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Synthetic Biology

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This EPTA Briefing Note gives an overview of the main concepts of synthetic biology as well as the current state of the debate on policy and governance issues that are induced by it.

WHAT IS SYNTHETIC BIOLOGY?

There is no individual definition of synthetic biology (SB), but two perspectives dominate the understanding and communication of SB: On the one hand, researchers promote the idea of applying engineering principles to biology or of "biology becoming technology" and vice versa. On the other hand, the term is being applied as an umbrella for new technologies that allow a more comprehensive or fundamental manipulation of biological systems as compared to "classical" genetic engineering. Important methods and approaches in the SB field are:

> the chemical synthesis of large pieces of DNA up to complete genomes;

> the *de novo* design of metabolic pathways for the production of specific molecules, and the implementation of their genetic basis in microorganisms and higher organisms;

> the reduction of existing cells to their minimum ("top-down") or the construction of synthetic cells by assembling non-living chemical components ("bottom-up"), both with the aim to use such a construct as a host or a chassis for tailor-made metabolic pathways.

ENGINEERING LIFE

Engineering work in general is based on standardisation, which allows rational construction and a reliable production of useful goods. Against this background, researchers seek to introduce a high level of standardisation, predictability and reproducibility to biology as well. For example, registered and characterised biological parts would allow scientists to apply them easily, relying on their proper function in any given construction. To arrive at such parts, storing and displaying gathered information in a comprehensive way is a prerequisite.

As SB heavily relies on expertise from many fields, boundaries between scientific disciplines tend to blur. Today, chemists and biologists work side by side with physicists, engineers, IT scientists and many others. They not only contribute their specific knowledge but also influence the

SUMMARY

> Synthetic biology might be the next wave of biotechnology, characterised by a convergence of molecular and systems biology, chemistry, nanotechnology, and IT.

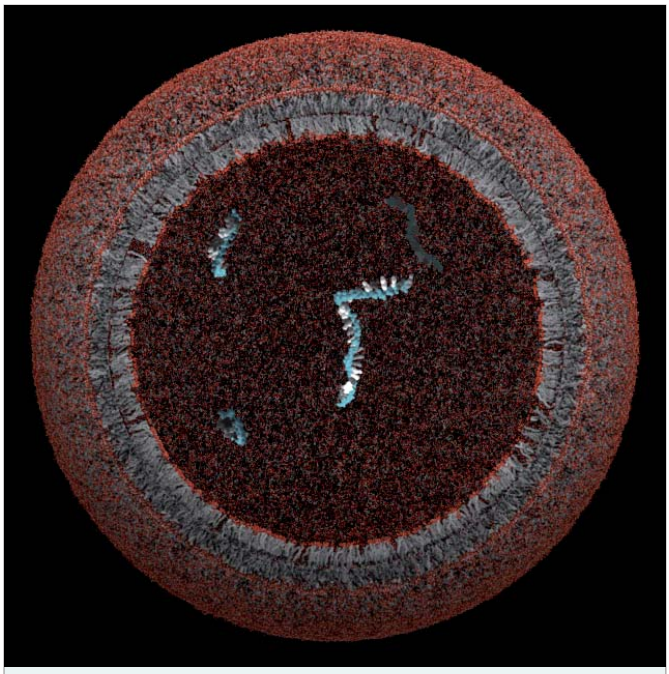
> It is necessary to distinguish between
1) incremental new steps in biotechnology,
2) approaches that aim at the synthesis of organisms beyond the classical approach, and
3) visionary approaches of creating artificial organisms without reference in nature. First-generation applications of synthetic biology are expected in such diverse fields as biofuels, malaria medicine, bioremediation, and new materials.

> Biosafety concerns are related to uncontrolled spreading of modified organisms that are toxic or can seriously harm biodiversity. Easy access to standardised modules for DNA synthesis also raises fear of bioterror and implies the need for biosecurity measures.

> For the time being, new regulatory initiatives are not necessary. Public authorities still need to prepare for possible breakthroughs in research by
- constant observation of research results to be prepared for adopting new or modified regulatory frameworks,
- organizing platforms for exchange among those active in laboratories, governance offices and civil society,
- engaging in international coordination and shared efforts on necessary regulations,
- providing for information and involvement of the broader public.

way the work is done along the traditions in their field. Derived from traditions in the IT sector, SB scientists often include playful elements in their work. For example, the International Genetically Engineered Machine competition (iGEM) encourages university students to use and develop biological parts ("BioBricks"™) for new (and sometimes funny) biological functions in microorganisms.

Realistically, though, reaching goals like "building new organisms from scratch" cannot be expected in the near or midterm future. The synthesis of the complete genome of the bacterium *Mycoplasma genitalium* by Craig Venter was not equivalent to "creating life" as often reported in the media, because it more or less copied the genome of a naturally occurring organism.



Artificial protocells with the properties of living cells shall be assembled from biochemical substances.

Source: Harvard Medical School/Massachusetts General Hospital

SYNTHETIC BIOLOGY APPLICATIONS

Most of the hitherto projected applications of SB do not pertain to fundamental new product innovations. They rather represent additional technological options in the areas of energy, chemicals, medicine/health, and environmental services.

Regarding the potential market volume, SB technologies could have the largest economic effect in the energy and chemical industries, both relying on hydrocarbons as starting material. BP and Exxon have massively invested in projects investigating improved biofuel production with a specific focus on SB technologies.

The pharmaceutical industry and other medical areas are important potential fields of application for SB, such as regarding the identification of disease mechanisms, drug discovery, the development of therapeutic strategies and, in particular, drug production. The most advanced example of a successful SB application is the production of a precursor of the anti-malaria compound (Artemisinin) from the wormwood plant. As a result, much larger quantities of the drug can be provided regardless of the season and at a lower price.

Bioremediation, the biological rehabilitation of contaminated sites using specific microbes, is another promising approach of SB. Better solutions for particular problems concerning toxic pollutants could be of great relevance for certain areas or regions. In addition, experts say that the diversity of naturally occurring bacteria provides better opportunities to fight contamination.

RESEARCH AND INNOVATION POLICIES

The first SB research department was founded in 2003 at the Lawrence Berkeley Laboratories, and the United States are still leading. Nevertheless, the European Commission was early in starting a broad research funding scheme for SB. In the Sixth Framework Programme for Research and Technological Development (FP6), at least 25 million euros were spent for scientific research in SB as well as on its ethical, legal, social and economic implications (ELSI). Up to 2007, the amount spent for public funding of SB projects was higher in Europe than in the United States. From 2008 on, the United States Department of Energy funded SB bioenergy research with more than 100 million USD per year.

National funding programmes for SB have been established in many European countries, especially in the UK and Switzerland. In France and Germany, most research related to SB has been funded by general biotech programmes. In both countries, there are important scientific institutions active in SB research and industrial firms as well. The only European enterprise dealing with SB biofuel production, "Global Bioenergies" is located in France, and Germany is the home country of several of the world's leading companies for DNA synthesis. ELSI research on SB was funded e.g. in the UK, Germany, the Netherlands and Austria.

A specific topic in SB is that of intellectual property rights. As in the IT sector, "open source" approaches play an important role. Synthetic biologists aim at creating biological parts and circuits for a potentially broad scope of applications as well as modular components and standards for assembly and performance. To support this, many researchers call for transparency and sharing of research results and methods. A prominent example is the MIT Registry of Standard Biological Parts: resear-

chers subscribing to the registry may use any "BioBrick"™ and all data, but they must disclose their results. This is in contrast to the traditional practise of intellectual property protection in biotechnology as a prerequisite to attract investors. Many experts doubt that an open-source model can be reasonably maintained once SB has entered commercial application. Most policy reports on SB emphasize that the main challenge for the European innovation system will be the development and establishment of a research environment that satisfies the needs of different players.

REGULATORY DEMAND

Biosafety principles and practices aim at preventing the unintentional release of pathogens and/or toxins ("keeping bad bugs from people"). Challenges from synthetic organisms are expected to come up in a medium or long-term perspective only. Biosecurity seeks to prevent the intentional release of pathogens and/or toxins ("keeping bad people from bugs"). In this regard, possible problems from SB are already addressed today.

Biosafety

All regulations on genetic engineering pertain to SB as well. As with genetic engineering, the contained use of microorganisms in closed systems (regulated by EU directive 2009/41/EC) has to be distinguished from the deliberate release (EU directive 2001/18/EC) of organisms produced with the help of SB technologies into the environment. Today, most experts consider SB not to be fundamentally different from genetic engineering, so regulation and the principles of risk assessment are considered to be adequate. For contained use, SB in general is not expected to cause fundamentally new questions even in the medium-term.

However, according to the International Risk Governance Council (IRGC), risk assessment principles may come under challenge "once modification is pursued at the 'deep' systemic level that synthetic biology should enable". Thus, deliberate release would raise problems, if the principles of familiarity and substantial equivalence could not be applied any more. So far, GM plants have been approved for commercial use, because they are not considered substantially different except for the introduced trait(s). This approach will not suffice, if SB would create fundamentally new organisms.

Although most experts consider a global governance regime for SB safety aspects necessary, differences between the European and the US regulatory approaches persist. Members of the US Presidential Commission for the Study of Bioethical Issues (PCSBI) and the European Group on Ethics (EGE) converged on many issues, but regarding biosafety, the EGE has taken a stricter stance recommending prior risk assessment and the application of the precautionary principle. The PCSBI advocates a less restrictive approach of "prudent vigilance".

Civil society organisations like the ETC Group call for a moratorium and have brought this issue to the Convention on Biological Diversity conference in Nagoya in 2010.

Biosecurity

With a view to international terrorism, the possible spill-over of relevant SB knowledge and its deliberate misuse became an issue of governance dis-

PROJECTS AND SELECTED PUBLICATIONS OF EPTA NETWORK MEMBERS

DBT (The Danish Board of Technology) (www.tekno.dk):
Synthetic Biology: Challenges and Debates, Newsletter No. 281, June 2011

DBT and The Danish Council of Ethics (etiskraad.dk):
Synthetic Biology – A discussion paper, May 2011

IST (Institute Society & Technology, Flemish Parliament, Belgium) (www.samenlevingentechnologie.be):
Synthetic Biology (running project)

ITA (Institute of Technology Assessment, Austria) (www.oeaw.ac.at/ita/):
SYN-BIOSAFE – Safety and Ethical Aspects of Synthetic Biology (completed project),
COSY – Communicating Synthetic Biology (completed);
STEPE - Sensitive Technologies and European Public Ethics (completed);
Reflexive Systems Biology (running project)

NBT (The Norwegian Board of Technology) (www.teknologiradet.no):
Synthetic Biology: Remaking Life? (running project)

OPECST (Parliamentary Office for Evaluation of Scientific and Technological Options, France) (www.senat.fr/opecst):
The stakes of synthetic biology (running project)

POST (Parliamentary Office of Science and Technology, United Kingdom) (www.parliament.uk/post):
Synthetic biology, POSTnote 298, January 2008

Rathenau Institute (Netherlands)(www.rathenau.nl):
Key technologies: Synthetic biology (running project);
Constructing Life – Early social reflections on the emerging field of synthetic biology, December 2006;
Constructing Life – The World of Synthetic Biology, November 2007

STOA (Science and Technology Options Assessment at the European Parliament) (www.europarl.europa.eu/stoa/):
Making perfect life. Bioengineering in the 21st century. Interim study, March 2010 (running project)

TAB (Office of Technology Assessment at the German Bundestag) (www.tab-beim-bundestag.de):
Synthetic Biology (running project)

course especially in the United States. Obviously, synthesising pathogenic organisms (such as viruses) using freely available sequence information through commercial DNA providers must be prevented.

While some plead for enforced self-regulation and monitoring by the research community, the International Risk Governance Council recently asked for the implementation of internationally standardised procedures as well as for the creation of an international, systemically organised approach to promoting a "culture of responsibility", backed up by legal mechanisms, along with surveillance and intelligence on deliberate threats. However, much SB work is carried out in countries where regulations would be difficult to enforce, and effectively controlling potential SB weapon activities will be difficult.

A specific "blend" of biosafety and biosecurity challenges ("keeping incompetent people from dangerous bugs") could result from SB activities being adopted in the DIY – or "biohacker" – community. It is subject to debate whether the increase of the number of potential users unaware of risks should cause concern.

PUBLIC DISCOURSE

So far, the public discourse on synthetic biology is still in its infancy in many countries, and awareness is low among the public. According to the 2010 Eurobarometer survey regarding public perception of new technologies, citizens, if at all, are most interested in risks and benefits. As with other technology fields, people tend to support applications with health or environmental benefits, so e.g. creating microbes to produce fuel from biological waste finds positive resonance. In contrast, as previously with GMOs, the deliberate release of modified organisms into the environment probably would raise public opposition, especially if organisms are labelled "synthetic".

Reporting on synthetic biology has intensified in recent years – and was mainly driven by protagonist researchers such as Craig Venter actively promoting the field. Apparently, it is the notion of "artificial life" put forward by parts of the research community that triggers media interest. Reporting often goes along with sceptical sentiments transported in metaphors like "playing god" or "tinkering with nature".

OUTLOOK

The question is how national and supranational political bodies can adequately prepare themselves institutionally and methodologically for the political and societal challenges induced by SB. One main challenge for policy making is to come to terms with uncertainties and ambiguities regarding the novelty of SB compared to genetic engineering and the related problem of assessing the actual potential of SB innovations in the short and medium-term.

The concept of SB is still in the making and the field's boundaries are yet to be defined. There seems to be a broad consensus that for the time being new regulatory initiatives are not necessary. Nevertheless, public authorities may prepare for possible breakthroughs in research that would have a bearing on existing regulations and, at the same time, contribute to responsible research and innovation in this area by stimulating and (co-) organising a broad process of societal deliberation on SB, its potential benefits, risks and promises.

As a prerequisite for a sober reflection on the aims of SB as well as on appropriate regulatory regimes, it will be important to explain that many expectations are exaggerated. Furthermore, any (perceived) bias in initiatives to stimulate a debate – such as "educating" the public to prevent "misleading" perceptions – will not help to induce an open societal learning process on the social, political and ethical implications of SB. Since public perception and discourse presently are in an embryonic state, spaces for debate among those concerned are needed rather than public campaigns.

Developing an effective mixed system of self-regulation, control and surveillance will be a complex and long-term activity. It could benefit from the continuous work of TA institutions to keep the level of awareness high (beyond the waves of media reporting) and to stimulate and shape expert and public discourse.

The EPTA network was formally established in 1990 under the patronage of the President of the European Parliament, Mr Enrique Baron Crespo. The network is made up by technology assessment institutions in Europe advising parliaments on the possible social, economic and environmental impact of new sciences and technologies. The common aim is to provide impartial and high-quality accounts and reports of developments in issues such as for example bioethics and biotechnology, public health, environment and energy, ICTs, and R&D policy (www.eptanetwork.org).

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