SYNTHETIC BIOLOGY

"Biomassacre" illustration by the Beehive Design Collective

At COP 11, government negotiators will be asked to consider bringing a new and emerging area of industrial activity under the oversight of the Convention on Biological Diversity. Synthetic Biology is a burgeoning technological field that builds artificial genetic systems and programmes lifeforms for industrial use. It urgently requires effective governance.

This briefing details ten key points to consider.

10 key points for delegates

1. The Synthetic Biology industry is global, well financed and rapidly expanding with products already in the marketplace.
2. Synthetic Biology can be clearly defined.
3. Synthetic Biology differs from recombinant DNA technologies.
4. Synthetic Biology is controversial.
5. Synthetic Biology has not yet come under any national or global oversight.
6. Synthetic Biology governance is best dealt with under the CBD and its protocols.
7. Synthetic Biology threatens the conservation of biological diversity.
8. Synthetic Biology threatens the sustainable use of biological diversity.
9. Synthetic Biology threatens the equitable sharing of benefits arising from genetic resources.
10. Synthetic Biology activities can be brought under an enforceable moratorium on environmental release and commercial use.

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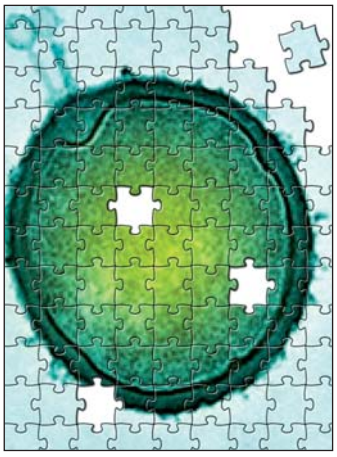
1. The Synthetic Biology industry is global, well financed and rapidly expanding with products already in the marketplace.

Synthetic biology may not be well known by the public but a broad range of industrial sectors are reporting growing activity and investment, and there are products already on the market. According to BCC Research, the global market for synthetic biology products was US$1.6 billion in 2011 and is expected to rise to $10.8 billion by 2016. While three quarters of that activity has so far been oil and chemical companies developing and marketing next generation biofuels, bioplastics and commodity chemicals, the industry is now switching focus to produce materials formerly sourced from natural plant products – such as rubber, food flavours, fragrances and essential oils as well as natural medicinal compounds. Examples of synthetic biology products already on the market include maize-sourced bioplastics sold by DuPont and Archer Daniels Midland, biosynthesized 'natural' grapefruit flavour sold by Allylix of San Diego (USA) and biodiesel sold in Brazil by Amyris, Inc. (USA). (The price of Amyris stock has recently plummeted due to technical problems, including an inability to scale up operations as expected.) A 2012 survey by ETC Group found that leading global investors and developers of synthetic biology products include 6 of the 10 largest chemical companies, 6 of the 10 largest energy companies, 6 of the ten largest grain traders and the world's 7 largest pharmaceutical companies. These and other financial players have in turn invested billions of dollars in over 100 'pure-play' synthetic biology companies. A recent survey of the scientific landscape of synthetic biology published in early 2012 by Dr. Paul Oldham and colleagues identified almost 3000 synthetic biology researchers in 40 countries funded by 530 different entities – primarily headquartered in the global North.



2. Synthetic Biology can be clearly defined.

Following a number of key policy investigations, there are emerging clear and shared definitions of the field that can guide future oversight, monitoring and reporting activities. Definitions of synthetic biology commonly make reference to:

1. the chemical synthesis of biological components, particularly the construction of synthetic DNA, and
2. the design and use of those synthetic components as interchangeable parts and 'circuits' to produce engineered novel organisms and systems intended to perform specific functions.

Three examples:

EU: "Synthetic Biology is the engineering of biological components and systems that do not exist in nature and the re-engineering of existing biological elements; it is determined on the intentional design of artificial biological systems rather than on the understanding of natural biology." – European Commission, DG Research (2005)

The Netherlands: "Synthetic Biology focuses on the design and synthesis of artificial genes and complete biological systems, and on changing existing organisms, aimed at acquiring useful functions." – Committee on Genetic Modification (COGEM, 2006)

USA: "Synthetic biology is the name given to an emerging field of research that combines elements of biology, engineering, genetics, chemistry, and computer science. The diverse but related endeavors that fall under its umbrella rely on chemically synthesized DNA, along with standardized and automatable processes, to create new biochemical systems or organisms with novel or enhanced characteristics." – Presidential Commission for the Study of Bioethical Issues, Report on Synthetic Biology (2011)

3. Synthetic Biology differs from recombinant DNA technologies.

While synthetic biology incorporates the techniques of molecular biology and has been referred to as 'extreme genetic engineering,' there are significant differences from the recombinant DNA technology in use when biotech governance arrangements were framed:

- Synthetic biology uses synthetically constructed parts such as 'artificial cells,' ribosomes, strands of synthetic DNA, novel nucleic acids or amino acids not sourced from nature.
- Synthetic biologists construct engineered gene circuits or 'metabolic pathways' from the bottom-up out of engineered 'parts' rather than taking sequences from existing (natural) organisms.
- Synthetic biologists use computer algorithms to 'evolve' and radically alter genetic sequences using computer software before building and deploying them in the laboratory.
- Some synthetic biologists use 'gene shuffling,' 'refactoring' and other techniques that alter or delete hundreds or even thousands of genetic elements in an organism at once.
- Synthetic biologists increasingly use new 'whole genome assembly' techniques to build an entire microbial genome from scratch all at once instead of the traditional 'gene gun' insertions or vector techniques of recombinant DNA.
- Synthetic biologists use massively parallel robotic genetic engineering platforms to construct thousands or even millions of variants of an organism rather than engineering one organism at a time.

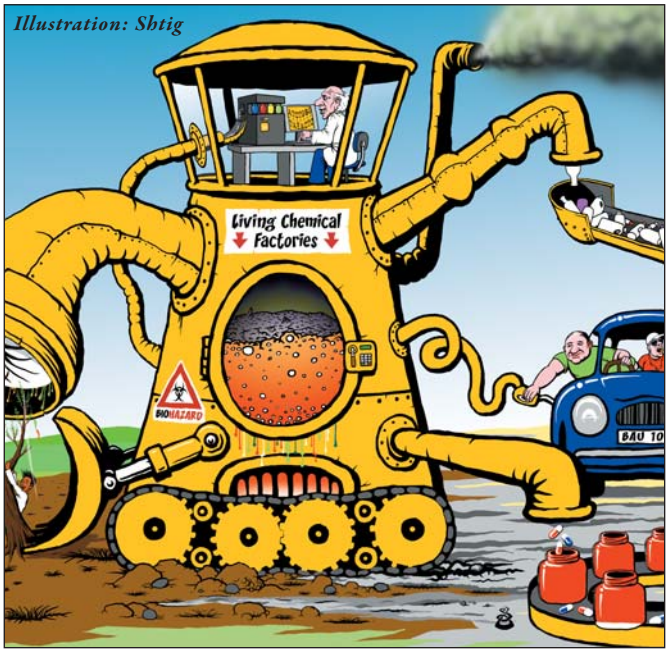


Illustration: Shtig

In short, synthetic biology allows for a form of genetic engineering that is much faster and much higher in volume with an unprecedented degree of novelty and complexity than previous recombinant DNA techniques.

4. Synthetic Biology is controversial.

Because of the speed of its commercial development and the industrial potential of this new platform, civil society, social movements, ethicists and others have begun to raise concerns about the field. In 2012, over 113 organisations, including trade unions, environmental groups, faith groups, farmers' organisations and science groups, launched 'Principles for the Oversight of Synthetic Biology." Since 2007, governments and policy experts have authored over 40 papers on the governance challenges and risks of synthetic biology and the number of expert commissions, international conferences and other processes examining the environmental, ethical, legal and social implications is on the rise.

> ***"Genetic engineering involves shuffling the cards of life, moving genes across species; synthetic biology introduces new jokers into the pack. Genetic engineering is limited to genes that naturally exist; synthetic biology provides the technology to create life that has not and could not have naturally existed."***
> – Julian Savulescu, transhumanist philosopher, Oxford University, UK

5. Synthetic Biology has not yet come under any national or global oversight.

Although parts of existing national laws and regulations may, in theory, apply to some aspects of synthetic biology, there is no comprehensive oversight apparatus at national or international levels. There have been repeated calls for such a framework to be established from insurers, civil society and policy reviews. Not only is there no validated risk assessment model for the biosafety of organisms and parts developed through synthetic biology, but also existing risk assessment concepts such as 'substantial equivalence' are even less relevant in light of the degree of novelty of organisms created through synthetic biology. Meanwhile, existing national and global biosafety, biosecurity and benefit sharing procedures and agreements are not adequate to deal with the digital aspects of synthetic biology or the volume and complexity of novel organisms. While the strict definition of a Living Modified Organism (LMO) under the Cartagena Protocol arguably embraces the products of synthetic biology, the working of the Protocol was not framed with synthetic biology in mind: It does not cover the virtual (digital) transfer of DNA sequences, which is routine with synthetic biology; it does not cover transfer of synthetic biological parts even though parts 'kits' can now be readily acquired and reconstituted into a viable organism; and it allows free movement of synthetic organisms destined for contained use without considering the different containment needs. By focusing on the physical transfer of material, the Nagoya Protocol on Access and Benefit Sharing similarly neglects the routine synthesis of genetic parts and metabolic pathways from digital genomic data, creating a loophole that makes possible the 'digital biopiracy' of genetic resources.

> ***"The assessment methods for GMOs are based on a comparison of the altered organism with the natural organism on which they are based, considering each individual trait introduced. Synthetic biology will produce organisms with multiple traits from multiple organisms, and therefore it may be difficult to predict their properties."***
> – European Group on Ethics in Science and New Technologies, advisors to the European Commission, 'Ethics of Synthetic Biology,' 2009, p. 49.

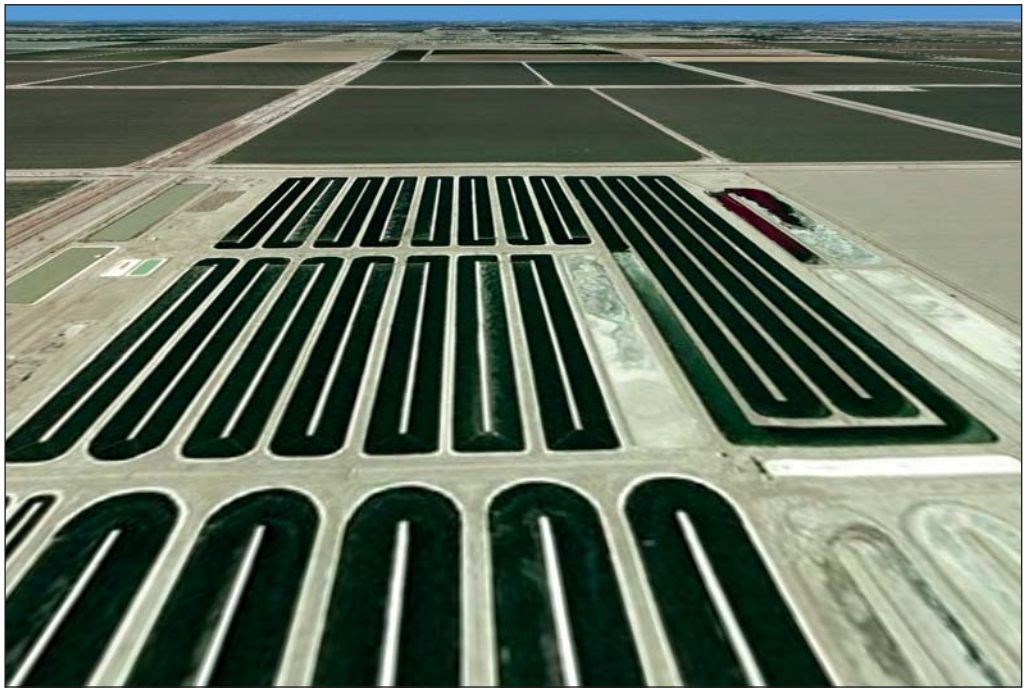
6. Synthetic Biology governance is best dealt with under the CBD and its protocols

If there were an 'emerging issue' that would seem tailor-made to the mandate of the Convention on Biological Diversity, it is synthetic biology. The Convention's expertise and history addressing global biological diversity and genetic resources make it especially well suited to face the challenges, even while developments in the field challenge the applicability of the CBD's protocols and existing decisions. The CBD is currently the only multilateral forum with a subsidiary expert body equally able to address questions of genetic science, equity and livelihoods and ecosystem-wide impacts. Ratification of the CBD is nearly universal.

7. Synthetic Biology threatens the conservation of biological diversity.

As has already been recognized in the establishment of the Cartagena Protocol, novel lifeforms can pose a direct threat to biological diversity and ecosystems safety. To date, not a single synthetic organism has undergone an environmental risk assessment. Leading areas of development for synthetic organisms include production of algae that will be released in ponds and waterways; development of microbes and enzymes able to break down wood, grasses and other cellulosic matter; and synthetic microbes intended for oil and gas extraction, remediation of soils and oil spill clean-up – all of which pose significant environmental release threats.

Following a six-month investigation, the US Commission for the Study of Bioethical Issues raised strong concerns about synthetic organisms being released into the environment, echoing concerns from the European Commission's group on ethics in science and new technologies, whose report noted a proposal from scientists recommending that, in the absence of clear biosafety data, all synthetic biology research take place in Biological Safety Level P3 or P4 laboratories.



A number of commercial synthetic biology companies have developed synthetic algal species intended for release into outdoor ponds such as these in Southern California.
Photo (cc): Pacific Northwest National Laboratory

Besides the direct biosafety threat of synthetic organisms to ecosystems, the emerging industry poses an economic threat to those whose livelihoods depend on biodiversity. Companies are employing synthetic microbes as biochemical 'factories' intended to ferment biomass to produce a range of high-value chemicals, including fuels. This in turn is intensifying an emerging grab on biomass from forests, grasslands, oceans and agricultural settings as well as the conversion of land to high-biomass monoculture crops such as cane sugar and eucalyptus. The land use change, greenhouse gas emissions, water and nutrient use associated with this new 'biomass-based' economy pose threats to biodiversity and ecosystem integrity across different biomes. Industrial synthetic biology applications that transform seaweed into fuels and chemicals directly impact conservation of marine biodiversity, just as synthetic microbes that transform crop residues into plastics and fuels impact the conservation of agricultural biodiversity.

8. Synthetic Biology threatens the sustainable use of biological diversity.

Because scale-up of production has proved unexpectedly difficult, initial investment in the development of fuels using synthetic biology is now giving way to a new strategy to use the same technologies to produce high-value natural products. In the crosshairs of this shift are markets in rubber, essential oils, flavourings, fragrances, medicinal compounds and cosmetic ingredients. This 'natural plant products' market is worth an estimated $65 billion annually and currently depends upon the knowledge, labour and farming practices of billions of small farmers and peasants – particularly in the global South. Synthetic biology's new business plan takes direct aim at the livelihoods of these essential stewards of biological diversity by offering cheaper synthetic alternatives that will not depend on specific growing regions, conditions or growers.

Examples of sustainable use practices under threat from synthetic biology include:

- Near term (2013-2014) commercialization of Isoprene (natural rubber) from DuPont collaborating with Goodyear and from Amyris collaborating with Michelin. 20 million smallholder families rely on agricultural production of natural rubber for their livelihood.
- Near term (2014) commercialisation of high quality vanillin (vanilla essence) –from Evolva SA (Switzerland). 200,000 people are involved in the production and curing of vanilla beans.
- Commercialization this year (2012) of vetiver oil produced by Allylix, Inc. of San Diego, USA. Vetiver is a key fragrance ingredient. In Haiti alone 60,000 people depend on vetiver production.

9. Synthetic Biology threatens the equitable sharing of benefits arising from genetic resources.

When the Parties to the CBD concluded negotiating the Nagoya Protocol on Access and Benefit Sharing, it was considered a step forward to ensure that biotechnology companies could not exploit genetic resources without the consent and sharing of benefits with the communities that have developed and stewarded those genetic resources. However the techniques of synthetic biology may have already undone any gains toward fairness made under the Nagoya Protocol.

> ***"We ought to be able to make any compound produced by a plant inside a microbe.... You need this drug: OK. We pull this piece, this part, and this one off the shelf. You put them into a microbe, and two weeks later out comes your product."***
> – Synthetic biologist Jay Keasling, quoted in Michael Specter, 'A Life of Its Own,' The New Yorker, 2009

While the Nagoya Protocol put in place rules for the physical transfer of genetic material, synthetic biologists routinely transfer genetic material digitally (as genetic code).

A farmer in Tanzania pollinates vanilla flowers. Vanillin is just one of many high-value natural products that the synthetic biology industry is working to synthesize artificially in a vat, potentially impacting rural livelihoods.
Photo (cc): Helen Graham

Today's digital biopirates can sequence DNA of indigenous flora in one location, upload that information to the Internet and then, in a matter of hours, synthesize that DNA in a laboratory on the other side of the globe. Like the digital 'piracy' of music, videos and books, digital piracy of genetic resources is now both easy and common.

Like other areas of biotechnology, synthetic biology has been subject to aggressive patenting, including ownership claims on synthetically constructed DNA, ribosomes, RNA, amino acids and cells, as well as related processes. Broad claims on metabolic pathways are also on the rise because they are key to producing whole classes of natural plant compounds. For example, Amyris, Inc. has aggressively patented the biosynthesis of isoprenoids – a class of over 55,000 natural compounds ranging from rubber and neem to ginger oil, palm oil, patchouli scent, pine oil and more.

10. Synthetic Biology activities can be brought under an enforceable moratorium on environmental release and commercial use.

At SBSTTA 16, Some Parties to the CBD proposed that a de facto moratorium be established to prevent environmental release or commercial use of synthetic genetic parts and living modified organisms produced by synthetic biology. The following recommendation from SBSTTA 16 will be considered by Parties at COP11 (Decision XVI/12 para 2):

> [4. Urges parties to the Convention on Biological Diversity, in accordance with the precautionary approach, which is key when dealing with new and emerging scientific and technological issues, to ensure that synthetic genetic parts and living modified organisms produced by synthetic biology are not released into the environment or approved for commercial use until there is an adequate scientific basis on which to justify such activities and due consideration is given to the associated risks for biological diversity, also including socioeconomic risks and risks to the environment, human health, food security, livelihoods, culture and traditional knowldege, practices and innovations;]

This proposal echoes calls from civil society and from specialized bodies considering the issue. For example, the US Presidential Commission for the Study of Bioethical Issues recognized the potential high risks anduncertainties of deliberate release of synthetic organisms, proposing that the US government must first "identify, as needed, reliable containment and control mechanisms."

Despite the rapid growth of synthetic biology, such a moratorium is currently feasible because there are still clear areas that can be monitored and regulated, including:

- There are a limited number of firms that provide the basic raw materials for DNA synthesis and a limited number of DNA synthesis companies. There have also been proposals from synthetic biologists that DNA synthesis machinery should be licensed and available only to licensed and regulated users.
- Digital access to a few common repositories of genetic parts – such as the BioBricks' registry of standard biological parts or GENBANK – can be monitored and subject to legal agreements restricting any environmental or commercial release of any organism.
- Expansion of the Nagoya Protocol to cover digital genetic sequences would go far to address digital biopiracy.
- Institutions known to be handling synthetic genetic parts or organisms can be required to maintain public registries of the genetic code of all unique novel organisms and to demonstrate effective containment and monitoring arrangements.
- New tools of science metrics and data visualization make it possible to pinpoint almost all of the key individuals and institutions involved in the field of synthetic biology, allowing for meaningful monitoring of the field, an essential prerequisite for governance.

Parties at COP11 must:

- Adopt a moratorium on the environmental release and commercial use of synthetic biology until there is an adequate scientific basis to justify their use and release, and until there exists the capability to assess associated risks for biodiversity, socio-economic risks, culture and traditional knowledge, practices and innovations.
- Support Option 2 from SBSTTA-16 Recommendation XVI/12, which would provide Parties with the most relevant information when considering risks posed by synthetic biology and involves consultation with local and indigenous communities, civil society, and other relevant parties.
- Request the Parties to the Cartagena Protocol on Biosafety to extend agreements to include synthetic biology in order to eliminate gaps that otherwise permit evasion of the Protocol's rules on the physical transfer of LMOs, such as digital importation of DNA sequences or importation of genetic 'parts' ready to be assembled.
- Request the Parties to the Nagoya Protocol on Access and Benefit Sharing to extend agreements to include digital genetic sequences and products of synthetic biology technologies.

Further information:

The International Civil Society Working Group on Synthetic Biology submission to SBSTTA on the Potential Impacts of Synthetic Biology on the Conservation and Sustainable Use of Biodiversity:
www.cbd.int/doc/emerging-issues/Int-Civil-Soc-WG-Synthetic-Biology-2011-013-en.pdf

ETC Group's online resource on Synthetic Biology:
www.etcgroup.org/issues/synthetic-biology

ETC Group contacts at COP 11:
Silvia Ribeiro - silvia@etcgroup.org
(mobile +52 1 55 2653 3330)
Neth Daño - Neth@etcgroup.org
(mobile +63 917 532 9369)

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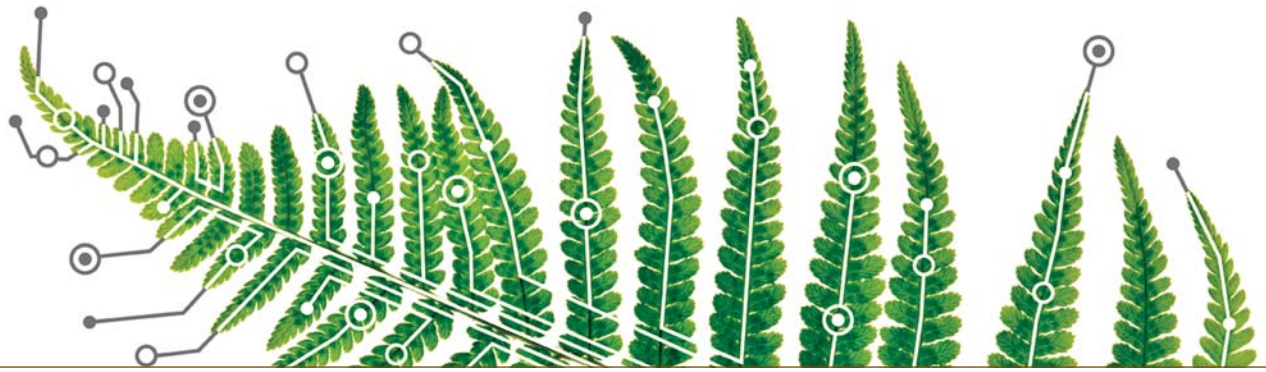

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