THE DANISH COUNCIL OF ETHICS

TEKNOLOGI-RÅDET
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SYNTHETIC BIOLOGY

A discussion paper

Synthetic Biology
A discussion paper

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Preface

This debate material is the result of a collaborative project on synthetic biology carried out by The Danish Board of Technology and The Danish Council of Ethics from April 2010 to April 2011. The aim has been to open a broad debate on synthetic biology beyond the boundaries of the professional research environment.

By way of dialogues with experts and other parties with knowledge of and interest in this subject we have attempted to shed light on a new development area within biotechnology and genetic engineering. We consider it important to discuss the perspectives in synthetic biology while this research area is still in its embryonic stages.

With this project we want to:

1) Impart knowledge on the nature of synthetic biology
2) Provide examples of the potential uses of synthetic biology
3) Present the dilemmas and challenges inherent in synthetic biology within areas such as research priorities, ethics, democratic handling, risk assessment and public regulation.

The Danish Council of Ethics and The Danish Board of Technology have set up a work group consisting of experts in biology, physics/chemistry, philosophy, risk communication and science presentation. These people have pinpointed the themes of the project, contributed specialist knowledge and written parts of the debate material. In January 2011 The Danish Council of Ethics and The Danish Board of Technology hosted a workshop on synthetic biology where the participants contributed various kinds of input to the debate material.

This material is intended to open a debate on synthetic biology, but also to suggest ways to handle the future challenges of synthetic biology in Denmark. The material does not offer any conclusive assessments of the potentials and challenges in synthetic biology.

The material will be distributed to a wide range of research environments, companies and public institutions with a potential stake in synthetic biology. Since one of the most significant problems in relation to synthetic biology concerns the possible need for new legislation, we have included political decision-makers and public authorities in the target audience as well. Furthermore, the material is submitted to the participants in the workshop and to a wide circle of institutions in regular contact with The Danish Board of Technology and The Danish Council of Ethics.

EA work group on synthetic biology within the framework of The Danish Council of Ethics has commented on various versions of the material. The material as such, however, has not been processed by The Danish Council of Ethics. The Danish Council of Ethics and The Danish Board of Technology would like to thank the work group for a very strong commitment to the whole project and for major contributions to the design of the debate material.

The work group consists of :

Birger Lindberg Møller, The Faculty of Life Sciences, University of Copenhagen
Gunna Christiansen, The Danish Council of Ethics
Jakob Vedelsby, freelance journalist
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Thomas Breck, The Danish Centre for Risk Communication

Assessments in brief

The work group's assessments of synthetic biology and suggestions for further debate

The 21st century is characterised by major investment and strong faith in new biotech research and by visions of bio-based societies with a number of potentially useful improvements of everyday life. By way of ground-breaking advances in biotechnology we hope to be able to find new forms of energy that are not based on fossil resources and to develop new products that can help us control and remove pollution, new or improved medicine, new sustainable materials and substitutes for harmful chemical substances. In addition, there is great interest in new insights into the fundamental "building blocks of life."

However, the 21st century is also characterised by a critical stance towards certain areas of biotechnology, in part, due to the development of genetically modified plants in recent decades and because of scientific research trends that some consider ethically dubious. Biological and genetic research and developments can lead to improvements and new sustainable solutions, but it can also have negative consequences for humans, nature and the environment. Moreover, such consequences can be considered a warning not to take the positive societal role of science and technology for granted.

This debate material seeks to contribute to an open, unprejudiced debate on synthetic biology in the making, including the positive expectations to the results of this research and the new knowledge it may afford us on the smallest units of life and their basic functions. But the material will also look at synthetic biology in a more critical light. It is important to include both positions in order to avoid polarizing the debate. And it is important to be able to aim at socially sound uses of scientific research, tenable research priorities and a socially informed science policy.

Synthetic biology can be described as a meeting between different disciplines. At present, synthetic biology has a lot in common with traditional biotechnology and genetic engineering, but it is based on a more radical vision of constructing living or life-like structures designed to perform particular tasks, much like engineers build computers and machines today. In implementing these visions molecular biologists and geneticists team up with nano engineers, computer scientists and chemists. This cooperation results in more than just new technologies and applications; it produces fundamental knowledge of life as such. The endeavour to construct living organisms from inanimate elements has always commanded considerable interest. Hitherto, however, successful outcomes of this intention have been confined to theoretical scenarios – within a sci-fi framework.

In sum, the work group behind this discussion paper evaluates the situation as follows:

- Synthetic biology is still in a very early phase of its development, so there is ample opportunity to be proactive in this area. This gives us a chance to promote a very inclusive interdisciplinary dialogue about the perspectives of synthetic biology with contributions from various researchers, companies, authorities and grassroots – so as to create an open exchange of ideas between private and public actors and stakeholders and between converging opinions and insights.

- We need an open dialogue about synthetic biology focussing on:
    - the increased possibilities of cooperation in

Danish research communities
- the potential applications of synthetic biology in relation to the environment, energy, health, agriculture etc.
- the environmental, medical, ethical, legal and social aspects of synthetic biology, including the necessity of continually re-assessing the adequacy of public regulations
- the prioritization of research funds in light of Denmark's position in global research
- the mapping of the activities of the international research communities

- In the opinion of the work group, synthetic biology involves only limited risks in its present stage, and there is currently no need for new legislation for this particular area.

- It is important to work for a responsible manage ment of research and development in synthetic biology. A responsible development of new prod-ucts within the field of synthetic biology requires individual researchers and authorities alike to exercise great caution and vigilance.

- We need a continual assessment of the need for regulations of the pursuit of new research and development potentials in order to maximize use-value and minimize damaging and harmful ef-fects. It may prove advantageous to have clear guidelines for the achievement of safety and security in biotech research and development, but such guidelines should not be allowed to obstruct or constrain possible scientific developments or check creative research potentials.

- The public at large is a crucial stakeholder and must be continually involved in the ethical and value-oriented aspects of the discussion, e.g. the question of acceptable and unacceptable uses of synthetic biology, the determination of the extent to which research in synthetic biology should be publicly funded, the definition of acceptable risks and the settlement of the social and cultural signifi cance of synthetic biology.

- The impact of synthetic biology will be global. It is imperative that individual countries enter into international collaboration on the potentials of synthetic biology and help make the necessary regulations a common concern. The global nature of the issues at stake calls for transparency, coordi-nation and shared information and practices.

- Cooperation between researchers, developers, patent-holders, companies and authorities must be stimulated and promoted in order to create synergies and innovation strategies.

- Risk assessment must be integrated in biotechno logical research as such and not just relegated to special forums, and we need to develop more specific tools for the control and regulation of the possible damages and risks involved in synthetic biology.

Synthetic biology – a point of view by Maja Horst

In Denmark, we need to discuss our research priorities. We do not have the resources required to do all the things we would like to do. Nor do we have sufficient resources to compete with big countries with huge research budgets for extensive initiatives. When we have tried to fund strategic research in the past, the sums involved have often been so small that it is almost worse than nothing, because it makes researchers jump from one little project to another without really getting anywhere.

Real advances in synthetic biology involve heavy expenditure – and it takes years to procure the necessary funds. Politically and democratically, we may not be ready for such obligations. For a number of reasons, however, Denmark must continue to have experts who can understand, explain and adapt the knowledge produced abroad. Even if we cannot afford to invest in major projects, it is probably a good idea to let Danish scientists continue to conduct research in synthetic biology to the extent they consider it relevant for their areas of expertise. In light of these circumstances we need to discuss whether we should earmark specific amounts for synthetic biology or finance such research through the unspecified funds allocated to basic research programs in general.

Furthermore, we need to consider whether our public regulation system is suitably organized. The current division into sectors and disciplines is a relic of the past and may be ill-suited for new research areas such as synthetic biology. The field of synthetic biology cuts across IT, bio engineering and health, but these areas are typically regulated separately. As science becomes ever more interdisciplinary, the public regulation should follow suit.

Synthetic biology – a point of view by Sune Holm

Do all organisms have a moral status? Ethical discussions of synthetic biology often raise the question of whether living beings are entitled to be treated with moral consideration. If you believe all living beings have a moral status, synthetic biology is apt to raise the question of whether it alters the moral status of an organism that it has been designed and created by humans as a means to a specific end. The most widespread opinion among moral philosophers is that we should only show consideration for beings that are able to feel pain. The fact that an organism is animate is not in itself sufficient reason to grant it moral status.

According to another tradition, however, all living beings have a right to be treated with moral consideration, not necessarily because all living beings originate from a divine creator, or because it would ultimately be to our disadvantage if we did not treat all living being with the proper respect, but because our actions can both harm and benefit these organisms. For instance, we often say that it is bad for a tree if you deprive it of water and sunlight or that living, animate beings can become ill, even if they cannot feel anything. It is important to keep in mind, though, that claiming a moral status for all living beings is not the same as saying that it is always wrong to kill them. Acknowledging that a tree or a yeast cell has a moral status may simply carry less weight than other considerations.

Synthetic biology – a point of view by Gunna Christiansen

When I believe synthetic biology has great potential, it is not so much because we can already point to a lot of concrete results, but rather because the premise looks highly promising in a technological perspective. In synthetic biology, the complexity of living organisms is replaced by simple designs. The problem faced by GMO researchers trying to understand what happens inside complex natural cells when you insert a few new genes, is precisely what synthetic biology seeks to solve by assuming an unprecedented degree of control over the fundamental structure of the organism by picking the most suitable designs from animate as well as inanimate nature creating a kind of mini-cyborgs that are hard to place within our customary moral categories.

But maybe it is precisely the unlimited character of these possibilities that causes concern. The first question to arise is probably whether such 'tailor-made' organisms will react or conduct themselves in unforeseen ways? Another possible concern is related to our sense of nature. Arguably, the idea of nature as a set of building blocks is a symbol of the ever more intensive exploitation of nature which, according to many, has already gone too far. Is exploiting nature at odds with showing humility and respect towards it? Not necessarily. But we must face the fact that redefining nature may lead to gradual changes in our views of what we are permitted to do to it.

Registries such as BioBricks and techniques for synthesis of DNA and proteins will give a tremendous boost to the development that began with genetic engineering. It is almost unthinkable that this would not, in time, result in concrete applications, including possible solutions to some of the most urgent societal problems in relation to energy, climate and health. But because the potential is so enormous, and because we cannot anticipate the scientific breakthroughs, it is currently impossible to tell whether synthetic biology will lead to this or that particular advantage or disadvantage. The ongoing activities within synthetic biology are deemed satisfactorily regulated by the present legislation for this area, including the regulations that apply to genetic engineering.

Synthetic biology must be allowed to develop, and I believe we must monitor this development. In this respect, it is important to have a debate focussing on the requests and concerns voiced by ordinary citizens.

Synthetic biology at issue

DEBATE

How can synthetic biology realistically contribute to positive societal developments – now and in the long term? And what role should Denmark play?

Why do we need a debate on synthetic biology? And how are we to conduct it?

There are at least three good reasons why it is relevant to debate a new area of technological development such as synthetic biology:

1) New technology can influence the organization of society and the conditions of our mind-set and our physical, social and cultural life. Therefore, society is obliged to inform citizens of new technologies and actively take a position on them.

2) The choice of technology is partly a result of a political prioritization of research and development funding. This prioritization should also take place on an enlightened and democratic basis.

3) We know from experience that new technologies can have positive as well as negative consequences.

The purpose of the debate is to inform about the technological possibilities, to ensure democratic influence on the technological choices and to increase the consensus on the directions and values that should underlie the technological development – including the risks we are willing to run in order to achieve the positive gains and opportunities offered by new technology.

As will appear from the present discussion paper, the purpose of research in synthetic biology is to contribute to the solution of problems and to help cover a number of societal needs. This is a beautiful ideal that no one could disagree with. Disagreements arise, however, once we raise the question of which societal problems to solve first. The answer to this question will depend a great deal on one's convictions and values. The work group behind this project considers it highly important that the debate on synthetic biology also focuses on our values and our understanding of the various problems – and not just on the possible solutions offered by synthetic biology.

Experiences from the GMO debate

Two decades of European controversy over genetically modified plants has given us a number of valuable experiences when it comes to the relations between risk, technology and society. According to one view, it is largely because of confusion and entrenchment that it has been almost impossible to find funding for research in the practical use of genetically modified plants. In turn, this has meant that researchers have only been able to fulfil a few of the many promises some saw in GMO. Now, some fear that a similarly adverse controversy over synthetic biology will lead to the same result and create mutual mistrust between scientists and citizens.

According to the opposite view, the public debate on genetically modified plants has shown that citizens actually are interested in taking part in debates on new technology. The debate also showed, however, that the citizens lose faith in science, if the research environments fail to take an active interest in how citizens feel about use, risk and ethics, and if they fail to achieve the promised results.

This latter point is reflected in the debate on the uses of medicine produced by way of genetic engineering. This debate has a different character, probably because citizens have been able to see a direct use-value right from the start, and because legislation for genetic engineering was enacted quite early in the process. This legislation protects the personnel working with genetic engineering, but also the surrounding environment. Also, we have witnessed no negative effects on humans, animals or nature in relation to genetic engineering, perhaps because of this legislation.

Facts about synthetic biology

One of the crucial visions for synthetic biology is the ability to produce biological components, systems, cells, organisms and life-like structures in a grey area between the animate and the inanimate. To a certain extent, synthetic biology constitutes a completely new field – especially the branch of synthetic biology that concerns the making of living organisms from new materials. If researchers succeed in this, it will open a vast range of new possibilities that we cannot yet link to particular purposes.

The other branch of synthetic biology, where you fabricate, isolate or purchase genes and combine them in new ways, is not a completely new departure in itself. What is new, however, is the use of research teams comprised of people with different backgrounds such as bio-informaticians, engineers, molecular biologists, chemists, physicists and medical doctors. And that you use computer-generated data to identify the relevant components, that you order them as BioBricks and combine them in new ways in order to make whole systems or simple organisms, e.g. bacteria, yeast cells or algae with the desired qualities. The first products have already been made and are about to be marketed.

The American researcher Craig Venter's synthetic genome is an example of this branch of synthetic biology. He has created a bacterium in which the cellular machinery (what you might call its hardware) derives from one organism, whereas the genes (the software, so to speak) derive from another organism. The idea with this 'prototype' of a new bacterium is to show that it is possible to transplant whole genomes into a new 'shell'. The point is that we will be able to design bacteria and use them to generate the products we want.

It remains a fact, however, that many of today's research projects labelled as 'synthetic biology' were previously categorized as genetic engineering, nano medicine or plant biotechnology. New designations are created not only for technical reason, but also in order to attract funding. On the other hand, emergent technologies will always contain many well-known elements in the initial stages. In other words, 'new' does not necessarily refer to the technique as such. Rather, it may at first denote a different vision or organization.

Biology as engineering

In many ways, synthetic biology is akin to traditional biotechnology, not least genetic engineering where the object is to modify the heredity of various organisms by moving a single or a few genes, typically from one species to another. Synthetic biology is more radical in its approach, however. It is often described as an endeavour to turn biology into a kind of engineering. In synthetic biology, you 'build with bricks', and these bricks are typically elements of living organisms such as genes, proteins or cell membranes, combined with elements of the 'inanimate' world such as electrodes, metal surfaces and nano fibres.

Major strands of synthetic biology aspire to look at biological systems much like an engineer would look at making a computer for instance: In order to make a system perform efficiently it is necessary to standardize the elements so as to make their function as controllable as possible regardless of the setting. For example, when you buy an external hard drive online, you can reasonably expect it to be compatible with the other parts of your PC. Correspondingly, synthesis biologists hope to develop standardized elements and modules that other synthesis biologists around the world will be able to insert in their biological constructions. Cells, for instance, are referred to as a kind of 'chassis' that will hold the various biological elements in a 'plug and play system' that can easily be realigned or re-programmed for new tasks.

Ownership and accessibility in synthetic biology

The engineering approach to biology is a long-standing phenomenon, but the technological development enables a far higher level of ambition for biological engineering. Today, a number of techniques have reached a stage where they can be used by ordinary laboratories. This applies to the identification of DNA sequences and the synthesis of DNA and proteins, for instance.

One of the most significant obstacles for molecular biological research has been the time and effort expended on the identification or fabrication of precisely those genetic components that would perform a particular task, e.g. a specific variant of an enzyme with a very special ability or capacity that the researcher may have found in nature. Consequently, researchers often hold such components close to the chest. It is clearly easiest to procure such components, if one has something to 'barter' with.

Within the international synthetic biology community there is currently a tendency to make single components available for free in the form of so-called 'BioBricks', i.e. building blocks that other researchers or companies can use in new combinations for patentable products. Several key laboratories working with synthetic biology have decided to place single components at free disposal managed by the BioBrick Foundation.

Synthetic biology differs from other research when it comes to the question of funding and ownership of the research results. In the Western world we have chosen to grant patents to new inventions, because we believe it is the best way to promote an innovative society. Large sections of the basic scientific research, however, cannot be expected to yield immediately patentable results. Here, private partners will typically have very little incentive to finance research projects.

As a result of this, basic research must be financed with public funds or by charitable foundations that do not invest with an eye to immediate profit, but rather to support research that can be expected to create greater knowledge and perhaps, in the long term, lead to commercial products as well. In recent decades public research institutions have also begun to take out patents and claim proprietary rights in various inventions. These institutions generally aim to sell off the rights to utilize such patents to private businesses, because they are typically the only players with sufficient resources to make the investments it requires to develop the original idea into a commercially viable product. Universities will then make agreements with investors and receive royalties from the products that result from the patents. This arrangement means that research results, funded by the public, is not immediately available for everyone to utilize practically and commercially.

In the last 30 years intellectual property law has undergone a series of disputed changes, not least within the area of biotechnology. The European patent directive from 1998 establishes that, in principle, one can take out patents for genes, if the 'invention' is covered by normal patent requirements such as inventiveness. Critics point out that a patent on a gene may bar other researchers from making further inventions or prevent scientists and doctors in testing patients for specific genes. In the 1990's, for example, the American company Myriad Genetics took out a patent for two mammary cancer genes (BRCA 1 and 2). They demanded substantial payments for genetic tests of patients and aggressively sought to hinder American and European hospitals in running independent tests for these genes. Such measures seem unusual, however. Generally, we must assume that holders of broad-range patens have an interest in licensing others to utilize their patents.

On the other hand, we must also expect the financial interests in synthetic biology to increase rapidly when this research gradually begins to result in marketable products. When that happens, it is not unlikely that the field of synthetic biology will run into similar discussions about the relations between research funding and the right to use the results.

Synthetic biology is still an emergent discipline

Generally speaking, synthetic biology unfolds at an early level of basic research. Consequently, it is exceedingly difficult to predict the concrete results, products, risks and ethical/moral challenges it will lead to 20, 30 or 40 years from now.

History shows us that some of the discoveries that have truly changed the world have been in the pipeline for many years before they finally broke through, whereas other inventions and discoveries have had almost instantaneous impacts and consequences. Nor can we be sure that expectations and predictions always come true – no matter how long we wait. In addition, it has proven almost impossible to foresee all the possibilities and risks that new technologies bring about in the course of time. Think of the first computers in the 1950's or the use of pesticides like DDT.

Approaches to research in synthetic biology

The top-down approach

In the top-down approach to synthetic biology researchers focus on simplifying cells. Usually, you begin with a living cell in which you remove genes from the genome until the latter has become so simple that the cell is only just capable of reproducing itself. Similarly, the genes can be disassembled and used as 'BioBricks' when manufacturing new organisms. New, artificially produced genomes can also be transplanted into living cells. This approach is anatural continuation of traditional genetic engineering and it is often referred to as 'radical genetic engineering' (see Figure 1 (A)).

The top-down method has the merit that, in principle, it operates with a living, modern cell which allows it to make use of molecular biological lab techniques. This, however, gives the method the same limitations as modern biological cells.

In May 2010 researchers from the American J. Craig Venter Institute announced that they had successfully constructed the first synthetic genome transplanted into an existing bacterium cell. Even though the genome constitutes less than 1 per cent of the biological machinery, this is truly a milestone after about 15 years of foundational the top-down research. The synthetic cell, known as Mycoplasma mycoides JCVI-syn1.0, proves that it is possible to design a genome on a computer, produce it chemically in a laboratory and transplant it into a recipient cell. This bacterium, then, is a new, self-replicating cell controlled only by the synthetic genome.

One particular vision for the top-down approach concerns a re-programming of organisms by way of standardized genetic parts, i.e. BioBricks. Jay Keasling's research team at University of California in San Francisco has developed a yeast cell secreting the antimalarial drug artemisinin in such quantities that a large-scale production is planned to begin in 2012. Successful research in this vein presupposes that the many different genetic components are highly accessible and fully described. Here, accessible means that testing the function of the various genes or gene variants in an organism is a relatively fast procedure. This is a prerequisite, because the interplay between genes and organism is so complex in general that it is quite impossible to know for sure in advance whether a gene will serve a particular function sufficiently well

The bottom-up approach

In the bottom-up approach researchers seek to put together a biological system with a minimal degree of life –a so-called proto-cell – from inanimate, inorganic and organic materials. One variant of this approach works with materials that are essentially different from modern biological molecules (see Figure 1 (B)). Another variant uses components from existing biological cells (see Figure 1 (C)).

The bottom-up method is a natural continuation of the studies in the origin of life and scientific research in artificial life, e.g. experiments with life in media such as robots and computer network.

The advantage of the bottom-up method is that it can use all kinds of materials as building blocks, including biological, inorganic and electronic components. This frees the method from the usual biological constraints. The big scientific challenge is the construction of a living machine from scratch.

By way of example, a Japanese research team in Osaka headed by Tesuya Yomo has developed a design for a minimal synthetic cell which they are now in the process of implementing. This artificial cell consists of an artificial cell membrane filled with artificially manufactured biochemical components with the capacity to replicate an artificial DNA. The cells are ‘fed’ so they can grow and replicate their DNA.

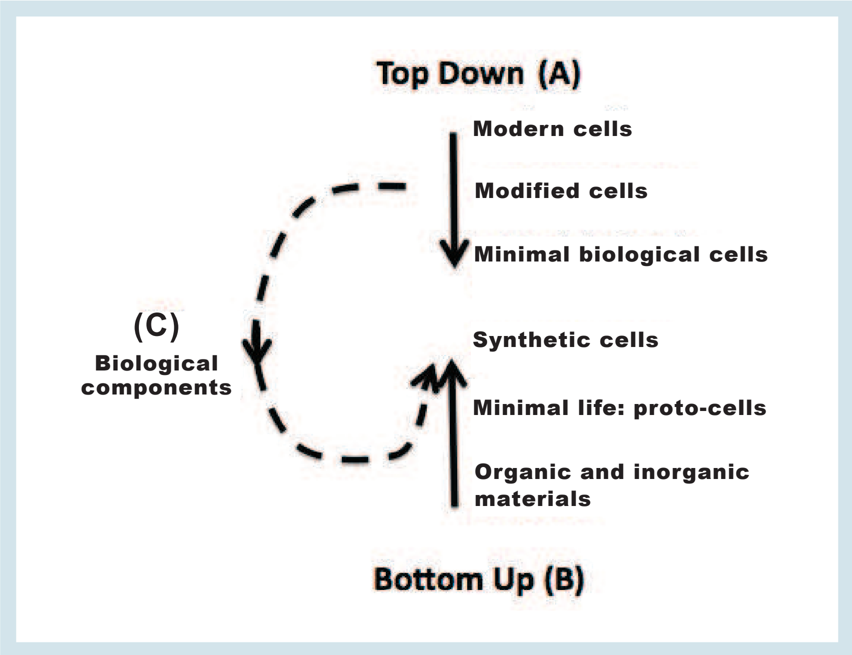


Figure 1: The two basic approaches in synthetic biology

Subsequently the individual cell is artificially divided into two new daughter cells. When repeating this artificial life cycle, the researchers expect a cell type with a specific DNA to gradually dominate the popu lation, because its particular qualities will give it the most favourable conditions of growth. If this assumption proves correct, Yomo and his team believe they will have established an evolution which is considered one of the decisive criteria for ‘life’.

In the section on proto-cells we will also describe the research team centred on the Danish artificial life scientist Steen Rasmussen and its endeavour to create artificial cells using the bottom-up method. Although in different ways Yomo’s and Rasmussen’s artificial cells give us an idea of the progress achieved in basic research concerning the creation of artificial life from the ground up using biological and non-biological components respectively.

We have not yet managed to create artificial life in the laboratory – neither by way of the bottom-up or the top-down method.

The reach of synthetic biology in 2011

The first major international congress on synthetic biology was held in the US in 2004 (“SynBio 1.0”), but the research environment for synthetic biology is already quite well-established. Today, research in synthetic biology takes place at universities and research institutions, in public laboratories and companies, all over the world – most notably in America, Europe, China and Japan.

In the US, current investments in synthetic biology amount to an estimated 1 billion dollars annually, the bulk of which comes from the National Institute of Health (NIH) followed by the Department of Energy and the Pentagon, respectively. Private foundations and companies have also begun to invest in the area – especially the oil industry and major non-profit foundations financing research in alternative energy sources.

So far, the EU has allocated €30 million from The Framework Programmes for Research and Technological Development to synthetic biology[1] and approx. €18 million to the borderland between synthetic biology and IT[2]. The Danish Ministry of Science has prioritized this area with DKK120 million from the so-called UNIK Pool. For a five year period this amount will fund a research centre for synthetic biology headed by a group of nano and plant biotech researchers from the University of Copenhagen. In addition, bottom-up synthetic biology has been sponsored by about DKK40 million from The Danish National Research Foundation and The University of Southern Denmark (SDU) for five years funding of the of the Centre for Fundamental Living Technology at The University of Southern Denmark. In Denmark, research in synthetic biology currently takes place at the University of Copenhagen, The University of Southern Denmark, the Technical University of Denmark and the University of Aarhus.

Examples of leading research centres

You can get an idea of what goes on in synthetic biology by visiting the websites of the leading research centres. Here follows a few examples from the US and the EU:

SynBERC – The Synthetic Biology Engineering Research Centre (US):
http://www.synberc.org/

BioBricks Foundation (US):
www.biobricks.org

Jay Keasling's laboratory (US):
http://keaslinglab.lbl.gov/wiki/index.php/Main_Page

UNIK Synthetic Biology (Denmark):
http://www.plbio.life.ku.dk/Centre/UNIK_Syntesebiologi.aspx

Centre for Fundamental Living Technology (Denmark):
http://www.sdu.dk/flint

Centre for Synthetic Biology and Innovation (UK):
www3.imperial.ac.uk/syntheticbiology

1 The EU's efforts are described as somewhat dawdling in Capurro et al. (17.11.2009): Ethics of Synthetic Biology. Opinion of the European Group on Ethics in Science and New Technologies to the European Commission.
2 As part of the EC FET project PACE and the EC FET programmes Chembio-IT and FET Open.

Synthetic biology and values

DEBATE

There is a distinct possibility that synthetic biology will gradually blur the contemporary differentiation between life and machine. Most people agree that there are moral rules for our treatment of living objects, while few would object to the making, destruction or modification of mere machinery. In order to avoid giving machines the same status as animals or humans and so as to prevent the future treatment of all living beings as machines we must find new ways to distinguish between animate and inanimate. But how are we to define a new meaningful moral distinction between the life we make ourselves and naturally created life?

Synthetic biology means new challenges

Synthetic biology involves ethical, legal and social challenges. We must examine whether existing laws are adequate and whether we need to establish a code of conduct for research in synthetic biology.

Synthetic biology is a relatively recent discipline. Consequently, the ethical agenda for this area is only just beginning to take form. Already, however, several of the world's leading research centres have initiated attempts to include ethics and security in the earliest project conceptualizations. Mainly, these efforts derive from a strong wish to avoid the polarization that followed from the debate on genetically modified plants (GMO).

Two decades of debate on genetically modified plants has shown that the research environments must take an interest in how citizens perceive use-value, risk and ethics, if they want to win the confidence of the public. Also steps must be taken to avoid turning the issue of synthetic biology into an arena of special interests, partisan views and religious notions.

A diffuse debate

As mentioned, synthetic biology challenges a number of culturally rooted distinctions between animate and inanimate, natural and artificial for instance. We know from experience that misgivings about biotechnology will often appear diffuse and hazy in the public debate. Not least because such misgivings typically borrow phrases and narrations from the world of fiction: Scientists 'play God' or 'behave like Doctor Frankenstein'[3], and we are headed for a 'Brave new world'[4] .

Researchers and scientists have often been partly to blame for distorting the implications of new technology. In the 1990's, for instance, many geneticists referred to genes as 'the book of life' or the 'code of life'. By doing so they helped introduce far-reaching perspectives that other researchers have since had reason to regret and deplore. Such perspectives made the debate unduly high-pitched and gave the impression that biotechnology was more

3 Mary Shelley, Frankenstein (orig. 1818). On the significance of Frankenstein and other myths in the public debate on biology and biotechnology, see Jon Turvey: Frankenstein's Footsteps, Yale University Press 1998.
4 Aldous Huxley, Brave New World (orig. 1932)

revolutionary than it really was – technically as well as ethically.

In a televised debate on genetic engineering molecular biologist and Nobel Prize winner James Watson, who along with Francis Crick discovered the structure of DNA in 1953, was once asked if it would be fair to say that he "played God?" He answered: "Well, if we don't, who will!" A similar remark fell recently when another Nobel Prize winner, Craig Venter's collaborator Hamilton Smith, was asked if researchers active in synthetic biology "played God". "We are not playing!" he answered drily.

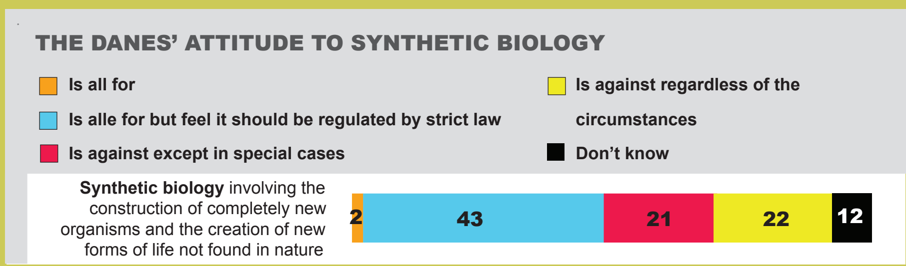
Crude images and high-flown expressions – whether they derive from experts or laymen – can have a tendency to present the matter in a highly polarized light, as a case of either-or, which is not necessarily conducive to a nuanced and balanced debate.

Likewise, it is not always clear what we are actually saying when we state, in opinion polls, that what happens in the laboratories is 'unethical', 'unnatural' or 'hazardous'. The Eurobarometer survey presented above shows that many of the citizens who consider genetically modified food 'dangerous' still think that this technology should be promoted. However, the survey also tells us that only very few of the respondents had ever heard of synthetic biology. There is every reason, then, to avoid drawing too unequivocal conclusions from such surveys.

In a democracy perspective, this work group is of the opinion that the regulation of synthetic biology should safeguard the harmony between developments within synthetic biology and the concerns and demands of the citizens. Citizen concerns, however, are not necessarily limited to health and environment; they may also relate to questions of justice and power. Surveys of citizen attitudes to technology generally give the impression that a majority of the population considers economic growth and financial profit insufficient justification and that people are far more positive when it comes to technologies that aim to improve health or solve societal problems such as climate change.

The Danes' attitude to synthetic biology

According to a Eurobarometer survey from 2010:



Source: http://ec.europa.eu/public_opinion/archives/eb_special_359_340_en.htm#341

Many Danes accept the new technology, it would seem, provided it is sufficiently regulated and that there is an adequate level of preparedness in case of emergencies. Among Danes with some knowledge of synthetic biology 68 per cent were mostly interested in the possible risks associated with synthetic biology, whereas 36 per cent were mostly concerned about the social and ethical problems. In addition, the survey showed that 94 per cent of the Danes have confidence in researchers working in synthetic biology. The survey also demonstrates that Danes are among those who are most willing to run a risk, if it is for a good enough purpose. At the same time, the Danish population ranks as the people who are most aware that synthetic biology can have unintentional, negative consequences.

Man's relation to nature

There is no indication that synthetic biology will be able to fabricate or re-design anything other than microorganisms such as yeast cells and bacteria for many years to come. Science has been modifying the genetic properties of such organisms for years, e.g. in order to produce insulin. Nor do we find it morally objectionable, under normal circumstances, to kill such organisms, since they only possess morally relevant qualities like consciousness or sense of pain to a very limited degree.

Some have expressed concern that synthetic biology – and not least its underlying 'mechanistic' view of life – may intensify or lead to a changed and perhaps less respectful view of nature. As an adherent of synthetic biology you need not subscribe to a particular view of nature. Whether the choice of synthetic biology as the answer to the challenges of our time will change Man's relation to nature – and whether this is problematic or not – remains an open question.

No guarantee of results

Synthetic biology is a hazardous research area in the sense that there is significant risk, at least within some research areas, that no concrete products or methods will ensue from the efforts. On the other hand, there is also a chance of considerable gains, if this research turns out to produce ground-breaking results such as new energy forms or new solutions to pollution or disease.

Research results, however, are nor simply ordered and delivered by pushing a button. Research and development is not something that proceeds in a linear fashion, and there is no guarantee of ground-breaking results when investing in synthetic biology. There is a risk, then, that we end up spending resources on synthetic biology that we could have allocated to other, less revolutionary, less high-tech and less radical solutions that would nonetheless have been better suited as remedies to crucial societal problems.

Examples of the visions for synthetic biology

DEBATE

In attempting to harmonize research in synthetic biology with the public's views and demands, is it possible to map which research areas to cultivate and which areas to abandon in favour of other activities?

This section presents a number of examples of the concrete uses of synthetic biology. As mentioned, research in synthetic biology has not yet moved from basic research to concrete applications and it is still uncertain whether it will, in fact, lead to the desired results.

Medicine based on synthetic biology

Doctor in a cell

Medical drugs work by impeding a pathogenic organism or process for example. The drug needs to reach the particular place in the body where it is supposed to have an effect. Many drugs are hindered in reaching their destination, because they are hard to dissolve or because they are metabolized too quickly. By encapsulating the medicine in small liposomes (microscopic fat bubbles) it can be protected against catabolism. Alternatively, prodrugs (precursors to the medically active compound) can be connected to the phosphor-lipids in the liposomes and released once these carriers reach the place where the medicine is supposed to work.

In poisoning cases where a toxin is to be removed from the bloodstream, synthetic biology may be able to indicate new solution models focussing on the modules in the BioBricks collection mentioned earlier. One procedure will be to encase the enzymes that decompose the toxin in small nano membranes and insert these in liposomes (see Figure 2). The liposome membrane will contain a transporter feeding the toxin into the liposome. This concentrates the toxin inside the liposome containing the enzyme system that is able to break down the toxin.

Globally, researchers have developed a number of technologies that can determine which substances a particular transporter is able to feed through a membrane and into a liposome. Collections of approx. 2,000 different transporters have been established. Likewise, collections of the so-called cytochrom P450 enzymes are well under way. These enzymes can also break down toxins and be inserted in nano membranes. Danish researchers have already established a sizeable collection of glycosyl transferases with the capacity to attach sugar molecules to the decomposed toxins thereby decreasing their toxicity and increasing the possibility of excretion.

In spite of these advances it will take many years for this technology to reach the point where it can be used for human medical treatment. The development of what The Centre for Synthetic Biology at The University of Copenhagen describes as "Toxin Terminator Technology" requires testing of many different enzyme systems and transporters.

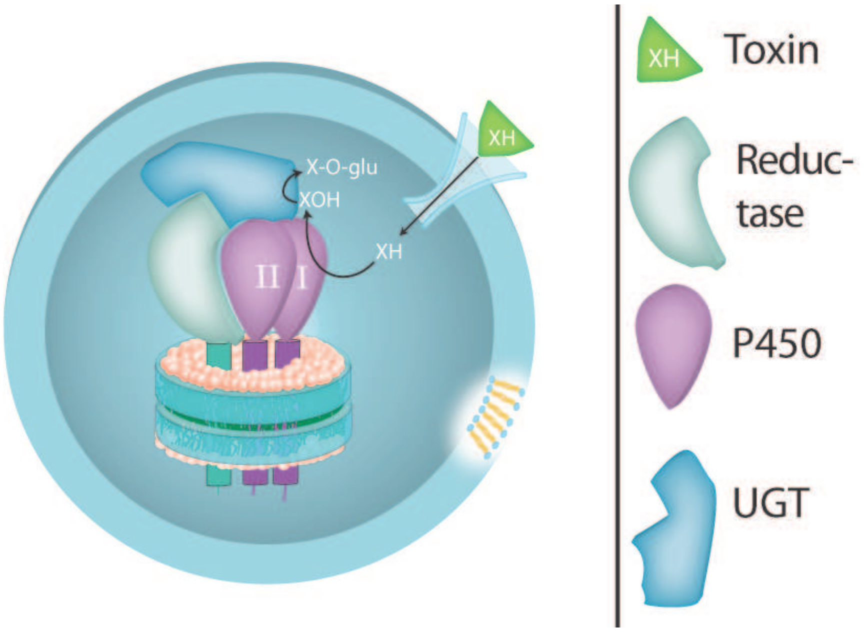


Figure 2

This is an illustration of a nano membrane in a liposome. The nano membrane will contain enzymes that break down toxins fed into the liposome membrane by the transporter protein. The development of this technology is still in its incipient stages. Current research efforts focus on the insertion of enzymes in the nano membrane.

Photosynthesis and synthetic biology

Harvesting the rays of the sun

The solar power hitting the Earth in 1.3 hours is equal to Man's total energy consumption in an entire year. Solar energy can be captured by way of solar cells turning solar power into electricity.

Plants are also able to use sunlight as a source of energy, but they do so in a much more sophisticated way. Using the carbon dioxide in the air as a source of carbon and sunlight as a source of energy plants can form all the organic substances they need through photosynthesis. But they can do more than that. Since they cannot 'run away' when attacked by microorganisms and animals they defend themselves by developing a number of often rather complicated bioactive defensive substances. Many of these substances are used as medical remedies for human diseases. Taxol, for instance, is used in cancer treatment, and morphine, of course, is used in pain management.

Photosynthesis enables plants to efficiently transform sunlight into chemical energy in the carbon hydrates, proteins, fats etc. With great precision the rays of the sun are captured by green antennae molecules and transformed into chemical energy in the very centre of the reactions.

It is plant processes such as these that researchers are now trying to imitate. In all these processes the crucial reactions are controlled by enzyme systems. The function of these enzyme systems can be examined scientifically by building them into nano membranes or liposomes. That makes it possible to combine the systems in new ways and fit them with new functional properties in living cells.

Light-driven chemical synthesis

In a series of experiments conducted in recent years, Danish researchers have managed to connect one of the enzyme complexes involved in photosynthesis, found in the chlorophyll granules in living plants, to other natural membrane enzymes involved in complex syntheses of bioactive substances. By combining the two enzyme systems these researchers have succeeded in constructing a synthetic biological system producing useful, complex substances with sunlight as the only necessary source of energy. This system makes it possible to achieve a highly efficient synthesis working at much higher speed than what we can observe in the plants themselves. The ground-breaking character of this system is due to the achieved combination of the photosynthetic processes and the synthesis of complicated chemical substances with specific medical effects, for instance.

In earlier attempts to construct artificial synthesis systems for such substances it has been necessary to add very expensive co-factors (e.g. ATP and NADPH) in order to be able to make the biological processes work. In the new synthesis, however, these co-factors have been replaced by light. This holds great promise, not only considered as a challenging research project but also, in a wider sense, as a first step on the way to sustainable production systems using solar power instead of fossil fuels. An improved development of solar power will reduce the use of CO2-polluting energy sources such as coal, oil and natural gas.

From laboratory to market

It remains uncertain if and when Man's use of solar power by way of photosynthesis will become an everyday phenomenon. To a large extent, it depends on whether it will be possible to create stable and workable production systems.

The speed of technological development will also depend on the establishment of a market for artificial photosynthesis. As long as fossil fuels remain relatively cheap, the demand for alternative energy will be limited. The moment oil prices begin to rise, research in the alternatives will grow accordingly. The global focus on climate changes also helps accelerate the development of environment-friendly energy forms.

Proto-cells

Artificial life

Using the bottom-up method researchers at The Centre for Fundamental Living Technology (FLinT) at The University of Southern Denmark have managed to create life-like and living processes from simple organic and inorganic elements. The purpose is to achieve a deeper understanding of what life really is. The bottom-up design employed in FLinT's so-called minimal proto-cells frees researchers from the limitations inherent in the biochemical complexity characterizing cells brought about by evolution. Minimal proto-cells allow them to choose the elements that are best and most practical to work with.

There is general agreement that life can be created by making three different molecular structures interact – an information system, a metabolism and a container (see Figure (A)). This is the premise for the proto-cells manufactured at FLinT and other research institutions across the world. In addition, this system must be able to undergo evolution through some kind of iterative life-cycle (see Figure (B)).

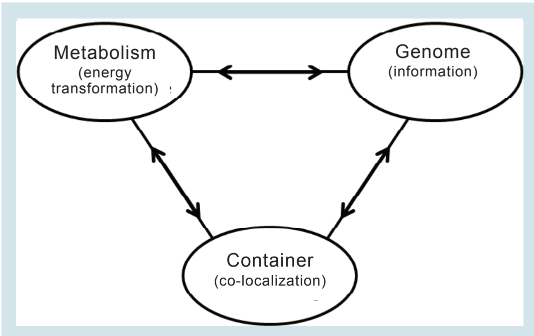


Figure A

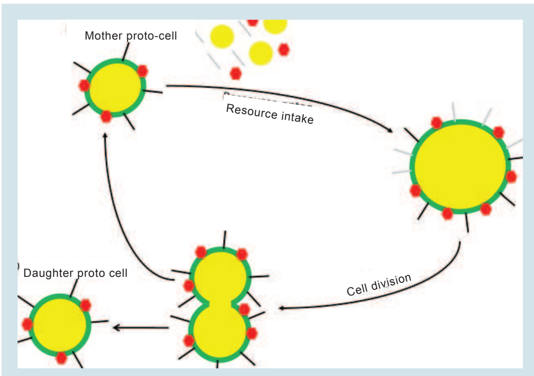


Figure B

In order for artificial proto-cells to be defined as life they must meet the following three criteria:

1) The proto-cell must have a localized identity, i.e. a delimitation from the surrounding environment. This requires a specific container to which the metabolism and the information system are attached. The container can be a vesicle or a drop of oil. So as to make the proto-cell as simple as possible the information as well as the metabolism molecules are attached to the external side of the container which greatly simplifies the exchange of resources and excrements with the surroundings. This has been achieved in a laboratory setting.

2) The proto-cell must be able to grow and divide itself, i.e. to transform resources from the environment into building blocks (metabolism). In FLinT's proto-cells a particular DNA-base pairing in an information molecule controls the transformation (metabolism) of an oil-like resource molecule into a fatty acid. Under certain conditions, these fatty acid molecules make the container so unstable that it divides itself. Proto-cell division can also take place artificially by means of manual modification of the system. This, too, has been achieved in the laboratory.

3) The proto-cell must be able to demonstrate evolution. It must be equipped with an information system that is copied and transmitted as heredity. According to the definition, information molecules must also, at least partly, control the growth and division process. Selection is possible if the proto-cell population is subjected to limited resources. Proto-cells with slightly different information molecules will grow and divide in slightly different ways. The proto cells with the information molecules best suited to control the most efficient life cycle will have the best growth conditions and gradually come to dominate the population – and when this happens the population can be said to have undergone a primitive form of evolution. This, however, has not yet been achieved in the laboratory.

A fully integrated lifecycle including all three processes has not yet been established in any laboratory, but various combinations of the three processes have been realized.

Living technologies

In theory, the technological applications of artificial, living processes are estimated to be extensive in the long term. As physical process, life can be implemented in various systems – including systems not based on chemistry or biology. Hence, basic research in the fabrication of proto-cells is part of a wider research field focused on the examination of the artificial production of living processes in computer network and robots.

As mentioned, most of this work takes place at the level of basic research, and its outcome remains uncertain. It is possible that we will come to base our technologies on living processes in the future. The great advantage of such technologies is that, like existing life forms, they would be robust, highly adaptive, sustainable, self-repairing and capable of developing new qualities according to our shifting demands.

The EU funds a number of strategic research projects focused on the development of living processes within various media. Currently, the FLinT centre takes part in the management of three of these European projects (ECCell, MATCHIT and COBRA). These research efforts unfold in the borderland between nano, bio and formation technology. What these projects have in common is that they examine how to create and eventually utilize living and life-like processes in a technological context.

One of the concrete technological visions for these EU-sponsored projects is the establishment of a basis for the development of a so-called "Sustainable Personal Fabricator Network." In principle, this network is intended to be able to produce almost all the objects we humans need. Imagine an extension of our personal computers with an extremely advanced biological 3D-printer which is also able to control bio fabrication (along the lines of a very advanced bread maker). This opens the possibility that every single person will be able to design and produce complex objects in a simple and sustainable way.

The risks involved in synthetic biology

DEBATE

How can we prevent the use of synthetic biology for harmful purposes without causing major obstructions to the development of beneficial application?

The challenges of synthetic biology

Like any other field of technology synthetic biology can be of service to human beings and human society, but it can also lend itself to abuse. If we chose to make use of the potential inherent in synthetic biology, it is of crucial importance that we do what we can to minimize the possibilities of abuse.

As mentioned, it is impossible to predict the exact risks and possibilities that synthetic biology will lead to. We will be dealing with a process, then, in which the authorities will have to revise expectations and assessments continually as our knowledge increases. The work group suggests the following five risk types as basis for this continual re-assessment: [5]

Negative environmental impacts: A situation in which synthetic microorganisms can have unintended negative consequences in their interaction with other organisms.

Genetic spill-over: Any genetic exchange between a synthetic and a natural biological unit may result in a genetic spill-over effect. This problem is identical with the so-called' gene flow' between various plant species. This gene flow will include trans-genetic plants in which some of the genes are transmitted to cultivated plants or wild plants by way of cross-pollination.

Run-off risk: This problem is best known from nano technology and concerns the risk that synthetic material gets out of hand. Hypothetical doomsday scenarios include the 'grey goo' problem[6]. Since synthetic biology is subject to the same limitations and conditions as all other kinds of life on this planet, this development is not very likely. One way of limiting the risk of 'grey goo' is to give all the artificial organisms set free in natural environments a limited life span once they leave the laboratory. Critics, however, have pointed out[7] that even with a limited life span there is still a risk that such organisms will mutate and break free of their own limitations. Also, other critics have made clear that even if animal testing shows that a given synthetic microorganism does not cause disease, there is no telling how new organisms will work in the human body.

Deadly diseases and bioterror: Synthetic biology has the potential to create and possibly disseminate harmful diseases. Some feel[8] that the technological obstacles involved make it more likely that the destructive potential of synthetic biology will be employed by governments rather than by terrorists. Furthermore, if bioterror really occurred, it would most likely involve traditional biological weapons rather than synthetic biological weapons.

5 Following Arjun Bhutkar.
6 The 'grey goo' problem is defined as an ecological apocalypse, i.e. the total destruction of the ecosystem caused by uncontrolled multiplying organisms either breaking down or absorbing vital material.
7 B. Tucker & Raymond A. Zilinskas
8 Keller (2009)

As bio-techniques become increasingly widespread and simplified, and in light of the growing amounts of information available on the internet, there is a distinct possibility that we will one day see DIY bio weapons. Manuals and ingredients can be found on the internet in the form of construction kits with DNA sequences coding for different qualities and various chemical substances and equipment. Furthermore, many genomes have been described in public databases, and anyone can enter gene databases and pick out selected gene sequences. As a result, people with some professional insight may experiment with living organisms and organizations may produce biological weapons and use them for terror. On the other hand, making bio weapons would seem to require a sizeable laboratory, something along the lines of, say, an average university lab. Until now, we have only seen very few examples of bio terror. The latest occurrence was a number of letters containing anthrax bacteria back in 2001 in the U.S. Developing terrifying biological weapons does not require synthetic biology – such weapons already exist.

Aside from the risk of bio terror there is growing concern about the risk of 'bio error'. Bio error reflects the real danger that synthetic biology – even in authorized and publicly controlled laboratories – may lead to accidental leaks of synthetic organisms harming Man or nature.

Regulating synthetic biology today (2011)

In order to counter these risks Denmark has implemented laws and regulations in accordance with the EU directive from 1990 on "The Contained Use of Genetically Modified Organisms". The following laws apply for synthetic biology in Denmark:

- Executive Order on Genetic Engineering and the Working Environment No. 910, 11/09/2008
- Executive Order on Changes in Executive Order on Genetic Engineering and the Working Environment nr. 88 – 22/01/2010
- The Consolidated Environment and Genetic Engineering Act No. 869, 12/06/2010

According to the present regulation all work within synthetic biology, research as well as production, must be approved by the authorities. Legally, genetically modified organisms are defined as "organisms containing new combinations of genetic material which would not come into being naturally." One is required to notify the relevant authorities of any work involving genetic engineering and await approval on the basis of "an overall assessment of the risks involved in the biological systems in relation human safety and health and the environment in general."

Watermarkning

Ten students from The University of Southern Denmark won the 2010 iGEM Special Prize for Safety in Synthetic Biology thanks to their suggestion of 'watermarking' synthetic biological organisms. Inspired by J. Craig Venter's experiments with the first watermarking of a bacterium in May 2010, they suggested an international injunction to "watermark" synthetic bio products. All laboratories, institutions and companies could be issued with a unique ID number which would be recorded in an internationally accessible database. The watermark on a rogue bacterium makes it possible to contact the originators and obtain information on how to neutralize the bacterium. This would be a viable way to handle possible bio errors.

Source: http://2010.igem.org/Team:SDU-Denmark/safety-d

Assessment points include whether the organism is poisonous or pathogenic for humans, whether it has any survival advantage over natural microorganisms which would enable it to establish itself in nature. Furthermore, the risk assessment of any use of synthetic biology must consider the possible threats to the wellbeing of humans, animals, plants and the environment. Work facilities for synthetic biology must be secured and steps must be taken to ensure that no biological material can escape. When launching a commercial production of a synthetic bio product, the company must document that the product in question is assessed to be safe in relation to the dangers and risks mentioned above.

In addition, it is prohibited to work with an organism if safer, alternative organisms are available. Safety assessments are based on how contagious and dangerous the organism is. If it is possible to find suitable and less dangerous biological systems that are compatible with the task at hand, researchers and developers are required by law to employ such systems as opposed to less safe systems.

According to Danish law, genetically modified organisms can only be fabricated, used, imported, transported, released, sold or marketed as part of research projects and large-scale experiments with the approval of the Danish Minister for the Environment or the relevant public authority. In Europe as well as in America there are also rules for import and export of 'dual use' technologies which also includes synthetic bio products.

For all the areas of our society where potentially dangerous technologies are employed, we have laws establishing certain safety measures. Similar safety measures to be implemented in biological machines have been suggested for the area of synthetic biology. It could be built-in safety devices that cause the system to self-destruct, if it does not work as intended. Another option is to ensure that biological machines cannot survive without particular signals or specific amino acids[9] or by rendering the synthetically created DNA sequences illegible for nature so as to prevent them from spreading[10].

Another possibility is to develop guidelines for companies synthetizing DNA, making them screen the DNA produced for pathogens or sequences that might be harmful for human beings. By introducing such screenings it might be possible to prevent terrorists from ordering DNA sequences with dangerous potentials[11].

DEBATE

Is synthetic biology covered by sufficient regulation in Denmark? Do we need further international guidelines and standards that oblige individual countries to control and monitor the activities within synthetic biology?

Leaving synthetic biology unpursued: possible drawbacks

When developing new technology, it is easy to become hypnotized by the risks involved and to forget that the alternatives may involve other risks and problems and that there may be drawbacks to refraining from developing the technology in question.

Research and development has led to threats against health and the environment – even if the aim has been to help find solutions to problems faced by

9 An idea known from Michael Crichton's highly popular book Jurassic Park where animals cannot produce a necessary amino acid, lysine, and therefore automatically die unless they are supplied with this amino acid.
10 Neumann et al., "Encoding multiple unnatural amino acids via evolution of a quadruplet-decoding ribosome, Nature 464, p. 441-444, March 18th 2010.
11 This kind of legislation is about to be enacted in the U.S. For further information on this law, please consult "Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA" (available at http://www.phe.gov/Preparedness/legal/guidance/syndna/Pages/default.asp).

humanity. This was certainly the outcome in the case of the explosive development in pesticides and other almost non-biodegradable chemicals. But modern research has also resulted in useful inventions that might have been checked if society had taken a restrictive stance towards the technology at an early stage.

Depending on the technological potential of synthetic biology, Denmark may incur economic losses and reduced welfare by opting out of research and development within this field. Generally, the technological development has been highly important for Denmark's competitive power and production, e.g. in agriculture, pharmaceuticals and energy. Politically, high-tech jobs are considered to be the backbone of the future Danish economy. Regulation putting Denmark at a disadvantage as compared to other countries will distort Danish competiveness and possibly lead to a loss of commercial opportunities. Therefore, researchers and companies alike emphasize that legal limitations and restrictions must be implemented internationally.

Sources and links

The following experts have been interviewed and delivered significant contributions to the drafting and writing of this discussion paper:

Birger Lindberg Møller, Professor, Dr. Scient., Head of Centre for Synthetic Biology and The Villum Kann Rasmussen Research Centre Pro-Active Plants.

Gunna Christiansen, Professor, Institute of Medical Microbiology and Immunology at Aarhus University.

John-Erik Stig Hansen, Consultant Doctor, Dr. Med., Head of Centre for Bio Security and Bio Preparedness, The National Serum Institute.

Maja Horst, Senior Lecturer, Ph.D., Department of Organization, Copenhagen Business School.

Steen Rasmussen, Professor, Head of Centre for Fundamental Living Technology, The University of Southern Denmark and the EC project under Chembio-IT.

Sune Holm, philosopher, post.doc., Department of Media, Cognition and Communication, University of Copenhagen.

Thomas Bjørnholm, Professor, former head of The Nano Science Centre at The University of Copenhagen, as of September 2010 deputy rector of The University of Copenhagen.

Thomas Breck, senior consultant at The Danish Centre for Risk Communication.

In addition, ph.d. students Wendie Jørgensen and Anders Albertsen as well as BS-student Mike Barnkob, all from The University of Southern Denmark, have helped write the section on proto cells, page 22.

The following written sources have been consulted in the making of this discussion paper:

"Ethics of Synthetic Biology". Report no. 25, 17/11/2009, The European Group on Ethics in Science and New Technologies (EGE). Link: http://ec.europa.eu/european_group_ethics/docs/opinion25_en.pdf

"Ethical Issues in Synthetic Biology". Report from The Hastings Center, Garrison, New York, 2009. Link: http://www.synbioproject.org/process/assets/files/6334/synbio3.pdf

"Synthetic Biology – A Nest Pathfinder Initiative". Report from The EU Commission, Directorate-General for Research, 2007. Link: ftp://ftp.cordis.europa.eu/pub/nest/docs/5-nest-synthetic-080507.pdf

"A synthetic creation story". Article in Nature by Philip Ball. Link: http://www.nature.com/news/2010/100524/full/news.2010.261.html

"Extreme Genetic Engineering – an Introduction to Synthetic Biology". Report from ETC Group, 2007. Link: http://www.etcgroup.org/upload/publication/602/01/synbioreportweb.pdf

Synthetic Biology – The Technoscience and Its Societal Consequences. Springer Science+Business Media B.V. 2009. Link: http://www.springerlink.com/content/w96l83/front-matter.pdf

Balmer A., Martin P., 2008, Synthetic Biology: Social and Ethical Challenges, Institute for Science and Society, University of Nottingham. http://www.bbsrc.ac.uk/web/FILES/Reviews/0806_synthetic_biology.pdf

IRGC 2008, Concept note: Synthetic Biology: Risk and Opportunities of an emerging field, International Risk Governance Council, Geneva. http://www.irgc.org/IMG/pdf/IRGC_ConceptNote_SyntheticBiology_Final_30April.pdf

Parliamentary Office of Science and Technology (POST), POSTNOTE – Synthetic Biology, January 2008, N° 298. http://www.parliament.uk/documents/post/postpn298.pdf

Schmidt M., 2008, Diffusion of synthetic biology: a challenge to biosafety, Syst Synth Biol, June 2008. http://www.synbiosafe.eu/uploads///pdf/Diffusion_of_synthetic_biology.pdf

Synthetic biology: a view from SCENIHR. http://ec.europa.eu/health/dialogue_collaboration/docs/ev_20100318_co14.pdf

Synthetic Biology: scope, applications and implications. The Royal Academy of Engineering, UK. http://www.raeng.org.uk/news/publications/list/reports/Synthetic_biology.pdf

Europeans and biotechnology in 2010: Winds of Change? Science in Society and Food, Agriculture, Fisheries, & Biotechnology, EU. http://ec.europa.eu/public_opinion/archives/ebs/ebs_341_winds_en.pdf

Living technology working group documents, Initiative for Science, Society and Policy (ISSP), University of Southern Denmark. Link: http://www.science-society-policy.org/living-technology

Various articles in Danish and international scientific periodicals and newspapers.

Online resources:

http://www.synbiosafe.eu/

http://www.synbioproject.org/

http://bbf.openwetware.org/

http://syntheticbiology.org/

http://www.youtube.com/watch?v=_DUrpfcAzNY. (A video on the ethical dilemmas in relation to artificial life.)

SYNTHETIC BIOLOGY

THE DANISH COUNCIL OF ETHICS

TEKNOLOGI-RÅDET
THE DANISH BOARD OF TECHNOLOGY