

# SYNTHETIC BIOLOGY: FINAL TECHNOLOGISATION OF LIFE – OR NO NEWS AT ALL?

Synthetic biology currently represents a prime example of a »hope, hype and fear technology«. On the one hand, it has a close methodological connection with genetic engineering while, on the other hand, being close to nanotechnology and converging technologies in discursive terms. Even though there is as yet no consensus about the essence and prospects of synthetic biology, it is regarded by many as the key direction in which developments are heading in biosciences – with the latter being seen in turn as the defining science of the 21st century, following in the footsteps of physics in the 19th century and chemistry in the 20th. This paper will show that a certain discrepancy can be identified between the extent of the expectations, hopes and fears under discussion and the available fund of knowledge or of specifically foreseeable potential applications.

- > Construction of chemical systems (new biomolecules) corresponding to biological models such that these systems manifest certain properties of living organisms
- > Reduction of organisms to rudimentary system components by installing standardised modular biological parts (»BioBricks«) for the purpose of creating biological circuits that respond to external stimuli«

One characteristic feature of hope, hype and fear technologies, without doubt, is that every debate about it is preceded by a discussion of its definition or whether there is a common understanding of what it means. Although this seems absolutely inevitable with a new technology or a new branch of science, the question about definitions and understanding has a different meaning in the three examples of nanotechnology (central theme of paper by C. Revermann), converging technologies (TAB 2008) and synthetic biology: that is because the question is whether the current status of knowledge, data and technology allows a new, discrete field to be assumed – or whether this is just a relabelling of incremental progress or a new name for something long familiar.

## IN SEARCH OF A COMMON UNDERSTANDING

Almost every paper which addresses the prospects, opportunities and risks of synthetic biology reflects and comments on what differentiates it from a mere further development of genetic engineering – which for its part can be very well demarcated because the targeted modification of naturally occurring DNA can be defined as the intersection of all genetic engineering applications.

The understanding which forms the basis for the current TAB project on synthetic biology has been defined as follows (<http://www.tab-beim-bundestag.de/en/research/u9800.html>): »Synthetic biology is the designation for a field at the interface of biology, chemistry, biotechnology, engineering science, and information technology. It is based on findings and methods from molecular and systems biology, in particular the decoding of entire genomes and the technological advances in the synthesis and analysis of nucleic acids. The idea underlying synthetic biology is the creation of new biological systems that do not occur as such in nature and the design of individual molecules, cells and organisms that exhibit new properties with the aid of procedures from molecular biology and standardised principles and methods from engineering science. In doing this, different strategies are being followed:

- > Mechanical, synthetic production and sequencing of DNA
- > Synthesis of protocells with the properties of living cells with the aid of biochemical substances lacking a concrete biological model
- > Construction of minimal cells with synthetically produced genomes
- > Integration of artificial biochemical systems in living organisms to achieve new properties

This description deliberately avoids an advance positioning on the news value of synthetic biology and serves as a starting point so that, as a result of the systematic capture of application potentials and risks, it is even possible to discuss whether the term and content are really forward-looking and relevant, i.e. whether there is even a cause for hope and fear.

The antipole to such a position which is initially about searching is formed by those who understand or postulate the creation of »artificial life« as the core goal of synthetic biology and place it at the centre of the debate. This almost inevitably gives rise to the question of the legitimacy of »playing God« as a metaphor for the philosophical and theological discussion of necessary and desirable limits on human action when interacting with nature. »Synthetic biology shifts human interaction with nature from the paradigm of manipulation to that of creation,« write, for example, Boldt et al. (2009, p. 80); »Vom Veränderer zum Schöpfer« (From modifier to creator) is the title of a paper by the Director of the TAB (Grunwald 2010a). Similar formulations have been used since the emergence of genetic engineering in the 1970s for almost every important biomedical development (prenatal and pre-implantation diagnosis, cloning, stem cell use), and they reliably generated public attention, though

this is mainly characterised by fear and less by hope (see below).

And how could hype arise? Where can these exaggerated hopes come from? The easiest way to explain these is to select a third perspective on the issue of synthetic biology, i.e. the assumption of the systematic and synergistic merging of biomedical and engineering developments in what are termed converging technologies (Coenen et al. 2009; TAB 2008). »Biology is becoming technology« and »Technology is becoming biology« – according to the »Making Perfect Life« project of the European Technology Assessment Group these are two megatrends which will shape our technical and economic future (ETAG 2010). Based on this assessment there is a clear assumption that synthetic biology is positively predestined to be *the* key technology for resolving mankind's future problems because it unites all the major technologies.

Overall it may be assumed, both in the case of synthetic biology and also for other technological developments, that the extent of hope, hype and fear is greatly influenced by the chosen perspective and the resulting preoccupation with the potentials. The considerations outlined below are intended to substantiate three assumptions relating to synthetic biology:

- > To date there have been – surprisingly – few hopes in the sense of target applications, or they have been far from specific.
- > Exaggerations mainly accompany the topos of the creation of artificial life – and have less impact than might be expected.
- > For various reasons the fears that could be mobilised have been contained to date within comparatively tight limits.

## HOPE: IMPROVED MICROBES AND DIVERSE ACQUISITION OF KNOWLEDGE

The same applications for synthetic biology are repeatedly cited as the future prospect (e.g. in the overview studies on the potentials of synthetic biology in box 2): bioenergy and raw materials production with optimised or »newly designed« microorganisms, biosensors for environmental monitoring and medical diagnostics and various strategies for the manufacture of pharmaceuticals and new therapy and vaccine variants.

However, a precise analysis of the applications concretely pursued and developed a little further to date, such as took place at a workshop of the Engineering Life project ([www.engineeringlife.de](http://www.engineeringlife.de)) (König et al. 2011) which is sponsored by the BMBF (Germany's Federal Ministry of Education and Research) reveals that practically no or scarcely any example can be identified which cannot be regarded as a mere further development of molecular biological and genetic engineering methods which have been in use for some time – or vice versa that qualitatively delimitable approaches, such as the comprehensive »construction« and »implementation« of new metabolic pathways in bacteria or yeasts or even the complete *de novo* design of microorganisms, currently still constitute basic research without any certainty of technical feasibility and utility.

With reference to synthetic biology, therefore, it is particularly relevant to ask whether the current status of research is really such that it is possible to talk of a new development stage in applied biosciences or even a paradigm shift. Many scientists regard synthetic biology to date more as an almost playful, experimental use

of new technical options without any fundamental strategic importance – along the lines of the International Genetically Engineered Machine competition, iGEM (<http://ung.igem.org>), set up by Massachusetts Institute of Technology (MIT) and run annually since 2003 in which groups of students vie for the most original and forward-looking projects using BioBricks. Perhaps the greatest consensus among scientists working in this field could be that the methods brought together under the synthetic biology label constitute a gain in knowledge in basic research, particularly with reference to the functioning of genes and genomes but also of other molecules and cell components without direct applications having necessarily to result from them.

## HYPE: »LEBEN 3.0« AND – YET AGAIN – SAVING THE WORLD

Hype – i.e. an exaggerated expectation of the future potential – can only accompany spectacular scientific successes which are easily communicable to the wider community in the case of synthetic biology to a limited extent. The primary opportunity for dramatisation is the image of the artificial production of life in the laboratory – which, even though it can hardly withstand serious scrutiny, has a centuries-old tradition to call on. It is no surprise on the one hand, therefore, that a clear interest has developed in the humanities and arts for an interdisciplinary debate on the potential significance of synthetic biology (e.g. the proceedings of the »Leben 3.0 and die Zukunft der Evolution« [Life 3.0 and the Future of Evolution] conference of the Berlin-Brandenburg Academy of Sciences and Humanities in cooperation with the Berlin Medical Historical Museum of the Charité University Hospital on

16/17 September 2010; Gerhardt et al. 2011) and, on the other hand, that the visual arts are addressing the issue, especially through the medium of the cinema (such as in May of this year in Vienna at Bio:Fiction, the world's first film festival devoted to this theme; www.bio-fiction.com).

Some scientists are presenting the complete synthesis of genomes, i.e. the central genetic information of a cell or organism, as the current variant of creating life. Following the successful sequencing of the genomes of three viruses – including the reconstructed virus of the Spanish flu of 1918 – by 2005, scientists from the laboratories of Craig Venter, probably the greatest media star among genome researchers, reported the complete synthesis of a bacterium genome which is many times greater (see Schummer 2011 in relation to this and the following). The to date greatest public sensation was generated by a press release from the J. Craig Venter Institute in May 2010 which stated that scientists had created the first synthetic, self-reproducing bacterium cell. As Joachim Schummer emphasises in his book »The Craft of Gods: The Artificial Creation of Life in the Laboratory«, the press release contains an unusually detailed exposition of the scientific methodology which, in conjunction with a superficial reading of the related scientific paper, would have made clear that this is nothing to do with a *de novo* creation of life in the laboratory, but merely a further step in the use of large DNA molecules and a targeted manipulation of bacterium cells. At the same time, however, the message of the »synthetic genome« and the »synthetic cell« was declared so prominently and further hyped in interviews that artificial life was the media message that emerged after all (Schummer 2011, p. 113 ff.). This also occurs as a result of people equating »synthetic cell« with »artificial cell«

(i.e. without a natural paradigm) in everyday speech. Interestingly, the religious implication in the sense of »playing God« occurred almost only in Catholic- and Hindu-dominated countries or media (including a large part of the German press), whereas Protestant, Islamic and Jewish voices tended more towards the »Frankenstein« or »Pandora's Box« image as a warning against possible uncontrollable dangers (Schummer 2011, p. 119 ff.).

All these images give rise more easily to scary (see below) messages about alleged artificial life than hopeful ones – the latter requires a connection with humanity's great challenges: world food affairs, global health, global energy and raw materials demand or resolving global environmental problems. However, it seems that the current status of synthetic biology does not really allow these positive hype goals or visions to be underpinned. One probable reason for this is that practically all of those involved emphasise that only microorganisms will be manipulated for the foreseeable future. In medicine this results in possible application prospects for simpler and more efficient production of complicated pharmaceutical molecules or for the optimisation of gene therapy processes using better vectors, i.e. vehicles for introducing the therapeutic DNA or RNA molecules. Neither of these is a revolutionary new approach, which therefore means that projections relating to synthetic biology do not offer any completely new prospects in medicine.

A »hype message« is most easily associated with renewable raw materials and fuel production with the aid of algae and other protozoa »designed« *de novo*. The primary goal which can be defined here is to resolve the food vs. fuel problem with regard to the use of agricultural land and the

protection of natural ecosystems (e.g. World Economic Forum 2010). This problem and its repercussions on food prices and the world food situation have become a central political and social point of contention with reference to the use of scientific and/or technical options. If visions of synthetic biology could render plausible a means of producing raw materials and fuels which saves land and resources, this would represent an ideal trigger for hype.

However, the communication of this vision has yet to really gain momentum. One reason could be that the debate on the global demand for energy and raw materials has become extremely complex, differentiated and controversial in recent years – completely independently of the developments in synthetic biology (SRU 2007; TAB 2010; WBGU 2009). It is difficult, therefore, for simplified proposed solutions and left-field visions to have an impact, in scientifically and politically relevant circles at least, but also in serious media. If genuine hype is to be generated here, it would have to be possible to report substantive results, e.g. relating to an increase in efficiency from the use of synthetic biology – but this is apparently not the case to date.

Because of their experience with the hope, hype and fear technology cycles up till now, secondary research and government funding bodies now react, depending on their point of view, as if this is all quite normal or with almost slightly hasty submissiveness. The natural sciences underpinning technology are scarcely able to meet the relevant demands with reference to producing new knowledge and developments. This results in the same old examples and considerations being brought up again and again, a reflex action which hardly any relevant institution is able to elude.

So, where is the hype in synthetic biology? Or does it not actually exist, and is it all just measured hopes without any exaggeration? The large number of projects, reports and statements actually indicates that it must exist. One possible suspicion is that the hype surrounding synthetic biology is something that happens in the »observer community« (from the field of technology assessment and innovation analysis, philosophy of technology and bioethics, in other political consultancy and research funding bodies) – as it were in the »discursive superstructure« of synthetic biology.

## FEAR: MONSTER GERMS FROM THE GARAGE AND OTHER GHOULS

Particular fears can be caused especially if something is entirely new or unknown, if it has the potential to cause significant damage or if people feel they may be especially affected by it.

Because of the lack of fundamental difference from previous developments in molecular biology and related research and applied fields, no concrete risk scenarios are actually emerging, given the current development status of synthetic biology. All the restrained statements on synthetic biology are in agreement here. At the same time they mostly also point out that this could change in the event of possible major development strides and that close, ongoing monitoring and analysis are therefore needed (please see in this regard the studies on the potentials of synthetic biology in box 2).

Such a step would be the »construction« of massively modified microorganisms, especially if they were to be used in the environment, outside of bioreactors. Such releases have not yet taken place, and many scientists regard this as unjustifiable. A recurrent idea is the

thought of using synthetic biology methods to incorporate mechanisms in the future microbe creations which will prevent uncontrolled reproduction, e.g. by using molecules which do not occur in nature as a kind of »genetic firewall« (Marlière et al. 2011; Schmidt 2010).

However, more concrete fears are directed not only towards the targeted, monitored use of organisms or substances manufactured by means of synthetic biology, but also towards those produced by amateurs in garage laboratories, whether intentionally or simply accidentally. This would be the other side of the coin from the playful/creative attempts by academics and researchers – if a relevant number of people were actually to start using BioBricks for fun or to scare others.

It is generally agreed that genetic engineering can now be carried out with comparatively little expertise and relatively inexpensive equipment. What is unclear, however, is how many »DNA DIYers« are already at work. However, the self-regulation within the associations of companies which are contracted by customers to produce large DNA molecules commercially as a raw material demonstrates that this danger is not regarded as irrelevant. In this the member companies undertake to check DNA orders for possible sequences of pathogens or toxins and also to document the orders and report suspicious orders to the authorities (IASB 2009).

On the other hand, attempts to impute an even greater danger to biodiversity

### BOX 1: SELECTED EUROPEAN AND GERMAN TA STUDIES AND INNOVATION ANALYSES IN SYNTHETIC BIOLOGY

- > »TESSY – Towards a European Strategy for Synthetic Biology« (Fraunhofer ISI, Karlsruhe; on behalf of the EU Commission; concluded 2009): analysis of the issue from the perspective of research and innovation strategies
- > »SYNBIOSAFE: Safety and ethical aspects of synthetic biology« (ITA and IDC Vienna, University of Zurich, ISTHMUS SARL Paris; on behalf of the EU Commission; concluded 2009): analysis of safety-related and ethical aspects and the public debate on the issue
- > »SYNTH-ETHICS« (Technical University of Delft, Dutch research institute TNO, the University of Padua, the Australian National University and ITAS, Karlsruhe; on behalf of the EU Commission; concluded 2011): analysis of ethical, legal and social implications
- > »Making Perfect Life« (members of the European Technology Assessment Group: Rathenau Institute, The Hague, Fraunhofer ISI, Karlsruhe, ITA, Vienna, ITAS, Karlsruhe; on behalf of STOA, the TA panel of the European Parliament): Synthetic biology (»Engineering of Living Artefacts«) is one of four sub-themes (in addition to »Engineering of the Body, of the Brain and of Intelligent Artefacts«)
- > »Engineering Life« (Institute for Ethics and History in Medicine and Centre for Biological Signalling Studies (BIOSS) at the University of Freiburg; ITAS, Karlsruhe; Theological Faculty of the University of Erlangen-Nuremberg; funded by the BMBF; start 2010): reflection on the ethical/philosophical and theological relevance of synthetic biology; analysis of the potential applications and statutory framework for dealing with potential threats
- > »SynBioTA – innovation and technology assessment of synthetic biology« (University of Bremen; funded by the BMBF; start 2010): comprehensive analysis of potential with reference to future focuses of research policy

or the biosphere as a whole from the visions of synthetic biology than is represented by »classic« gene technology and generate public debate have remained astonishingly low-key. It may be assumed that the declared opponents are also finding it difficult to communicate a plausible definition and vision of synthetic biology which could be even scarier than the applications and objectives hitherto for genetic engineering. The warning against selling off nature and against the unforeseeable consequences for the environment and health and the scares about the world view and the (patenting) intentions of scientists, industry and government were intensive enough with (green) gene technology and cannot be convincingly further intensified by adding the attribute »extreme« (»extreme genetic engineering« was the label applied to synthetic biology for a time by the ETC Group; ETC 2008).

The attempt to postulate a new form of protection, »evolutionary integrity«, and to introduce it into the debate about the protection of biodiversity, as in the case of the German non-governmental organisation »Testbiotech«, which is critical of gene technology (Then/Hamberger 2010), is a more interesting concept. However, it is not yet possible to say whether this will fall on good soil and will perhaps be able to move the scientific debate forwards.

In addition to these worries about the intended (»biosecurity«) and unintended (»biosafety«) consequences for the environment and health, the ethical and theological concerns about mankind's possible arrogance in shaping nature improperly to fit his own desires must be seen as part of the fears and anxieties about synthetic biology. Here, too, however, there are two factors which mean that, given the current state of synthetic biology,

the warnings against playing God will ultimately have little effect: firstly, because, for the foreseeable future according to practically all scientists, the issue primarily involves microorganisms which are to be modified and shaped for human purposes, and secondly, because – as with the concerns about biosecurity and biosafety – horror stories have always been circulated warning of eventual overstepping of limits, such as the breeding of humans, in connection with much more advanced or even established technologies (preimplantation diagnosis, stem cell research, cloning, germline therapy). If synthetic biology is to cause specific and new fears, it would need more plausible scenarios than hitherto which would presumably have to refer at least to higher plants or animals.

### GOVERNMENT STRATEGIES: PROMOTING RESEARCH AND DIALOGUE

The systematic monitoring of new scientific and technical developments with possible social, especially socio-economic relevance has been practised by all major industrial countries for years. The EU Commission addressed synthetic biology as long ago as December 2003 under New and Emerging Science and Technology (NEST) and announced a project tender in the autumn of 2005 with a value of 50 million euros. The major part of this went on scientific research projects, but a range of projects relating to the ethical, legal and social analysis and technology assessment (TA) of synthetic biology were also commissioned (box 1). In recent years reports and statements have been published by various bodies and institutes which advise governments, including in the Netherlands, the UK, Switzerland, Germany and the US (box 2).

A rigorous comparison of these documents in terms of relevant differences is beyond the scope of this paper, though a few striking areas of commonality may be mentioned:

- > None of the reports exaggerates the opportunities or risks of synthetic biology, which is not surprising in light of the constantly more comprehensive, deliberative approach, but is due to the early and as yet unclear development stage as described of most synthetic biology projects.
- > Nevertheless, synthetic biology is judged to be an important development field with major potential that should be promoted systematically and comprehensively.
- > All the statements from European countries and the EU at least clearly declare that a very important intention is to address the possible risks intensively from the outset, for precautionary reasons, on the one hand, and in order, on the other hand, to prevent a resulting debate in society blocking the use of potential opportunities.
- > The key recommendations on action resulting from this are the consistent continued monitoring of the scientific and technical field, including a regular review of whether national and transnational funding and regulatory measures appear appropriate, together with a comprehensive social dialogue on the opportunities and risks and how to deal with them. The guiding principle is good governance in the sense of planned action by responsible government, scientific and business representatives.

It is clear that the analyses and assessments of synthetic biology are shaped by earlier experience with the associated technology fields – emerging or new technologies, technical sciences or whatever you wish to call them – of

**BOX 2: SELECTED REPORTS AND STATEMENTS ON THE POTENTIALS OF SYNTHETIC BIOLOGY**

- > *Netherlands*: Commission on Genetic Modification (COGEM) (2008): Biological machines? Anticipating developments in synthetic biology.
- > *Germany*: Deutsche Forschungsgemeinschaft (DFG), Deutsche Akademie der Technikwissenschaften (acatech), Deutsche Akademie der Naturforscher Leopoldina (2009): Synthetische Biologie – Stellungnahme.
- > *United Kingdom*: The Royal Academy of Engineering (ed.) (2009): Synthetic Biology: Scope, Applications and Implications. The Royal Academy of Engineering (ed.) (2009): Synthetic Biology: public dialogue on synthetic biology. Biotechnology and Biological Sciences Research Council (BBSRC), Engineering and Physical Sciences Research Council (EPSRC), Sciencewise – ERC (2010): Synthetic Biology Dialogue.
- > *Switzerland*: Schweizerische Eidgenössische Ethikkommission für die Biotechnologie im Ausserhumanbereich (EKAH) (2010): Synthetische Biologie – Ethische Überlegungen.
- > *EU*: European Group on Ethics in Science and New Technologies (EGE) (ed.) (2009): Ethics of synthetic biology.
- > *Member States of the EU*: The European Academies Science Advisory Council (EASAC) (2011): Realising European potential in synthetic biology: scientific opportunities and good governance.
- > *USA*: Presidential Commission for the Study of Bioethical Issues (2010): New Directions. The Ethics of Synthetic Biology and Emerging Technologies.

gene technology and nanotechnology. Following the largely hostile political and social response to green gene technology – in particular the planting of transgenic crops – in Europe in the 1990s which was seen, at least by its proponents, as a disastrous failure and was blamed by many observers on poor communication, nanotechnology in the first decade of the new millennium offered an example of a significantly more complex, varied and assured discourse (as made clear in the paper by C. Revermann in this section).

In synthetic biology it is almost possible to gain the impression that the debate about opportunities and risks, while not in principle coming too soon, is nonetheless slightly too feverish. The fundamental uncertainty stated at the outset as to whether this is a meaningfully discrete field of science and technology leads to major problems of understanding, particularly with the general public, in association

with the far from clear application prospects in the attempted public debate to date. In the case of synthetic biology, scientists and politicians are evidently especially susceptible to the Collingridge dilemma, with which TA and forward-looking technology design are fundamentally faced (Collingridge 1980; Grunwald 2010b): If you don't want to be too late, you'll have to find your way in the dark.

For the German situation an evident but surprising feature should be noted when dealing with the problem of definition and understanding related to synthetic biology: while important professional associations and special interest groups within the German scientific community, especially the Leopoldina and acatech national academies, started to work extensively on the issue of synthetic biology as early as 2008 (box 2) and the Bundestag, as a consequence of initial soundings in its parliamentary

Ethics Committee, commissioned the TAB with its current project, the relevant ministry, although also commissioning two TA projects (box 1), has otherwise consistently avoided using the term »synthetic biology« in its funding programmes. This becomes particularly clear in the Biotechnology 2020+ strategy process which includes practically all the R&D approaches which are usually covered under synthetic biology without using the label (see the »official« presentation of the strategy process in Wirsching 2011). One consequence of this is that the Federal Government stated in March 2011 in its response to a minor interpellation by the Social Democrats (SPD) in the German Bundestag that it has funded »no research and development projects to date specifically in synthetic biology« (Bundesregierung 2011, p. 2). The impression could be given that Germany is lagging behind in this technological field or is concealing its involvement, as was suspected promptly by critics (Testbiotech 2011). Neither appears very plausible – perhaps the BMBF has simply decided to wait and see whether the term »synthetic biology« really catches on in the long term or falls out of fashion in just a few years, to be replaced by a different buzzword in the biosciences.

At any rate, the BMBF is thus closer to the researchers in the natural and technical sciences who frequently – unlike many external observers – do not use the term synthetic biology at all in relation to their projects. And, when dealing with the potentials of synthetic biology, this almost antiquated refusal to use the fashionable term can be seen at least as a prompt to repeatedly ask what the common feature really is in the different R&D lines mentioned initially.

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