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zur biodiversitätsforschung
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Synthetic Biology

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Participants of the “International Genetically Engineered Machine” (iGEM 2016) competition in Boston

Photo: http://2016.igem.org

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GEFÖRDERT VOM

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We are many - and will be much more!

This is the message from events such as the "International Genetically Engineered Machine" competition (iGEM 2016) when looking at the development of the number of participants: while in 2013 191 teams took part in the competition, in 2016 already 299 student teams participated! The iGEM competition is an annual, worldwide event for high school, undergraduate and post-graduate students interested in the field of genetic engineering (the Cartagena Protocol uses the term "modern biotechnology"). They work all summer long in multidisciplinary teams to build genetically engineered systems using standard biological parts called BioBricks. iGEM teams work inside and outside the lab.

The cover picture of this fact sheet illustrates the fact that genetic engineering has become a very diverse and extremely dynamic field of research, which within a short period of time has considerably extended its research biotope with a variety of research foci e.g. in FP 6 and FP 7, conferences, competitions, scientific journals, and receives considerable public perception as well as funding. The reason for this revival of genetic engineering is the promise of "synthetic biology" and its genetic and cell biology innovations to now allow for a more precise manipulation of DNA fragments in species-hosting organisms. Also related innovative methods such as TALEN or CRISPR-Cas9 link to synthetic biology, as they provide more and more specific tools to manipulate genetic regulation. The resulting organisms could for example produce proteins and other biological products in large quantities for food, medicine and/or fuel.

This "synthetic biology" is in fact genetic engineering 2.0: synthetically modified organisms (SMOs) promise a billion-dollar business - and are also suspected of simultaneously threatening the livelihoods of millions of tropical small farmers producing e.g. coconut oil, vanilla, saffron, stevia or rubber that could possibly be substituted by products from SMOs (ICSWGSB 2016). With respect to biological diversity, there are sectors such as agriculture, chemical production, energy, and pharmaceuticals where a growing number of organisms, components and products of genetic engineering may interact with biological diversity (CBD-SBSTTA 2016, SEP 2016).

Concerning the objectives of the Convention on Biological Diversity (CBD), genetic engineering and synthetic biology represent "a dilemma: while the technology might be able to provide innovations which help reduce some of the environmental problems existing today, it also poses large and potentially unforeseeable risks to ecosystems. It cautions that careful consideration of the risks, benefits and ethics of these techniques should be undertaken as a priority." (FCRN 2016)

Relationship between synthetic biology and biological diversity

Synthetic biology is closely related to issues associated with the conservation and sustainable use of biological diversity: medical and nutritional applications may lead to healthier populations, and industrial applications of synthetic biology may lead to alternative methods to manufacture products, such as chemicals and other materials, which are currently produced from natural sources, thereby reducing the impacts associated with the extraction of natural resources. The idea that species conservation may profit by changing the traits of species – with regard to fertility or pathogen

resistance for example, has to be explored further as specifity of interactions and risk management are not explored yet (Johnson et al. 2016). The shift away from nature-based towards biotechnology-based economies would deeply change socioeconomic patterns in rural economies of low-income countries. Furthermore, synthetic biology is associated with ethical issues such as potential changes in people's perception of nature. Finally, there are considerable safety issues associated with genetic engineering: the accidental release of SMOs into the environment, the deliberate marketing of products from e.g. DIY biology, the accidental transfer of genes to wild populations, or the production of biological weapons and novel pathogens for malevolent purposes pose high risks for the survival of humankind on Earth (SEP 2016).

Genetic engineering may have both positive and negative effects on the conservation and sustainable use of biodiversity (Redford et al. 2014). Thus, the CBD report on synthetic biology discusses potential benefits as well as potential adverse effects from synthetic biology on biodiversity in relation to the three CBD objectives conservation and sustainable use of biodiversity as well as fair and equitable sharing of the benefits of biological diversity (CBD-SBSTTA 2016). A selection of the most important potential impacts from synthetic biology on biodiversity is presented in box 1 (CBD-SBSTTA 2016, SEP 2016).

Box 1: Selected potential impacts from synthetic biology on biodiversity

Potential benefits

A key potential benefit of synthetic biology is the contribution to the understanding of biological systems from the molecular to the ecosystems level.

- Bioremediation may contribute to the restoration of ecosystems and may even be able to restore extinct species.
- Agricultural and agroforestry applications such as improved pest control may reduce the impact of human land use on biodiversity, in particular on pollinators and other non-target organisms, through reduced chemical pesticide/herbicide use.
- Synthesisation of products currently extracted from plants and animals may reduce the pressure on threatened species.
- Invasive species may be eradicated through the application of gene drives in their populations.

Potential risks

Potential risks of synthetic biology with respect to biological diversity may result from direct and indirect, intended or unintended, as well as immediate or delayed effects. These effects may occur at the genetic, species, or ecosystem level.

- Transfer of genetic material to wild populations may lead to a loss of genetic diversity, the spread of harmful characteristics, toxic effects on other species, and destruction of habitats.
- Replacement of natural products may lead to changes in the agricultural practices of communities, which may adversely affect traditional crops, practices and livelihoods.
- Large-scale increase in the use of biomass crops, as well as changes in patterns of extraction of biomass, minerals and other sources of energy, may lead to changes in land use as well as to reduction of soil fertility and structure.
- Inappropriate access without benefit sharing due to the use of sequenced data without material transfer agreements under the Nagoya Protocol.
- Indigenous peoples and local communities will not necessarily support or benefit from the utilization of genetic resources in synthetic biology.

Current debates in relation to biological diversity

The CBD is the only international body currently assessing the potential risks and benefits from synthetic biology on biological diversity. With synthetic biology rapidly transforming the impact of genetic engineering or modern biotechnology on biodiversity, "it is urgent that international governance arrangements are kept updated and made relevant." (ICSWGSB 2016)

According to the advice already issued by SBSTTA-20 and the Ad-Hoc Technical Expert Group (AHTEG) on Synthetic Biology in document UNEP/CBD/SBSTTA/20/8 (CBD-SBSTTA 2016), Parties are expected to discuss *inter alia* an operational definition of synthetic biology, a precautionary approach towards gene drives, the implications of biopiracy (digital theft and use of DNA) for both the CBD and the Nagoya Protocol, how to address impacts of synthetic biology on the sustainable use of biodiversity, and the elaboration of risk assessment guidance on synthetic biology.

Main issues for consideration by COP-13

According to its revised annotated provisional agenda (UNEP/CBD/COP/13/2/Rev.1), COP will handle synthetic biology – in contrast to SBSTTA – not as an emerging issue. However, there are hopes to extend the AHTEG on Synthetic Biology to make synthetic biology a standing item in the CBD and to keep the discussion about the issue within the CBD process alive.

The discussion is expected to concentrate here on the following issues closely linked to the conservation and sustainable use of biodiversity:

- **Operational definition of synthetic biology**
  Debates about synthetic biology in relation to biological diversity tackle topics such as the need for a clear definition of the term "synthetic biology". The associated techniques have the potential to greatly advance and alter applications such as biomedicine and plant breeding. In future, it will no longer be clear whether a genomic transformation is the result of a natural mutation, a conventional breeding method, or a targeted intervention from genetic engineering. This development has led to the blurring of differentiability and thus provoked a highly controversial debate on what should actually be called a "genetically modified organism" and what has to be regulated accordingly and what not. This raises the question of how to define synthetic biology within the CBD and whether or not the definition of modern biotechnology (Cartagena Protocol, Art. 3) should be revised.
  Within the framework of the CBD, the term is proposed to be defined as follows to: “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.” (CBD-SBSTTA 2016: 4) However, outside the CBD process there are a number of additional definitions for the term (see SEP 2016: 6). Until now, the CBD failed to adopt a definition for use within the Convention and its Protocols.
  One suggestion is to develop something like a "living list" which collates products and techniques which are currently seen as belonging to synthetic biology – or not (ICSWGSB 2016).

- **Precautionary approach towards gene drives and ecosystem integrity governance**
  "The precautionary principle must be central to addressing the threats of synthetic biology to biodiversity. In the EU, the precautionary principle plays a key role in policy design: applied as a tool to follow developments in a sector and continuously verify that the conditions for the acceptability of a given innovation are fulfilled (...). In the case of synthetic biology, the precautionary principle is an important element of ethical debates and legal decision making and will help to protect the environment from harm." (SEP 2016: 30) It is worth noting that the precautionary principle is of course already applied to genetic engineering in the CBD and its Cartagena Protocol. There is reason to extend its validity to the phenomenon of synthetic biology. Currently, synthetic biology is not specifically regulated; for the US no specific regulations are expected (Suppan 2014), for Europe – and Germany – decisions whether there specific rules for synthetic biology – and genome editing – are necessary or whether it is covered completely by the current gentechnological law are expected for 2018.
  Linked to this question is how modified microorganisms, fungi, plants, and animals change evolutionary pathways; how for example does the use of SMOs for degraded ecosystems shape the biological interactions within the ecosystem? How are those synthetically modified species, functions, and services monitored for achieving the Aichi targets? In some respects, synthetic biology understood as bioengineering can be compared with climate engineering (c.f. Solé 2015) and poses similar governance questions to the CBD and its Parties.

- **Impacts on sustainable use**
  While procedures exist within the CBD to evaluate direct biosafety impacts of engineered organisms on biological diversity (through the Cartagena Protocol) and to establish access and benefit-sharing arrangements (through the Nagoya Protocol) there is no mechanism for Parties to raise and assess the impact of genetic engineering developments on sustainable use of biodiversity – particularly the indirect impacts of products created through genetic engineering (e.g. large scale changes in land management and loss of sustainable livelihoods as a result of natural products being replaced by synthetic ones) which may be significant. Such indirect effects and sustainable use implications are often socioeconomic impacts in the first instance, but later reveal serious biodiversity implications (ICSWGSB 2016).
  As COP moves forward with addressing synthetic biology within the CBD, the Parties should establish a body, process or mechanism for assessing socioeconomic and indirect impacts of genetic engineering with particular attention to issues of sustainable use. If a novel biosynthesis of a natural commodity in one location threatens sustainable use within a Party's border (e.g. biosynthesis of natural products elsewhere threatens traditional livelihoods) then there needs to be a forum for a country to raise concerns and seek redress. Such a process can be pursued through making synthetic biology a standing item in the CBD or by raising the item under sustainable use (ibid.).

- **Impacts on fair access to genetic resources (ABS – Access and benefit sharing)**
  Modern technologies increasingly use virtual or digital information on genes. It is not clear whether this can be considered "genetic resources" or "genetic material" in accordance with the definitions contained in Article 2 of the Convention" (CBD 2015: 80). Therefore, the applicability of the Nagoya Protocol is unclear, and may re-open the discourse on biopiracy, increasing the risk of "digital thefts" (ICSWGSB 2015).

Glossary

BioBricks BioBrick parts are DNA sequences which are designed to assemble larger synthetic biological circuits from individual parts and combinations of parts with defined functions. The intention is to incorporate them into living cells to construct new biological systems.

DIY bio DIY bio (Do-it-yourself biology) a movement in which individuals, teams, and small organisations use the same methods as traditional research institutions in genetic engineering. This may be done as a hobby, as a not-for-profit endeavor, or for profit to start a business. Other terms are garage biology, biohacking or wetware hacking.

Gene drive Technique that circumvents the natural rules of sexual reproduction and increases the odds that a gene will be passed on to offspring, allowing them to spread to all members of a population. It can be used to spread particular genetic alterations (e.g. re-engineering or eradication) through targeted wild populations over many generations. By altering the traits of entire populations of organisms, gene drive systems have the potential to irreversibly alter our natural environment.

Genome editing Type of genetic engineering (e.g. CRISPR-Cas9/-Cpf1, ZFN, TALEN) to selectively cut and modify DNA. Genes can be inserted, removed, or turned off using engineered nucleases (GEEN).

Literature and further reading

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