SynBio Politics

Bringing synthetic biology into debate

Virgil Rerimassie & Dirk Stemerding

Rathenau Instituut

The **Rathenau Instituut** promotes the formation of political and public opinion on science and technology. To this end, the Institute studies the organization and development of science systems, publishes about social impact of new technologies, and organizes debates on issues and dilemmas in science and technology.

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Publisher: Rathenau Instituut, The Hague
Editor Intermezzi: Tjalling Swierstra, Marianne Boenink with the assistance of Hanneke Berman, Anika Haacke and Elena Chernovich
Design and layout: Smidswater, The Hague
Photos: Shutterstock, Science Photo, Hilbert Krane

Preferred citation:
Rerimassie, V. & D. Stemerding, SynBio Politics - Bringing synthetic biology into debate. Rathenau Instituut 2014, The Hague

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Preface

In 2011 the Dutch Rathenau Instituut organized a Meeting of Young Minds. In this meeting 'politicians of the future' – representing Dutch Political Youth Organizations – debated synthetic biology with 'scientists of the future' – participants from the international iGEM student competition.
The debate made vividly clear that synthetic biology raises a lot of interest in its potential applications and a lot of questions about risk, ownership and society's relationship with nature. In this publication the reader will find a report of the Meeting of Young Minds, but it has more to offer. It is primarily a plea for a more engaging process of political and societal opinion making about synthetic biology.

As soon as synthetic biology started to emerge we have seen a lively international debate about the promises and implications of this new field of science. Up to now however, this debate is largely confined to academic circles. A couple of years ago, the Rathenau Instituut extensively mapped the dynamics of this international debate.
Four different countries – the United States, the Netherlands, the United Kingdom and Germany – were studied to identify the most important issues and actors involved. Among the main players in this debate we find first of all the pioneers within the field itself, especially when it comes to issues of risk and intellectual property rights. Other important contributions come from ethicists and social scientists belonging to the international community of scholars studying the ethical, legal and social implications (ELSI) of new science and technology. It has resulted in an impressive pile of reports with reflections on synthetic biology and its societal implications. The report *Constructing Life*, published by the Rathenau Instituut in 2006, was one of the first contributions to this international debate.

In scientific circles, the process of opinion making is therefore in full swing. However, as we argue in this report, this process also calls for engagement from society. Synthetic biology offers huge potential for novel drugs and vaccines, as well as for 'greener' chemicals and biofuels. Nonetheless, this field also brings with it various challenges, ranging from regulatory issues of biosafety, biosecurity and intellectual property rights to potential environmental and socio-economic risks and related ethical questions. It is thus essential to establish an open dialogue between stakeholders, including the public, concerning the technology's potential benefits and risks and to explore possibilities for 'collaborative shaping' of the field. An important initiative in this regard is the funding by the European Commission of *Synenergene*, a large European project aiming at responsible research and innovation in synthetic biology.

The report *SynBio Politics* is a contribution to this initiative and an invitation to political parties and NGO's to actively engage with it. Although it was originally published as a contribution to the Dutch debate, its message is equally important for the discussion in Europe and internationally.

Jan Staman, director Rathenau Instituut

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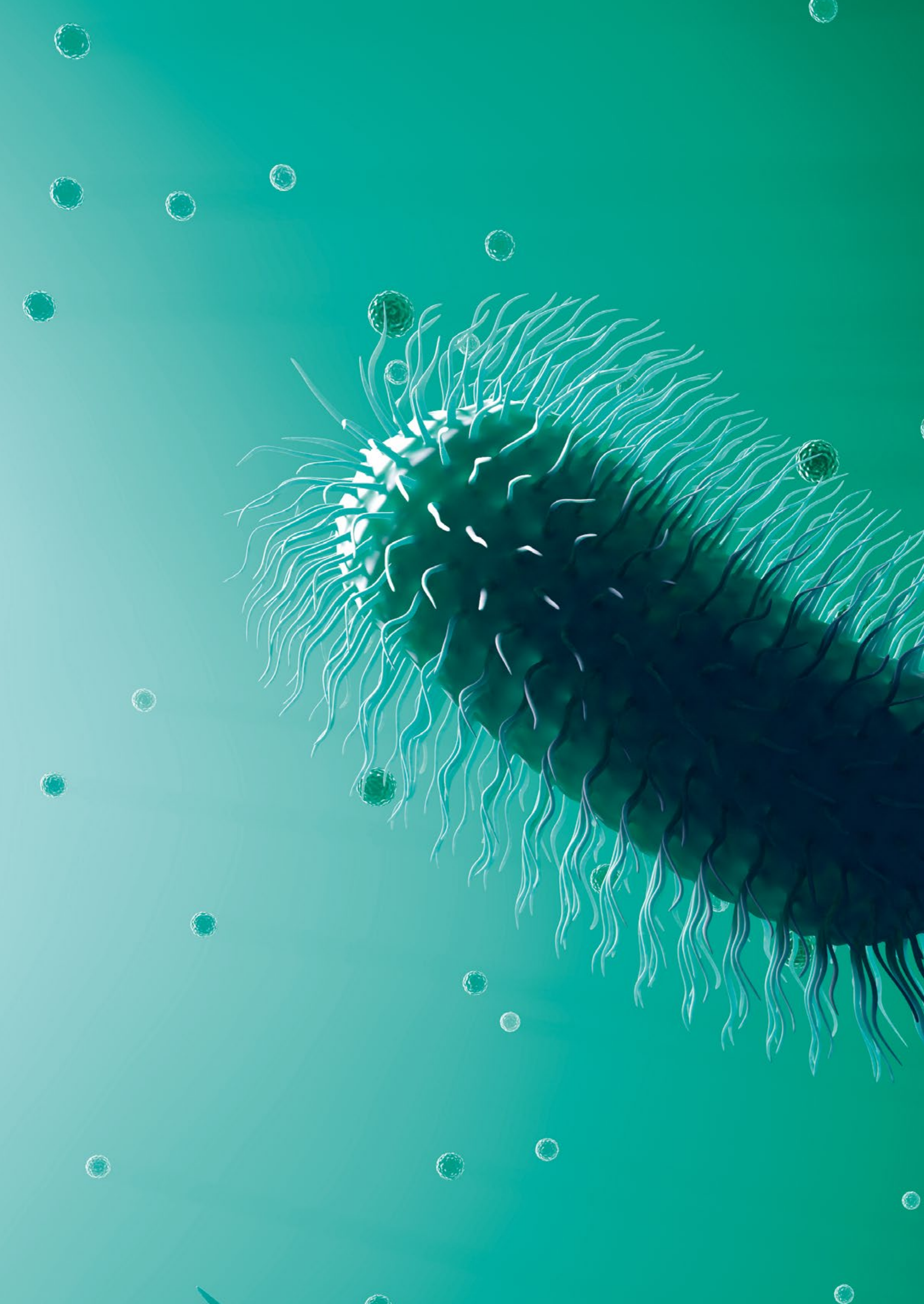
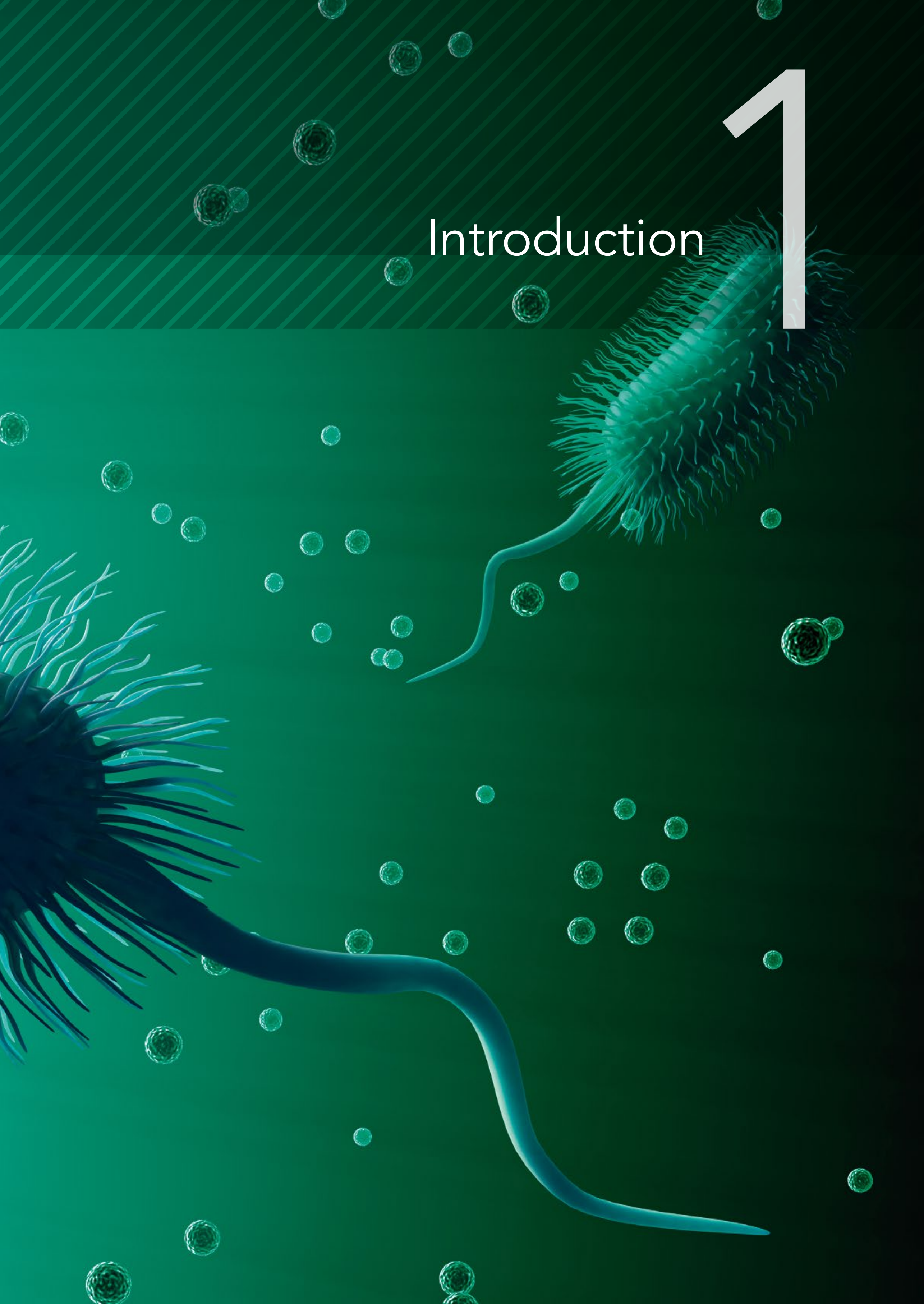


1 Introduction



1 Introduction

> ***As you know, scientists have announced a milestone in the emerging field of cellular and genetic engineering research known as synthetic biology. While scientists have used DNA to develop genetically modified cells for many years, for the first time, all of the natural genetic material in a bacterial cell has been replaced with a synthetic set of genes. This development raises the prospect of important benefits, such as the ability to accelerate vaccine development. At the same time, it raises genuine concerns, and so we must consider carefully the implications of this research (PCSBI 2010, p.vi).***

With the above words, President Barack Obama opened his dedicatory letter to the newly installed Commission for the Study of Bioethical Issues. According to the U.S. President, it is crucial to carefully monitor synthetic biology, the new phase in the development of biotechnology.

In synthetic biology, scientists explore and unravel genetic material and parts of organisms. With that knowledge they design new biological systems and that offers a world of possibilities: drugs that are produced by artificial bacteria, heavily genetically modified algae to produce biofuels, possibly bringing back extinct animals like the mammoth or even creating artificial life. The ambitions in synthetic biology are thought provoking and expectations are running high indeed.

1.1 Back in time

In 2006 the Rathenau Instituut started examining the societal aspects of synthetic biology. In that year, it published the report *Constructing Life*, an introduction to synthetic biology (de Vriend 2006). Worldwide, this publication was the first survey study of societal aspects of this emerging field of science. A year later, the Dutch edition *Leven Maken* was published and the ensuing *Report to Parliament* (In Dutch: *Bericht aan het Parlement*). Following these activities the Dutch Labour Party (Partij van de Arbeid) raised questions about synthetic biology in the parliament.[1] Since then, the Rathenau Instituut has closely monitored developments in synthetic biology and undertook various activities related to this theme.

Eight years have passed since the publication of *Constructing Life* and the *Report to Parliament*. Developments in synthetic biology have certainly progressed during that period. Craig Venter, for instance, known for his contributions to the unravelling of the human genome, announced in 2010

1 Annex to Papers of Parliament, Aanhangsel Handelingen II 2007/2008, nr. 2070800670.

that his team had succeeded in creating a bacterium with a fully synthetic genome[2] (Gibson et al. 2010). In the Netherlands too there has been increasing research activity in the field of synthetic biology. Thus in 2008 the *Groningen Centre for Synthetic Biology* was established. Currently, there are academic research groups active in this field in Delft, Eindhoven, Amsterdam, Nijmegen and Wageningen.

Along with the advances in synthetic biology there is also an increasing number of organizations exploring the societal aspects of the emerging field, and putting these on the agenda. Among others, the *European Group on Ethics* and *the International Risk Governance Council* have issued opinions on this subject. In the project *Making Perfect Life*, which was carried out for the European Parliament, and led by the Rathenau Instituut, synthetic biology was prominently discussed (Schmidt & Torgersen 2012). Other Dutch organizations have also been investigating the potential impacts of synthetic biology, among them the *Commission on Genetic Modification* (COGEM), the *Royal Netherlands Academy of Arts and Sciences* (KNAW) and the *Dutch Health Council* (Gezondheidsraad).

In the meantime, several critical non-governmental organizations (NGO's) also made themselves heard, such as the *ETC Group*[3] *and Friends of the Earth*.

Despite these efforts a broader societal and political debate on synthetic biology has not yet started (Stemerding & Van Est 2013; Stemerding & Rerimassie 2013). That is not really surprising. A 2010 Eurobarometer Report shows that public awareness about synthetic biology is very low. An amazing 83 % of EU citizens have never heard of synthetic biology (Eurobarometer 2010).

2 The genome is the set of all genes of an organism; the genetic blueprint of an organism.
3 Action Group on Erosion, Technology and Concentration: www.etc.group.org.

1.2 iGEM

Synthetic biology, however, really appeals to young scientists. This is evident from the explosive growth of iGEM – the International Genetically Engineered Machines competition. This is a global competition for student teams in the field of synthetic biology. In this competition, students use standardized and interchangeable genetic building blocks (BioBricks™) to design microorganisms with new properties. For this purpose they have access to the so-called *Registry of Standard Biological Parts*, an open source database of genetic building blocks.[4] As part of their projects, students also design new building blocks by themselves that are then added to the database, so that the number of BioBricks™ and their availability is continuously growing.

iGEM began in 2003 as a summer course for students at the Massachusetts Institute of Technology. In 2004 the course was transformed into a competition in which five different teams participated. Meanwhile iGEM has become a global competition and in 2014 around 250 teams from all over the globe took part.[5] Although these projects last only a few months, the results are often impressive. The competition testifies not only of enthusiasm for this new area of science, but also of the potential of synthetic biology (see text box about iGEM project).

The subjects tackled by the students are highly diverse, ranging from applications focused on the environment or medicine, to more playful delights, such as developing bacteria with a banana fragrance. In 2010 the Technical University Delft iGEM team made it to the main Dutch TV news NOS Journaal with their work on a bacterium that ‘eats up’ oil, inspired at that moment by the oil spill in the Gulf of Mexico.[6]

4 http://partsregistry.org.

5 See: http://igem.org/Team_List?year=2014.

6 http://2010.igem.org/Team:TU_Delft. The movie is available on http://nos.nl/uitzending/16142-20100616-225000-nos-journaal-op-3.html. The iGEM-project starts at 3:45 minutes.

iGEM-project highlighted:

Project AuxIn: new bacteria deployed in the battle against bottom erosion

IGEM-finalist 2011, Imperial College London (http://2011.igem.org/Team:Imperial_College_London)

The Imperial College London (ICL team) has engineered E. coli bacteria to accelerate plant root development. The bacteria were designed to respond to a chemical released by the roots of germinating seed, whereby the bacteria are actively taken up by the roots. As a second step, the bacteria were designed to express auxin, a plant hormone which promotes root formation. Thirdly, a safety mechanism was designed to prevent horizontal gene transfer from the modified bacteria to existing soil bacteria. By sowing seeds coated with the modified bacteria in areas at risk of erosion, plants may increase the stability of soil as a result of enhanced root growth. In this way engineered E. coli bacteria may help to prevent soil erosion and desertification, a massive problem in arid areas of the world.

Human practice work was seen by the team as crucial for the framing of their project and to ensure that the design of the AuxIn system would respect all relevant social, ethical and legal issues. One important aspect considered by the team were the advantages of an approach using engineered bacteria rather than engineered plants. Existing approaches to improve drought-tolerant crop plants via genetic engineering might be a viable alternative. However, considering a world-wide problem such as desertification will require a lot of different plant species to be engineered and some of these species may be very difficult to engineer genetically. Using a bacterial delivery system based on naturally existing symbiosis between bacteria and plants might help to overcome these difficulties.

While the AuxIn project remained at a proof-of-concept stage, the team undertook a number of activities with the aim to develop a future implementation plan for their product, taking into account specifications of seed coat design, local conditions and practices of planting in regions where the product will have to be implemented, issues of patenting, and environmental safety requirements. A special and highly important component of the team's human practice work were numerous consultations during the early design stages of the project with plant scientists, ecologists, social scientists and NGO's, including two discussion panels and a visit at Syngenta, a company specializing in agricultural products and research. The team also undertook several outreach activities, including the writing of a script set in a future world where the technology designed in the project has been widely implemented.

1.3 Meeting of Young Minds

Due to iGEM's explosive growth, the organization decided in 2011 to organize separate competitions in three global regions. That year the African-European preliminaries, or *Jamboree* in iGEM jargon, were held in Amsterdam. The Rathenau Instituut took up this opportunity to boost the still modest societal and political debate on synthetic biology. On the evening preceding the European iGEM Jamboree, the Rathenau Instituut held a *Meeting of Young Minds*: a debate between 'future synthetic biologists' and 'future Dutch politicians'. Both groups will not only play an important role in seizing the opportunities that synthetic biology offers, but also in addressing risks and other issues that this technological development entails.

In this debate the iGEM community represented future synthetic biologists. A key part of the work of iGEM teams is the *policy & practices* element. This implies that the iGEM participants do not only work on their project inside the laboratory, but also pay attention to the societal aspects of their research. Often, students seek the public debate, for example in the form of workshops for a wider audience or guest lectures at schools. The idea of a *Meeting of Young Minds* therefore fitted in well into the culture of iGEM and a new generation of researchers who like to engage in conversation with society.

We have looked for politicians of the future in circles of the Dutch political youth organizations (PYO's). Almost every Dutch political party has an active youth organization, often with impressive membership numbers. The Rathenau Instituut found seven PYO's willing to meet the challenge to develop a vision on synthetic biology, and to enter into debate with iGEM students during the *Meeting of Young Minds*.

In exploring this new subject, the Rathenau Instituut assisted the PYO's in various ways. Relevant information was available on the Instituut's website[7] enand together with the iGEM team from the Technical University Delft a *Jumpstart Meeting*[8] was organized. During this meeting, several experts in the field of synthetic biology informed the PYO's and these aspiring young politicians could also take a look inside biotechnology laboratories at this university. Furthermore, the Rathenau Instituut developed future scenarios on synthetic biology in the form of 'vignettes', short stories inspired by potential applications researchers are contemplating, and societal issues that would come into play.[9] With these vignettes we aimed to make the significance and impact of this field more concrete, as a starting point for discussions and opinion making about the futures that this new field could bring. In this report we have included, as interludes, two of these vignettes. On 30 September 2011 the moment had come and six representatives of the Dutch PYO's crossed swords

7 http://www.rathenau.nl/themas/thema/project/synthetische-biologie/synbio-info.html.

8 For a video report of the Jumpstart meeting see this link: http://goo.gl/rWRHNl .

9 See: http://www.rathenau.nl/themas/thema/project/synthetische-biologie/what-are-tech-moral-vignettes.html.

with each other and with six iGEM team members during the *Meeting of Young Minds* in the auditorium of the VU University in Amsterdam. The result was a lively debate on the future of synthetic biology (see Chapter 3).

1.4 How to proceed?

For the Rathenau Instituut the *Meeting of Young Minds* was an exciting step towards a broader societal and political debate on synthetic biology. The societal significance and risks of synthetic biology have already been appropriately addressed in a growing number of studies, but these are mostly academic in character. What is still missing is a broader process of *societal and political opinion making* on synthetic biology. How is the aim of synthetic biology valued from the perspective of societal and (partisan) political movements? Do we want to embrace the opportunities offered by synthetic biology, and if so, how can we deal with potential risks? Or might we exceed limits with synthetic biology that should not be overstepped?

Synthetic biology raises questions that may challenge established frames of mind. How should NGO's and political parties with strong feelings about environmental issues deal with the tension between the *unnatural* character of synthetic biology and the opportunities that synthetic biology has to offer in the field of *sustainability*? Another tension is palpable in the question whether we are not 'playing God' with the aim of *engineering life* in synthetic biology. How will Christian and other religion-based organizations and political parties value synthetic biology in the light of this issue?

1.5 Purpose and scope of this report

This report aims to inform and to inspire. We wish to inform about on-going developments in synthetic biology, the potential ethical and societal issues raised by these developments, and the debate about these issues at the *Meeting of Young Minds*. On this basis we hope to inspire a further process of formulating political and societal views on synthetic biology. To this end, chapter 2 provides a glimpse into the world of synthetic biology and into the discussions on this subject. Chapter 3 provides an analysis of the debate at the *Meeting of Young Minds*. We conclude in chapter 4 with an epilogue on synthetic biology from a societal and political perspective. As *intermezzi* you will find some columns and vignettes in this report.

References

European Commission (2010). *Science and Technology. Special Eurobarometer 340/Wave 73.1.* Brussels: European Commission.

Gibson, D. et al. (2010). 'Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome'. In: *Science* 329, no. 5987, pp. 52-56.

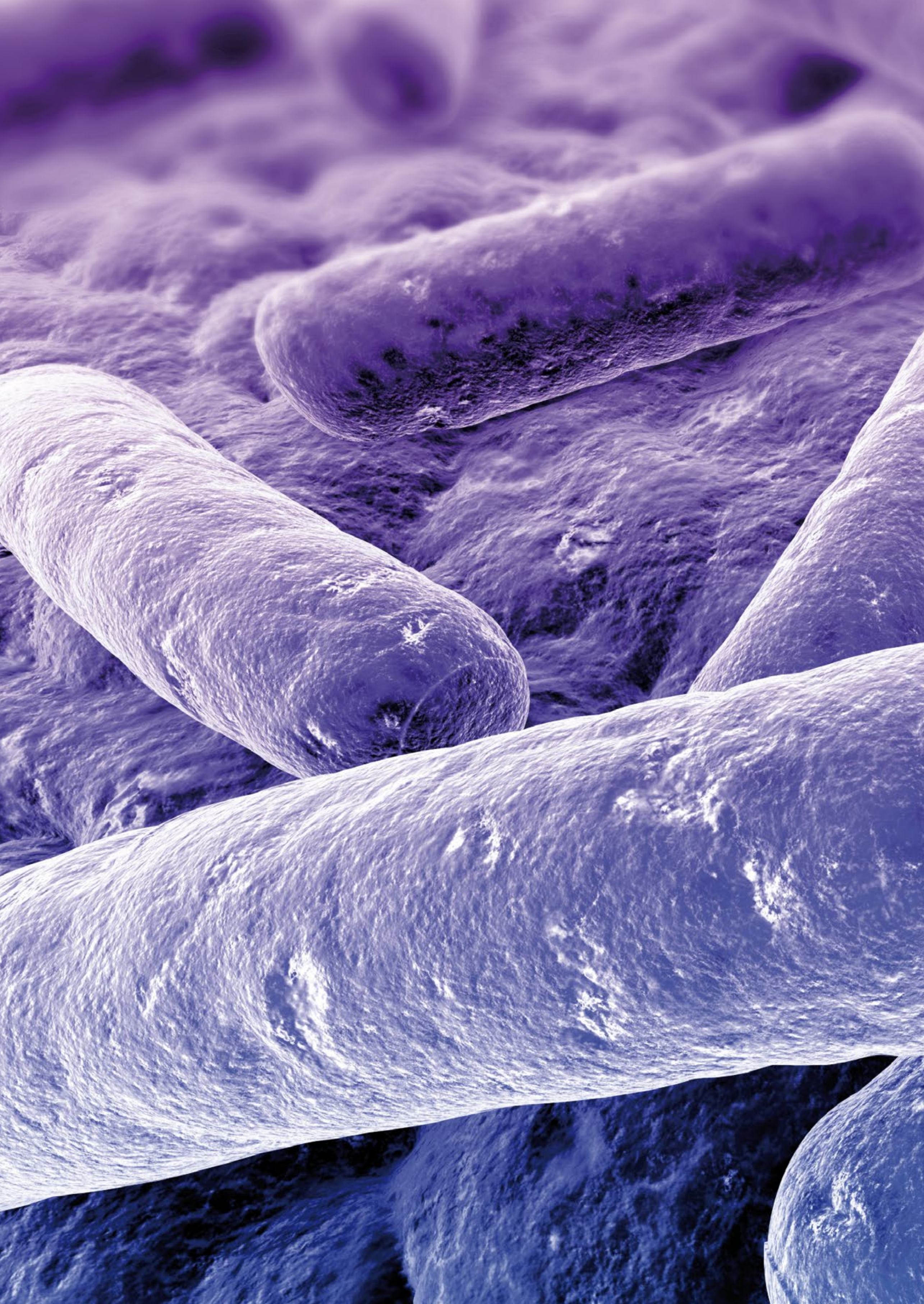
Presidential Commission for the Study of Bioethical Issues. (2010). *New Directions. The Ethics of Synthetic Biology and Emerging Technologies.* Washington: Presidential Commission for the Study of Bioethical Issues. http://www.bioethics.gov/documents/synthetic-biology/PCSBI-Synthetic-Biology-Report-12.16.10.pdf

Schmidt, M. & H. Torgersen (2012). Standardizing synthetic biology: contributing to the bioeconomy? In: Est R. van & D. Stemerding (eds), *Making Perfect Life: European governance challenges in 21st century bio-engineering.* Final Report. Science and Technology Options Assessment (STOA). Brussels, European Union: 161-231.

Stemerding, D. & V. Rerimassie. (2013). *Discourses on synthetic biology in Europe. Working paper 1305.* The Hague: Rathenau Instituut. http://www.rathenau.nl/uploads/tx_tferathenau/Working_Paper_Discourses_on_Synthetic_Biology_in_Europe_01.pdf

Stemerding, D. & Rinie van Est (eds.). (2013). *Geen debat zonder publiek. Het opkomende debat over synthetische biologie ontleed.* The Hague: Rathenau Instituut. http://www.rathenau.nl/uploads/tx_tferathenau/Rapport_Geen_Debat_Zonder_Publiek.pdf

Vriend, H. de (2006). Constructing Life. *Early Social Reflections on the Emerging Field of Synthetic Biology.* The Hague: Rathenau Instituut. http://www.rathenau.nl/uploads/tx_tferathenau/BAP_Synthetic_biology_nov2007.pdf



2
A peek into the world of synthetic biology

2 A peek into the world of synthetic biology

In this chapter we take a look at the dynamic world of synthetic biology. As a starting point we take our previous *Report to Parliament* (in Dutch: *Bericht aan het Parlement*). Meanwhile, however, almost seven years have passed and developments have moved forwards. Therefore, this chapter starts by outlining a number of current developments in synthetic biology. The chapter then discusses some of the main areas of application. Researchers in the field hope that synthetic biology may contribute to addressing grand challenges societies are facing. Finally, we discuss in this chapter the possible risks of synthetic biology, as well as broader social and ethical issues.

This chapter is mainly based on various national and international reports on synthetic biology already referred to in the introduction. We have also made grateful use of the book, *Synthetic Biology. Man as creator? (Synthetische Biologie. De mens als schepper?)* by the Dutch science journalist Arno Schrauwers and synthetic biologist Bert Poolman.

2.1 A new engineering science

"When considered as a piece of machinery, nature is imperfect and should and can be revised and improved". This quote from MIT researcher Drew Endy, one of the pioneers of synthetic biology, summarized the revolutionary nature of synthetic biology as a new and emerging science (Van Est et al. 2007). Craig Venter, another high-profile researcher in this area, was quoted in The New York Times as follows: "This is the step everyone has always been talking about. Once we have learned how to read the genome, we can now also start writing it." (De Vriend 2006).

This new scientific field strives for the complete control of the basic building blocks of life. An important driver for synthetic biologists in the pursuit of this control, is to design organisms, which can lead to useful functions for society, for example in the areas of health, energy and the environment.

The pursuit of controlling nature is not new. Take for instance the age-old history of agriculture and the breeding of plant and animal species. The 1953 discovery of the DNA structure by Watson and Crick laid the foundations for a new form of control over life. Twenty years later, Cohen and Jalal succeeded to cut DNA out of a particular organism and pasting it into another organism, back then unheard of and revolutionary (Cohen et al. 1973). This so-called *recombinant DNA technology* opened the ability to take a gene from a crab into a lettuce, or to incorporate the human gene for insulin into bacteria (Van den Belt 2009). Now, sixty years after Watson and Crick's discoveries, we are again on the threshold of a new phase in the development biotechnology.

As is often the case in emerging fields of science, the definition and delimitation of synthetic biology is subject of much debate (COGEM 2008, EGE 2009). What we can say with certainty at least, is that the aims of synthetic biologists reach much higher than usual in biotechnology. Up to now biotechnologists were engaged in relatively modest modifications to existing DNA within organisms. Starting from genetic modification, the research field of synthetic biologists is moving gradually into the field of rational design of life forms that are becoming more and more estranged from what we may find in nature (De Vriend et al. 2007). In the report *Biological machines?* (2008) The Dutch COGEM uses the following definition of synthetic biology, derived from an expert group of the European Commission:

"Synthetic biology is the engineering of biology: the synthesis of complex, biologically based (or inspired) systems, which display functions that do not exist in nature. This engineering perspective may be applied at all levels of the hierarchy of biological structures – from individual molecules to whole cells, tissues and organisms. In essence, synthetic biology will enable the design of 'biological systems' in a rational and systematic way."[10]

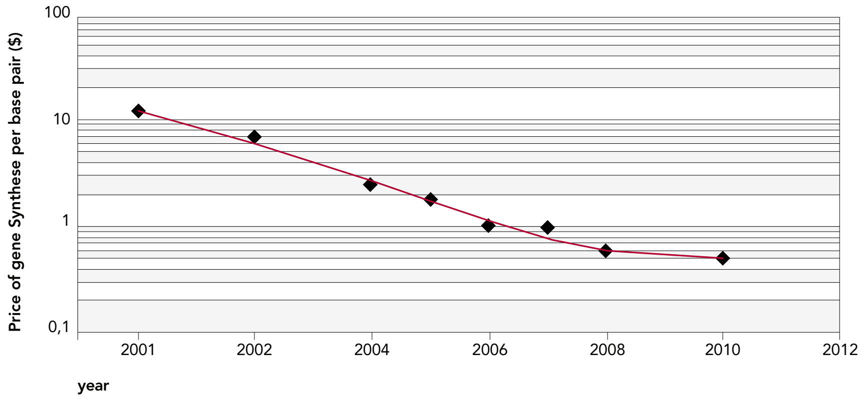
Does synthetic biology really provide options different from DNA technologies that we already know? The answer must be yes, even though the transition from conventional biotechnology approaches to synthetic biology is obviously a gradual process.

In biotechnology, up to now, scientists were dependent on existing genetic material that they had to isolate from organisms. Synthetic biologists are increasingly released from this limitation. They can make use of DNA chemically *synthesized* by specialized commercial companies. This enables synthetic biologists to create more complex systems than hitherto possible (POST 2008; EGE 2009). Moreover, technologies for DNA synthesis rapidly become more sophisticated and the price per DNA-letter keeps on decreasing (see Figure 2.1).

These developments usher in the dream of being able to 'create' life. In their work synthetic biologists take on the *engineering* role. Looking at a cell, they observe a system of cooperating nano-machines. As mentioned earlier, according to synthetic biology pioneer Drew Endy, up to now in biology it was always 'nature at work'. However, "when considered as a piece of machinery, nature is imperfect

10 Recently, the European Scientific Committee on Health and Environmental Risks (SCHER), Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) and Scientific Committee on Consumer Safety (SCCS) (2014) published the following definition of synthetic biology: "Synthetic biology is the application of science, technology and engineering to facilitate and accelerate the design, manufacture and/or modification of genetic materials in living organisms."

Figure 2.1 Price rate of DNA synthesis in the past decade (Source: Runco & Coleman 2011)



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and should and can be revised and improved" (De Vriend 2006). In line with this engineering vision, synthetic biologists draw inspiration from electrical engineering. This is evident in the approach they employ to design and build organisms. Just like transistors, diodes, capacitors and switches, DNA building blocks have specific characteristics and thus they can fulfil exact and predictable functions. The standardization of these building blocks is high on the agenda of synthetic biology (De Vriend et al. 2007; EPTA 2011).

2.1.1 Power from convergence

Synthetic biology is strongly driven by the convergence of different disciplines. Therefore, in synthetic biology, molecular biologists and chemists share the lab with physicists, civil engineers and IT specialists. Indeed, many leading synthetic biologists have no background in biology at all. For example, the aforementioned Drew Endy has a background in civil engineering and Tom Knight, another pioneer in synthetic biology, is originally an IT specialist (Schrauwers & Poolman 2011).

Synthetic biology is therefore a good example of so-called NBIC convergence, involving four key scientific areas: nanotechnology, biotechnology, information technology and cognitive science (hence the acronym NBIC). At the intersections of these scientific domains, new important scientific developments occur in areas such as ambient intelligence, molecular medicine, persuasive technologies, brain-machine interactions and synthetic biology (Swierstra et al. 2009; Van Est & Stemerding 2012). Synthetic biology is especially driven by the convergence of biotechnology with two other NBIC disciplines: information technology and nanotechnology.

Information technology plays an indispensable role in synthetic biology. It is crucial for mapping and analysis of large amounts of genetic material, and for modelling and designing biological systems. Nanotechnology plays an important role in making these biological systems and the development of new technology for reading and writing DNA. With this technology, the four different nucleotides that make up DNA - represented by the letters A, T, C and G - can be placed in any desired sequence in order to create the required building blocks (Van Est et al. 2007).

2.2 Life on the drawing board

For the time being, synthetic biologists are primarily engaged with micro-organisms in the laboratory, although cautious steps are already made to cells of higher organisms. However, people who dream of designing a pet or wish to admire a unicorn or griffin at the zoo still need to have a lot of patience. This of course does not diminish the importance and potential of synthetic biology as a new phase in biotechnology. Much is already possible even today. Indeed, in 2005 researchers succeeded to emulate Jurassic Park™ at a micro level. They managed, by using synthetic DNA, to recreate the extinct Spanish influenza virus. In addition to gaining knowledge of the cause of flu pandemics, this achievement also raised a fierce debate about potential risks. A century ago the Spanish flu virus caused a worldwide flu epidemic that claimed between twenty and fifty million lives (De Vriend et al. 2007).

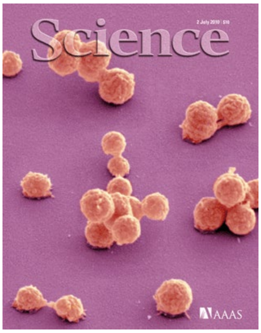
What can synthetic biology offer us today in terms of developments and opportunities? In the following section, we discuss these developments and opportunities by distinguishing between a number of different engineering approaches that are visible in the emerging field of synthetic biology.

2.2.1 Searching for a minimal cell

In this first engineering approach, with Craig Venter as its main ambassador, researchers deconstruct existing organisms to determine the minimum number of genes required by a living cell. Their ultimate objective is the creation of a *minimal cell*, wherein the genetic information has been reduced to a minimum size necessary for simple cellular life. By minimizing the number of genes, you could limit the complexity of the biological processes in the cell, allowing one to better predict and control them. Using this approach, we not only learn about evolutionary processes, but we can also develop a minimal cell into a biological base system or chassis into which new biological systems can be designed (De Vriend et al. 2007). In the future, Venter hopes to design and develop bacteria based on a minimal cell, able to produce hydrogen or to filter out CO_2 in the air, thus enabling to tackle the challenges of energy production and global warming (Schrauwers & Poolman 2011).

Venter has not yet succeeded to create a minimal cell, but his research follows a specific roadmap, with each step creating press coverage for his work. Thus in 2007, Venter could announce that the complete chromosome of the bacterium *M. genitalium* had been synthesized. In 2009 the Venter Institute succeeded in transplanting the chromosome of *M. mycoides*, a distant relative of *M. genitalium*, into the cell of a different bacterial strain, M. capricolum (Schrauwers & Poolman 2011). By May 2010, the Institute created a real stir in the media, saying that it had created a fully functional synthetic genome for the first time and had built it into a microorganism named M. *mycoides* JCVIsyn1.0. (Gibson et al. 2010). The chromosome was synthesized on the basis of genetic information available in computer databases. In the words of Venter: "The first species.... to have its parents be a computer" (Henderson, 2010). Thus Venter demonstrated that it is possible in the laboratory to synthesize a complete DNA strand being fully functional within a microorganism, laying the foundation for the design of a minimal cell. To prove that it actually was a synthetic DNA molecule, several watermarks were fitted in into the DNA sequence, including the names of the 46 researchers who participated and the Institute's email address (Schrauwers & Poolman 2011).

Although there was a lot of positive response to this particular achievement, not everyone is quite happy with it. The *ETC Group* for instance is watching developments in synthetic biology with much concern. They baptized Venter's bacteria 'Synthia' and see its creation as symbolic of the profit-driven haste of synthetic biologists to come up with results without understanding the potential risks (ETC Group, 2010). ETC Group's Pat Mooney says: "This is a Pandora's box moment – like the splitting of the atom or the cloning of Dolly the sheep – we will all have to deal with the fall-out from this alarming experiment."[11]



The Science cover with the M. mycoides JCVI-syn1.0, developed by the J. Craig Venter Institute (Science, July 2010)

11 See: http://www.dailymail.co.uk/sciencetech/article-1279988/Artificial-life-created-Craig-Venter--wipe-humanity.html.

Venter is by no means the only one looking for a minimal cell. In the Netherlands, researchers are also active in this field. Microbiologists from the University of Wageningen announced that by using a new method they could quickly and relatively cheaply remove excess DNA from the bacterium Pseudomonas putida. The researchers from the Wageningen *Synthetic Biology and Systems Biology group* expect that ultimately over half of the genome of this bacterium can be erased.[12]

In the beginning of 2014 an international research team, led by Jeff Boeke at New York University's institute for systems genetics, announced that they managed to fully synthesize a complex chromosome from brewer's yeast and successfully transplanted it into a yeast cell. During the project that spanned seven years, the research group redesigned one of the chromosomes of the organism by removing non-essential genes. The crucial difference with earlier breakthroughs following this approach is that it involved the synthesis of a chromosome from an organism that is 'eukaryotic', with a far more complex organization of the cell, like plants and animals (Sample 2014; Annaluru et al. 2014).

2.2.2 Building with living Lego® bricks

The idea behind this second engineering approach is to design standardized genetic building blocks which can be used to reprogram microorganisms, for the purpose of research and useful applications. These genetic elements are constructed in such a way, that they can be combined in different ways as independent modules. You can compare it to Lego®. Microorganisms essentially serve in this approach as a 'motherboard' or 'chassis'.

This approach is the foundation for the Registry of Biological Parts at MIT: the online open source catalogue of standardized genetic building blocks, BioBricks™ as described in the introduction. This catalogue is one of the most important tools for iGEM, the international design competition for students in the field of synthetic biology. In this engineering approach the growing knowledge about genetic biodiversity, the increasing speed with which DNA can be read and written, and the development of models in systems biology[13] all come in very handy (Schrauwers & Poolman 2011).

The above developments fit well in with established practices of industrial *metabolic pathway engineering* whereby pathways in microorganisms are modified in order to be able to produce medicines and other useful products. Until now, this practice has mostly been a matter of trial and error. With the rise of systems biology and synthetic biology this is changing. Metabolic routes can be

12 See: http://www.wur.nl/NL/nieuwsagenda/nieuws/R_Kleinere_genomen_.htm

13 The KNAW Academy strategic study New Biology describes systems biology as follows: "[...] a biological system is herein described as a complex set of processes in which the contributions of the individual processes can be clearly made visible in their relative positions. Thus, we are better able to do predictions on the effectiveness of an intervention in a system" (KNAW 2011, p. 35).

simulated in computer models and by using computer aided design increasingly complex genetic building blocks can be designed and built. This allows researchers on the basis of *rational design* to adjust existing organisms in a targeted way or to build 'new' designs (De Vriend & Stemerding 2011).

In the further development of this approach, the research group of the American synthetic biologist Jay Keasling plays a leading role. His research focuses in particular on the design of basal metabolic pathways in microorganisms with a multi-use nature. The compounds formed in these metabolic pathways may serve as starting point for the production of a range of useful substances. Bacteria are thus converted to production platforms with various applications in the fields of pharmaceuticals, chemicals and fuel. James Carothers, a former researcher in the Keasling group, is convinced that the development of such biological *multi-use* platforms, combined with engineering design approaches, will enable the rapid engineering of safe and effective synthetic biology technologies that can address key problems in health, environment and resources on a global scale (Carothers 2013).

MIT Synthetic biologist Drew Endy with vials filled with BioBricks™

2.2.3 Automated evolution

George Church, active at Harvard and MIT, and veteran in the field of *genome sequencing*, is developing a different approach to introduce desired properties into microorganisms. Whereas the above engineering approaches are to a large extent based on human engineering ingenuity, Church wants to harness nature's design and assembly power to do the work.

In 2009, researchers from his group presented their 'evolution machine' called MAGE or in full, Multiplex-Automation of Genome Engineering (Wang et al.

2009). Assisted by MAGE, large-scale genetic changes can be entered into microorganisms on the basis of which these organisms will evolve in a certain direction in the shortest time span. Thus in three days, using MAGE, the researchers were able to produce as many as 15 billion genetic variants of *E. coli*, from which the desired variants were selected in a smart way. With conventional technology, this would have taken the researchers many months, if not years of work. "The strength of this method is that combinations of mutations can be introduced that have not yet been thought of at the drawing board. In fact, the organism does the work – creating the effect of random gene mutation – and the researcher's contribution is developing a proper selection system" (Schrauwers & Poolman 2011, p 114).

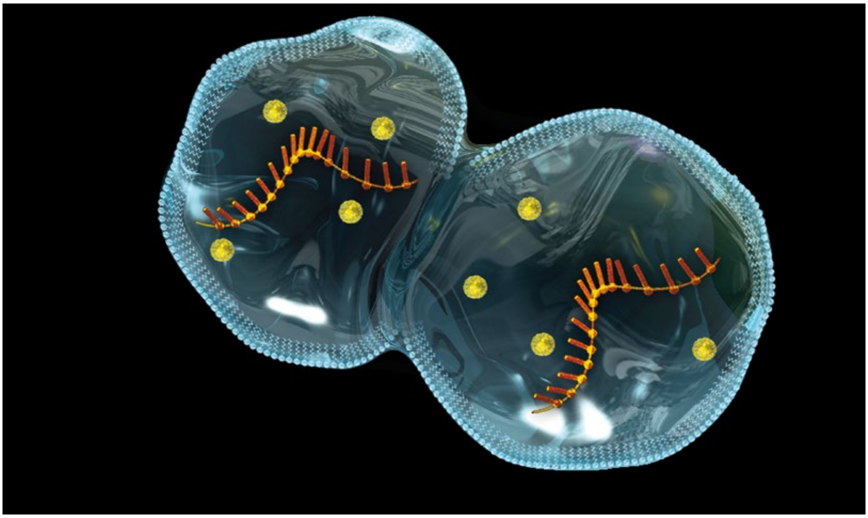
2.2.4 Creation 2.0

"If we look at the chemical elements that make up living systems, we notice that nature has only made frugal use of the periodic table of elements" (Schrauwers & Poolman 2011, p. 12). With this remark Schrauwers and Poolman pose the tantalizing question of whether life is possible with a little wider selection of the elements that are available on earth.

Some synthetic biologists aim to build systems based on non-natural genomes, showing that we are not bound by the conventional DNA/RNA. Their aim is to create a separate "nature" through XNA's, where the X stands for xeno (foreign), that cannot mix with the existing nature, or in jargon, has a high degree of orthogonality. Such foreign systems preclude undesired exchange of mutations, as new unnatural genes cannot interfere with that of existing (micro)organisms (Schrauwers & Poolman 2011; Torgersen et al. 2010). The first conference on xenobiology 'XB1' was held in May 2014. According to the conference website Xenobiology "is the endeavour to overcome the constraints imposed by evolution on natural living organisms. It is taking shape as an emerging field in the context of synthetic biology, encompassing the design, generation and evolution of alternative forms of life. The foundational conference XB1 aims to gather scientists, engineers, designers, policy makers and other stakeholders to chart the paths toward an entirely novel biodiversity".[14]

Indeed, 2014 turned out to be a landmark year for this approach. Recently, a group of U.S. based researchers created the first-ever living organism carrying an expanded genetic code and passing it down to future generations. The group led by Floyd Romesberg successfully added DNA containing a base pair made up by two synthetic nucleotides – for simplicity dubbed 'X' and 'Y' – to an *E. Coli*. As hoped for, the unnatural base pair did not significantly affect the growth of the microorganism and the synthetic code was also inherited by succeeding generations. Thus, the researchers created the first organism that stably propagates an expanded genetic alphabet (Sample 2014; Malyshev et al. 2014).

14 See: http://xb1genoa.com/.



Artistic image of a proto-cell

Other synthetic biologists are working on 'proto-cells'. These are artificial cells with properties of living cells. The Dutch report *Synthetic biology: creating opportunities* defines proto-cells as follows: "A simple self-assembling nanosystem consisting of three basic components: a metabolic system, a molecule able to store information and a membrane that keeps the system together" (Dutch Health Council 2008, p.40). Although this type of research is only at its infancy, and still far away from useful applications, it certainly testifies to the ambitions of synthetic biologists dreaming of making synthetic life.

2.2.5 Why not just do it yourself?

A typical feature of the engineering approach in synthetic biology is its aim to simplify the technical construction of biological devices and systems as much as possible. A lot of information on standardized biological parts is available online. Thus synthetic biology has great attraction for non-professional scientists who in their own kitchen or garage would like to get to work with bacteria and BioBricks™. Designer Tuur van Balen is a good example. He shows how even without a firm foundation in biotechnology you can get notable results. In his contribution to the *Next Nature Power Show* in Amsterdam, he showed how to transform yogurt bacteria, by using BioBricks™ from the Registry of Biological Parts, into a Prozac-production system.[15]

Do-It-Yourself Biology or DIYbio communities like to identify themselves with 'hackers' and 'geeks', who eventually have become famous with 'garage' innovations (Wohlsen 2011). Up to now, the activities of these amateur biologists are modest and their experiments are mostly simple and playful (Van Boheemen & De Vriend 2014). This playful and open nature is also part of the culture of

15 See: http://www.youtube.com/watch?v=Co8NOnErrPU.

synthetic biology, whereby some of its proponents hold democratization of biotechnology in high esteem (Carlson 2010). In Europe, the DIYbio movement is small in size, but new initiatives begin to crop up. Some enthusiasts have managed to build community laboratories with instruments bought on eBay, as happened in Paris.[16]

EU research programs in the field of synthetic biology

The first research department in synthetic biology was founded in 2003 at the Lawrence Berkeley Laboratories, and the United States are still leading. Nevertheless, the European Commission was quite early in starting a broad research funding scheme for synthetic biology. In the Sixth Framework Program for Research and Technological Development (FP6), at least 25 million euros were spent for scientific research in synthetic biology as well as on its ethical, legal, social and economic implications (EPTA 2011, p. 2).

More recently, from 2012 to 2014, came the establishment of ERASynBio, an initiative aimed at the development and coordination of synthetic biology in the European research area. One of the important aims of this initiative was to comprehensively map national and transnational funding schemes, funded synthetic biology projects, relevant strategies and reports, and active companies, in order to develop a strategic vision. According to these mapping activities, about €450 million of public research funding was allocated to synthetic biology from 2004 to 2014 (ERASynBio 2014).

16 See: http://www.lapaillasse.org/.

2.3 The promises of synthetic biology

Section 2 gave an impression of different approaches in synthetic biology. Being an engineering science, synthetic biology not only involves acquisition of knowledge, but even more so work on applications. Many researchers regard synthetic biology as an important key in addressing global challenges in the areas of energy, climate and healthcare. In this section we look at some of these potential applications.

2.3.1 Bio-economy and environmental issues

To begin with, synthetic biology could contribute to a future bio-economy. This bio-economy – or bio-based economy – is an economy in which fossil fuels are as much as possible replaced by sustainably produced biomass (Asveld et al. 2011). One of the potential applications of synthetic biology is production of biofuels. Some bacteria are able to convert vegetable biomass into butanol, but do quite an inefficient job, so that yields remain low. In order to address these problems, synthetic biologists have transformed E. coli bacteria into a variant that is much more efficient and therefore more interesting for the industry (PCSBI 2010; EGE 2009). Major oil companies such as Shell, Exxon Mobil and BP are investing hundreds of millions of Euros in such research (EPTA 2011). In the Netherlands there are also activities in this field, taking place in consortia of universities and companies like *BE-Basic*[17] and *BioSolar Cells.*[18]

Another example is the use of algae to produce biodiesel. According to researchers, algae have certain advantages compared to plant material. Algae are high in oil content and have a high growth rate, can be grown in production systems on land or in water and do not claim areas with good soil, necessary for growing food crops. By-products emerging during production of biodiesel from algae can be used in other ways, for example as animal feed (PCSBI 2010). In the Netherlands AlgaePARC in Wageningen has been established in 2011 as an important centre for algae research.[19]

In a future bio-economy, biomass should also be used wherever possible as a raw material for producing quality products, as an alternative source to existing petrochemical production (Asveld et al. 2011). The previous section described how in the vision of researchers, by using synthetic biology, microorganisms could be developed into multi-use platforms for making all kinds of useful substances. Multinationals DuPont and Tate & Lyle already use converted microorganisms for a process transforming corn sugar into a key ingredient for the production of fibres (De Vriend & Stemerding 2011).

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17 http://www.be-basic.org/home.html.
18 http://www.biosolarcells.nl/.
19 http://www.algaeparc.com/.

A possible application of synthetic biology in addressing environmental issues is bioremediation, the use of biological processes to turn a contaminated environment back to its original condition. For this purpose, microorganisms are used that can accumulate and break down certain substances. Researchers may use synthetic biology in developing microorganisms able to efficiently tackle extremely stubborn contaminants, such as heavy metals, nuclear waste and pesticides (EGE 2009; PCSBI 2010). IGEM-teams are regularly engaged in projects aiming at this type of practical applications. In the introduction we already gave the example of the Delft research team in 2010, with their design of a bacterium that can digest crude oil pollution.

2.3.2 Health

Health is another frequently mentioned field for potential applications of synthetic biology. In fact, the first known application that was attributed to synthetic biology has been in the field of medicine. With generous financial support from the Bill and Melinda Gates Foundation, the Jay Keasling team at UC Berkeley ingeniously managed to develop yeast cells producing artemisinic acid, the basis for the malaria drug *artemisinin* that is extracted from the sweet wormwood plant. In 2013 UC Berkeley announced that a pharmaceutical company had launched large scale production of artemisinin based on Keasling's work.[20]

The George Church group recently used MAGE as a tool to develop E. coli bacteria that are able to make significant amounts of lycopene, a pigment found in tomatoes and possibly having cancer-inhibiting effects.

These two examples demonstrate how synthetic biology may be used to fabricate medicinal substances we already know from nature. Synthetic biology can however also be used to create medicinal substances that do not occur in nature. Thus, the *Centre for Synthetic Biology* at Groningen University uses synthetic biology to develop new kinds of antibiotics. This Centre also uses synthetic biology in a completely different way as a technique for developing targeted drug delivery by means of synthetic membrane vesicles. This approach could be applied to fight tumours in a much more targeted way (Schrauwers & Poolman 2011; EGE 2008). By means of synthetic biology, targeted drug delivery could also be used to insert in the body active viruses or bacteria, so-called living therapeutics (De Vriend et al. 2007).

Finally, biosensors can be mentioned as a potential contribution of synthetic biology to public health, particularly in developing countries, as for example biosensors for testing drinking water for harmful substances. Every year, 100 million people fall victim to arsenic poisoning after drinking contaminated ground water, often with deadly results. In 2006 this problem inspired the

20 See: http://newscenter.berkeley.edu/2013/04/11/launch-of-antimalarial-drug-a-triumph-for-uc-berkeley-synthetic-biology/.

Column - It’s technology, stupid!

The book ‘Synthetic biology : man as creator’ (in Dutch: ‘Synthetische biologie: de mens als schepper’) puts an emerging area of science on the map for a wider audience. This is important, because creation of life raises questions and dilemmas that affect everyone. Are we ready for that?

It is the holy grail of biology: creating new life. The understanding of the essence of life has captivated generations of biologists. Although it will take many years before we are really able to create life itself from dead matter, rapid developments in molecular biology bring the possibility of creating life ever closer.

We can already read life. Much has been unravelled about DNA, the sample sheet of life. Now we are about to also write life. With computer programs, we can already design complete gene networks (in silico). We can also perform targeted interventions in how cells work and change their properties.

That is just the beginning. During the next decades new knowledge and capabilities will bring unprecedented new applications within reach. For example, the prolonging of life, disease prediction and prevention and the development of new food crops, new materials and new raw materials for industry.

These are developments that will greatly influence and change our society – but also affect us as individuals. This presents new challenges to which we will have to find an answer.

How do we deal with financing of new medical technologies? What opportunities and risks do genetically modified crops engender? How do we ensure that we are not the only ones who have access to these new technologies, but also people in developing countries?

Do we dare to take on this risky but promising adventure? And if so, what will it take? To start with, we need a long-term vision of our role and our aims, coupled with long-term investment in research, education and development.

But a mentality change is also required, so that technology will become sexy again. In a country like the Netherlands, students think science is dull and nerdy and rather opt for an office job in the service sector than for technical training or a career in the lab.

There is need of action – including political action to increase the much needed influx of young talent. We will have to convey much better how exciting and challenging research and innovation can be. It can be an adventure, an opportunity to discover things that no one before you has found out. How to create new life, for example.

In short, it’s technology, stupid!

Bert Poolman
Synthetic Biologist

iGEM team at Edinburgh to design a bacterial biosensor, which should be able to detect arsenic quickly and cheaply.[21] With this design, the team won the prize for the best *real-world application*. Other iGEM teams also went to work with biosensors. A 2009 design by the Cambridge iGEM team, called *E. Chromi* even won iGEM's top prize, the *BioBrick Trophy*. The team focused on the development of bacteria that under certain environmental conditions produce a colour visible with the naked eye.[22] Such biosensors can indeed be used also for other than medical purposes. An example mentioned by the *Presidential Commission for the Study of Bioethical Issues* in its report on synthetic biology, is the development of biosensors for monitoring soil fertility in agriculture (PCSBI 2010).

2.4 Risks

Both internationally and in the Netherlands, in discussions on synthetic biology from the outset attention was paid not only to the opportunities but also to the risks of this emerging field of science. The risk discussions concentrate in particular on issues of safety in laboratories and the environment and issues related to possible abuse of knowledge. The first kind of risks relate to *biosafety* – 'keeping bad bugs from people' – and the second kind to *biosecurity* – 'keeping bad people from bugs' (EPTA 2011, p. 3).

2.4.1 Biosafety

The discussion on biosafety is about the potential risks to humans and the environment, an area that has long been at issue in the public debate on genetically modified organisms (GMOs). It involves the risks of working with microorganisms with novel (potentially harmful) traits and their possible escape. An important and recurring question in the debate is whether we have sufficient knowledge to assess the risks involved and control them, especially given possible irreversible effects of the spread of GMOs into the environment.

Due to the development of synthetic biology these questions remain recurring themes on the agenda (De Vriend et al. 2007; EGE 2009, International Risk Governance Council 2010). Synthetic biologists themselves have taken the lead in this discussion, but also had to face critical reactions from NGO's that advocate stricter regulation. In 2012, 111 international NGO's – including the ETC Group and Friends of the Earth – called for strict supervision of synthetic biology and strict application of the precautionary principle "to protect the planet and its inhabitants against the risks of synthetic biology and synthetic biology related products." (Friends of the Earth, CTA & ETC Group 2012, p.1).

21 See: http://parts.mit.edu/wiki/index.php/Arsenic_Biosensor.

22 See: http://2009.igem.org/Team:Cambridge.

Among experts a broad international consensus prevails that the existing regulations for GMOs still suffice as a framework for assessing and managing the risks of synthetic biology (EPTA 2011).[23] A few years ago this view was also expressed in the Netherlands by the COGEM in the report *Biological Machines*?, anticipating developments in synthetic biology (COGEM 2008). At the same time there is a concern that existing biosafety rules may come under pressure by developments in synthetic biology, as in the future synthesized microorganisms may become more and more different from organisms that we are already familiar with (International Risk Governance Council 2010, COGEM 2013).

A major focus in this discussion is to assess the knowledge needed in the area of risk analysis, in order to properly judge new developments in the field of synthetic biology. This particularly applies to situations in which synthetic organisms are released into the natural environment. Some authors therefore argued in *Nature* to timely invest in ecological risk studies (Dana et al. 2012). Interestingly, it is conceivable that synthetic biology creates opportunities to reduce the risks to the environment, by the development of organisms that cannot survive under natural conditions and will be genetically isolated from natural populations (see also Schmidt 2010).

Recently, the international debate on synthetic biology was fuelled by the success of a synthetic biology start-up company dedicated to the development of glowing plants, which attracted a considerable amount of funding via the crowdsourcing website 'Kickstarter' (Callaway 2013). Only three days after the launch of the project in April 2013 the initial funding goal of $65.000 was reached. The project gained considerable press coverage and ended up with $484,013, by the end of the campaign. More than 8.000 persons financially supported the project and will in return be rewarded with seeds to plant their very own glowing plant.[24] While some are apparently eager to own a plant altered by means of synthetic biology, others are highly critical towards the idea of individual citizens being able to plant GM crops wherever they please, and the related potential 'SynBio pollution'.[25] In any case, shipping of the seeds is expected in fall 2014, for now however only in the United States, given more stringent GMO regulation regimes elsewhere, such as in the EU.

23 In its opinion on synthetic biology, the European Group on Ethics on gives an overview of European and global regulation in the field of GMOs (EGE 2009, pp. 27-35). Such an overview is also available on the COGEM website on Genetic Modification, including the regulations as applicable in the Netherlands: http://www.cogem.net/index.cfm/nl/genetische-modificatie/wetten-en-regels/.

24 See: www.glowingplant.com and https://www.kickstarter.com/projects/antonyevans/glowing-plants-natural-lighting-with-no-electricity.

25 See for instance: http://www.etcgroup.org/kickstopper.

2.4.2 Biosecurity

Concerns about possible abuse of biological knowledge have also a longer history associated with the development of biotechnology, mostly related to the possible development of biological weapons. Since the attacks of 9/11, the attention in this debate has shifted to the threat of bioterrorism and thus explicitly to the role of malicious individuals and groups. As a result, researchers in the life sciences are facing measures and responsibilities in the area of biosecurity to ensure that knowledge does not fall into the wrong hands. In this context, the *Royal Netherlands Academy of Arts and Sciences* has a designed a scientific code of conduct for biosecurity (KNAW 2007).

An important aim of synthetic biology is to simplify the construction of biological devices and systems. This aim has evoked fears that synthetic biology could become an instrument of abuse in the hands of malicious individuals. With growing possibilities for DNA synthesis and freely accessible information about viruses on the internet, it might become more easy in a not too distant future to construct dangerous viruses (Garfinkel et al. 2007). Firms commercially providing synthetic DNA have therefore made mutual agreements on screening orders from customers for potential risks of abuse. At the same time, it remains crucial for synthetic biologists and the future development of science that knowledge and materials can be freely shared.

Biosecurity thus implies a tension between control oriented security measures and the pursuit of openness in the scientific community (Stemerding et al. 2011). In the autumn of 2011 this tension became very clear in an international debate about research in Rotterdam, in which a dangerous bird flu virus had been made transmissible between people via air. The discussion centred on the question whether the possibility of misuse would justify restrictions to publication of the results of this research (KNAW 2013). Although the Rotterdam study involved only classical virology research, it raises questions that are also obviously significant in the context of future developments in synthetic biology (Jefferson et al. 2014).

2.5 Broader issues

In the introduction we have noted that Dutch political parties have thus far hardly considered the significance and implications of synthetic biology for society. This also applies to NGO's in the Netherlands. Internationally, we see a lively debate inspired by a well-established tradition of reflection on the *ethical, legal and social implications* (ELSI) of new and emerging science and technology. This debate is mainly taking place in academic circles, with occasional contributions from NGO's. In addition to social scientists and ethicists, scientists and technologists are playing an active role, sometimes even a leading role. In these ELSI debates, not only potential risks are receiving attention, but also broader societal issues raised by synthetic biology.

2.5.1 Justice

A much-debated issue in ELSI discussions about new and emerging science and technology is the extent to which the expected benefits and downsides are distributed fairly, particularly from a global point of view. This issue has been raised also in discussions about synthetic biology. For example, the Presidential Commission for the Study of Bioethical Issues states that: "Emerging technologies like synthetic biology will have global impacts. For this reason, every nation has a responsibility to champion fair and just systems to promote wide availability of information and fairly distribute the burdens and benefits of new technologies" (PCSBI 2010, p.5). The opinion of the European Group of Ethics further adds that not only global fairness is at stake, but also fairness with regard to future generations. Justice therefore implies, according to the EGE, that issues of *sustainability* have to be taken into account in synbio research and innovation (EGE 2009).

From the point of view of justice the role of patenting is especially controversial in synthetic biology (Oye & Wellhausen 2009). Researchers striving for strong patent positions stand opposite to researchers and also public organizations that advocate an open source model. Intellectual property is often seen as an important prerequisite to commercially exploit new knowledge. It implies that third parties may not use valuable knowledge for commercial purposes without permission. However, there are also experiences showing that patents can significantly hinder innovation. An often-mentioned example is the 'Golden Rice' project, where permission had to be obtained for the use of no less than seventy biotechnology patents, spanning 32 different owners, in order to operate this project (Van den Belt 2009).

From this perspective, Craig Venter's broad patent applications in synthetic biology have become an issue of debate. Venter's applications do not only relate to the concept of a minimal cell (a concept that still has to be realized), but also to the more generic tools of synthetic biology, like the creation and transfer of synthetic genomes (Dutch Health council 2008). International NGO's have criticized Venter's business strategy, highlighting the unjust consequences of monopolization caused by such far-reaching forms of patenting (Friends of the Earth, CTA & ETC Group 2012). Their branding of Venter's companies as *MicrobeSoft* clearly suggests what example these critics have in mind (Dutch Health council 2008).

The BioBricks Foundation, known for its Registry of Standard Biological Parts, has been established precisely with the aim to guarantee free access to standard biological parts in order to facilitate and speed up innovation in synthetic biology. As one of the founders of the BioBricks movement, Drew Endy has expressed clear concerns about radical forms of patenting. He fears a 'Balkanization' of basic biological functions (Van den Belt 2009).

2.5.2 Naturalness

Notions of 'culture' and 'nature' express often deeply felt ways in which people define their relationship with their non-human environment. In our society, different views exist about which intervention in nature is acceptable or appropriate and what moral limits should be taken into consideration (De Vriend et al. 2007). Developments in biotechnology may evoke strong feelings of unnaturalness and discomfort. The 2010 Eurobarometer survey shows that EU citizens remain invariably sceptical about genetically modified (GM) food. Of all EU citizens 70 % believe that GM food is 'fundamentally unnatural' and 61% have uncomfortable feelings about GM food (Eurobarometer 2010).

It is highly likely that synthetic biology, with aims strongly framed in terms of 'engineering' and 'control', will raise similar feelings of uneasiness, especially when its products are making their way to consumer markets. The Belgium firm Ecover for example, has announced plans to shift from palm kernel oil to an algal oil as a basic ingredient for their soap products. For Ecover (according to its own website a pioneer in green innovation[26]), the oil represents a 'natural' and sustainable alternative for palm kernel oil, which is considered to be an important cause of deforestation of tropical rain forests (Strom 2014). According to a coalition of NGO's however, including the ETC Group and Friends of the Earth, the algal oil is far from natural and sustainable as it is produced by means of synthetic biology. They launched a petition Synthetic is not natural, urging Ecover to 'keep extreme genetic engineering out of "natural" products'.[27] The use of synthetic biology thus seems to raise a tension between notions of sustainability and naturalness that may prove difficult to reconcile.

2.5.3 Notions of life

What is life? Developments in synthetic biology could easily give the impression that life is reducible to being just DNA. Many people feel uncomfortable with such a reductionist approach to life (De Vriend et al. 2007). If we see life as something precious, the idea of *manipulability* of life may evoke resistance. Synthetic biology may also affect the boundary between what should be considered 'living' and 'non-living' (Van den Belt 2009; EGE 2009). Living beings are awarded intrinsic value precisely because of the fact that they are 'alive'. In synthetic biology, we meet combinations of terms that, from that perspective, are difficult to reconcile, like *artificial life* or *biological machines*. Is synthetic biology still about living 'beings' or is it merely about artificially manufactured things? For now, synthetic biologists are mostly dealing with microorganisms, for which most people will not get instant warm feelings. But it is not inconceivable that in the future organisms will be 'created' with a higher level of cuddliness (see for example the scenario described in Intermezzo II).

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26 See: http://us.ecover.com/en/.
27 See: http://www.syntheticisnotnatural.com/.

2.5.4 Playing God?

Another question arising in discussions about synthetic biology is whether we are ‘playing God’ if ‘we are creating life’ (Torgersen et al. 2010). The question also resonates in the subtitle, given by journalist Arno Schrauwers and synthetic biologist Bert Poolman to their book *Synthetic biology: man as creator?* (in Dutch: *Synthetische biologie: De mens als schepper?*). The media also seem keen to seize on this metaphor. An early Business Week report about Venter’s investigation of the minimal genome was titled “Playing God in the lab”.
In May 2007, Newsweek magazine put the phrase ‘Playing God’ prominently on the cover when reporting on Venter’s work. Some researchers seem to stir up the fire with some irony, as in the reply of Venter’s colleague and Nobel laureate Hamilton Smith: “We are not playing!”. James Watson, famous for his work on the structure of DNA, for his part explained before a committee of the British House of Commons: “If scientists don’t play God, who else is going to?” (Van den Belt 2009).

How synthetic biology relates to the notion of ‘playing God’ has been thoroughly examined in European project called SYNTH-ETHICS. According to the findings from this project, the notion of playing God allows different interpretations in religious and philosophical terms. Indeed, it can be argued that Christianity actually has a positive stance towards human intervention in nature, that is: “Nature is not a sacred or divine reality that man must leave alone. Rather, it is a gift offered by the Creator to the human community, entrusted to the intelligence and moral responsibility of men and women” (Link 2009). However that may be, it is too easy to dismiss the theme of ‘playing God’ as pure sensationalism. Synthetic biology could well come to be at odds with religious beliefs in our society. Moreover, we can also see the playing God metaphor as an expression of a more general culturally entrenched discomfort with engineering life (Dabrock 2009, Kaebnick 2009).

Referenties

Annaluru, N. et al. (2014). *'Total Synthesis of a Functional Designer Eukaryotic Chromosome'*. Science 1249252, Published online 27 March 2014.

Asveld, L. et al. (eds.). (2011). *Naar de kern van de bio-economie. De duurzame beloftes van biomassa in perspectief.* Den Haag: Rathenau Instituut. http://www.rathenau.nl/uploads/tx_tferathenau/Rapport_Biobased_Economy_Rathenau_Instituut.pdf

Belt, H. van den. (2009). *'Het leven op de tekentafel'*. In: Swierstra, T. et al. (eds.). *Leven als bouwpakket.* Den Haag: Rathenau Instituut, pp. 104-119. http://www.rathenau.nl/uploads/tx_tferathenau/Leven_als_bouwpakket.pdf

Boheemen, P. van & H. de Vriend. (2014) *Do It Yourself Biology. Een verkenning van ontwikkelingen in Nederland.* CGM 2014-03. Bilthoven: COGEM.

Callaway, E. (2013) *'Glowing plants spark debate'*. Nature 498, pp. 15–16.

Carlson, R. (2010). *Biology is Technology. The Promise, Peril and New Business of Engineering Life.* Cambridge: Harvard University Press.

Carothers, J. (2013). *'Design-driven, multi-use research agendas to enable applied synthetic biology for global health'.* Systems and Synthetic Biology 7(3), pp. 79-86.

Commissie Genetische Modificatie. (2008). *Biologische machines? Het anticiperen op ontwikkelingen in de synthetische biologie. COGEM signalering CGM/080925-01*. Bilthoven: Commissie Genetische Modificatie. http://www.cogem.net/index.cfm/nl/publicaties/publicatie/biologische-machines

Commissie Genetische Modificatie. (2013). *Synthetic Biology. Update 2013. Anticipating developments in synthetic biology COGEM Topic Report* CGM/130117-01. Bilthoven: Commissie Genetische Modificatie. http://www.cogem.net/index.cfm/en/publications/publicatie/synthetic-biology-update-2013

Cohen, S.N. et al. (1973). *'Construction of Biologically Functional Bacterial Plasmids in Vitro'*. In: PNAS 70, pp. 3240-3244.

Dabrock, P. (2009). 'Playing God? Synthetic Biology as a Theological and Ethical Challenge'. In: *Systems and Synthetic Biology* 3, no. 3, pp. 47-54.

Dana, G. et al. (2012). *'Synthetic Biology. Four Steps to Avoid a Synthetic-Biology Disaster'*. In: Nature 483, no. 7387, p. 29.

European Group on Ethics. (2009). *Ethics of Synthetic Biology. Opinion no. 25.* Brussels: European Commission. http://ec.europa.eu/bepa/european-group-ethics/docs/opinion25_en.pdf

EPTA. (2011). *Synthetic Biology. Briefing note no. 1. EPTA [n.p.].* http://www.rathenau.nl/fileadmin/user_upload/rathenau/Projecten/Synthetische_biologie/EPTA_briefingnote_syntheticbiology.pdf

ERASynBio. (2014). Next steps for European synthetic biology: A strategic vision from ERA-SynBio. European Research Area Network for the Development and Coordination of Synthetic Biology in Europe. https://www.erasynbio.eu/lw_resource/datapool/_items/item_59/erasynbiostrategicvision.pdf

Est, R. van et al. (2007). *Synthetische biologie. Nieuw leven in het biodebat.* The Hague: Rathenau Instituut. http://www.rathenau.nl/uploads/tx_tferathenau/BAP_Synthetische_biologie_sept_2007.pdf

Est. R. van et al., *'Kunstmatig leven verdient helder debat'*. In: de Volkskrant, 12 februari 2008. http://www.volkskrant.nl/vk/nl/2844/Archief/archief/article/detail/898598/2008/02/12/Kunstmatig-leven-verdient-helder-debat.dhtml

Est R. van & D. Stemerding (eds.). (2012) Making perfect life: European governance challenges in 21st century bio-engineering. Science and Technology Options Assessment, Brussels. http://www.rathenau.nl/en/publications/publication/making-perfect-life-study-summary.html

ETC Group. (2010). *Synthia is Alive… and Breeding. Panacea or Pandora's Box?* Ottawa: ETC Group. http://www.etcgroup.org/upload/publication/pdf_file/ETCVenterSynthiaMay202010.pdf

Friends of the Earth, CTA & ETC Group. (2012). *The Principles for the Oversight of Synthetic Biology.* Washington: Friends of the Earth. http://libcloud.s3.amazonaws.com/93/11/7/1204/1/Principles_for_the_oversight_of_synthetic_biology.pdf

Garfinkel, M. et al. (2007). *Synthetic Genomics. Options for Governance.* La Jolla: Synthetic Genomics. http://www.jcvi.org/cms/fileadmin/site/research/projects/synthetic-genomics-report/synthetic-genomics-report.pdf

Gibson, D. et al. (2010). 'Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome'. In: *Science* 329, no. 5987, pp. 52-56.

Gezondheidsraad, RGO & KNAW (2008). *Synthetische biologie: kansen creëren.* Den Haag: Gezondheidsraad. http://www.gezondheidsraad.nl/nl/adviezen/synthetische-biologie-kansen-cre-ren

Gezondheidsraad, Commissie Genetische Modificatie & Commissie Biotechnologie bij Dieren. (2010). *Trendanalyse Biotechnologie 2009. Mondiaal momentum.* Den Haag: Gezondheidsraad. http://www.gezondheidsraad.nl/sites/default/files/Trendanalyse%202009.pdf

Henderson, M., *'Scientists Create Artificial Life in Laboratory'*. In: The Times, 21 May 2010.

International Risk Governance Council. (2010). *Guidelines for the Appropriate Risk Governance of Synthetic Biology.* Geneva: International Risk Governance Council. http://www.irgc.org/IMG/pdf/irgc_SB_final_07jan_web.pdf

Jefferson, C. et al. (2014). *Synthetic Biology and Biosecurity: How Scared Should We Be?* Workshop Report. London: King's College London. http://www.kcl.ac.uk/newsevents/news/newsrecords/docs/Jefferson-et-al-2014-Synthetic-Biology-and-Biosecurity.pdf

Kaebnick, G. (2009). 'Should Moral Objections to Synthetic Biology Affect Public Policy?' In: *Nature Biotechnology 27*, no. 12, pp. 1106-1108.

KNAW (2007). *A Code of Conduct for Biosecurity.* Amsterdam: Koninklijke Akademie van Wetenschappen. http://www.knaw.nl/en/news/publications/a-code-of-conduct-for-biosecurity

KNAW (2013). Improving biosecurity. Assessments of dual-use research. Amsterdam: Koninklijke Akademie van Wetenschappen. http://www.knaw.nl/en/news/publications/improving-biosecurity

Link, H. (2011). 'In-depth analysis of outstanding philosophical issues in': *SYNTH-ETHICS Report WP1: Identification of ethical issues and analysis of public discourse*, pp. 40–49

Malyshev, D.A. et al. (2014). 'A semi-synthetic organism with an expanded genetic alphabet'. In: Nature 509, pp. 385-388 (15 May 2014). http://www.nature.com/nature/journal/v509/n7500/full/nature13314.html

Oye, K.A. & R. Wellhausen (2009). 'The intellectual commons and property in synthetic biology'. In: Schmidt, M. et al. (eds) *Synthetic Biology: the Technoscience and its Societal Consequences.* Dordrecht: Springer, pp. 221-139.

Parliamentary Office of Science and Technology. (2008). *Synthetic Biology. Postnote no. 298*. London: Parliamentary Office of Science and Technology. http://www.parliament.uk/documents/post/postpn298.pdf

Presidential Commission for the Study of Bioethical Issues. (2010). *New Directions. The Ethics of Synthetic Biology and Emerging Technologies.* Washington: Presidential Commission for the Study of Bioethical Issues. http://www.bioethics.gov/documents/synthetic-biology/PCSBI-Synthetic-Biology-Report-12.16.10.pdf

Runco, L. & J. Coleman. (2011). 'Harnessing DNA Synthesis to Develop Rapid Responses to Emerging and Pandemic Pathogens'. In: *Journal of Pathogens.*

Sample, I., 'Designer' chromosome for brewer's yeast built from scratch'. In: *The Guardian*, 27 March 2014. http://www.theguardian.com/science/2014/mar/27/designer-chromosome-brewers-yeast-eukaryotic-saccharomyces-cerevisiae

Sample, I., 'First life forms to pass on artificial DNA engineered by US scientists'. In: *The Guardian*, 7 May 2014. http://www.theguardian.com/world/2014/may/07/living-organism-pass-down-artificial-dna-us-scientists

Schmidt, M. (2010). 'Xenobiology: A New Form of Life as the Ultimate Biosafety Tool'. In: *BioEssays 32*, no. 4, pp. 322-331.

Schrauwers, A. & B. Poolman. (2011). *Synthetische biologie. De mens als schepper?* Diemen: Veen Magazines.

Scientific Committee on Health and Environmental Risks, Scientific Committee on Emerging and Newly Identified Health Risks, and Scientific Committee on Consumer Safety (2014). *Opinion on Synthetic Biology I Definition. Brussels: European Commission.* http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_044.pdf

Stemerding, D. et al. (2011). *Implementing Biosecurity in (Bio-)Scientific Research in the Netherlands.* Den Haag: Rathenau Instituut. http://www.rathenau.nl/uploads/tx_tferathenau/Rathenau_Policy_brief_-_biosecurity_and_bio-scientific_research_Nov_2011_-_2.pdf

Strom, S., 'Companies Quietly Apply Biofuel Tools to Household Products'. In: *The New York Times*, 30 May 2014. http://www.nytimes.com/2014/05/31/business/biofuel-tools-applied-to-household-soaps.html?smid=tw-share&_r=2

Swierstra, T. et al. (2009). *Leven als bouwpakket.* Zoetermeer: Uitgeverij Klement. http://www.rathenau.nl/publicaties/leven-als-bouwpakket.html

Torgersen, H. et al. (2010). 'Engineering of Living Artefacts: Synthetic Biology'. In: Van Est, R. et al. (red.). *Making Perfect Life. Bioengineering (in) the 21st Century. Monitoring Report Phase II*. Brussels: STOA. http://www.rathenau.nl/uploads/tx_tferathenau/Making_Perfect_Life_-_Monitoring_Report_-_Phase_II.pdf

Vriend, H. de. (2006). Constructing Life. Early social reflections on the emerging field of synthetic biology. The Hague: Rathenau Instituut. http://www.synbiosafe.eu/uploads/pdf/Rathenau%20Constructing%20Life%20 2006.pdf

Vriend, H. de et al. (2007). *Leven Maken. Maatschappelijke reflectie op de opkomst van synthetische biologie*. The Hague: Rathenau Instituut. http://www.rathenau.nl/uploads/tx_tferathenau/Leven_Maken.pdf

Wang, H. et al. (2009). 'Programming Cells by Multiplex Genome Engineering and Accelerated Evolution'. In: *Nature* 460, no. 7257, pp. 894-898.

Intermezzo

This land is your land,
this land is my land

This land is your land, this land is my land

> Synthetic biology might contribute to the development of biofuels through two different kinds of processes. Firstly, synthetic biologists can use synthetic DNA to tailor-make enzymes that can break down biomass much more efficiently than traditional methods. These synthetic enzymes, which can now be tailored towards specific types of biomass (like woodchips, corn stalks or sugar cane) increase the rate at which biomass is broken down into sugars that can then be fermented into ethanol or other types of fuels. A second approach is to create synthetic organisms (like synthetic algae) that can produce fuels directly from sunlight, water and fertilizers. Scientists are trying to customize these organisms (or 'living chemical factories' as they are often referred to) in such a way that the oil they produce is chemically similar (or even identical) to the oils we use in our current transportation and energy infrastructure. Large surfaces of land (and shallow waters) will be required for the production of biomass and the direct production of biofuels through algae. Where will this land be found, and under what conditions will it be purchased?
>
> *ETC Group. (2010). 'The New Biomassters. Synthetic Biology and the Next Assault on Biodiversity and Livelihoods'. http://www.etcgroup.org/en/node/5232*

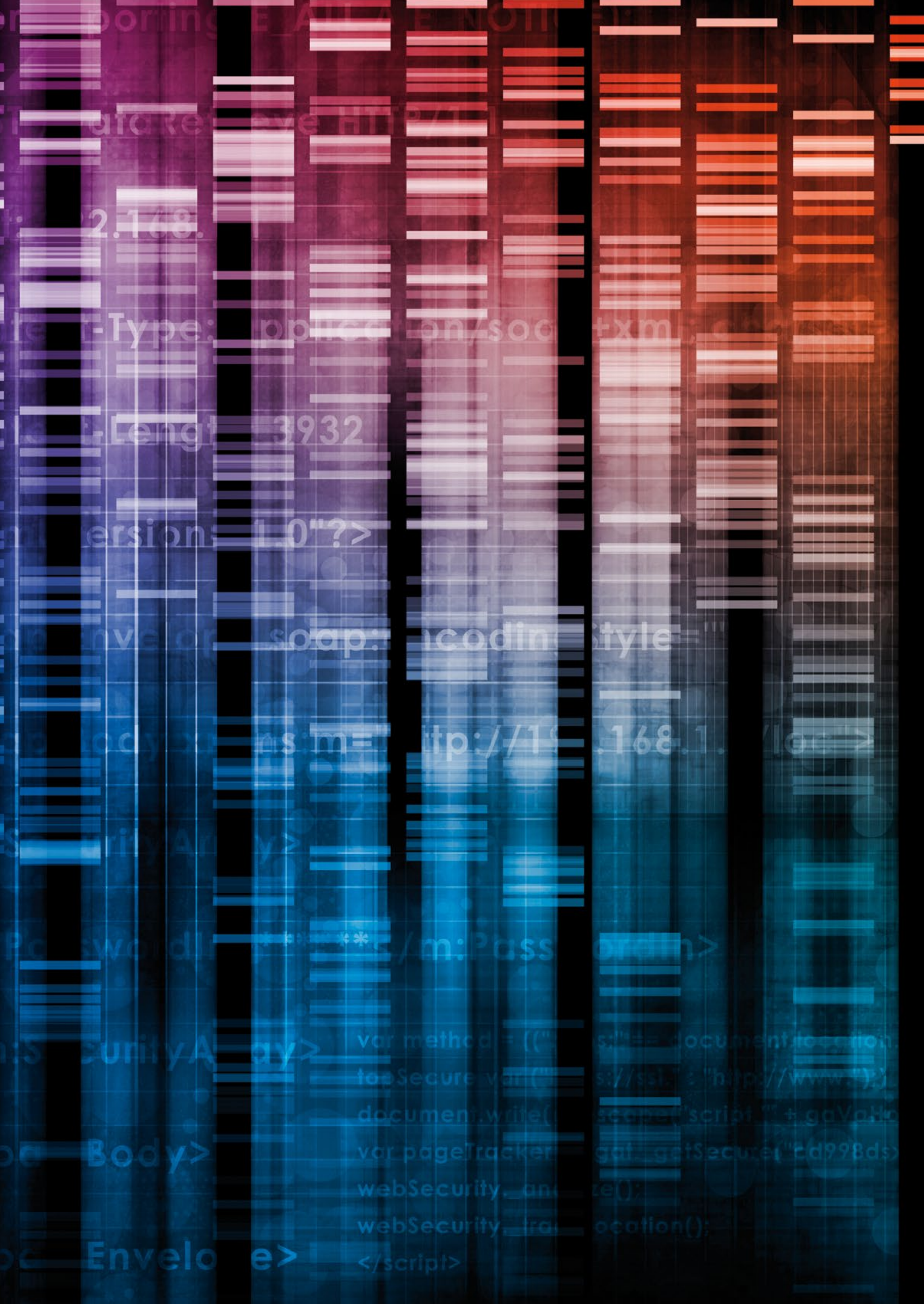
Wearily he looked down at the protesters outside the window. It's ironic, he thought, as I could be standing there myself, waving banners and yelling slogans, because I fully agree with them. But they are protesting against me. For years, everyone had been worrying about the depletion of fossil fuel. Not anymore, thanks to synthetic biologists like himself. He and his colleagues had helped create new generations of bio-oils that were no longer produced from the edible parts of plants – like sugarcane or corn – but from useless biomass (wood, weeds) or produced by algae. And what a success their bio-oil had been! It was plenty, clean to produce, cheap, and most importantly, it had put an end to the dependence of the industrialized countries on countries with large reserves of fossil oil but with questionable political regimes.

Of course, producing bio-oil in large quantities did require immense surfaces of land and shallow water. So, big companies had busied themselves for years buying large stretches of land and water in developing countries in Africa and South America. Mind you, they didn't purchase productive areas that could be used for industrial agriculture, but only marginal, idle, degraded, abandoned wastelands. So, no one took much notice. But in recent years, highly critical reports had started to appear, pointing out that these supposedly useless stretches of lands – natural forests, grasslands, deserts and wetlands – had been home to millions of indigenous peoples, most of whom had by now been relocated by their own, often corrupt, governments. Habitats, societies and livelihoods that had sustained local peoples for centuries were destroyed in the course of a few years. Instead of being able to set up and manage their own small companies and self-sustaining local economies, farmers were lured or forced into selling their land and working as temporary employees instead, thus increasing their dependence on the global north.

Furthermore, the large monoculture plantations had destroyed some of the most diverse ecosystems on the planet. Marine ecosystems and the more fragile ecosystems in deserts and wetlands had been devastated by the commercial growth of algae and the sowing of new varieties of grasses and crops that had been engineered to be drought-tolerant. Some reports even claimed that by destroying these eco-systems, bio-oil had actually exacerbated climate change rather than diminishing the problem, as these eco-systems had played a crucial role in regulating climate.

'But why lay all this misery on my doorstep?', he wondered. Did these protesters think that he had wanted all these bad things to happen, that he liked it? Of course not! As a citizen he shared all their concerns, and yes, somebody ought to do something to help these victims. But that was something for politicians. As a scientist, he didn't feel a twinge of regret or remorse. Science and technology bring good things, it is society that then goes on and messes things up.

He opened the window and shouted "Go take your protest to the politicians! I am a scientist I am not responsible for what people do with my inventions! Don't blame me!"



3

Meeting of Young Minds

3 Meeting of Young Minds

Politicians of the future and scientists of the future debate synthetic biology

On Friday night September 30, 2011 the Rathenau Instituut organized a Meeting of Young Minds. In this meeting, Dutch Political Youth Organizations (PYO's) entered into debate on synthetic biology, among each other and with students of iGEM (the *international Genetically Engineered Machine* competition). In the run-up to the debate, the PYO's were immersed in the public debate on synthetic biology and they put their vision to paper in propositions. From these propositions, the Rathenau Instituut selected three themes on which the PYO's clearly seemed to disagree. That part of the debate led to three rounds each with its own theme: promises, regulation and ownership. In each round two spokesmen for two different PYO's were facing each other. After an initial confrontation between the two spokespersons, other PYO's and iGEM students could also join in the debate.

What are the fears, hopes and expectations of future politicians and scientists, regarding synthetic biology as a future technology? In response to this question, we present in this chapter an analysis of the debate at the Meeting of Young Minds. We first examine the different attitudes towards science and technology that emerge in the visions of the PYO's on synthetic biology. We use a typology of *basic attitudes*, based on research of the Rathenau Instituut into perceptions of science and technology among citizens. We then focus our analysis on some of the most sensitive themes in the debate, referring to a number of recurrent *key narratives* in public debates about science and technology. In the conclusion, we compare the Meeting of Young Minds debate with existing international ELSI discussions about synthetic biology.

3.1 Different basic attitudes

In debates within society about new technologies, we come across different basic attitudes, shaping individual opinions no matter what kind of technology it is about. The Rathenau Instituut has charted these basic attitudes in a study in which more than a thousand Dutch individuals were asked to give their opinions on technology (Brom et al. 2011). Four groups have been distinguished: *ambassadors, functionalists, worried persons and sceptics.*

The *ambassadors* see the benefits of technology above all and find that its development should be minimally hindered by laws and regulations. *Functionalists* also find that technological progress has great potential, but they want to effectively protect people from adverse impacts of technological developments. *Worried persons* not only attach great importance to protection of people, but also find that there are certain limits to technological developments that must never be overstepped. Sceptics are not convinced that technology leads to social progress and at the same time do not find it necessary to protect citizens against negative impacts.

The differences between these attitudes highlight two major divisions. First, the extent to which one thinks that science and technology will ensure social progress. With the ambassadors and functionalists, confidence in scientific progress is great, but for worried persons and sceptics this is much less the case. Ambassadors and functionalists, on the other hand, differ in the degree to which they adhere to regulations and the same goes for worried persons and sceptics.

The study, in which these attitudes are mapped, also shows connections with political preferences. *Ambassadors* relatively often prefer the Dutch political parties D66 (liberal democrats) and VVD (moderate right wing). *Functionalists* often feel relatively at home in one of the left wing or Christian-democrat parties. *Worried persons* may align themselves with any party, but their voices are mostly represented by the *Christian Union* and the *Party for the Animals*. Sceptics often have no clear political preference. Figure 3.1 shows how the different attitudes are connected with the political spectrum.[28]

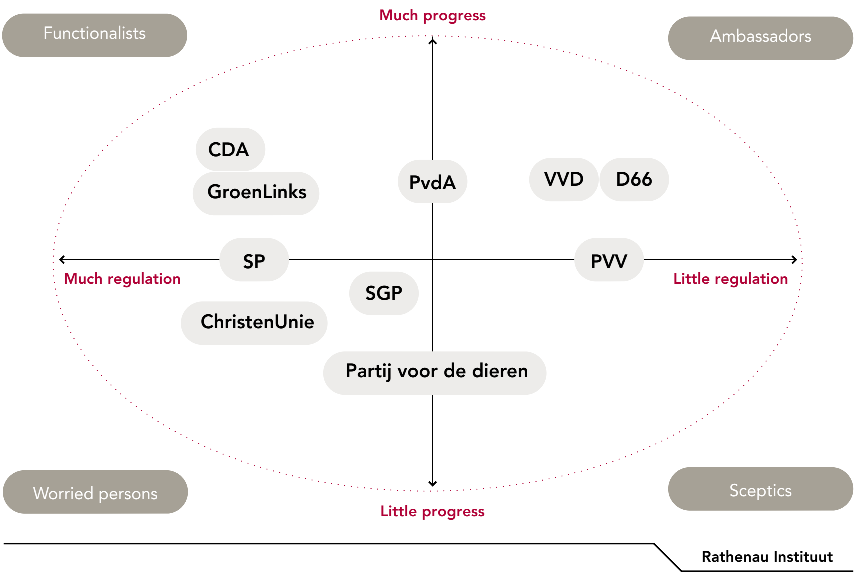
3.2 Political youth speaking out

Do we find these basic attitudes also reflected in the debate held during the Meeting of Young Minds?[29] Synthetic biology is a technology of the future, and applications are being promised, but are not yet clearly visible. Especially in this situation of uncertainty, expectations will be strongly shaped by basic attitudes

28 The Dutch political landscape can roughly be typified as follows: CDA (Christian Democrats), GroenLinks (Green Party), PvdA (Labour Party), VVD (moderate right wing), D66 (Liberal Democrats), SP (Socialist Party), PVV (right wing), SGP (Reformed Political Party), ChristenUnie (Christian Union), Partij voor de Dieren (Animal welfare party).

29 To get an impression of the debate see this link: https://www.youtube.com/watch?v=g5YPUFUayTo

Figure 3.1 Basic attitudes towards technology and political preferences (Adapted from Brom et al. 2011)



towards new technologies. This is also true for the positions of the different PYO's in the debate.[30]

Ambassadors and functionalists

"Just imagine what the impact will be on innovation if you want to stop everything until you're sure that it leads to a great invention that will solve worldwide hunger or something (...) I would say that synthetic biology offers enormous opportunities and there is simply no world that exists without risks." (Jonge Democraten/Young Democrats).

Here a true ambassador is speaking out. Technological innovation may bring many wonderful things, but it must be given space. Whoever wants to impose restrictions in advance to new technologies, does not give progress a chance. For many political youngsters the promise of technological progress is inspiring and enticing. However, from a more functionalist attitude some participants also stressed the possible downsides.

"When I heard about synthetic biology for the first time, I thought, wow, that's great, that really makes it possible to create biofuels and perhaps even to

30 The participating PYO's are the following: Young Democrats (linked to D66, liberal democrats), DWARS (linked to GroenLinks, green party), Young Socialists (linked to the PvdA, labour party), PINK! (linked to the Partij voor de Dieren, animal welfare party), CDJA (linked to CDA, Christian democrats), SGPJ (linked to SGP, the [Christian] reformed political party) and PerspectieF (linked to ChristenUnie, Christian Union).

address the climate problem (...) but it also got me thinking about the horror scenarios when it falls into the hands of people with wrong intentions, as in bioterrorism. My belief is that we cannot stop technological developments (...) We should not be afraid of the things we do not know. We need to look at what these new technologies can do in our society and we must use them in a safe and responsible manner." (DWARS)

For an ambassador, openness is the best weapon against abuse of knowledge, because you simply cannot predict everything that might happen.

"We must have faith in scientists. We think that scientists usually are not out to create super weapons or to start other calamity (...) the best weapon against abuse is transparency." (Jonge Democraten/Young Democrats)

Even being a functionalist you cannot be against transparency of course. Yet there is reason for caution.

"We think it is good to have as much openness as possible (...) but openness towards the outside world can be very dangerous, because with that knowledge someone like Ahmadinejad of Iran could work on new ways of waging war." (DWARS)

For the functionalist regulation is thus called for, obviously for security reasons, but also because of ethical implications. But whether regulation is needed, has to be viewed on a case-by-case basis.

"Therefore we cannot just say: this field of science is good and therefore it is allowed, and that field of science is bad and should be banned." (Jonge Socialisten/Young Socialists)

Worried persons and sceptics

Worried persons were also present among the PYO spokespersons. In their positions we see a lot more reluctance towards synthetic biology. If you let scientists just go their own way, it will soon be too late to avoid negative consequences. Scientists are mainly driven by curiosity and high hopes of new discoveries. Whereas ambassadors believe in transparency, worried persons rather see the opposite.

"Scientists tend to keep everything secret until the big moment of publication has arrived. Until then, they will share as little information as possible. And once the publication is out in the open, research has been finished and you are actually overtaken by events." (CDJA)

From the left: Christian van 't Hof (moderator), Eline van Nistelrooij (DWARS), David Zomerdijk (Young Socialists) and Mark Ruitenbeek (CDJA)

From the outset, politicians will have to set boundaries to technological developments especially when consequences of such developments cannot be foreseen.

"You shouldn't give scientists a blank check. First you need to discuss, which developments mankind can afford (...) We should expect no paradise from synthetic biology (...) perhaps expectations will not come true. My argument is that as a politician you have the responsibility to check things." (SGP Youth & PerspectieF)[31]

Especially when it comes to changing the properties of DNA at a fundamental level, for worried persons caution is called for. What if we change nature in ways that we do not always understand?

"Some biologists see it as improving nature. We do not find this a desirable development and we believe that this only should be allowed in exceptional cases (...) for example, only for the development of new drugs for very serious diseases (...) If you're talking about synthetic biology in the sense of improving or creating organisms, I think that goes very far indeed and then you have to be very strict in your regulations." (CDJA)

How far do we want to go in terms of control over 'life' and 'nature' by means of synthetic biology? iGEM students from Louvain, Belgium, have tried to make bacteria that stimulate ice growth. Imagine, one of them asked herself, you could thus save the polar bears? For the group of worried persons however this would be a really disturbing idea.

31 The SGP and ChristenUnie are two small Christian parties and that often work together and delegate a single spokesperson to represent both parties, as was the case in the Meeting of Young Minds.

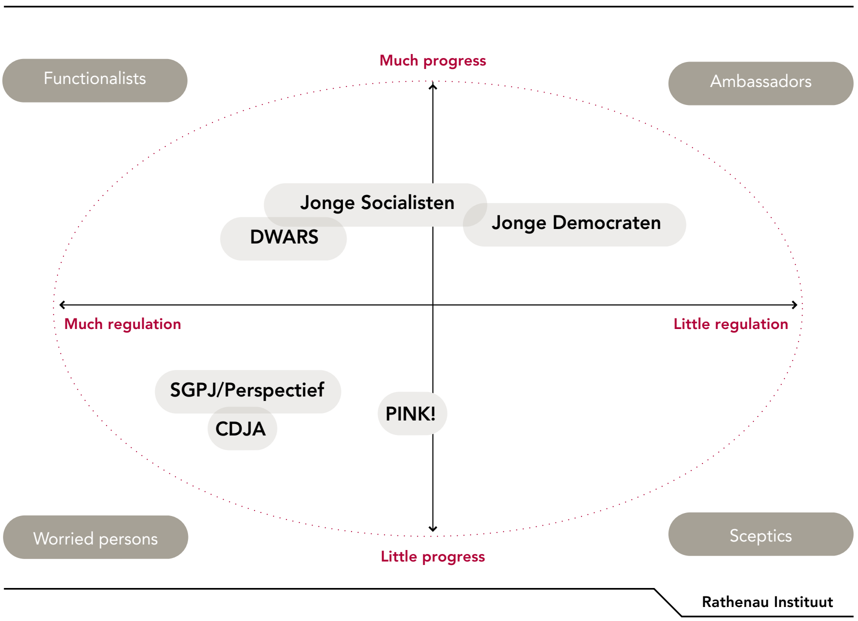
"I'd mainly wonder what impact that would have on the environment, if we are going to create new ice-sheets in the Arctic. No, really (...) I do not believe in it." (PINK!)

We are less likely to find the attitude of the sceptic among the political youth. Because sceptics do believe neither in technology, nor in politics. Yet, we occasionally heard a sceptical voice, especially from the side of the worried participants.

"Individual people and individual scientists sometimes do amazing things, but what we are less good at, is to give direction to society as a whole (...) Do we think we know how to perfect nature? (...) Before we start making nature 2.0 it is high time to first learn to appreciate the original (...) With technology in itself, nothing is wrong. In the distant future, we might do beautiful things using synthetic biology. However, good technology plus bad politics equates a bad outcome." (PINK!)

Figure 3.1 showed particular connections between basic attitudes towards technology on the one hand, and political preferences on the other. If we look at the attitudes of the PYO's regarding synthetic biology, we find in many respects a similar pattern of connections, as shown in Figure 3.2.

Figuur 3.2 Basic PYO attitudes to synthetic biology



The Young Democrats manifested themselves as *ambassadors* during the Meeting of Young Minds. Both the Green Party Youth (DWARS) as well as the Young Socialists took a predominantly *functionalist* position. The *worried* voices during the debate came from the three Christian PYO's – CDJA, SGP Youth, and PerspectieF (Christian Union Youth) – and the entirely different youth branch of the Animal Welfare Party *PINK!* Compared to the pattern visible in Figure 3.1, the CDJA position in this list is surprising, since in Figure 3.1 the official CDA is clearly connected to the functionalist part of the spectrum. That is interesting because it shows that the PYO position is not only based on predetermined political attitudes, but also by a particular appreciation of synthetic biology as a new engineering science of life. Precisely at the point where technology affects life itself, we may expect that a more worried attitude may prevail among the Christian parties.

3.3. Five key narratives

The different views on synthetic biology in the debate at the Meeting of Young Minds will be further discussed in this chapter in the light of some key narratives that can be found in public discussions about new and emerging technologies. In recent years, several studies have been published of public perceptions about nanotechnology. In one of these studies, based on a series of focus group discussions, researchers have identified five key narratives in public debates on science and technology which they consider to be deeply rooted in our culture (Macnaghten et al 2010):

1. Be careful what you wish for
2. Opening Pandora's box
3. Messing with nature
4. Kept in the dark
5. The rich get richer and the poor get poorer

These narratives especially articulate the concerns that people may have about new and emerging technologies such as nanotechnology. In other words they elucidate particularly sensitive and controversial themes in discussions about science and technology. The narrative 'Be careful what you wish for' is about the promises of new technology, which are often equally tempting as dangerous. 'Opening Pandora's box' refers to the potentially uncontrollable consequences of new technology. 'Messing with nature' expresses the conviction that nature has limits that cannot be overstepped with impunity by scientists and technologists. 'Kept in the dark' expresses a feeling of people's powerlessness in the face of scientific and technological developments that are stretching beyond their imagination and cannot be stopped. Finally, there is the narrative of 'The rich get richer and the poor get poorer'. Within this narrative, the prevailing belief is that science and technology are dominated by commercial interests and will reinforce existing forms of inequality.

As we will see below, these narratives are not difficult to recognize in the debate at the Meeting of Young Minds. However, given the different basic attitudes towards science and technology among the participants in the debate, we can also expect different responses to the themes expressed in these narratives.

Be careful what you wish for
Should one be careful indeed towards the promises of synthetic biology? We saw that for many of the political youngsters, the promise of technological progress is inspiring and alluring. That is certainly the case with iGEM students for whom synthetic biology is above all an opportunity to be seized.

"Do we really want to deprive ourselves of the opportunity that synthetic biology offers us to undo the damage that we have caused to our planet?" (iGEM student, Imperial College London)

And, what will happen if we don't take advantage of synthetic biology? Is it wise to hold back just because of potential risks?

"Even if it brings new risks, it may also improve our lives and that is an important point to consider in thinking about a technology such as synthetic biology." (Jonge Socialisten/Young Socialists)

From the standpoint of the worried however, it rather befits us to be modest. We should not strive for just anything, just because we are able to do it. And perhaps we can do very well without synthetic biology.

"Sometimes, you let yourself be carried away by the huge potential of a new discovery and you become blind to the risks and the wider consequences. You need to be careful with that (...) try to avoid risks as much as possible, and whatever way you go, always stay on your guard." (CDJA)

"We don't even need this technology for many of the problems we face. Hunger in the developing world is not a matter of food production but of distribution. For our environmental problems, we also have solutions available. We just need to use them." (PINK!)

One of the iGEM participants disagreed with this.

"Why can't we invent means to fix our problems in ways much faster than trying to convince everyone to change their behaviour?" (iGEM student, KU Leuven)

Opening Pandora's box

Even among those who believe in the blessings of technological progress, there is the fear for unanticipated consequences. Most PYO's have no serious objections against 'synthetic bacteria' with useful applications that are well contained inside a reactor vessel. However, things become different as soon as we start to think about releasing synthetic organisms into the open.

"We are extremely cautious about releasing products into the environment, because it can be harmful for ecosystems. This can have serious unpredictable consequences." (DWARS)

Column: Scientists must reach out to politics and society

Synthetic biology will dramatically change our view of the world and its 'make-ability' - and according to some, it has already done so. However, politicians and policymakers have little attention for the social impact of this new scientific field.

iGEM, the international competition of students in synthetic biology, shows what synthetic biology potentially can do: save the environment, solve the fuel crisis and develop advanced medicines. Of course, many of those far-reaching ideas will never get launched. Yet iGEM has delivered plenty of excellent, innovative ideas and a number of them may be realized.

Perhaps it will take years before the true potential of synthetic biology is fully unfolding. And maybe it will also change science and society in other ways than we now predict. Yet we must now prepare for what lies ahead. The main challenge is: allowing room for innovation in all areas, but also ensuring safe and socially responsible research.

Synthetic biology will present us with important ethical and scientific questions. The public may have quite a different viewpoint from that of scientists. iGEM shows that young scientists are aware of the societal challenges and issues associated with synthetic biology. What we need is a dialogue between scientists, politicians and society.

Rebekka Bauer
Member iGEM Team, Imperial College London: Project Auxin , finalist 2011

As mentioned, some PYO's would like to put restrictions not only to the products but also the knowledge of synthetic biology, if there is the danger that information could fall into the wrong hands. Another more principal question is how far we want to go in redesigning nature.

"I wonder where you draw the line, starting from working with micro-life to working with human cells, producing combinations of cells and improving people." (iGEM student, University of Potsdam)

This question was not really answered by most PYO's, but for the group of worried persons there is a clear limit.

"With unicellular organisms in the lab you can control what you're doing (...) although even then you should not use the tools of synthetic biology lightly. Proceeding to larger organisms such as mice and lab rats, which could escape (...) then the risks become higher and more stringent regulations are called for. And when you come to humans, to me that is really a step too far. We should not use human embryonic stem cells in this field." (CDJA)

iGEM member Rebekka Bauer takes the floor during the debate

Messing with nature

As a technology aiming at 'making life', synthetic biology obviously raises the question of what life really is. Should we confer to life a special status, denying us the possibility to have life at our disposal? One of the PYO's had strong views about this question, at least regarding life at the cellular level.

"Modern biology shows us that the properties of life are determined by molecules, molecules that control themselves. We are essentially talking about a nanomachine ... That implies that life itself has no special moral status, compared to other machines. And that brings us to the proposition that a cell is nothing but a machine that we can produce and change."
(Jonge Democraten/Young Democrats)

We have already seen that the idea of the makeability of life and nature was not received with enthusiasm by all PYO's. Even if one doesn't assign life as such a special moral status, it is more than a phenomenon at cellular level.

"When it comes to multi-cellular organisms that can feel pain, can see, can experience their environment as purposeful, like animals and people, life makes a real difference. I really would like to know who is prepared to support a full ban on biotechnology and synthetic biology in animals (...) and then of course we also have plants and single cellular organisms (...) even then I still think it's too easy to say that it is nothing more than a machine that we may construct and change at our discretion because you should always worry about consequences." (PINK!)

Indeed, life on earth has evolved into a delicate and balanced universe of species that are in mutual equilibrium.

"From a Christian democratic perspective, we see it as God's creation that we as stewards must preserve for the next generation. As a room full of scientists, you would prefer I think the Darwinian approach (...) also from that approach it involves a balance that has been established over billions of years (...) an equilibrium that is very delicate and easy to disrupt." (CDJA)

However, as one of the iGEM participants argued, even at this evolutionary level ambitions of synthetic biology can be defined in terms of makeability.

"Synthetic biology aims to learn from nature in order to use it for our own purposes. Being a politician you would like to see a society that evolves, and with synthetic biology, we can manage to control this evolution."
(iGEM student, Descartes University, Paris).

And besides, isn't that something we actually have done for a long time already?

"The consequences of changing nature through biotechnology and synthetic biology are not necessarily and fundamentally different from traditional breeding or from traditional genetic modification (...) Therefore, I rather see continuity than a fundamental difference." (Jonge Democraten/Young Democrats)

The idea, however, that people have traditionally moulded nature to their will, is for some PYO 's more cause for concern than for reassurance. Hubris is lurking.

"My position is mainly a response to the idea that we as humans can improve nature. What I definitely do not want to argue is that nature is without flaws. As a confident evolutionist, I know only too well that nature is imperfect in many ways. But I think it would be silly to believe that mankind can easily change that (...) We must guard ourselves from the idea that we know better and can just make life perfect." (PINK!)

Kept in the dark

In the Meeting of Young Minds debate two visions of technological development were confronting each other. Some PYO's see technological development as something that cannot be stopped. For others the main worry is that technology develops without our notice and takes us by surprise. In reaction, we heard pleas for openness and trust, both from the ambassadors among the PYO's and from iGEM teams.

"There is so much distrust of science and scientists. If you rely on doctors for your own life, why not trust scientists?" (iGEM student, Freiburg University)

For the worried amongst the PYO's it is not just a matter of trust, but also of political responsibility to provide steering to scientific and technological developments. Or should politicians give free room to scientists and technologists instead?

"As government and as politicians, we should not just accept what is going on. In providing a significant amount of money to technological developments we should know why we spend it. Just watching what happens and letting it happen, for me that's all too easy and passive." (CDJA)

"Being politicians, you must be very careful with defining in advance what knowledge may or may not be developed. You are in great danger of hampering science. That does not seem desirable and if you do that, there will still be private organizations conducting research in synthetic biology." (DWARS)

Can this difference be bridged by a code of conduct for synthetic biologists, as suggested by one of the iGEM teams, or by broad-based committees to discuss developments in synthetic biology, as suggested by some PYO's? Or do we need more public engagement, as advocated by one of the iGEM participants?

"I think all of this is really about finding the right balance. We have to properly manage our expectations of synthetic biology. It is true that some of us are too optimistic about the potential of this technology (...) Openness is therefore very important, and in Great Britain we do that by engaging people, as a political tool to enhance public awareness." (iGEM student, University College London)

The rich get richer and the poor get poorer

Striving for the makeability of life also raises questions about ownership. If life is a machine, as argued by one of the PYO's, there is little room for disagreement about this question.

"We think it's obvious and evident, if you have managed to create life in the lab, when you have artificial life, although we know it's not there yet, then you should be allowed to patent this life as an invention."
(Jonge Democraten/Young Democrats)

Another PYO representative saw this as a typical example of a political word game: first define life as a machine and then suggest it necessarily follows that life can be patented.

"Suppose that in the international community of synthetic biologists something is found – say a therapy for a particular disease, such as AIDS – and that this invention is patented in the United States. As a result it is marketed for a lot of money in African countries that desperately need it. Would you say that this is fair, that there are no ethical objections to patenting life that way?" (DWARS)

Although the problem was not denied, it was questioned whether it had specifically to do with synthetic biology. From the audience of iGEM students it elicited a passionate argument for open source as a model for synthetic biology. Nevertheless, one participant resisted the idea.

"I'd like to show another side of the problem, because there is only one person here who has declared himself in favour of patenting and you are all advocating open source. But do you know how open source actually originated? It comes from the world of information technology in which it takes no more than a few hundred or thousand dollars to buy a computer and start programming. That is very different from synthetic biology, requiring facilities taking millions of dollars. Everyone sees patents as a way for companies to make money, but to be honest, we as researchers really need patents in order to get paid for our job."
(iGEM student, University College London)

Another iGEM student considered open source only as part of the answer to the question of how technology can be made available and useful to people in different parts of the world.

"You can't just develop technology and say, 'This is what we can create, it is now for you to use it.' I think one should take a hard look at the situation in different parts of the world, and wonder how you can improve that situation, how in practice people can make best use of a technology. And I think there are many aid organizations, which already have a lot of relevant experience and for us it is very important therefore to collaborate with them. Many iGEM teams are trying to do that, even though we do not always notice it." (iGEM student, Imperial College London)

3.4 Conclusion: lessons from the debate

The themes discussed during the Meeting of Young Minds not only provided us with insight into the opinions of PYO's and iGEM students on synthetic biology, but also showed concerns that recur as key narratives in any public debate about new and emerging science and technology. How do we deal with promises and risks? How far do we go with interventions in our natural environment? How much freedom do we allow scientists and engineers? How do we find a balance between commercial interests and the public good? Indeed, the issues raised during the Meeting of Young Minds were in many respects not specific for synthetic biology. The different positions in this debate also clearly reflected more general basic attitudes in our society towards science and technology.

However, the Meeting of Young Minds also showed that synthetic biology raises especially sensitive issues as a new and emerging engineering science of life. The different opinions about synthetic biology are highly coloured by normative conceptions of life and nature, also touching upon ideas about ownership and commercialization of knowledge. What does the Meeting of Young Minds debate tell us about these issues compared to the already ongoing international ELSI debate on synthetic biology as discussed in the previous chapter? ELSI debates generally focus on possible applications of new technologies and potential risks to humans and the environment. These issues also received most attention in the ongoing debate on synthetic biology so far. Broader social and ethical issues have been mentioned in the debate, but have been given relatively little attention. The Meeting of Young Minds not only provided a platform for future politicians and scientists to make an active contribution to the debate, but has also shown that broader social and ethical issues may play an important role in shaping public opinion about synthetic biology (see also chapter 4).

Column: Time to make noise about new life

"I believe an officially organized public dialogue only makes sense if it can focus on specific, well defined applications within a reasonable time ahead." The Dutch Minister of Economic Affairs Maria van der Hoeven wrote this on 17 December 2009, answering parliamentary questions from the Christian party SGP on so-called NBIC technologies, including synthetic biology.

Googling (in 2011) the terms 'synthetic biology debate' (in Dutch) only produced ten hits, mostly from 2007 and 2008. On the site of the Dutch House of Representatives the subject is missing and also governmental reports on synthetic biology are scarce. In the Dutch 'Trend Analysis Biotechnology 2009' synthetic biology is almost ignored with only eighteen summary lines in a 144-page report.

In the Netherlands, strangely enough, there has hardly been any debate about synthetic biology. It is true, we don't see many practical applications yet, but why should we wait with a public debate, especially when we consider that synthetic biology may have profound consequences for individuals and society. It may be about hydrogen bacteria or diesel fungi, but also about enhanced versions of human beings. Or, just to put things in sharp focus, creating an all-devouring virus. Why then are we hardly discussing it?

Developments in synthetic biology mainly unfold in silence within scientific laboratories. However, the subject is far too important to be left to scientists alone. It concerns all of us. It is up to politics then to put the debate on synthetic biology on the societal agenda: as an opportunity for our knowledge economy, so ardently desired, but constantly thwarted by the government, and furthermore as a discussion topic for the general public.

The Dutch newspaper Volkskrant of 12 February 2008 carried the headline 'Artificial life deserves clear debate'. That debate never happened. So let us make noise about new life right now rather than tomorrow!

Arno Schrauwers
Science Journalist

If we take a look at the ELSI debate in the Netherlands, we see that until now the contribution of existing policy advisory bodies in the debate on synthetic biology has been limited. In the reports released some years ago by the Dutch Health Council and COGEM, attention was focused primarily on opportunities and risks of synthetic biology. With regard to broader social and ethical issues, political and societal debate is still to be awaited. We therefore hope that the Meeting of Young Minds will prove to be an inspiring step in the ongoing process of political and societal opinion making.

Thanks to the following spokespeople in the debate:
Political youth organisations
Pablo Moleman (PINK!)
Eline van Nistelrooij (DWARS)
Mark Ruitenbeek (CDJA)
Arjan van de Waerdt (SGP-jongeren & PerspectieF)
Gijsbert Werner (Jonge Democraten)
David Zomerdijk (Jonge Socialisten)

iGEM-students
Rebekka Bauer (Imperial College London)
Alfred Ho (University College London)
Paul Kaufman (Universiteit Potsdam)
Edward Kwarteng (Descartes Universiteit Parijs)
Rüdiger Trojok (Universiteit Freiburg)
Katrien Vandermeeren (Katholieke Universiteit Leuven)

References

Brom, F.W.A. et al. (2011). *Beleving van technologie en wetenschap. Een segmentatieonderzoek.* Den Haag: Rathenau Instituut. http://www.rathenau.nl/publicaties/beleving-van-technologie-en-wetenschap.html

Macnaghten, P. et al. (2010). 'Narrative and public engagement. Some findings from the DEEPEN project'. In: Schomberg, R. von et al. (red.). *Understanding public debate on nanotechnologies.* Options for framing public policy. Brussel: Europese Commissie. http://ec.europa.eu/research/science-society/document_library/pdf_06/understanding-public-debate-on-nanotechnologies_en.pdf

Intermezzo

The Light-Emitting Fish kit

The Light-Emitting Fish kit

Researchers have succeeded in creating animals with specific characteristics by inserting genes coding for a specific trait in animal embryos. One of the first applications, now commercially available, was a 'GloFish®': a fish with skin that glows in the dark. There are also glow-in-the-dark-pigs and Turkish Angora cats with a protein that makes their skin glow when exposed to ultraviolet light. Synthetic biology might add to a future in which we can playfully re-create our own forms of life.

http://www.glofish.com/
http://www.dailytech.com/South+Korean+Scientists+Clone+Glowing+Cat/article10042.htm

"Look, my dad brought me a luminous fish kit!" Ann was holding a colorful box with an inscription on it. The inscription said: Light-Emitting Fish (LEF) Create your own special toy! Her classmates were crowding around her and looking curiously.

"What is it?"

"Can you make a fish?"

"Will it be alive?" "Does it glow?"

"Is it a toy, really?"

They kept asking questions and everybody wanted her to answer. Fortunately, she knew something about synthetic biology. Her father was a bioengineer and for the last five years he had worked on the development of kits enabling people to modify their pets. The LEF was the first product to be put on the market. He had given her one of the first prototypes as a present for her twelfth birthday. And he had been right, it made quite an impression on her class mates!

"You need fish laying eggs and then you should inject the stuff in this kit into the eggs. They call the stuff BioBricks. These bricks are responsible for color, smell, or any other characteristic. This kit has bricks that make your fish glow. So when fish grow from the eggs, they will glow in the dark! They are also going to offer kits to produce fish with any colour you like."

"Wow, that's cool!" "I would like that!"

"My dad says I can do it this Saturday when he's at home to help me. If it works, I'll bring one for the school aquarium!"

A few months later

"Ann", Ms. Verger asked, "whatever happened to your luminous fish? Didn't you promise to bring us one for the school aquarium?"

"Ehh, maybe I did… But, I don't have one anymore." "Oh, why's that? Didn't your kit work out?"

"Yes it did! They actually glowed so much my father had to put a towel over the aquarium when he wanted to take a nap on the couch! At first I really thought they were cute. But after a few weeks I got bored with them and we threw them away."

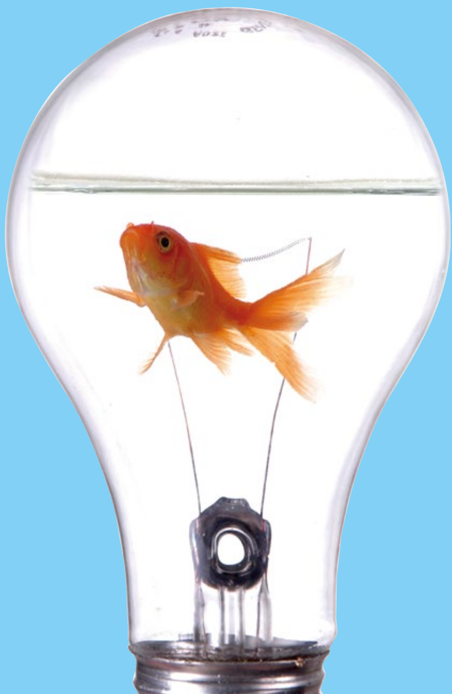
"Oh, that's too bad… Did you release them in the neighborhood pond?"

"No, according to my father we were not allowed to release them outside. So we had to put them in the trash bin for chemicals."

"But … that's really awful! You can't simply throw away a living being as if it's a can of paint!" "They're just toys, Ms. Verger. My father says the kits for creating colourful cats are almost finished. Shall I ask him whether I can have one for school?"

"Well, it's nice of you to offer that, Ann. But I don't think school needs a cat, whatever its colour."

Ms Verger finished the conversation and put the children back to work. While they were doing their history project, she reflected on the previous discussion. Usually Ann was a sensitive girl, perfectly willing to acknowledge the needs of others. The other children had not seemed too shocked either.
She sighed, it was a sign of the times. Society was so crazy about synthetic biology these days! She decided that the topic was too important to leave it at this and made a note to put the issue on the agenda of the teacher association's meeting next month. If selling kits like these could not be forbidden, at least schools could teach children the difference between toys and living beings.



4 Conclusion: a plea for political and societal opinion making

4 Conclusion: a plea for political and societal opinion making

As a new engineering science, synthetic biology not only raises high expectations, but also a multitude of questions about potential risks, ownership of knowledge and creating life. To a large extent the issues raised relate to developments that may play out in the future and are highly uncertain. These are therefore not issues that easily lend themselves to a parliamentary or public debate. However, as synthetic biology evolves and grows, sometimes in spurts, these issues will become topical.

This publication is therefore a plea for more political and societal opinion making about synthetic biology, in preparation for discussions that will undoubtedly arrive in the future. With the Meeting of Young Minds debate the Rathenau Instituut aimed to make a contribution. However, further steps must be taken forward. The ongoing international ELSI discussion has already yielded a lot of material on the issues raised by synthetic biology. What it now comes down to is a further consideration from the perspective of political parties and NGO's as a prelude to a broader public debate. In this concluding chapter, we present suggestions based on our experiences with technology assessment and the discussions held on synthetic biology up to now.

4.1 Experiences with technology assessment

In technology assessment (TA) we can distinguish three approaches and all three can also be recognized in activities related to synthetic biology. One approach with a long tradition focuses on *pro-active regulation* of the potential risks of new scientific and technological developments. In the case of synthetic biology, this involves issues of biosafety and biosecurity. Gradually, however, in TA more attention has been given to wider societal and ethical (ELSI) issues and an approach that focuses on *public discussion* of these issues. In a number of countries this has led to survey research on public attitudes about synthetic biology and occasionally to initiatives focused on dialogue in the form of focus groups. Finally, a form of TA has emerged that contributes to reflection on the development and societal embedding of technology in *direct interaction with scientists and technologists*. Examples of this in the field of synthetic biology are still scarce. Most noteworthy is the *policy and practices* part of the iGEM projects, in which young researchers not only reflect on the societal aspects of their work, but often also actively search for audiences to inform or to start discussions. Also the EU-project SYNENERGENE is aimed at fostering responsible research and innovation (RRI) in synthetic biology.[32]

32 www.synenergene.eu

These activities all contribute to a process of political and societal opinion making, but in practice connection between these activities is often lacking. Proactive regulation focuses on politics, while initiatives aimed at public discussion or interaction with scientists have much less connection with political decision-making. A more direct involvement of political parties and NGO's could help to establish a connection between these different activities and may contribute to an agenda for a broad-based and pro-active process of opinion formation about synthetic biology from a political and societal perspective.

In 2007, in a Report to the Parliament on synthetic biology, the Rathenau Instituut has made recommendations related to biosafety, bioterrorism, and abuse of patent applications, ethics and society. At that time these recommendations were aimed at the government. What we are now advocating is a broader process of political and societal opinion making. Based on the above three TA approaches, we distinguish below three key themes that should be central to this process: (1) risk and regulation, (2) society and nature, and (3) research and innovation. In the case of synthetic biology each of these themes is associated with more specific issues and key values that are at stake. This yields an agenda of more or less defined issues that can be picked up on in a process of political and societal opinion making, and that have been discussed in various ways in the Meeting of Young Minds (see chapter 3).

Recommendations from the Report to Parliament (2007)

Biological safety:

- *In the short term the Ministry of Environment (In Dutch: Volkshuisvesting, Ruimtelijke Ordening en Milieubeheer, VROM) should start investigating security risks of synthetic biology;*
- *and at European level should put on the agenda whether existing regulations must be amended;*

Abuse and bioterrorism:

- *The National Coordinator for Counterterrorism should take initiative for national and international cooperation to prevent bioterrorism with synthetic biological agents;*
- *the Ministry of Education (In Dutch: Onderwijs, Cultuur en Wetenschap, OCW) should increase the safety awareness of biotechnology researchers;*

Intellectual property:

- *The Ministries of Economic Affairs and OCW should investigate whether open source approaches can be stimulated in publicly funded genetic engineering research;*

Ethics and Society:

- *The government should create space for social engagement and reflection on fundamental ethical issues. This does not require regulation, but facilitation.*

4.2 Risks and regulation

TA practices have traditionally focused on possible risks of technology and its regulation. In the field of synthetic biology it involves issues of biosafety and biosecurity. In addition to safety as a value the question at issue here is how to deal with risks that are highly uncertain. According to the precautionary principle, these risks should be excluded as much as possible. The Meeting of Young Minds debate showed that given different basic attitudes towards technology, this principle is valued in significantly different ways.

Biosafety issues in the field of synthetic biology are covered by established regulations for risk assessment of genetically modified organisms (GMO's). In the Netherlands COGEM is responsible for advising on the implementation of this legislation. The development of synthetic biology raises two issues in particular. The first issue is whether the existing GMO regulation can still be considered as sufficient to assess future developments in the field of synthetic biology. A second related issue is how to timely provide knowledge needed to properly assess new developments in synthetic biology. These issues will especially play out in situations in which 'synthetic organisms' are released into the environment. Given the uncertainties inherent in this kind of development, public debate on these issues will most likely focus on the weight to be given to the precautionary principle.

Biosecurity issues have been raised in synthetic biology because the engineering approach pursued could allow for abuse for purposes of bioterrorism. Until now, the emphasis in addressing these issues was on self-regulation. Thus agreements on screening incoming external orders have been made internationally between producers of synthetic DNA. Laboratory scientists are also expected to be alert to possible abuse of knowledge and materials. Related to this, the Royal Netherlands Academy of Arts and Sciences KNAW has developed a code of conduct for biosecurity. However, this code is not actively supported and it is not clear to what extent the code contributes to awareness of biosecurity among scientists. The code assumes that legislation in the field of biosafety contributes to biosecurity as well. A Policy Brief of the Rathenau Instituut on this subject has questioned this, because biosafety and biosecurity are quite different issues in a number of ways.[33] The concern for biosafety is based on trust and openness, whereas the care for biosecurity is based on organized distrust and secrecy. Attention to biosafety therefore does not simply contribute to biosecurity. In the Rathenau Policy Brief it has also been noted that the Netherlands lacks a provision under which the biosecurity implications of developments in the field of life sciences and synthetic biology can be signalled, as COGEM already does for biosafety.

Important considerations in the field of risk and regulation:

- *How sustainable are the current GMO regulations for the assessment of biosafety risks of synthetic biology and how to timely provide the knowledge needed to assess these risks in future?*
- *How to ensure timely detection of biosecurity risks of synthetic biology and to which degree can we rely on self-regulation of companies and scientists in dealing with these risks?*
- *What weight to assign to the precautionary principle in the assessment of the biosafety and biosecurity risks of synthetic biology?*

33 See: http://www.rathenau.nl/uploads/tx_tferathenau/Rathenau_Policy_brief_-_biosecurity_and_bio-scientific_research_Nov_2011_-_2.pdf.

4.3 Society and nature

Confidence in the safety of synthetic biology is an important prerequisite for its social acceptance. Apart from that the Meeting of Young Minds has shown that other values are also of great importance. In public discussions about synthetic biology, the values of justice, sustainability and naturalness may play a decisive role for the public support that synthetic biology will be able to acquire. Three issues could give rise to public debate and resistance to synthetic biology.

The ongoing discussion on *patenting* in biotechnology is also clearly important in synthetic biology, where 'open source' is seen by the founders of the Biobricks Foundation as essential for the success of an engineering approach based on publicly available biological building blocks. Diametrically opposed are U.S. companies like Synthetic Genomics and Amyris, both working on commercial applications of synthetic biology based on patents. The main concern of NGO's in this discussion is a looming monopolization of knowledge by a small number of globally active companies, including existing oil company giants, which invest heavily in the development of new biofuels. Issues of monopolization could undermine public support for synthetic biology, as we have also seen in the GMO debate. The dominance of a company like Monsanto has significantly contributed to the existing societal resistance to GMO's.

A related issue is the way commercialization of synthetic biology may contribute to new forms of *global exploitation* of raw materials in the form of plant-based and other sources of biomass. If this commercial exploitation would claim large amounts of arable land in developing countries for the development of a bio-based economy in Europe and other industrialized or industrializing regions, this could not only be at the expense of necessary food production, but also lead to aggravating existing economic inequalities in the world. NGO's already emphatically voice their concern on this topic.

At the same time there is a strong belief that new forms of bio-based production may contribute to sustainability, a vision that is propagated for example by the Dutch chemical company DSM in an enthused way. Synthetic biology would be able to fulfil its role in applications that allow for much smarter and more efficient use of biomass. For example, by utilization of vegetable matter, which up to now remains as waste, or by using algae as a source of biomass that is so far hardly at all exploited. However, doing so will require new and more radical forms of engineering plants and algae as a feedstock for renewable bio-based production. Here, the values of sustainability are at odds with those of naturalness. Especially from religiously inspired attitudes, this could be a point of concern and discussion in the public appreciation of synthetic biology.

Important considerations in the field of society and nature:

- *How to deal with the tension between the existing practice of patenting in biotechnology and the pursuit of innovation in synthetic biology based on equal access to knowledge?*
- *How to create guarantees for the development of synthetic biology that meets criteria of global environmental and social sustainability?*
- *To what extent does sustainability-oriented development of synthetic biology also require respect for naturalness and life?*

4.4 Research and innovation

Synthetic biology is still to a large extent in the stage of laboratory research. Its promises can only be realized on the basis of global investments in research and innovation in this area. In addition, expectations will have to be continuously adjusted and researchers and funding parties will continually have to face new options and decisions. The Meeting of Young Minds has shown that important values are at stake here, such as the freedom of research, openness and trust, especially calling for transparency.

The question is how this transparency could be most effectively achieved. It is not only about publishing and monitoring ongoing developments in synthetic biology, but also about their political and societal significance. What are the important choices to be made in research, what related considerations are important, and what would be the result of these choices for future innovations and developments in society? Political and societal opinion making about such issues would be served by the elaboration and critical consideration of road maps and scenarios for synthetic biology in a societal context, in which possible futures are outlined and their meaning and implications are made tangible.

This requires a more direct interaction between scientists, political parties and NGO's as a basis for future-oriented political and social explorations of synthetic biology. To some extent this interaction already exists in the form of ELSI discussions and is also sought in various ways by students and researchers active in the growing iGEM community within synthetic biology. In doing so, the iGEM community significantly contributes to this important culture of openness in the international community of researchers in synthetic biology. This culture of openness provides opportunities for greater involvement of political parties and NGO's in joint process of political and societal opinion making.

Important considerations in the field of research and innovation:

- *What are key priorities for innovation in synthetic biology?*
- *What are related socially desirable scenarios for the future development of synthetic biology?*

4.5 Connecting the dots

Although in many respects synthetic biology may still be in its infancy and is still unknown to the general public, it is not too early for political and societal opinion making. Indeed, investments are already made in synthetic biology in the hope for a better future. If in future we do not want to be caught off guard by the issues raised by synthetic biology, it is important that politics and society be prepared. In the above, we have therefore highlighted various issues as agenda for a process of political and societal opinion making. Political parties and NGO's can take the lead in anticipating these issues, and we especially see a role for scientific bureaus and other think tanks within these organizations. The political youth organizations have been taking the first move.

In another respect it is also important that political parties and NGO's play an active role in the debate on synthetic biology. Until now, the debate takes place in various arenas, which to some extent coincide with the three different TA approaches. An important arena for issues of risk and regulation are national and international agencies active in regulation or self-regulation in the field of biosafety and biosecurity, as well as more general authoritative advisory committees such as the International Risk Governance Council (IRGC), the American National Scientific Advisory Board for Biosecurity (NSABB), and the European Group on Ethics (EGE). An arena partly linked to this, but also to be distinguished is formed by scientists from a variety of backgrounds involved in discussions in which the societal significance and implications of synthetic biology are considered from a predominantly academic ELSI perspective. Finally, an international coalition of NGO's has positioned itself as an arena for public debate on synthetic biology, the main voices being the ETC Group and Friends of the Earth.

As contributions to a process of political and societal opinion making, the activities in each of these arenas is important, but as we have argued in the preceding sections, they must also be interrelated. Indeed, in the vision of the Rathenau Instituut, political (partisan) and societal organizations can and should play an important role in connecting the debates that are going on in the various arenas. In this way, these organizations may contribute to a process of 'responsible research and innovation' (RRI) in synthetic biology and other emerging fields of science and technology, explicitly pursued in the innovation policies of the European Union.

About the authors

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Who was Rathenau?

The Rathenau Instituut is named after Professor G.W. Rathenau (1911-1989), who was successively professor of experimental physics at the University of Amsterdam, director of the Philips Physics Laboratory in Eindhoven, and a member of the Scientific Advisory Council on Government Policy. He achieved national fame as chairman of the commission formed in 1978 to investigate the societal implications of micro-electronics. One of the commission's recommendations was that there should be ongoing and systematic monitoring of the societal significance of all technological advances. Rathenau's activities led to the foundation of the Netherlands Organization for Technology Assessment (NOTA) in 1986. On 2 June 1994, this organization was renamed 'the Rathenau Instituut'.