



Background document for the SYNBIOSAFE e-conference

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1. INTRODUCTION

1.1. Aims and scope of the SYNBIOSAFE e-conference

Synthetic biology is becoming one of the hottest new fields of biology, with the potential to revolutionize the way we do biotechnology today. By applying the toolbox of engineering disciplines to biology, a whole set of potential applications are made possible ranging very widely across scientific and engineering disciplines. Some of the potential benefits of synthetic biology, such as the development of low-cost drugs or the production of chemicals and energy by engineered bacteria are enormous. There are, however, also potential and perceived risks related to deliberate or accidental damage. In order to ensure a vital and successful development of this new scientific field and in addition to addressing its potential benefits, it is absolutely necessary to gather information about risks and to devise biosafety strategies to minimize them. Also, ethical issues of synthetic biology are just beginning to be explored, with few ethicists specifically focusing on the area of synthetic biology. While a few undertakings on safety and ethics have recently started in the US, our project SYNBIOSAFE is the first initiative in Europe that focuses particularly on the safety, security and ethical concerns and tries to facilitate a socially acceptable development of synthetic biology. We have co-organized the safety/security and ethical sessions at the SB 3.0 in Zurich last June, and since then have carried out a survey among leading European synbio practitioners regarding their viewpoints on safety, security and ethical issues (to be published soon). Now we would like to share our thoughts and discuss the selected issues with a wider group of experts and interested stakeholders. This is why we are carrying out an **open online conference** - or e-conference – on the internet as part of our activities. The aim of this open e-conference is to further stimulate a debate on these issues in a proactive way at a relatively early stage. The discussions and consultations during the e-conference will be an important contribution to the production of our final recommendations, which will be delivered to national governments, international organizations, research centres, universities, and other stakeholders at the end of 2008.

1.2. Participation at the e-conference

We encourage you to actively participate in the online discussion. You are welcome to submit your professional expertise, opinion, or point of view at our e-conference. The participation is open to everybody interested in the ethical, safety and security issues of synthetic biology. It is very easy to take part:

Registration

1. Go to our website www.synbiosafe.eu/forum and click “**Register**”
2. Agree to terms and complete registration
3. Open the registration email in your mailbox and confirm (click the link)

Login and post your message

1. Go to our website www.synbiosafe.eu/forum and click “**Login**”
2. Go to the category of your interest.
3. If you want to add a new topic: just click “**new topic**” and post your text.
4. If you want to reply to an existing topic, just click “**post reply**” and write your text.
5. Finally click “**submit**”.

You can add new topics or reply to other topics as often as you want and we encourage you to take advantage of this special opportunity to discuss the societal issues of synthetic biology with a global community.

Some of the most important challenges – from our point of view - are explained in the following chapters. We look forward to discussing these issues with you. If you would like to suggest other issues, you are equally welcome to share them with us.

2. ETHICAL ISSUES IN SYNTHETIC BIOLOGY

2.1. Background

In this input paper two different attitudes towards ethical issues in Synthetic Biology (SB) are described. According to position A there are different types of ethical issues raised by SB. According to position B it is not important to discuss ethical issues in this context.

Position A: There are ethical issues that should be discussed

Creation of new life forms: “Creating life” is the most extreme form of control over other organisms. The possibility of creating living organisms bestows a new status and responsibility on scientists and society. Moreover, from a position that argues for an obligation to respect all living organisms or nature as whole, the creation of new life may be ethically problematic. The catch phrase: “scientists are playing god”, used in the context of SB and other new biotechnologies, expresses the uneasiness triggered by the idea of living organisms being designed and created by human beings.

Blurring of the boundary between living organisms and machines: SB products have features of living organisms as well as that of machines. This leads to a blurring of the border between these two categories and may have ethical consequences given that the separation between living and non-living matter is key to several ethical and philosophical approaches.

Patenting issues: Recent patent application on a modified *Mycoplasma* bacterium has drawn protests by NGOs partly because the patent claims rights on basic ideas that have not been realised yet. This can be considered unethical because such ideas should be, it is argued, freely accessible (see also the IPR chapter).

SB in human beings: SB may lead to potential applications in human cells and to new developments for gene therapy in adults as well as to modifications of human embryos. These techniques could be valuable tools in treatment of diseases but could also be applied to non-therapeutic purposes such as human enhancement, leading to another set of ethical questions.

The “synbio-divide”: The “digital divide”, “genetic divide” or “nano-divide” describe large gaps between geographic areas and socio-economic factors regarding to the opportunities to access the technologies. Analogous to these “divides” is the danger that the unequal chances to profit from SB might lead to a “synbio-divide”, which raises ethical issues such as justice and equity in access and power.

Position B: There is no need to discuss ethical issues

There are no new ethical issues in Synthetic Biology: As SB is closely related to gene technology and nanotechnology, most of the ethical issues have been discussed in those contexts before. In this light an open discussion on ethical questions connected to SB is considered unnecessary.

Ethical issues are really about public concern: Since the 1980s bioethical issues are often discussed in the public arena, making them more pressing and relevant than if discussed among experts only. This could seem to indicate that ethical issues are in fact no more than a reflection of public perception. If the public can be convinced of the innocuousness and sound principles of SB then no further ethical discussion is necessary.

Ethical issues are culture-relative: Values, principles, norms and intuitions, which play an important role in ethical evaluation, are culture-dependent. Given that SB research takes place at the international level and that there are significant cultural (and perhaps moral) differences across social groups, countries or even continents, such ethical debates are useless in the

international arena. The development and ethical evaluation of SB will in the end depend on the local ethical and regulatory frameworks.

Ethical debates may influence technology development nevertheless: Although ethical issues, together with risk claims, are often considered to be reflections of public concerns only, ensuing debates on ethics and/or risk are said to have entailed restrictive regulation in some cases. Thus, some scientists think such debates eventually may impede technology development through the generation of hostile public perceptions and/or restrictive regulation.

2.2. Ethical questions to be discussed

- Are there any new ethical issues related to synthetic biology, if yes, which ones?
- How do similar ethical debates in other technologies affect the ethical discussion in SB? Does it make it redundant and useless?
- Is the synthesis/creation of a living organism (or parts of it) per se ethically problematic, if yes, why?
- Does the design of living machines, entities that are “part organisms part machine” raise ethical or philosophical problems?
- Are patents on a “synthetic life form” or parts of it unethical?
- Should synthetic biology in human medicine be supported, if yes, up to what point?
- Is synthetic biology widening the divide between the rich and the poor?
- What is the impact of public concerns in determining ethical issues?

3. BIOSAFETY OF SYNTHETIC BIOLOGY

3.1. Background

For a discussion of the biosecurity implications of synthetic biology it is important to start with a distinction between the terms “biosafety” and “biosecurity”. While biosafety covers measures that aim to prevent the unintentional exposure to pathogens and toxins, or their accidental release, biosecurity measures focus on the prevention of theft, misuse, or intentional release of pathogens and toxins. Thus, biosafety and biosecurity are inextricably linked, with the latter building on the former.

Biosafety vs. biosecurity: Up to now most concerns – especially from the US - on potential new risk of synthetic genomics and synthetic biology referred to biosecurity threats. Given the past biotech debates in Europe it is likely that the European public, the media, NGOs and also scientists could be more concerned with safety issues rather than security issues. Will synthetic biology deepen the transatlantic divide opened up during past biotech debates?

Anything new? In order to focus on the biosafety risks from a scientific point of view it is necessary to distinguish as clearly as possible the safety issues that arise in synthetic biology from those associated with other life science activities. Many scientists argue that synthetic biology opens up fascinating new opportunities for the future bioeconomy while on the other hand when asked about the biosafety risks they unenthusiastically comment that these will remain the same as before. Is it really possible that such a promising new enabling technology will only yield useful and desired outcomes and doesn't automatically create new unintended consequences?

New challenges for risk assessment: In traditional genetic engineering the risk assessment is based on the donor organisms. Most transgenic organisms so far contain genes from relatively few parental organisms. In synthetic biology, however, the situation changes because

organisms can be created with a large number of genetic donors or even without any natural templates at all. Also instead of changing only few genes, with synthetic biology we will be able to create completely new genetic networks without known counterparts in nature. Given the absence of natural templates as a basis for solid evaluation, how can a risk assessment be carried out under such circumstances?

Controlled environmental release: Some foreseen SB applications such as environmental biosensors or bioremediation require deliberate releases into the environment. Given the shortcomings of current risk assessment practices in the light of synthetic biology, how can we make sure the novel organism fulfils only the tasks we engineered in it and does not behave in an unexpected and harmful way once it is beyond the reach of human intervention?

Future applications for food or medicine: Synthetic biology is still in a very early stage and most potential applications still lie ahead, however, some applications could raise new biosafety questions in the future. As an example we can have a look at the project ideas brought forward by some iGEM teams. In one example it was proposed to engineer the human gut bacteria *Lactobacillus casei* to make vitamins and essential amino acids to solve vitamin deficiencies in third world countries. This – hypothetical - strain would be able to detect the concentration of the vitamin or other essential compounds and synthesize more of it if required. Other developments currently in the pipeline aim to design synthetic gene networks (such as oscillators) in human cells in order to produce context depending biochemicals such as insulin. What would happen to the production of the biochemical compound if the network fails? Can these safety concerns be considered already in the design process?

New biosafety systems: Synthetic biology could improve the design of new and unconventional biosafety systems. One aspect would be the engineering of artificial dependencies on certain biochemical compounds into an organism for higher external control. In other words an organism would only survive as long as this specific biochemical compound is available in the environment or supplied by humans. Another approach would be the design of alternative biochemical systems, or in other words the creation of a parallel biological system that can not directly interact or exchange genes with regular organisms. A possible way to achieve this aim is the use of alternative base pairs, or the use of non-DNA/non-RNA nucleotides, or the use of other “orthogonal” biochemical systems.

Biohacking: Some synthetic biologists argue for an open source approach enabling also individuals outside the traditional biotech community to engineer living systems. As an ultimate consequence this would mean that anybody who wants to could invent a biological system and pull it off, without having to go through a big research process to do it. If this would become a reality then we will see a large number of biohackers and garage biologists who design and produce new life forms as they please, with no oversight in place.

3.2. Biosafety questions to be discussed

- Does synthetic biology raise new biosafety questions, and if yes, which ones?
- Do we need a new kind of risk assessment? How should it look like?
- Should we consider environmental release of “synthetic” organisms under the current biosafety framework?
- Can we include safety concerns already in the design process of novel SB applications?
- How feasible are new biosafety systems based on alternative biochemical systems?
- How realistic is the biohacker scenario? What should be done to prevent biosafety risks caused by unaccountable garage biologists?

4. BIOSECURITY OF SYNTHETIC BIOLOGY

4.1. Background

In addition to the biosafety issues mentioned in the preceding section, there are several biosecurity ramifications of the emerging field of synthetic biology that need close attention. Although reports on and assessments in the field of synthetic biology most of the time make reference to potential risks, these are neither spelled out in detail nor are potential measures to discuss such biosecurity risks developed in great detail. One exception is Tucker and Zilinskas (2006: 31) who distinguish three categories of potential risks from developments in synthetic biology.

“First, synthetic microorganisms might escape from a research laboratory or containment facility, proliferate out of control, and cause environmental damage or threaten public health. Second, a synthetic microorganism developed for some applied purpose might cause harmful side effects after being deliberately released into the open environment. Third, outlaw states, terrorist organizations, or individuals might exploit synthetic biology for hostile or malicious purposes.”

The likelihood of these risks materializing will in part depend on the degree of diffusion of SB knowledge and skills. Given the de-skilling agenda (i.e. the simplification of engineering life) inherent in some of the SB approaches being pursued, it would seem prudent to expect large-scale diffusion and conceptualize governance measures accordingly so as to prevent the above risks from becoming reality. However, any governance and/or regulatory measures will have to rely on the involvement of the scientific community who is pushing forward the boundaries of knowledge in this emerging area. Such involvement, in turn, requires that synthetic biology practitioners are aware of the dual-use character of much of their work. As a recently conducted study shows, such awareness is mostly non-existent among a set of 20 leading European synthetic biologists¹. This raises questions as to the advisability of letting this scientific community govern itself with a view to preventing the misuse of its findings and products and the extent and form of potential oversight mechanisms.

4.2. Biosecurity questions to be discussed

From a European governance perspective, several questions need to be addressed in order to prevent the most serious biosecurity risk, i.e. the malign misuse of advances in synthetic biology:

- How best to raise the low level of biosecurity awareness among European SB practitioners? What is the role of education in such an awareness-raising effort?
- In light of the current low awareness level, to what extent can the SB community be expected to successfully govern itself and thereby prevent the misuse of newly created knowledge and skills? Are unified screening methods for DNA sequences sufficient?
- How can we encourage and institutionalize a higher level of interaction between the SB and biosecurity communities?
- Do we need a European Biosecurity Oversight Organisation as part of a comprehensive governance framework for SB (and the life sciences more generally)? If yes, what would its role and competencies be?
- Which form should a constructive transatlantic dialogue on the biosecurity implications of SB take?

¹ see http://www.synbiosafe.eu/uploads///pdf/Synbiosafe-Biosecurity_awareness_in_Europe_Kelle.pdf

5. OTHER ISSUES

Apart from the three areas described above, there are of course also other important societal issues at stake in relation to synthetic biology. The following brief chapters try to summarize the open challenges.

5.1. IPR: patents versus open source

The aspired applications and related profit of SB inevitably raise questions about intellectual property rights. At which stage and to which extent should SB innovations and inventions be protected? As observed by O'Malley *et al.*² different strategies are applied in different branches within SB. Whereas synthetic biologists in the bioengineering field call for open access to the basic elements of their technology, the synthetic genomics branch aims to patent basic ideas (see ethics section). The tight relation of synthetic biology with systems biology and other basic research areas makes it difficult to distinguish between discovery and inventions, adding to the complexity of the discussion.

5.1.1. IPR questions to be discussed

- What is the more appropriate strategy for SB: patents or open source?
- In which areas of SB is patenting justified?
- How can scientific knowledge remain accessible in spite of patented applications?

5.2. Regulation and governance

If ethical, biosafety and biosecurity impacts of SB are taken seriously, the question comes up how this novel technology should be regulated. Should we be guided by the worst-case scenario or rather the most probable scenario? Different regulatory mechanisms may follow the former or the latter principle. Some pro and con arguments of three regulation models are listed.

Self-regulation by scientists

pro: Since laws are too slow scientists are best placed to regulate their science according to the latest developments; Scientists and engineers are the experts in their field and no one is better placed to know which regulations are appropriate.

contra: Synthetic Biologists are biased and cannot objectively judge which regulations are necessary. Researchers active in the field may have a profound self interest in avoiding any cumbersome regulation while other actors might consider regulation necessary.

Participatory approach involving several stakeholders (including civil societies)

pro: Since the whole society will be affected by the consequences of SB, different stakeholders should be involved in setting up the regulatory framework. Involving many views and different kinds of expertise in setting up a regulatory framework makes the result both sounder and more acceptable to many stakeholders.

contra: A participatory approach would impede the development of SB due to negative hype and ungrounded fears. Furthermore, it would be impossible to find a compromise between the different parties. The only way to regulate such a new technology is through a governmental legislative approach.

International guidelines

pro: Since research in SB is done at the international level the only efficient way to regulate it is through international guidelines.

² Maureen A. O'Malley, Alexander Powell, Jonathan F. Davies, Jane Calvert 2008. Knowledge-making distinctions in synthetic biology. BioEssays. Volume 30, Issue 1, Pages 57 - 65

contra: International guidelines are not realistic because it will be difficult to find a common ground that is universally acceptable.

5.2.1. Regulatory questions to be discussed

- Do we need new regulatory approaches for SB or are the existing regulatory frameworks sufficient?
- Should the precautionary principle be applied? What would be the outcome?
- Which of the described models is the most appropriate approaches to regulate SB?

5.3. Public perception, communication and the media

Public support for new technologies cannot be taken for granted. The examples of negative public perceptions on agricultural biotechnology in some countries and of popular moral positions against stem-cell research show that ensuing regulatory restrictions can seriously impede the implementation of a new technology. Synthetic biology is said to contain elements that are prone to elicit negative public sentiments, such as the promise to create new living organisms. Many issues discussed in terms of ethical relevance have their counterparts in popular perceptions (see above). Technology developers often fear hostile public reactions with the next wave of technology in general, and with Synthetic Biology in particular, which they try to avoid. A major issue here is how to deal with a public debate – to engage in or to avoid it?

Proactive communication?

Pro: By actively approaching the media and engaging in public relation activities, the scientific point of view can be better conveyed to the public. Stimulating a broad public debate involving NGOs and other sceptical actors may render the debate more sensible and take the steam off.

Contra: Environmental NGOs and sensationalist media reporting cannot be prevented from spreading unwarranted fears and denouncing new technologies. Any public debate could lead to a generally negative public perception, which in turn may induce politics to enact restrictive regulation.

5.3.1. Public perception questions to be discussed

- Is there a danger that SB will meet the same resistance in the public as, for example, agricultural biotechnology?
- What is the most appropriate way to deal with upcoming public debates?
- Should scientists and technology developers actively stimulate and engage in a public debate?

