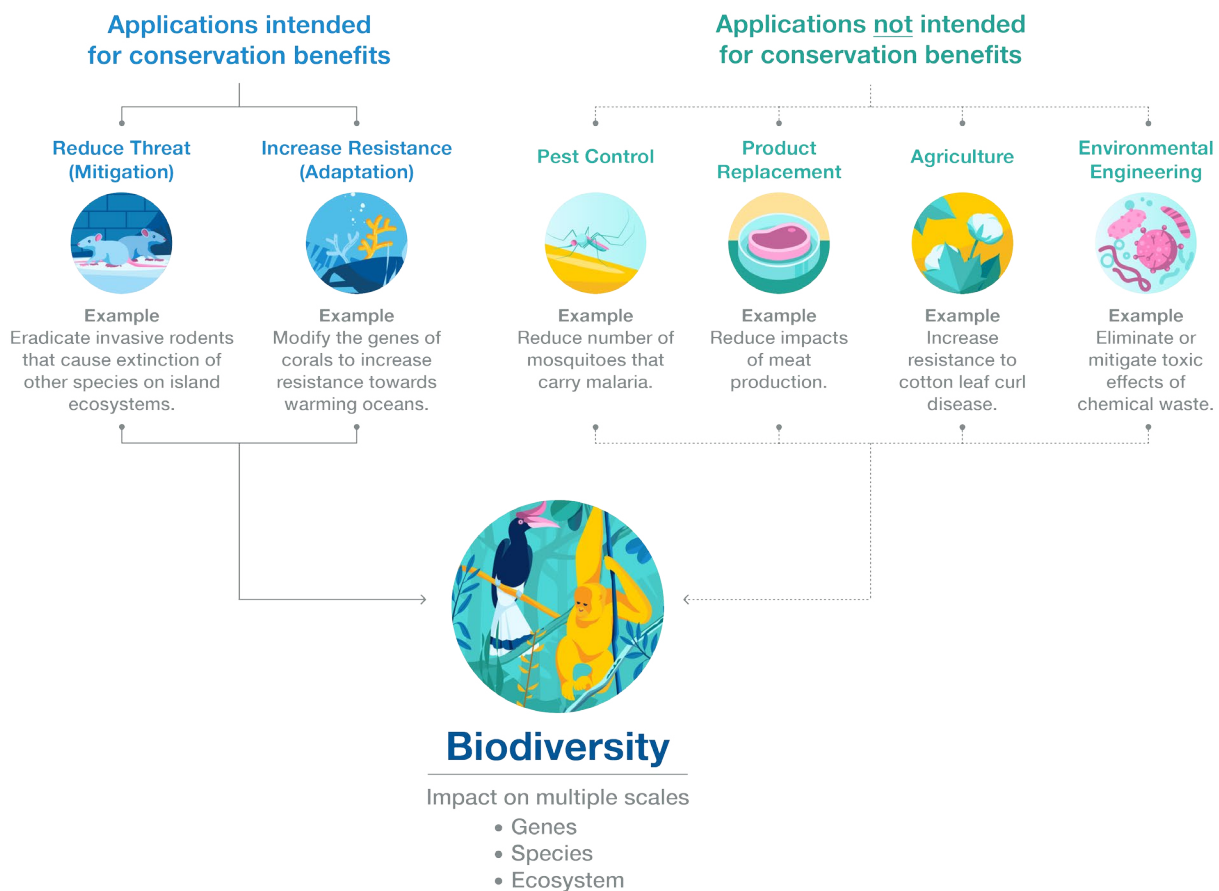


Figure 5 Ways that synthetic biology can affect conservation

example of adaptation might be to modify the genes of corals to increase their ability to resist the impacts of warming oceans resulting from climate change.

Applications in the second major category are not designed with a specific conservation end in mind, but could have an indirect impact, either positive or negative. For example, efforts to eliminate or greatly reduce the mosquitoes that carry malaria using synthetic biology approaches could eliminate a major cause of infant mortality in sub-Saharan Africa, a global public health priority. If these efforts, combining synthetic biology and more traditional approaches, are effective, changing demographic patterns and urbanisation could lead to significant changes in patterns of land use, with unknown impacts on biodiversity, though the same may be true for any effective disease-elimination programme.

— Evidence

Building on the work that has already taken place within the Convention on Biological Diversity, this assessment seeks to provide IUCN with a clear understanding, based on the best available evidence, of the issues regarding gene drive systems and other aspects of synthetic biology that are relevant to and may have an impact – positive or negative – on biodiversity conservation. While the idea that conservation needs to be an evidence-based endeavour is surprisingly recent, the argument for it is compelling: conservation practice needs to be rigorous and defensible, building on impartial standards that are free from ideology or political bias yet transparent in its advocacy for the natural world. From its inception, conservation biology has seen itself as analogous to medicine: a crisis discipline rooted in but not fully contained by the scientific method. As such, the development of evidence-based medical practice has been a powerful model for the move toward a similar expansion of the use of evidence in conservation.

There are, however, two challenges to developing an evidence-based approach to synthetic biology and conservation as mandated by the IUCN Resolution. The first is that the intersection of the two fields offers a perfect illustration of a “wicked problem”: ill-defined, with no clear boundaries, no right answer,

and dependent upon context and political judgement for resolution. The second is that while synthetic biology is making rapid advances, most of these with conservation relevance are still confined to the laboratory. Experience applying synthetic biology tools and techniques to actual conservation problems in real land- and seascapes is next-to-none. So we are confronting potential risks and potential benefits with limited data; determining what counts as the best available knowledge for assessing synthetic biology for conservation is a challenge in and of itself.

Application of synthetic biology to conservation is in its earliest stage. That makes the requirement that this assessment use an evidence-based approach more challenging but even more vital. While policy debates necessarily engage values and preferences, claims in support of or opposition to synthetic biology that draw primarily from rhetoric need to be distinguished from those grounded in evidence. This assessment thus aims to shed light on the state of the field, with the potential benefits and harms discernible to date. It cannot be, and does not aim to be, a comprehensive risk assessment. Rather, the goal of this assessment is to inform future deliberations and increase the understanding of the different ways that evidence regarding the potential impact of synthetic biology on conservation is generated, used and interpreted.

— The road ahead

This assessment is the beginning of a process that will lead to the development and approval of an IUCN policy to guide the Director General, Commissions and Members, and also draw far greater public attention to the topic of synthetic biology and biodiversity conservation. Such attention is essential, given the potential impact of scientific discoveries and policy decisions that may be just over the horizon, as well as the need for broad partnerships to address the challenges that the conservation and synthetic biology communities will inevitably face.

One crucial element of this process will be recognising and soliciting indigenous and traditional perspectives on synthetic biology. Some work in this regard is already underway, for example with tribal communities and

the potential deployment of genetically engineered American chestnut trees in historic territories of the Haudenosaunee peoples in the north-eastern US. Other efforts focus on Māori communities in New Zealand, starting from an understanding that there is no single Māori “perspective” on synthetic biology, but rather, many, and understanding this range of views requires deep engagement with diverse members of potentially affected communities.

Scientists, lawyers, ethicists and others have also begun to ponder the consequences of synthetic biology. And the world’s publics are also beginning to realise that they must pay attention to the ramifications of this complex and far-reaching field. The points of contact between conservation and synthetic biology are extensive, and the questions profound, yet for the most part people working in those fields remain apart, sharing little common language or common understanding of the problems they seek to address and the opportunities that each may provide the other. This assessment reveals that the dialogue between the synthetic biology and conservation communities can be productive, and in particular that not only do synthetic biologists have an important role to play in informing the future of conservation, but also the converse: conservationists have an important role to play in informing the development of synthetic biology.

— Coda

This technical assessment was released for review in September 2018, and 756 comments were received from a broad range of actors including civil society and governments. On 18 November 2018, a presentation of the assessment was made to about 130 people at the Fourteenth Conference of the Parties to the Convention on Biological Diversity in Sharm el Sheikh, Egypt. Both opportunities for comment generated a diversity of responses both positive and negative, including criticisms of the choice of authors and limitations of the process. The Technical Subgroup was aware of many of these concerns (see above) but the comment and review process offered a valuable opportunity to re-emphasise key issues. Specifically,

some raised the concern that the assessment authors did not represent the full diversity of actors who might be affected by applications of synthetic biology and engineered gene drive, and did include those who work directly on synthetic biology applications.

These are valid concerns: it is impossible for the authorship of such an assessment to span the full diversity of geography, discipline and life-ways; and to be possible, the assessment did indeed engage with those who are highly knowledgeable about the technologies, especially those who have been working at the frontiers of innovation. A further concern based on comments and subsequent published interviews was that applications of synthetic biology to the conservation and sustainable use of biological diversity, such as those included in this assessment, serve as a “smoke screen” for gaining social or regulatory approvals that would benefit future, detrimental applications of these technologies.

Recognising these concerns, this assessment was built on the assumption that potential uses of synthetic biology and engineered gene drive systems need to be considered on a case-by-case basis. The fact that one application may be beneficial in a certain social, political, economic and ecological context does not imply that the same technology would be beneficial in another context. Furthermore, different applications require different assessments, even if some knowledge is transferable. Advocates on both extremes lump all synthetic biology applications together for summary judgement. This lumping masks the complexity of the issues in favour of highly charged politics that fail to notice when different applications of synthetic biology could be beneficial, detrimental or a mix of both. Thus, this assessment should not be read as a judgement – positive or negative – on all synthetic biology or even all conservation applications of synthetic biology. Rather, it serves as an initial discussion of factors that will need to be considered in case-by-case decision making by the full range of appropriate stakeholders, operating with free access to all information, and informed by the framework of the precautionary principle.

Key messages

Each of the major sections of the Key Messages are linked to the parts (chapters or sections) of the Assessment from which it is drawn. Each of the sections is further qualified with an indication of the confidence with which it is held using a system modified from IPBES (IPBES, 2016) and the Intergovernmental Panel on Climate Change (Moss & Schneider, 2000) (Figure 6).

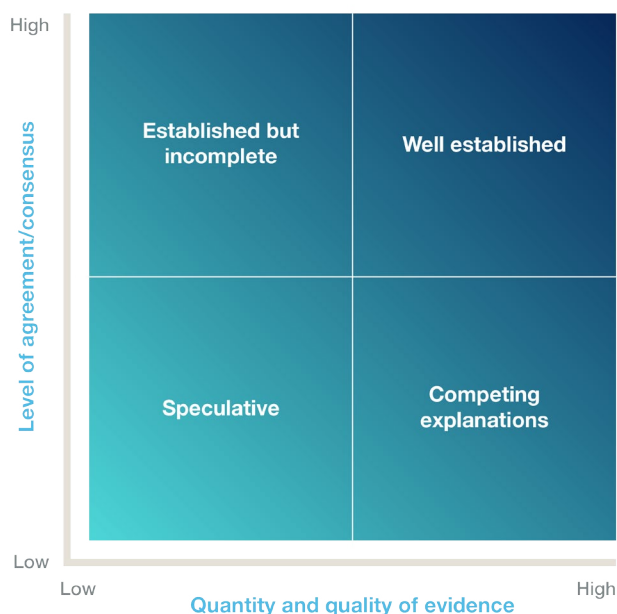


Figure 6 Qualitative uncertainty terms. Synthesis of Moss and Schneider (2000) and IPBES (2016).

1. Conservation implications

Synthetic biology and engineered gene drive have important implications for the conservation and sustainable use of biological diversity {1.1, 4.3} that are both direct {5} and indirect {6} (*well established*). While most synthetic biology and gene drive products are not designed as conservation applications {1.6} (*well established*), some of these will nonetheless have substantial impacts on conservation practices and outcomes {6.1} (*established but incomplete*).

2. New tools

New tools are needed for effective conservation and sustainable use of biological diversity {1.1} (*well established*). In recent years, global, regional

and national measures promoting biodiversity conservation have resulted in some successes, but biodiversity continues to decline globally {4.3} (*well established*). Biodiversity conservation requires the continued application of proven approaches, but scaling these efforts up to the level necessary to reverse the declines will continue to be a major challenge, given the seemingly intractable nature of some of the threats {5.1} (*well established*). Some synthetic biology and engineered gene drive applications, if appropriately designed and targeted, could enhance biodiversity conservation, for example, by mitigating threats {5.2} and increasing species' resilience to them {5.3} (*speculative*).

3. Rapid growth

The practice of synthetic biology is increasing rapidly, with major developments being promised and some delivered across multiple sectors {1.6} (*well established*). Over the last 15 years there has been a five-fold growth in companies with public and private investment approaching US\$ 10 billion over this period {1.6} (*established but incomplete*). Synthetic biology labs are found throughout the world in academic, corporate and non-traditional spaces like community biotech labs; increasingly young people are being taught to use these technologies {6.6} (*well established*). The distributed nature of access to synthetic biology techniques (*well established*) presents both opportunities and challenges for the conservation community {1.6, 2.3, 6.6} (*speculative*).

4. Engineered gene drive

Engineered gene drive systems may be a transformative tool for direct conservation applications {5.2.1, 5.3.1} (*speculative*) as well as in other sectors like public health {6.3} (*speculative*), where they could have an indirect impact on conservation {5.2.1, 5.3.1, 6.3}. Engineered gene drive systems are still years away from any deployment {5.2.1, 5.3.1, 6.3} (*established but incomplete*) despite the fast pace at which this technology is being developed {1.4} (*competing explanations*). The expertise of the conservation community is vital to the responsible

development and deployment of engineered gene drive systems {5.2.1, 5.3.1, 6.3} (*well established*).

5. Beneficial conservation impacts

Synthetic biology and engineered gene drive may be beneficial to conservation and sustainable use of biodiversity {4–6} (*speculative*). For example, by protecting threatened species against disease or climate threats {5.3.1} (*speculative*), eradicating invasive species {5.2.1} (*speculative*), increasing genetic diversity in small populations of threatened species {5.3.1} (*speculative*), restoring a proxy of an extinct species {5.3.2} (*speculative*), remediating degraded ecosystems {6.5} (*speculative*), or product replacement {5.2.2, 6.4} (*established but incomplete*).

6. Detrimental conservation impacts

Synthetic biology and engineered gene drive may be detrimental to conservation and sustainable use of biodiversity {4–6} (*speculative*). Detrimental effects may stem from the movement of genes, or escape of engineered gene-drive-carrying organisms, impacting non-target populations or species {5.2-5.3, 6.2-6.4} (*speculative*), changes to ecological roles played by target organisms {5.2, 6.3} (*speculative*), broader ecosystem effects {6.2} (*speculative*), product replacement that exacerbates a conservation problem {5.2.2} (*competing explanations*), socio-economic effects of product replacement on livelihoods and on production and consumption patterns {6.4} (*competing explanations*), distracting funding from other conservation approaches {5.1, 5.4} (*speculative*), and moral hazard reducing the urgency and importance of biodiversity conservation {2.3, 5.1} (*speculative*).

7. Values and worldview

Values, worldviews, and lived experiences influence the development, assessment and governance of synthetic biology and engineered gene drive {2–3} (*well established*). Thus, to produce evidence for conservation-relevant decision making, scientific methods and norms operate within contexts defined by the framing of problems and solutions, the integration of multiple perspectives and types of expertise, and who is trusted to produce credible knowledge {3} (*well established*).

Community and stakeholder engagement have been proposed to help navigate this complexity {2.3, 3.4} (*established but incomplete*).

8. Indigenous and local communities

Indigenous and local communities are key actors in research, governance and decisions around synthetic biology and engineered gene drive for conservation (*well established*). Synthetic biology has potentially significant positive and negative impacts on local and indigenous communities, which manage, govern, reside in or depend on a large part of the world's biodiversity {5–6} (*well established*). Historically there has been limited engagement with indigenous and local communities at both the project and global level (*established but incomplete*). Recently there have been calls for recognition of the rights of indigenous and local communities in decision making around synthetic biology and engineered gene drive {2.1} (*well established*). There have been some attempts to involve them in synthetic biology initiatives {2.3} (*established but incomplete*).

9. Governance

Multiple existing governance structures are relevant to synthetic biology (*well established*), but synthetic biology and engineered gene drive raise questions and challenges for these frameworks (*competing explanations*). Relevant governance frameworks include international, regional and national legal frameworks as well as religious, customary and indigenous governance systems, and scientific norms and practices (*well established*) {2.2}. Challenges relate to the extent to which current and future synthetic biology and gene drive applications are covered by existing regulations, norms and processes (*competing explanations*), implementation and enforcement in the context of accessibility of parts and tools (*established but incomplete*), different levels of governance capacity among jurisdictions (*well established*), mechanisms to address environmental harm, particularly transboundary impacts (*established but incomplete*), and the ability of governance frameworks to keep up with the rapid pace of technological innovation (*competing explanations*) {2.3}.

10. Risk Assessment

This “Assessment of Synthetic Biology and Biodiversity Conservation” is neither a risk assessment of individual synthetic biology and gene drive applications, nor of these technologies as a whole {3.4, 4.3} (*well established*). The diversity of these applications, of the mechanisms that can be used, and of the contexts in which these would take place, precludes an assessment of risks and benefits

of this technology as a whole (*well established*).

This assessment reviews existing and proposed applications of synthetic biology and engineered gene drive systems that are relevant to conservation and explores how they may be beneficial and detrimental to the conservation and sustainable use of biodiversity. Benefits and risks to conservation from synthetic biology applications vary on a case-by-case basis.

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