Rathenau Instituut BaSyC Radboud University

Society and synthetic cells

A position paper by the Future Panel on Synthetic Life

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About this position paper

This position paper is the joint result of discussions about the social significance of synthetic cell developments between the fourteen members of the Future Panel over a period of two years. Responsibility for the content of the document rests with the Future Panel. The paper, however, does not necessarily reflect the policies or positions of the individual contributors, or the organizations with which they are affiliated.

The *Future Panel on Synthetic Life* was organised by the Rathenau Instituut in collaboration with Radboud University, as part of the BaSyC research programme (Building a Synthetic Cell), which is aimed at creating an autonomous, self-reproducing synthetic cell with a bottom-up approach, that is, through integration of molecular building blocks. BaSyC is financed by a *Gravitation grant* from the Dutch Ministry of Education, Culture and Science, in cooperation with the Netherlands Organization for Scientific Research (NWO), and by the participating research institutions.

Preface by Henk de Jong

In the ten-year Dutch research programme BaSyC, six institutes have the high ambition to build a synthetic cell, hoping to discover 'how life works'. Where until now biotechnology has been mainly concerned with improving existing forms of life, this programme is about creating new forms of life from the bottom up. This kind of research is growing worldwide and raises various existential questions about our view of what life is, the desired relationship between technology and nature, and the impact of synthetic cell technology on society.

For more than 35 years now, the Rathenau Instituut has been involved in research and debate about the impact of science, innovation, and technology on society. Previous debates on, for example, GM food and cloning, have shown that new biotechnologies can lead to social controversies. This begs the question: how can we organise a timely public conversation about adjusting and creating life?

As part of BaSyC, the Rathenau Instituut and the Radboud University took the opportunity to kick-start such a conversation through the Future Panel on Synthetic Life. For two years we organised multiple meetings that facilitated a conversation between fourteen technical and social experts. This resulted in an iterative discussion and writing process, where new challenges and dilemmas were uncovered with each step, and where individual statements grew into this position paper that was embraced by twelve members of the Future Panel.

The fact that not all participants supported the position paper seems, once again, to emphasise the potential controversial nature of synthetic cell technology and the need to carefully address the issues that are related to this development. That is why this position paper is such a valuable document. Together, it’s key challenges, dilemmas, and recommendations, form beautiful ingredients for a first conceptual public agenda. In this way, hopefully at this early stage of development, the paper can provide a basis for starting a broader debate about our future lives with or without the synthetic cell.

Drs. Henk de Jong

Director Rathenau Instituut

Preface by Annelien Bredenoord

How does life work? This is one of the most essential questions that has been addressed for centuries by theology and philosophy. It has been taken over by synthetic biology in the early years of 2000, with the aim of (re)designing existing and new biological entities such as enzymes, genetic systems and cells. The BaSyC consortium, whose acronym stands for *building a synthetic cell*, proposes to develop a synthetic cell from the bottom up.

As this position papers shows, many aspects of synthetic cell research are yet unknown. However, we do know that patterns in the ethics of emerging science and technology exist. There is an increasing awareness that these kinds of scientific developments require an effective and comprehensive approach to ethically guide these innovations into society.

In the early stage of development, it is still possible to influence the research itself, but it is difficult to anticipate how the research will impact society. Even though the meaning and implication of synthetic life is not known yet, early anticipation of its possible ethical and societal impact is of key importance. After all, these insights could help research consortia in developing best practices, in explicating hidden normativity with regard to foreseen users, in explicating goals and effects, and in explicating possibilities for abuse and unintended effects. Empirical research and participatory design can provide input to compose meaningful orientation and anticipatory governance to meaningfully guide the development and application of synthetic cells. This is even more important for enabling technology, such as synthetic biology, because it has a wide range of potential applications and impacts in a wide variety of contexts.

It is, therefore, very important that the *Future Panel on Synthetic Life* has recognised that the building of synthetic cells in the lab should be accompanied by building inclusive narratives to co-produce synthetic cells in a morally responsible way. This is, after all, the only way that society can enjoy the positive implications and effects of synthetic cell research and mitigate the ever-present negative sides of science and technology as much as possible, and redistribute the impacts as fair as possible in a democratic society.

Prof. dr. Annelien Bredenoord

Professor Ethics of Technologies, Erasmus School of Philosophy, Rector Magnificus Erasmus University Rotterdam, Member of the Dutch Senate

Aim and scope

BaSyC (Building a Synthetic Cell) is a Dutch research programme aimed at creating an autonomous, self-reproducing synthetic cell with a bottom-up approach, meaning through integration of molecular building blocks. Within the BaSyC consortium, the Rathenau Instituut and Radboud University Nijmegen are responsible for work package 6 on Philosophy, Ethics, and Public Debate. Part of this combined effort is devoted to the establishment and organisation of a societal expert panel called the *Future Panel on Synthetic Life* (in short: the Future Panel).

Diversity as a precondition
Diversity is an important consideration in research that focuses on the social dimensions of the synthetic cell. While shaping the Future Panel, diversity was one of the main conditions. Not only diversity in expertise, but also in moral beliefs, visions of nature and technology, and the relationship between technology and society.

As we are still grappling with the full complexity of the challenges ahead when it comes to the development of the synthetic cell, the panel consists of experts across the science and society spectrum. Based on a first scan of scientific literature and interviews with natural and social scientists, the Rathenau Instituut and Radboud University together composed a non-exhaustive list of relevant subjects that could be considered by the Future Panel. For each of these subjects, one or two experts were approached with the invitation to become a member of the Future Panel.

When deemed necessary by the panel or the organisation, additional expertise could be invited to subsequent panel meetings. After the first panel meeting, it was decided that there was a need for one additional panel member with expertise on intellectual property rights and other legal procedures related to the development of the synthetic cell. This was the only addition made to the original composition of the Future Panel.

In total, fourteen experts accepted the invitation to be part of the Future Panel (see appendix 1). In line with our strive for diversity, the panel includes members with expertise in: social science, public engagement, chemistry, physics, synthetic biology, legal procedures, ethics, media, bio-art, risk assessment and management, biotech industry and policy. Moreover, there are mutual differences amongst the panel members in their views of nature and technology and the relationship between them, and the relationship between (civil) society, industry, government, and academia and the role they play in the development of new (living) technology.

The Future Panel has been given the responsibility to:
- map the social challenges and dilemmas in a society that masters synthetic cell technology;
- identify the conditions under which the construction of a synthetic cell can be considered beneficial for society; and
- advise on how these conditions can be realised.

A starting point for the societal debate on the synthetic cell
The aim of the Future Panel is to create an initial agenda for future political, academic and public debate on the synthetic cell. The aim is not to steer the societal debate on the synthetic cell, nor to impose particular representations or narratives onto society. The meetings of the Future Panel, and the position paper that resulted from this, are merely meant as a starting point for initiating a broader societal debate.

This position paper summarises the most important points of conversation, shared insights and issues of debate from the Future Panel, presenting the key challenges and dilemmas and resulting in four key recommendations. The position paper provides pathways of analysis and options for action, without being prescriptive. The Future Panel recognises that many of the ideas and recommendations are still exploratory, hoping that this document will catalyse further discussion on the socially responsible development of synthetic cell technology.

Methodology and questions addressed by the Future Panel
The discussions within the Future Panel were spread out over four separate meetings that took place between January 2020 and December 2021. Most panelists met physically during the first meeting. Because of the COVID-19 pandemic, and being unable to meet in person, the second and third meeting were each split up into two shorter online sessions.

Before the start of the first Future Panel meeting, each panel member received a background paper containing information on the science dynamics surrounding the development of the synthetic cell. The background paper briefly described the developments in this emerging field; the diverging views on what a synthetic cell is, and several ethical and societal challenges believed to be important for the panel to consider (i.e. public beneficence, biosafety, biosecurity, possible worldview changes, commercial incentives, public concerns, and value-driven innovation).

The background paper was written by the Rathenau Instituut and was based on an extensive literature review and interviews with researchers engaged in the bottom-up development of a synthetic cell, as well as natural and social scientists in synthetic biology in general. The paper functioned as a joint starting point for the panel discussions, but in no way aimed to represent an exhaustive list of societal challenges and concerns.

The first panel meeting
The focus of the first Future Panel meeting (January 2020) was on identifying the most important topics that should be discussed within the panel during subsequent meetings. Questions that were addressed during this meeting were:

- what social challenges and dilemmas do we see (which issues are relevant for a future with a synthetic cell);
- how can we talk about these issues; and
- who should have a say in this?

During that first meeting, the panel indicated that it wanted to broaden the perspective and move beyond traditional framings of life-sciences-versus-society debates. The panel did not want to be limited by either a pro-contra or a risks-benefits debate, nor a debate about a narrow set of ethical issues concerning future applications. The panel sees science and technology not as something outside of society, economics and politics, but as an integral part of it. When considering developments concerning the synthetic cell, due attention should therefore be given to the social, economic and political contexts that shape these developments, and thus the ways of framing and power relations at work. As a result, the panel explored how and under what conditions science-society interactions could allow synthetic cell research to become a catalyst for socially responsible developments, for example by contributing to the Sustainable Development Goals as defined by the United Nations.

The second panel meeting
The issues identified during the first meeting were the subjects of discussion during the second Future Panel meeting (October, 2020). During the first session of the second Future Panel meeting, the discussions were centred around three subjects related to the synthetic cell: Biosafety (including biosecurity and risk assessment), Intellectual Property, and Public Concerns. The second online session of the second Future Panel meeting centred around four different domains related to the development of the synthetic cell: academia, civil society, government and industry.

For each of the above mentioned subjects and domains, one panel member with expertise on or interest in this specific subject or domain wrote a short statement (300-600 words) that functioned as the start of the discussions. The same panel member was also asked to moderate the discussions on that subject. Through multiple discussion rounds in break-out groups of three to four panel members, all panel members got the opportunity to respond to each statement and discuss each other's views on the specific subjects.

Questions that were central during the second meeting were:
- under what circumstances can building a synthetic cell be considered beneficial for society;
- to which societal challenges and public values should innovation contribute; and
- how are responsibilities and power dynamics taking shape between the involved governance domains and how should these be dealt with?

Directly after this second meeting, the same panel members that wrote the starting statements revised the statements based on the discussions. This resulted in seven statements by the Future Panel on the following topics:
1. biosafety, biosecurity, risk assessment;
2. public concerns;
3. intellectual property;
4. civil society (governance);
5. government (governance);
6. academia (governance); and
7. industry (governance).

Writing phase
In preparation for the third meeting, pairs of members of the panel were asked to further elaborate the seven statements with reference to three questions:
- what are the main developments;
- what are the main challenges; and
- what are your views on addressing these challenges?

By addressing these three questions, the panel made the final step in the discussion towards recommendations on how to address the identified issues. In other words, what transformations are needed to create a society in which it is possible to position synthetic cell research in the context of responsible and ecologically sustainable developments?

The writing pairs consisted of the panel member who wrote and rewrote the first statement on the specific subject (this was also the panel member with the most expertise on the subject) and a second panel member with a different expertise or perspective to challenge and broaden up the existing statement. For some pairs, a shortage in time and the difference in expertise posed some problems during this collaborative writing process. In addition, all communication and collaboration had to be organised online because of the COVID-19 pandemic.

This led to some differences in the division of effort and influence on the contents of the statements within the pairs. For other pairs however, the difference in expertise led to an exciting discussion and constructive collaboration. In addition, one panel member (with approval of the organisers) wrote an additional overarching and reflective statement on the relation between society and technology and the influence of the power relations within society on the development of new technologies. This contribution also enriched and sharpened the discussion within the panel about the interaction between technology and society.

As a result, the writing phase resulted in a set of strong final statements written by the panel. These final statements were then handed over to the editing team (consisting of two panel members, including the chair of the Future Panel, and two members of the project team). From this point onwards, the editing team was responsible for combining all statements and discussion reports into a first complete draft of a position paper.

The third panel meeting

That first complete draft was the starting point for the third meeting of the Future Panel, which consisted of two online sessions (February and May, 2021). The discussions during the third meeting were directly focused on the content of the position paper addressing questions that included:

- where are we in the process of writing the position paper;
- what is the scope and the purpose of the position paper;
- what does the panel think of the challenges and recommendations as presented in the paper? Where do we agree or disagree and why? Is it complete; and
- how do we present the position paper to the public? What is important in this? Who must be present? In addition, how do we make the most impact?

The first session of the third panel meeting was organised around the different chapters within the position paper. After a plenary start during which the panel members could express any first responses to the paper, the panel split up into smaller groups to discuss the separate chapters of the paper in more detail. Each panel member got the opportunity to sign up for two preferred subjects before the meeting which resulted in the layout of the groups. The members of the editing team were the moderators of the discussions. Besides the discussions during the meeting, the panel members got the opportunity to send in any written feedback on the first draft of the position paper.

Based on the discussions during the first online session (February, 2021) and the received written feedback, a second draft of the paper was written by the editing team, which formed the starting point for the second online session (May, 2021). Besides some substantive changes, the position paper was rewritten to be more accessible and to the point, with shorter chapters and stronger statements. Also, the conclusion and recommendations were completed.

The second draft of the position paper was shared with the panel before the second online session of the third Future Panel meeting. The discussions during this meeting were organised around the seven recommendations in the paper. The panel was again split up into small groups of three to four panel members and the members of the editing team were asked to moderate the discussions in the break-out sessions. The seven recommendations were divided over five slots and there was one open slot of which the subject was decided during the plenary part at the beginning of the meeting. In two rounds all panel members were randomly assigned to two slots.

During this second online session, the importance of the dilemmas that the panel was confronted with in their discussions was emphasised. The dilemmas not only show the difficulties of the assignment to organise the development of the synthetic cell in the context of a more responsible, just, and sustainable development, but also the diversity of the views and richness of the discussions within the panel. It was decided that the dilemmas should have a more central place within the position paper. In addition, the panel decided to merge the seven recommendations into four recommendations. Besides their feedback during the online session, the panel members also got the opportunity to hand in written feedback on the paper.

Finalizing the position paper

After the third meeting, the editing team finalised the position paper and sent the final draft version to the panel for a new feedback round, in which the panel members were asked to email their written feedback. After processing the feedback, there was one final feedback round that functioned as a final check of the contents by the panel and a way to extract any remaining factual inaccuracies before publication.

During this final stage it was stressed that, although the responsibility for the content of the document rests with the Future Panel, the paper does not necessarily reflect the policies or positions of the individual contributors, or the organizations with which they are affiliated. Moreover, two panel members decided to reject co-authorship of the position paper as they could not agree with the way their contributions were combined with those of others in the final position. This request was accepted (see at the end of appendix 1).

After the final feedback round the position paper was prepared for publication by adding illustrations to strengthen the core messages of the different chapters, and a grammar check. Moreover, Henk de Jong (ad interim director of the Rathenau

Instituut) and Annelien Bredenoord (who is a bioethics professor and a Member of the Dutch Senate) were invited to write the two prefaces of this publication. The position paper is to be presented by the Future Panel on Synthetic Life at a public meeting during the first half of 2022 and will be published prior to this meeting on the website of the Rathenau Instituut.

Summary

The BaSyC consortium, whose acronym stands for *building a synthetic cell*, proposes to develop a synthetic cell from the bottom up. In the context of this joined effort, the Rathenau Instituut and Radboud University Nijmegen have organised the *Future Panel on Synthetic Life*, consisting of societal experts, to explore the social challenges, dilemmas, and possible societal impacts of synthetic cell research, and to advise how this research may contribute to a fair and sustainable future. The goal for the Future Panel is to create an initial agenda for future political, academic, and public debate on the synthetic cell.

The profile of science and technology is two-sided. On the one hand, they act as drivers for problem-solving, progress, and emancipation, but techno-scientific innovation can also give rise to disruptive threats. Therefore, societal reflection should be timely and anticipatory. Rather than asking what risks and benefits are involved, the question will be how to engage society in such a way that synthetic cell research can become a joint endeavour, responsive to societal hopes and concerns. Consequently, the Future Panel aimed to:

- map the social challenges and dilemmas in a society where a synthetic cell exists;
- identify conditions under which synthetic cell technology can be considered beneficial for society; and
- advice on how these conditions can be realised.

To contribute to this, the Future Panel discussed the role and perspectives of key stakeholders (academia, government and governance, industry, and civil society), besides more specific issues like public responses, biosafety, biosecurity, and intellectual property rights during multiple online and offline meetings within a period of two years. This position paper summarises the most important points of conversation, shared insights, key challenges, dilemmas that were discussed during these meetings, resulting in four recommendations, as a starting point for further analysis and debate.

Key challenges

During the deliberations, the Future Panel encountered four overarching challenges.

1. The novelty of synthetic cell research makes it challenging to devise a methodology capable of anticipating public concerns in a domain where overt public attitudes do not exist as of yet.

2. As long as the existing power structures within the contexts that shape developments in science and technology are not explicitly addressed, the development of a synthetic cell will inevitably reproduce and may even strengthen existing power inequalities.
3. In order to involve civil society and allow citizens to articulate their views and concerns, besides factual information, the synthetic cell has to be positioned in a proper context: how to develop a responsible narrative that allows the public to actively relate to these developments?
4. Even though the BaSyC project is halfway, there are still many unknowns, even unknown unknowns. A key challenge is to connect social, ethical, and science perspectives, and dilemmas, ambitions, and uncertainties related to the building of a synthetic cell.

Dilemmas

During the panel discussions, many reasons have arisen, from different perspectives, for involving the general public, governments, industry and NGOs in an anticipatory way. However, doing this reveals some fundamental dilemmas and tensions that should be addressed.

1. The BaSyC project is curiosity-driven, aspiring to deepen our understanding of life. At the same time, our desire to know is driven by an impetus to control. How to practice synthetic cell research as a dialogue with nature rather than an appropriation and instrumentalisation of the living cell?
2. Many aspects of synthetic cell research are yet unknown. How to allow space for the unknown while, at the same time, opt for an anticipatory and imaginative approach to take the future social and ethical implications and concerns into account?
3. How to make research more inclusive by involving public, politics and policy in such a way that it is fostering and inspirational rather than detrimental for curiosity-driven experimentation and exploration?
4. Curiosity-driven science requires a great deal of specialism and thrives on serendipity. How to achieve convergence in science, involving multiple stakeholders and taking into account societal expectations and concerns, without frustrating the process of discovery?
5. Deliberation requires a dialogue across disciplines, languages, and levels of information. How to combine different vocabularies, perspectives, socio-cultural and time horizons in a meaningful way?
6. Within science and technology, and in particular biotechnology, there has long been a discussion about how to deal with knowledge and intellectual property rights. Should life be considered patentable or should life be seen as a common heritage that belongs to everybody?

7. How to deal with researchers who need to make their work openly accessible, and companies, incubators, and organisations that want to protect their invention?
8. Within projects of four to five years, researchers are under pressure to focus on and deliver scientific publications, while at the same time being encouraged to actively reflect on and engage with the potential societal impact of their work. How to balance conflicting expectations related to different time horizons?

Recommendations

The Future Panel proposes four recommendations for fostering a socially responsible development of the synthetic cell:

1. Ensure that the synthetic cell contributes to a fair and sustainable future

To foster sustainable synthetic cells, we need co-constructed narratives that allow us to explore how synthetic cells may contribute to a sustainable future. It is not enough to stimulate techno-scientific innovation as such. Governments must simultaneously stimulate social innovation, and promote broad stakeholder involvement in synthetic cell research.

2. Organise participation of civil society in synthetic cell research

In order to ensure that synthetic cell research contributes to a fair and sustainable society, an inclusive and participatory process of reflection is required, open to public intelligence, and sensitive to societal expectations and concerns. This requires innovative methods to engage the wisdom of the crowd. Meetings with societal stakeholders should be organised on relevant issues at different moments of the project and should be designed as in-between spaces in which different meanings, interests, and societal values come together and are made explicit.

3. Foster a socially responsive academic ecosystem

Rather than endorsing the status quo, synthetic cell research emphasises the importance of rethinking the university of the 21st century, where research and education must become more inclusive and interactive, bent on developing long-term partnerships with society: with industry and governmental organisations, but first and foremost with society at large. Societal reflection and interaction with society should be an integral part of academic research and education. Therefore, researchers must be empowered to engage with society in such a way that dialogue and interaction become an inherent part of their work, from design to publication.

4. Design social governance experiments aimed at renewing the regulatory landscape for new biotechnologies, including the synthetic cell
Ensuring that the synthetic cell may contribute to a more sustainable and socially equitable world requires an adequate social understanding of governance and regulatory systems. The current regulatory system is not prepared for that task. We need a new system, which does not reproduce previous polemics. Besides looking at risks, a more comprehensive regulatory regime would integrate questions concerning sustainability, human rights, ethics, and societal desirability. Governance experiments co-designed with societal actors are needed to gain insight into the contours of such a new regulatory landscape on synthetic biology or new biotechnologies, including the synthetic cell.

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Introduction

Building a better world

Global society is currently facing an epoch of unprecedented ecological disruption, with climate change and mass extinction among its most distressing symptoms. Although multiple complex processes are involved, the industrial revolution, beginning in the eighteenth century, played a decisive role, contributing over time to developments such as globalisation, consumerism and disruptive innovation. In important respects, the scientific revolution (which separated the domain of nature from that of the social through the emergence of the experimental method in the natural sciences) prepared the ground for this. Against this backdrop, the profile of science and technology came increasingly to be seen as having two sides. On the one hand, the technosciences can act as drivers for problem-solving, progress and emancipation – think of the development of vaccines or sustainable energy technologies. On the other hand, it can also give rise to disruptive threats. Think of how the internet was expected to bring people closer together, whereas in practice it has also helped to spread mass surveillance, as well as racial and religious hate and violence.

The Future Panel thus recognises that, in addition to producing great economic and societal benefits, technologies can also be harnessed — often by powerful parties — to produce large-scale violence, dehumanization and environmental destruction. Science and technology will often lead to a mix of positive and negative developments.

This insight should make us humble and demands that we raise the question of how to ensure that science and technology, or more generally technoscience, as much as possible can become part of the solution, i.e. how it can contribute to the development of a socially and ecologically sustainable and just global culture? When addressing this question, it is important to pay attention to the social, economic and political context in which the developments surrounding the synthetic cell take place and to the powerful or vulnerable position that various actors play within it (Wickson et al., 2017).

In contemporary public and scholarly debate, both in the natural sciences and in the social sciences and humanities, multiple authors are exploring such possibilities. In the quest for a sustainable and biocompatible technology, various ideas have been proposed, indicating a willingness to learn from and collaborate with nature, resulting in a technology that is nature-friendly rather than nature-harming. Concepts such as *biomimicry*, *biomimesis* or *homeotechnology* (aligning with nature, contrary to *allotechnology*) have drawn much attention (Benyus, 1997; Sloterdijk, 2001; Bensaude-Vincent & Benoit-Browaeys, 2011). A focus purely on the technological dimension of innovation will not suffice, however. Rather, technoscientific innovation needs to be part of a more comprehensive transition, requiring a broader attitude of change. Sustainability is not only a matter of sustainable technologies (as *products* of innovation), but also requires social innovation in terms of changing relationships, involving new ways of doing, knowing, framing and organizing the endeavour (Pel et al., 2020). In addition, the processes of technoscientific innovation must be reconsidered to make them more inclusive, interactive, and responsive to societal needs and concerns (Owen et al., 2012).

Against this backdrop, the BaSyC project represents a fascinating case study. How to involve public deliberation as an inherent dimension of the project's work? Rather than framing the question in terms of possible benefits and risks involved for society, we pose the question as to how projects such as BaSyC can become part of a broader transition, which not only entails technological, but also societal and normative developments. Besides zooming in on specific aspects, we also want to consider the broader landscape, by asking how and under what conditions the synthetic cell may disrupt or contribute to a fairer society in transition to sustainability, which is considered an open, responsive and deliberative process. In this introduction, we first briefly position the BaSyC project in the context of a more extended history of efforts to produce *living technologies* that mimic the basic signature features of living systems. Secondly, we briefly address the societal challenges we are facing. Finally, we outline the design of the report.

Building synthetic cells

In their efforts to understand the fundamental processes of life, scientists have attempted for a few decades to build various types of protocells, minimal cells or synthetic cells. Early work showed that abiotic components can demonstrate life-like behavior (Bedau & Parke, 2009). Studies of simple protocells began in the 1980s in the context of research into the origin of life and artificial life. The advances in synthetic biology during the past decades and in other research fields such as genomics, biocomputing, materials science and nanotechnology accelerated the pace of synthetic cell research.

The Dutch BaSyC (Building a Synthetic Cell) consortium is a collaborative, transdisciplinary effort to create an autonomous, self-reproducing synthetic cell through integration of molecular (bottom-up) building blocks (box 1). By building synthetic cells from individual molecular components, scientists aim to uncover the basic principles of life perceived as molecular building blocks and to foster our understanding of what that life is. This in turn will enable greater insight into the building blocks and molecular functioning of living systems, which may not only revolutionise biotechnology but also acquire a significant societal impact. Scientists imagine and speculate for example on developments such as smart devices for drug delivery, drug-screening, bio-nanodevices for molecular detection, self-healing (responsive) materials, nanoscale bioreactors, data storage and information processing.[1] However, not everyone is optimistic about the increase of control through the technological reproduction of life. Jasanoff (2019), for instance, warns that we should be wary that life does not devolve into just another object of conscious design, valued mainly for our ability to manipulate it, commodify it and profit from it.

Setting up a Future Panel

Against this background, the BaSyC consortium decided to establish a societal panel to explore scenarios for the future: the Future Panel. The panel had the task of examining the societal meanings and potential future impacts of the synthetic cell. To do so the panel includes members with expertise in: social science, public engagement, chemistry, physics, synthetic biology, legal procedures, ethics, media, bio-art, risk assessment and management, biotech-industry and policy.

The Future Panel is a joint initiative of the Rathenau Instituut and Radboud University within the BaSyC programme tasked with initiating a political and public debate on the societal, ethical and governance aspects surrounding the effort to build a synthetic cell. This is a challenging task, as we are dealing with a research endeavour that may require us to rethink some of the fundamental categories of our thinking, such as the line between the natural and the artificial, living and non-living, basic and applied research, science and technology, technology and democratic society.

The synthetic cell may be what has been called a *living technology* (Bedeau, 2010) that asks for a reflection on societal and ethical issues that may arise with its development. As Sandel (2004) phrased it: ‘When science moves faster than our moral understanding, we struggle to articulate our unease’. Yet, it is of utmost importance that we find ways to discuss transformative technologies like this one, as they may have a major disruptive impact on society. Jennifer Doudna, who received the Nobel prize in chemistry together with Emmanuelle Charpentier for their pioneering work on gene editing, emphasises how important it is to pro-actively explore and address ethical and societal issues involved in technoscientific innovation. This is a process which requires dialogue across disciplinary boundaries and across the science-society divide, a mutual learning process, forcing us to develop new insights and skills.

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[1] http://www.syntheticcell.eu/

Box 1 Bottom-up synthetic cell approach

In synthetic biology, the construction of new forms of life can involve different approaches and strategies. In the top-down approach, living cells are genetically and metabolically engineered with the aim to impart new functions, taking advantage of large-scale recombinant DNA technology. The work can involve the engineering of minimal cells and the introduction of synthetic genomes. In the bottom-up approach, also known as constructive approach, cells are constructed from molecular components, which can be natural or non-natural, and here the boundaries of chemistry and biology are explored. The Dutch BaSyC consortium takes the bottom-up synthetic cell approach and assembles biomolecular building blocks to create autonomous self-sustaining systems that can grow and replicate.

A minimal cell is a cell whose genome has been reduced by deleting as many genes as possible, which ultimately should lead to a cell with only essential genes and more room for introducing orthologous gene and metabolic networks. A protocell is any model that may or may not involve a self-assembled compartment, allowing chemical processes to take place within, aimed at explaining the functioning of more complex biological systems. An artificial cell uses a repertoire of naturally existing biomolecules, which is complemented with non-natural ones. Here, we define a synthetic cell as a complex system that can autonomously grow and sustain itself and is built from molecular components, provided to us by evolution. Such a bottom-up constructed cell may, provide mechanistic insight in the principles by which modern cellular life operates and to harness this for new functionalities and production of useful compounds.

Multiple questions emerge: What is needed to make the building of a synthetic cell beneficial to society, and how to take this on board in the further development of the research agenda? What societal challenges and concerns are involved in (living with) synthetic cells? What kind of values and norms should guide the development of synthetic life? What kind of framings of challenges and particular values in society are currently driving the development of synthetic cell-based innovations? What kind of governance arrangements need to be put in place to navigate synthetic cells through society? How will the synthetic cell transform the social world we live in? Intriguing questions specifically related to the synthetic cell include: To what extent does synthetic cell research reduce the bios (life) to a computable logos? What are the implications of such a computer-based understanding of cellular reproduction in a political sense and for the way we understand and know the world? Can the missing link between the inorganic and organic worlds be found in the creation of a synthetic cell? How is the relation between synthetic cell and the genetic code? The Future Panel has been invited to develop and address imaginative plausible futures in a participatory and anticipatory manner.

Synthetic cell research
The BaSyC consortium is funded through a so-called Gravitation grant (18.8 million euro) from the Dutch Ministry of Education, Culture and Science. Gravitation is the scientific excellence programme of the Netherlands Organization for Scientific Research (NWO), which supports large-scale, challenging research efforts. Led by Marileen Dogterom, professor of bionanoscience at Delft University of Technology, and supported by the participating research institutes, this consortium aims to create an autonomous, self-reproducing synthetic cell through integration of molecular building blocks and components.

Similar initiatives are taking place in other countries, for example in Germany the MaxSynBio programme is attempting to create a synthetic cell, funded by the Max Planck Society and the Federal Ministry of Education and Research. The University of Bristol has a multidisciplinary research centre, BrissynBio, which focusses on several strands of research within synthetic biology, among which the artificial cell.

In October 2019, the first SynCell symposium was held in Madrid. SynCell is an initiative in Europe to join the various European research networks and create a broader narrative within the larger European and other International funding programmes. At this symposium, researchers got together to design a European roadmap to build a synthetic cell.

In the United States, the top-down approach in synthetic biology has been more dominant, notably via the work of the J. Craig Venter Institute and the EBRC (Engineering Biology Research Center).[2] An informal network *Build-a-cell* has been set up in 2017, which supports scientists working together to build a diversity of synthetic cells, and in 2019 the National Science Foundation has invested $ 36 million in its *Understanding the Rules of Life* portfolio.

During the discussion at the European SynCell symposium, it became evident that the very concept of a synthetic cell is still evolving. A synthetic cell needs basic cellular components within a membrane, must be able to sustain itself, grow and reproduce, and needs to have some form of metabolism, with genetic information passed on to daughter cells. In their Opinion on Synthetic Biology, the scientific committees of the European Commission referred to the mantra of synthetic biology: ‘What I cannot create, I do not understand’, referring to physicist Richard Feynman’s famous words.[3]

Exploring future and present

The ability to create something does not imply that we can foresee the future consequences and implications. Synthetic cells are seen as a threshold technology, that will lead to qualitatively different applications than the ones currently developed in top-down synthetic biology. Even research into creating a synthetic cell itself will deliver new information, data, and technologies that may be valuable for qualitatively new kinds of applications (Bedau & Parke, 2009). There are hopes that synthetic cells will foster sustainability (through biomimicry) and provide new pathways for biomedicine, the energy problem, the world food crisis, and the environmental crisis. However, the technological, societal and economic benefits are all still hypothetical.

Applications that are under development in the medical field are, among others, smart drug delivery systems, Car-T like cells, self-healing and responsive materials, biohybrid materials, cosmetics, and medical diagnostic systems. Where green and white biotechnology are concerned, examples include artificial photosynthesis, bio-

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[2] https://ebrc.org/synberc/

[3] Scientific Committee on Emerging and Newly Identified Health Risks SCENIHR, Scientific Committee on Health and Environmental Risks SCHER, Scientific Committee on Consumer Safety SCCS. (2015). The Final Opinion on Synthetic Biology III: Risks to the environment and biodiversity related to synthetic biology and research priorities in the field of synthetic biology.

factories, synthetic meat, and taste enhancers. Additionattly, bottom-up synthetic biology is expected to bring new ways to sense, design, produce, test and measure molecules and materials, disrupting traditional ways of doing so. Yet, whether society will benefit from this will depend on many factors. It is for example important to maintain public legitimacy and support, to align commercial incentives with the public good, and to ensure that benefits outweigh societal risks (variously defined). Alongside benefits and (bio-safety, bio-security, etc.) risks, worldview implications may also be involved, as synthetic cells may affect the *symbolic order*, e.g. the way we define distinctions between natural and artificial, life and non-life, evolution and responsibility (Van den Belt, 2009).

Finally, if bottom-up synthetic biology and the creation of a synthetic cell will indeed revolutionise biotechnology, whether it will provide socially beneficial products will also depend on the alignment of commercial incentives with the common good. Commercial development is believed to be encouraged by intellectual property rights, although the desirability of the intellectual property system has a long history of being questioned (Palombi, 2009; Sterckx, 2006; Feeney, et al., 2018; Nuffield Council, 2012; Nelson, 2014). Therefore, this aspect should also be pro-actively addressed (Zwart, 2019). To foster positive scenarios and prevent current inequalities from increasing, democratic governance is needed (Habets et al., 2021) and the Future Panel is to address such concerns.

Governmental policies are often shaped by expectations of innovation and socio-economic growth. Science and technologies are often promoted under the assumption that they will provide economic and societal benefit. The development of *key enabling technologies* as nano and biotechnology are expected to reinforce economic competitiveness. Science and innovation are seen as indispensable in the pursuit of sustainable economic growth: the solutions to today's societal challenges are tomorrow's earning capacity.[4] Yet increasingly, the assumption that science and technology will lead to societal benefits as well as economic growth, is questioned. Hence policies need to extend beyond economic growth and risk-based regulation. We need to evaluate the anticipated social and sustainability value of a new technology and not assume that benefits will be demonstrated by market success. We need underlying values that help structure policies; values beyond safety and economic growth. Sustainable development goals, as adopted by all United Nations Member States in 2015, should guide biotechnology assessment. These goals include important human values such as equity, solidarity, sustainability and wellbeing. And the public needs to be involved in setting the agenda; the role of participants should not be limited to their role as consumers but

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[4] Report working group Science, Research, Development and Innovation for the Study Group Sustainable Growth, July 2016

should participate also as citizens (Macnaghten et al., 2019; Nuffield Council on Bioethics, 2012).

There are different ways of looking at technology and its relationship with society and politics. One idea is that technology has a strong dynamic of its own and that society must adapt to technology, preferably by anticipating the opportunities and risks of technology. From this perspective, the debate is about the advantages and disadvantages of technology and ways to amplify benefits and avoid or mitigate downsides.

The Future Panel builds on the view that technoscience and society *mutually* probe and question each other. Rather than asking what kind of risks and benefits are involved, the question will be how to involve and engage society in this project in such a manner that BaSyC can become a joint endeavour, responsive to societal hopes and concerns. Although social actors are indeed socially shaping technology, particular actors may have a greater influence than others. Technology developments thus often occur within asymmetrical social power relations that are easily reproduced. It is then important to consider the specific social, economic and political context in which technology takes shape.

Secondly, the Panel is aware of the fact that technical artefacts can mediate people's actions and the way they live their lives. In many ways, technology helps us in what we do and how we do it. Values and assumptions may be built into the new technologies we produce. In line with this, one could say that various (public) values can be put into the technology. Efficiency and private profit motive often play a central role in the development of technology. A social design process is needed that offers space for other often not-for-profit public values. This requires a critical value-driven approach to technology, also described as ethics or politics by design and/ or value-driven innovation (Rathenau Instituut, 2018).

In the following sections, we will first address the role and perspectives of key stakeholders: academia (researchers as stakeholders), government and governance, industry, and civil society. Next, we will zoom in on specific issues to address: public responses, biosafety, biosecurity and risk assessment, and intellectual property rights. In all sections, after a short introduction, key challenges are outlined, and it is indicated how these challenges could be addressed in a collaborative, participatory and anticipatory manner.

1 Academia: organise specialisation and convergence

We are witnessing drastic changes in the ways in which scientific research is designed and conducted. On the one hand, we see hyper-specialisation, resulting in a plethora of disciplines and sub-disciplines, each with their own methodologies, technologies, journals, etc. On the other hand, we notice convergence, where research aspires to combine mass and focus to address big and urgent scientific and/or societal challenges. Both trends evolve simultaneously, side by side, which is illustrated by the BaSyC and MaxSynBio programmes.

The building of a synthetic cell requires convergence. BaSyC profits from various disciplines, like physics, chemistry, biology, social sciences, and the humanities. However, the question *What is life?* transcends such disciplinary boundaries, and demands a collaborative mutual learning process. Convergence means that science aims to become more collaborative, inclusive and interactive, more sensitive to societal expectations and concerns, and better equipped to effectively address urgent and complex societal challenges.

Although convergence has a long history and is increasingly stimulated, academia is still mainly organised from a disciplinary perspective to, on the one hand, assure and maintain sufficient depth in the research and education, while on the other hand, to maintain existing roles and identities. Organizing convergence is therefore necessary, but challenging. Below we list five ways to tackle this challenge.

1.1 Stimulate convergence top-down and bottom-up

Collaboration to address major scientific and/or societal challenges may be initiated by researchers themselves (bottom-up), but may also be encouraged by research funding agencies (top-down). We believe that convergence only works, i.e. results in sustainable (long-term) change, if it reflects and supports a bottom-up drive towards convergence. This collaboration across disciplines can be reinforced and facilitated by funding strategies. The BaSyC programme combines a bottom-up and top-down dimension: it builds on ongoing cross-disciplinary collaborations among researchers themselves, but was developed in response to a so-called Gravitation call[5] that aims to foster convergence.

1.2 Treat synthetic cell research as technoscience

Synthetic cell research is often described as fundamental research. At the same time, this type of research tends to require innovative technologies, which should thus be developed as part of the research. It carries the promise that it may lead to technological innovation, perhaps even opening up a new technoscientific domain, where the synthetic cell is used as a scaffold for multiple purposes. It is impossible to predict how this research will develop, since innovation often depends heavily on serendipity. At the same time, synthetic cell research cannot be seen simply as

[5] Each year, the Ministry of Education, Culture and Science makes a structural budget available for encouraging research consortia that have the potential to belong to the absolute world top in the field of research or have already achieved that level. This programme previously existed under the name Depth Strategy support programme. Since 2012 the revised instrument has been called Gravitation.

basic research. It is better to speak of technoscience (Hottois, 2018), in which technologies play a central role in doing and directing research. In addition, research is often carried out and funded with the aim of developing and applying technology. This strong link between science and application demands timely reflection, social involvement, and societal responsiveness of researchers.

1.3 Organise societal anticipation and deliberation

The CRISPR-Cas9 story (box 2) shows that it is important to address possible societal, ethical, and legal issues in an anticipatory manner. Keeping bioethical deliberation in pace with technoscience is a political choice. Many successful instances of anticipatory reflection can be pointed out (box 3). Societal reflection and interaction with society should therefore be an integral part of synthetic cell research. This broadens the spectrum of questions, ranging from philosophical issues (e.g. the impact of synthetic cells on our world-view, our understanding of life and technology) via global policy issues (potential contribution to Sustainable Development Goals) up to legal and data management issues (e.g. intellectual property rights). Synthetic cell research can be inspired by previous experiences, like various bio-art initiatives, the Human Genome Project and the Netherlands Genomics Initiative (with their ELSA research in ethical, legal and societal aspects), and the risk and technology assessment activities within the Dutch Nano-R&D Programme NanoNextNL.

Box 2 The CRISPR-Cas9 story

Many examples can be given of scientific breakthroughs with a significant societal impact. An interesting recent example is CRISPR-Cas9, resulting in a Nobel Prize in chemistry for Jennifer Doudna and Emmanuelle Charpentier. In *A crack in creation: The new power to control evolution*, Doudna (2017) explains how the small, hyper-specialised CRISPR research community had never realised that this microbial molecular tool might have dramatic social consequences in multiple realms of applications. This overwhelming awareness forced her to acquire new, transdisciplinary skills in fields like science policy and communication, research ethics, and intellectual property rights (Zwart 2019).

1.4 Empower researchers to engage with society

Synthetic cell research needs both specialisation and convergence. The current academic system in particular stimulates specialisation. Encouraging societal responsiveness and interaction among academics requires adjustment of how science is organised and researchers are rewarded, otherwise it runs the risk of becoming an extra, rather than an integrated task. How can we ensure that, in addition to publishing in high-impact journals or finishing theses, there is also time and appreciation for societal interaction? We must make sure that insecure PhD researchers do not get mangled in between specialisation and convergence. With respect to the latter, the CRISPR-Cas9 story (box 2) showed how ill prepared Jennifer Doudna was for addressing the societal, governance, and ethical aspects of her breakthrough. Educational programmes should be adapted in such a way that researchers are empowered with those kinds of skills.

Box 3 The Oviedo Convention on Human Rights and Biomedicine

The Oviedo Convention on Human Rights and Biomedicine (1997)[6] represents the outcome of in-depth discussions at the European level on biomedical developments, in particular in genetics, acknowledging the potential perspectives, but also the greater possibility to modify genetic characteristics of human beings, raising concern about possible misuse and abuses, in particular the intentional modification of human genome. In addition, following the second international summit on human genome editing and the announcement of the use of CRISPR-Cas9 technologies on human embryos in China, the *Council of Europe Committee on Bioethics* issued a Statement on genome editing in December 2015.[7]

1.5 Proactively address data management issues

Most academics tend to favour open science and open access, but sensitive data can become controversial once they enter the public realm and may become the target of ownership claims. This also plays a role in, for instance, CRISPR-Cas9. Therefore, we should proactively address data management issues, along the line of data trust principles (see further chapter 8). EU legislation regarding data

[6] https://www.coe.int/en/web/bioethics/oviedo-convention
[7] https://www.coe.int/en/web/bioethics/emerging-technologies/

governance and data policies is currently being drafted and close interaction between technoscience and governance is called for. If open data sharing is the default, this has to be proactively organised. Shared data and digital tools enable increased output and quality, especially when scientists from different disciplines work together and approach problems in a more comprehensive manner. The latter is the standard in astronomy for several decades already.

2 Governments: synthetic cells for a more sustainable and just world

Governments stimulate and regulate technological development. When promoting technology, it is often assumed that its development will automatically benefit society as a whole. Such technological positivism is too easy. The question of whether and why we want to develop a particular technology, in this case the synthetic cell, must be openly discussed. Part of such a discussion is the question to what extent the government is able to properly regulate the technology and embed it responsibly in society. The inability to properly regulate technology can be a reason not to deploy or apply that technology.

How synthetic cell technology will develop is uncertain. While some may think that creating an artificial cell is impossible, others foresee a disruptive technology that is likely to have multisector impacts (Bedau et al., 2001:2010; Rasmussen et al., 2011). That raises the question of the social significance of a possible synthetic cell technology. The social impact of the synthetic cell is certainly not a given, but will result from continuously technological, economic and political shaping. This again raises various governance issues. Who will be involved in the regulation of synthetic cell developments? Based on which public values do we want to shape synthetic cell technology? And do governments have the capacity to responsibly embed technology in society?

The point of departure of the Future Panel is that governments should stimulate and regulate the development of the synthetic cell in such a way that it leads to a more sustainable and more socially just world. Stimulating technoscience is insufficient for such a task. Besides technological innovation, governments should also stimulate social innovation to embed emerging technoscientific developments in society and make current biotechnology policies future-proof, for example by taking into account the possible development of the synthetic cell.

2.1 Discuss the if, why and context of synthetic cells

Many discussions about the governance of technology follow the same pattern: this technology is coming, it will have a lot of impact, how are we going to shape it? In this way, the question of whether we want the technology at all is avoided. From a democratic perspective, however, the first question is whether and why we want to develop synthetic cell technology. This basic question should therefore be openly discussed.

The importance of such a discussion does not lie in a simple yes or no answer, if only because of the fact that it is difficult to determine what exactly is meant by synthetic cell technology. The starting point for the discussion is the question which goals or public values society would like to pursue. A fundamental ethical issue, for example, concerns the ability of the synthetic cell to self-replicate. Is this something we would like to pursue? If it works, will we be able to contain the proliferation of such cells? Sustainability is often put forward as an important reason for developing synthetic cell technology. It is important to identify and prioritise those kinds of public values. Subsequently, the question emerges whether the claim that synthetic cells may contribute to a more sustainable technology is plausible. In this way, it becomes possible to think about how to properly shape the development of synthetic cell technology based on such public values, moving the developments involved in the direction we want to go as a democratic society.

When discussing the usefulness, necessity and governance of the development of synthetic cell technology, we should consider that technology takes shape in a social, ecological, economical, and political context, often with unequal power relationships. Because existing interests and powers will try to develop technology to their advantage, technological progress does not automatically lead to social progress. The current environmental crisis (from climate change to the mass extinction of animals and plants) and the emergence of surveillance societies and the challenges of misinformation indicate that, besides being beneficial for society, new technologies can be misused. How to ensure that synthetic cell technologies are not used for oppressive or unsustainable purposes? A good discussion about synthetic cell technology, therefore, requires attention to the forces that shape its development and the way governments regulate this development.

2.2 Stimulate technical and social innovation

When such an open-minded discussion leads to social support for the development of synthetic cell technology, then the question arises how the government can stimulate and shape this development. Since living technologies are based on the principles of living systems, meaning autonomous performance such as growth and self-repair, and long-term out-of-equilibrium operation, various scientists argue that they promise a significantly more sustainable future. That possibility could be a good reason for government support. According to the Future Panel, it is the government's task to ensure that synthetic cell development contributes to a more sustainable and socially just world.

For such contributions, it is not enough to stimulate technoscientific innovation. Governments must simultaneously stimulate social innovation which is geared towards transforming existing structures that hinder pluralising and diversifying not only identities, but also knowledge that is deemed relevant and rigorous in society. A central guiding question is always what the objective of sustainability and social justice means in concrete terms for research programming and research practice. And besides a continuous alignment between those objectives and engineering work, there should be – again from the perspective of sustainability and social justice – a focus on developing and exploring societal and (global) governance issues, fair business models, and stimulating interaction between a diverse group of experts and stakeholders, including representatives from government, industry, and civil society organisations.

2.3 Renew regulatory landscape for biotechnologies

Although the development of the synthetic cell is still at an early (basic research) stage, it could potentially give rise to a new biotechnological development in line with GMOs and recombinant DNA research and CRISPR-Cas9. Thinking about how to regulate synthetic cell research should therefore use the experience from these regulatory challenges and debates. The current risk-based regulatory system has been developed over the last 40 years and has led to much discussion and dissatisfaction. The European Union needs to reconsider what has been developed over the last decades, in terms of governance and regulatory oversight. To anticipate the new wave of scientific innovation, we should start building a new system, which does not reproduce the same polemics. Besides looking at risks, a more comprehensive regulatory regime would integrate questions around sustainability, ethics and societal desirability. Large-scale experiments co-designed with societal actors are needed to gain insight into the outline of such a new regulatory landscape on synthetic biology or new biotechnologies, including the synthetic cell.

This is called anticipatory governance. It is important that the government is able to embed technology in society in an adequate way. At the moment, to question whether governments are able to properly regulate and socially embed emerging technology is justified. For example, the case of the internet shows that in the past two decades governments have not taken their responsibility in all kinds of areas, resulting in bad developments such as surveillance, loss of privacy, disinformation and market dominance of large tech companies. Thus governments need to regain their ability to develop and uphold useful policies for emerging technologies. This requires new ways of looking at research, innovation and institutional renewal.

3 Industrial domain: towards anticipatory governance

Companies, entrepreneurs, and industrial scientists will be interested in, or even excited about, the idea of building a synthetic cell bottom-up and the challenges involved, but the current technology readiness level (TRL) of the research is too low for making committed investments. At the moment, the potential applications of synthetic cells are difficult to foresee. Yet, or in the near future, the level of readiness of this technology may well increase, and this calls for a proactive attitude in which the future is explored together.

3.1 The challenge of long-term partnerships

Industry may be potentially interested in advanced sub-systems, e.g. biological sensors, biological components of smart devices and other emerging and enabling technologies developed in the context of synthetic cell research. The challenge is to develop long-term partnerships to make this work. Besides public-private partnerships in the sense of academia-industry collaborations, we need to develop multi-stakeholder ecosystems involving universities, industries and societal stakeholders, and imaginative narratives for opening-up plausible futures for synthetic cell applications. These narratives should not only focus on the technological developments, but also on ethical and governance aspects from the very beginning and active involvement of all partners involved.

The European programmes (e.g. Horizon Europe) can provide an optimal setting for academic-industrial exchange of information and ideas. The tension between short-term and long-term time scales may prove a challenge here. From the perspective of industry (and of society) there is a need for short-term solutions, whereas projects such as building a synthetic cell emphasise the importance of long-term, comprehensive understanding. Societal policymakers have pressing questions and desire quick impact, but this type of research requires long-term efforts. How to foster constructive interaction between these time scales? This requires sustainable networks of collaboration between academia and its societal ecosystem. Possible impact must be pro-actively addressed, but short timeframes and application focus may lead to fragmented development of the scientific fields in question and to unstable and unsustainable associated industrial networks.

BaSyC as a project that will run for ten years, with possible extensions into the future (notably on the European scale), offers opportunities for network building with industry. However, there is a dilemma for principal investigators (PIs) with respect to the choice between following their scientific curiosity and/or focusing on translational innovation. It is hard to do both. PIs and most PhDs and post-docs will probably like to focus on basic, high-impact research resulting in highly cited academic papers. Innovation requires a different skill- and mindset. In addition, the timeline for a doctorate or post-doctorate study is typically two to four years and includes a training component that may conflict with a fast route towards applications. Spin-out, start-up ventures are the most suitable vehicles to drive innovation, especially for products and technologies that are new to the world, but they also need significant (PI) time and energy to get started. This is an argument for industrial involvement at an early stage.

3.2 Convincing narratives

In addition, there is a need for credible and imaginative narratives that trigger further explorations and discussions, both in terms of scientific prospects and potential industrial applications. Such narratives require a participatory and inclusive methodology to be convincing. It should not be about selling science to society or preparing society for new applications. Rather, societal needs, expectations and concerns should be taken on board for such narratives to be motivating and trustworthy.

It is also important to define what industry actually is, e.g. does *food industry* mean big companies (big players), or does it include the small farmers and food producers as well? Who should be at the table when synthetic cells and their potential applications are being discussed? An important question, when it comes to exploring potential futures and potential applications, is to identify and involve relevant stakeholders early on in the innovation process.

Also, we should indicate and explore potential implications for synthetic cell research for addressing the UN Sustainable Development Goals (SDGs). Inspired by SDGs and the multi-stakeholder discussions at World Economic Forum meetings, multiple voices (representing natural sciences, social sciences, humanities, arts, civic society, etc.) with global mindsets could be brought together to jointly develop plausible future scenarios to inspire synthetic cell research. This could form a basis for the development of compelling narratives, which could help trigger industrial interest, funding and innovations.

4 Involving civil society

Looking into the perspectives of civil society representatives (e.g. non-governmental organisations, trade unions, social movements, local communities) is critical to ensure a robust and in-depth understanding and societal embedding of any development in science and technology. Such inquiry should involve the frames of reference that exist in the communities that are potentially impacted. The development of a synthetic cell is a challenging example of such a development as consequences for society may be significant. Although at this moment these consequences are uncertain and unknown. When thinking of involving civil society in the development of this new research area, fundamental challenges arise.

4.1 The challenge of (dis)trust in science

Over the last decades, public participation in science has mainly emerged as a way to inform and engage the public on scientific developments. These efforts often had the objective to convince members of the public of the relevance and necessity of a particular line of research. At the same time, more and more scientists are at least willing to communicate with citizens in other stages of the research process. The idea is that citizens have relevant insights and data that may contribute to the quality of the research as well as to the applicability of innovations and recommendations that may follow from new scientific insights. Another important reason for extending traditional science communication is the insight that scientists, without being aware, present their work together with all kinds of implicit interpretations, assumptions, interests, values and norms that may clash with those of other societal actors. Related to the synthetic cell, scientists might, for instance easily assume that non-scientists will not understand the scientific research, and thus cannot be useful in the stage of building a synthetic cell. Another assumption may be that non-scientists will always resist the unknown, and should therefore not be involved as long as science is in the making and possible applications are not yet clear.

Distrust in science arises when scientists deny that their research is value-driven and monopolise the truth, in the way they see it. Distrust may also result from mixing science and politics when it comes to policy development for solving complex problems. The fierce discussions about the development and implementation of COVID-19 measures is a clear example. According to their values that they might feel that are at stake, societal actors involve different contexts, emphasise different sensitivities and pose different questions than scientists do (Wynne, 1992).

Establishing, (re)gaining and maintaining public trust in science therefore asks for true and sincere participation of civil society in scientific research that may have important consequences for future society. Clearly, this applies to the development of a synthetic cell as well. In discussions with civil society actors that take part in such participation, different framings and possibly threatened societal values related to both existing and future concerns should be the main issue.

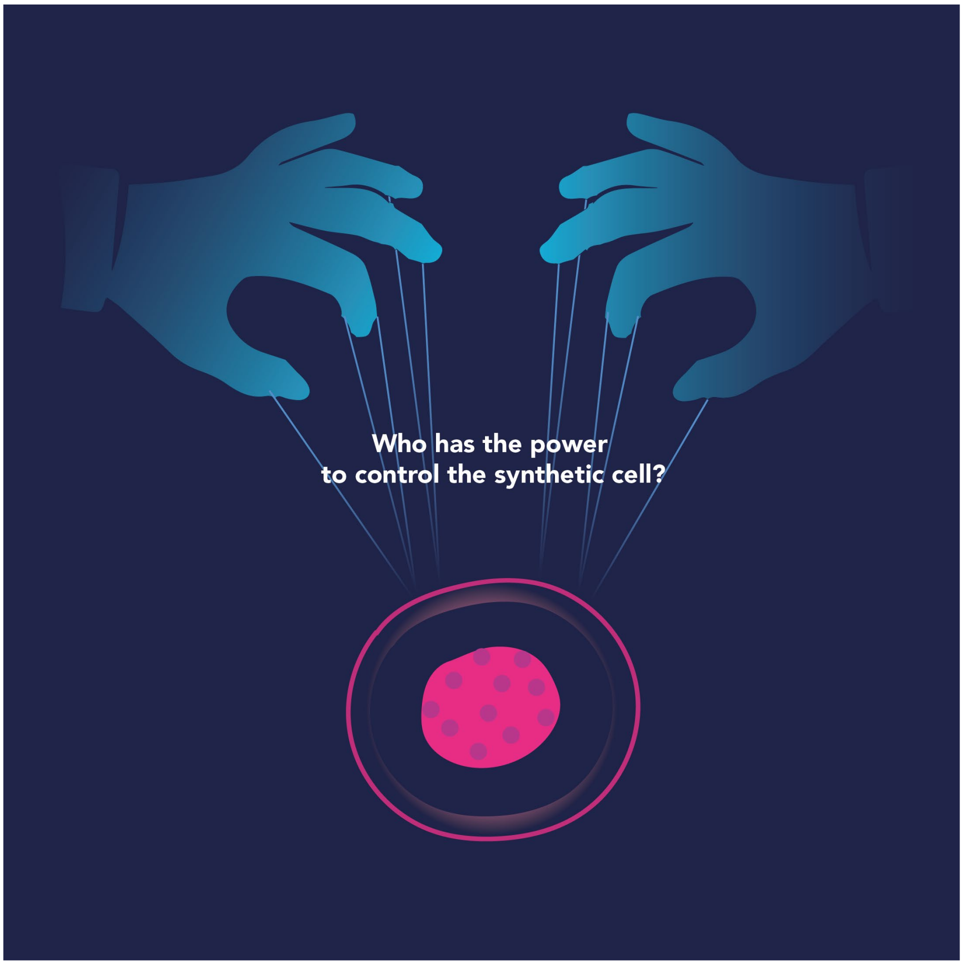
Last but not least, synthetic cell research is evolving against a backdrop of pervasive societal transitions. This is happening to such an extent that we should even raise the question whether concepts such as *civil society* and the *public sphere* are still valid. Due to developments related to social media and big tech companies, and contrary to what was expected when Internet emerged during the final decades of the twentieth century, contemporary societies have become increasingly fragmented. This is resulting in a proliferation of platforms where societal debate and exchange takes place. Participants no longer speak the same language, nor do they use or trust the same sources of information. This adds additional challenges to the objective of restoring transparency of and trust in science.

4.2 The challenge of reproducing power structures

Developments in science and technology take shape in specific social, economic and political contexts that include specific power structures. Science and technology are, for instance, developed according to specific standards, that are agreed upon and reproduced by the scientific community itself. Moreover, whether or not a specific question (e.g. What is life?) is being dealt with via scientific research is influenced by governments and other powerful institutions (Luhmann, 1990; 1995; Urry, 2004). When stressing public concerns, for example, the dichotomy between academic concerns and public concerns is reproduced and even strengthened: apparently these concerns are to be considered as fundamentally distinct. Scientists arguing that, by building a synthetic cell, they are just trying to understand what life is (so that it would not make sense to involve the public at this stage of research as they would not understand anything of what they are doing), may unintendedly reproduce and strengthen the societal division and the existing power structures as part of the academic context they are working in. In order to open-up the process of exploring the future implication of synthetic cell research, voices and perspectives from society must be enabled to become involved from the very outset.

Of course, science is partly driven by the curiosity and brilliance of individuals. However, the distinction between fundamental, curiosity-driven science and the development of applied technologies and how these could be used is not always as clear as scientists themselves would assume. Moreover, how much money is invested in science and on what research questions is determined by political choices. These are in turn influenced by lobbying activities from a wide range of stakeholders. Here we see again how science and politics are mixed via various structures.

In short, as long as power structures are not explicitly addressed, the development of a synthetic cell will inevitably reproduce and may even strengthen existing power inequalities between academia and society. Here, we find an important task for both natural scientists working on the development of the synthetic cell as well as civil society actors and social scientists who study science and technology from a critical perspective to guarantee a process that also takes into account social innovation.



4.3 The challenge of involving the public in science

Public participation can take many forms, such as science cafés, focus groups, interviews, debates and dialogues, user panels, polls, citizen science projects, etc..

Whatever form is chosen and whatever topics are being tackled, the common denominator is that the science domain is in the lead, with scientific institutions and scientists often determining the topics for the discussion, the format, the timing and the participants. Furthermore, they decide how to use and interpret the outcomes of the participation project. Taken together, the conventional approach to public participation is mostly supply-led: consciously or not, scientists tend to promote their ideas in such a way as to prevent the public from expressing opposition to their activities (see for instance Reincke, Bredenoord & Van Mil, 2020).

Moreover, it is often the case that many public or civil society related organisations do not have the power nor the resources to make their voices heard, even if they want to. It could, for instance, be the lack of time to be able to participate in a public participation setting. And there probably is always a large group of people that is not connected at all when it comes to participating in a science café or in a citizen science project because it would not fit in their daily practices. Moreover, many people may not feel comfortable to join such groups. As a result, whether or not represented by civil society organisations, mainly the 'usual suspects' - the highly educated white men and women – tend to participate. Special efforts should thus be employed to involve society in all its diversity and to explore new ways to connect science and the civil society.

4.4 Exploring FPIC as a new, radical approach

A complimentary way that may contribute to a balanced relationship between science and society is to adopt a needs-led approach. Initial considerations of such an approach may include questions such as: how did this area of science come into being? Who is likely to benefit from this area of research and how? What practices might be the outcomes of such disrupting research? Where do the resources come from to bring this research into being? How will future research be justified? What could be the implications of building a synthetic cell over time and space, across communities and generations? What are the uncertainties and unknowns related to the research, including potential consequences that may emerge over time? How to involve society in all its diversity?

By taking such considerations into account, new and more radical approaches of public participation could be explored. An inspiring but also controversial example is the *Free Prior Informed Consent approach (FPIC)*[8]. FPIC is an important principle that can protect the publics' rights to self-determination, consultation, and

[8] https://www.un.org/development/desa/indigenouspeoples/publications/2016/10/free-prior-and-informed-consent-an-indigenous-peoples-right-and-a-good-practice-for-local-communities-fao/#

participation in decision-making about issues that affect them. If synthetic cell scientists are to commit to FPIC, they themselves should take on the responsibility to seriously reflect its four elements, as defined by the United Nations Food and Agricultural Organisation (FAO)[9].

Free means that there is no manipulation and coercion of the public and that the process is self-directed by those that may be affected by the development of synthetic cell related technologies.

Prior implies that consent is sought sufficiently in advance of any activities being either commenced or authorised. Sufficient time should be guaranteed for the ongoing process of considering and reconsidering the economic, cultural, social, and political implications of the research.

Informed suggests that the participants to the process should be informed about key-points and developments. Not merely the uses of the research that are already envisaged, should be considered. Other possible uses as well as the economic and political interests underlying the development and deployment of any related technology and considerations of the public should constantly be taken into account as well.

Rather than a one-off event, consent is a process, which means that it can be reconsidered and even withdrawn, as new information may emerge and new experiences may add to existing understandings and reflections.

Scientists may argue that society would come to standstill if FPIC were to be implemented in all its facets: the discovery of CRISPR may have been prohibited, the technology underlying iPhone would maybe not have been developed, a COVID-19 vaccine would not have been developed within less than a year. Fundamental problems and dilemmas will indeed emerge when considering implementation of FPIC in the process of building a synthetic cell. Nevertheless, when societal dialogues about the synthetic cell would follow FPIC-like principles they would at least contribute to a turning point towards doing science by embracing participatory forms of (re)connecting the public. It may create an atmosphere that invites listening to each other and even to some 'unlearning' of what was considered the one and only way. In the next chapter on public responses, a number of design features of FPIC like approaches, as well as the substantive challenge concerning the constitution of public concerns will be elaborated.

[9] https://www.fao.org/home/en/

5 Public responses

As we saw in the previous chapter, anticipating public responses to emerging science and innovation is a major challenge for contemporary democracies. It is also a precondition for responsible innovation, including the task of how to align research and innovation with fundamental societal values. In this chapter we define a public response as a matter of interest or importance to someone, and thus as something that may include concerns and worries, but also hopes and dreams, or even more ephemeral experiences such as curiosity and wonder (see Callon et al., 2009; Wynne, 2001, 2006, 2016).

To map future public responses to the building of a synthetic cell, it is important that we explore both the concerns of the public and the concerns of the stakeholders about potential risks to the environment and human health, alongside wider responses associated with how the development of a synthetic cell is likely to transform and reconfigure social, ethical and economic life. For these reasons, we need to understand how socio-economic and cultural relations are inscribed in the development of synthetic cells. As said, by not involving voices and perspectives from society during the early stages of developing a synthetic cell, scientists may unconsciously inscribe their own tacit values into the research process and thereby reproduce existing power relations between experts and so-called non-experts. Even though the development of the synthetic cell involves scientists from all over the world, the tendency towards particular kinds of values and assumptions of societal benefit, which may not be universally shared, is strengthened at the same time.

The challenge of engaging with public responses on synthetic life is twofold:

1. to devise a methodology capable of anticipating public responses, although overt public attitudes do not yet exist; and
2. to understand the significance of public responses surrounding the construction of a synthetic cell, and of synthetic life more broadly.

5.1 The methodological challenge

There is an ecosystem of participatory and deliberative methods for including the public and stakeholders in early-stage discussions on science and innovation (Macnaghten and Chilvers, 2014). Such methods range from those designed to develop consensus on the social issues surrounding a particular technology or science (such as consensus conferences, consensus forums, citizens juries and constructive technology assessment), to those designed to open up ways of imagining the social issues and potential implications of science and innovation in-the-making (such as co-evolutionary scenarios, foresight activities and horizon scanning), to those aimed at disrupting existing science policy and problem-solving frames (such as co-design and interactional user research).

Rather than undertaking public engagement research after a controversial social or ethical question has arisen in relation to a new technology (Rogers-Hayden and Pidgeon, 2007), the challenge here is to craft an *upstream* deliberative methodology aimed at understanding how people develop views, attitudes and ethical values under conditions of unfamiliarity. The question then is if deliberative methodologies can give voice to the articulation of public views on topics on which participants — at least prior to the deliberative intervention — have poorly formed attitudes and standpoints. Can questions of political economy be integrated into public engagement dialogue processes? Is it realistic, feasible, or useful to conduct public engagement in fundamental research projects where applications are still distant? How can it be avoided that an emphasis on public engagement legitimates only those forms of research that have a utilitarian orientation, rather than encouraging curiosity-driven research too? Can deliberative processes provide reflective and critical citizen input as a counterweight to technocratic decision-making, capable of contesting rather than reinforcing existing relations of professional power and economic rationality?

5.2 Design features of best practices

To respond to these challenges, a number of design features can be identified as elements of best practice (Macnaghten 2021). The first design feature is sampling, determining who is involved in the deliberative research and who fits the criteria for selection. An interesting method may be the anticipatory focus group method. For public engagement research on synthetic life, it will be necessary to bring participants together on the basis of shared experience as a design feature (see Macnaghten and Myers, 2004; Morgan, 1996).

The second design feature is context. For public engagement research on synthetic life, it will be necessary to deliberate on social meanings and dynamics, to reflect on relevant everyday practices, and through deliberation to derive contextual factors deemed likely to be significant in the shaping of subsequent public responses.

The third design feature is framing. Given that the representation of a technology is never neutral, but always framed in particular ways and for particular purposes, care will be exercised to introduce the technology by offering participants an inclusive range of rhetorical resources and frames, without closing down or narrowing the issue from the start (Felt et al., 2007; Stirling, 2008). In-depth deliberation on these frames helps to facilitate involved actors to construct problem definitions, meanings, and moral evaluations.

The fourth design feature is moderation. A discussion group is a space in which a group identity and discourse can emerge. To ensure that discussions are not dominated by expert discourses and norms, it is necessary to include a moderator that is trained in the art and ethos of deliberation.

To summarise, we have set out the methodological challenge of designing an anticipatory public engagement methodology that aims at emancipatory technological development and the design of characteristics that can help address these challenges. We now address the substantive challenge concerning the constitution of public concerns.

5.3 The substantive challenge: cultural narratives

Public responses to the creation of a synthetic cell, and to synthetic life in general, will not emerge anew. The dynamics through which the unfamiliar will be rendered familiar will depend on how the technology, and the issues it raises, is embedded into everyday social life. Key questions will concern the following: what concerns people about the technology? What factors underpin and mediate these concerns? What narrative resources do people draw upon to make novel innovation readily sensible and meaningful? And how do these emerge and solidify in guided social interaction?

People are rarely completely for or against a particular technology. Nor do people respond in distributional terms, evaluating the benefits of the technology pitted against its harms. Rather, the way people construct their responses speak to the moral implications of the technology, its purposes, and transformative and transgressive potential.

The *Enlightenment narrative of science*, that imagines technology to bear clear social benefits, is a dominant narrative about the societal role of science and technology. In this narrative, technological progress almost automatically leads to social progress.

However, there are several other critical narratives, where people discern a connection between pleas for technological innovation and neo-liberal ideological values (e.g. individualism, conspicuous consumption, global inequalities, etc.). For those who are reluctant to adopt a modernist narrative of science, what counter-narratives are available to structure public responses (Bamberg and Andrews, 2004)? Macnaghten et al. (2019) identified five over-arching cultural narratives, each familiar in Western culture, which are continually enacted in deliberative discussions on new and emerging technology. The use of age-old narratives can be very useful in understanding an unfamiliar present and in developing a vocabulary for an imagined future, including why people feel impoverished agency in shaping technological choices and trajectories. These narratives articulate potential public concerns, which proponents of synthetic cell research should be able to address.

There is the *be careful what you wish for narrative*: the idea that getting exactly what you wish for may lead to unforeseen disaster and catastrophe (Dupuy, 2010: 155). Advanced technology-derived products and innovations may be desirable — and even offer the promise of perfection — but there is also the sense that getting exactly what you want may not ultimately be good for you, or society, or, ultimately, the planet.

Pandora's Box is the second narrative: the story of Pandora, the first woman, who was given a huge jar that she was instructed not to open. Out of curiosity, Pandora opened the lid and all the evils, miseries, diseases and illnesses that mankind previously had been spared from flew out and infected the world. Even though innovations were not born of evil intent, people use this narrative to explain why radical technological intervention on nature is seen as likely to release unforeseen perils.

A close variant with the former is the *messing with nature narrative* that relies on the ancient idea of nature as having sacred qualities that establishes norms or order to the human world that should not be transgressed.

The *kept in the dark narrative* is a different kind of story, deployed in contexts where people feel powerless in the face of an emerging technology. It speaks to the concept of alienation, in the modern sense of being disenfranchised from the research and development (R&D) innovation process.

A final narrative is *the rich get richer.* Again, largely a modern story, in so far as it is premised on the ideal of social equality as a foundational element in modernity, it speaks to the potential of emerging technology helping to exacerbate further injustice and inequality, both globally and locally.

These narratives have resulted from the earlier, so-called *DEEPEN project* that examined public responses to emerging nanotechnology. However, close variants have been witnessed in deliberative projects with the public on topics such as genetically modified foods and crops, gene editing technologies, geoengineering, and fracking. It is thus plausible, and indeed likely, that these kinds of narratives will be used to structure public responses to this new biotechnology, unless there is substantial integrative work from scientists and other actors to work through these narratives in ongoing and continuous co-design and interactional user research. Such research would require of scientists and policymakers to be open to the disruption of existing science policy and problem-solving frames. Clearly, what we need to research is not simply the content and composition of public concerns to a synthetic cell (and to synthetic life more broadly), but also the underlying cultural narratives through which concerns in a broad sense are articulated in public dialogue. Finally, this exercise should prepare the ground for producing convincing co-constructed narratives exploring how synthetic cell research could contribute to important societal goals such as sustainability and global justice. Developing such narratives collaboratively will help us to steer the future development of synthetic cell research in a desirable direction.

6 Biosafety, biosecurity, risk assessment

Biosafety and biosecurity refer to the prevention of risks to humans, animals, and the environment that may originate from living entities, like microorganisms and viruses. In recombinant DNA technology, biosafety risks that are taken into account are e.g. pathogenicity, gene transfer, and invasiveness. It remains to be seen if these are also applicable to a synthetic cell that is man-made from molecular building blocks.

The development of a synthetic cell is at its onset and one may have to define a timeline for the foreseeable developmental stages of the cell and, simultaneously, the risk assessment. Current research on the construction of life-like systems takes advantage of properties such as self-replication, repair, self-assembly of biomolecules, and the ability to develop out-of-equilibrium metabolic networks with complex functions. But a synthetic cell showing all these properties is still very far from realisation. When realised, the synthetic cell could also be very different from the natural cell, making it difficult to oversee what kind of risks may arise, and, therefore, the risks associated with conventional recombinant DNA technology may only partly apply. We suggest how to not only build on an existing technocratic approach to biosafety, biosecurity, and risk assessment, but also move beyond such approaches to create new ways of assessment that fit the challenges ahead.

6.1 The challenges

6.1.1 What to consider?

To be able to consider safety and security concerns for a synthetic cell, it is important to have an understanding of what the synthetic cell is. One can only think about concerns if one knows what kind of synthetic cell will be designed and what the purpose of that cell is. If the synthetic cell is evolving into a cell closely resembling a natural cell in that it can grow and replicate, one will have to consider invasiveness if the synthetic cell is released into the environment. Furthermore, concerns like passing genetic traits to other species need to be considered, as well as the evolutionary potential of a cell causing genetic and phenotypic instability. These concerns are typically regarded for a genetically modified cell.

A first assumption to dispel is that there will not be one design for the synthetic cell. Instead, there will be several possible designs of a synthetic cell, some will not have a genome, but be based on biomolecular assemblies with specific functions (vide infra). Moreover, the synthetic cell itself or its variants may function in different contexts.

To be able to anticipate on safety and security concerns of a synthetic cell, it is important to understand what precisely is meant or designed. The following questions can be helpful: from what components is the synthetic cell compiled? What are the characteristics that define the particular cell? How is the cell produced? What is the cell designed to do, what is its function, and what is the context of use?

Answers to these questions need to be collected during early steps in design and development of synthetic cells as they will guide the determination of potential concerns originating from the cell and the development of safety norms and practices. In the course of new developments of synthetic cells, such questions need to be reiterated in or respond to arising concerns.

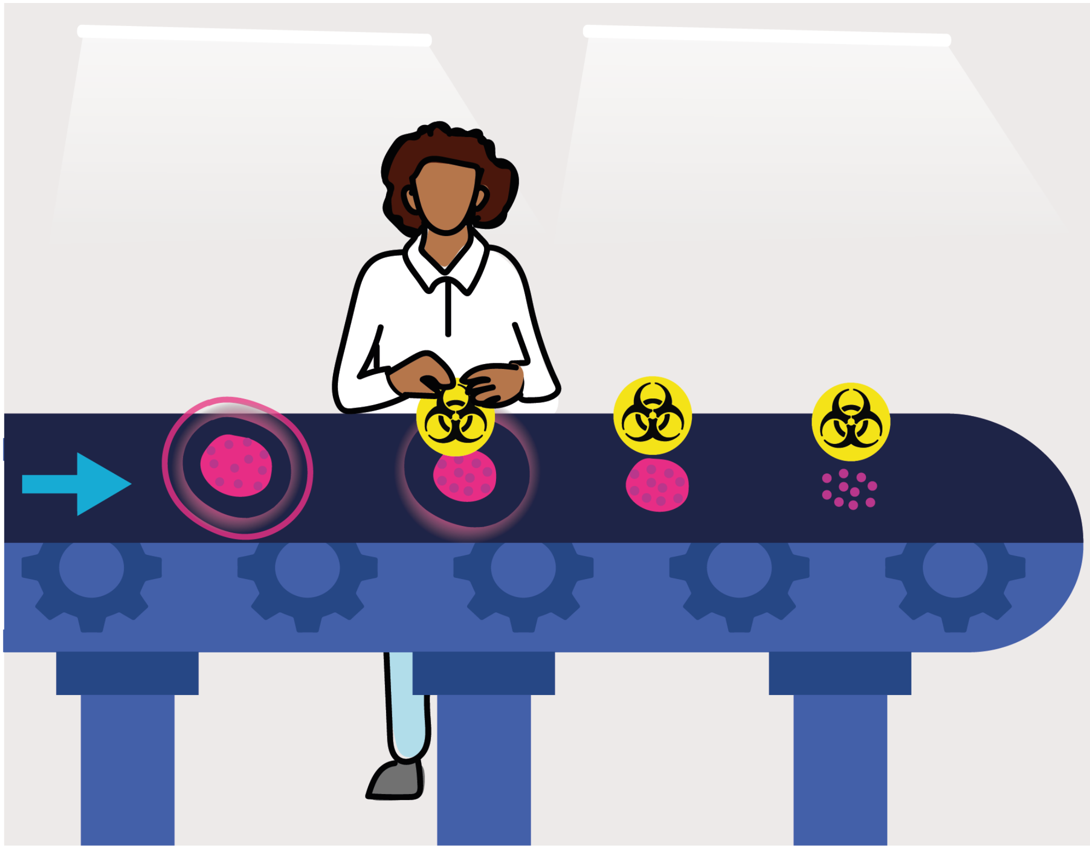
6.1.2 How to consider?

Concerns for human health and the environment that may arise from a synthetic cell might be different from, or additional to, those that are regarded for known living entities. It is premature to envision what kind of biosafety and biosecurity concerns may be relevant to a synthetic cell. At the same time, there is a need to devise ways to avoid the Collingridge dilemma, which indicates that in some instances, we can only learn about the risks after they materialise. It is advisable to keep an open mind towards *new* concerns possibly arising from yet *unknown* characteristics (such as interactions with living cells), functionalities and applications of the synthetic cell. The inclusion of a broad scope of stakeholders can shed a light on new concerns and consequences. This approach may broaden the discussion.

6.1.3 When to consider?

A technology that allows you to create something that does not yet exist, asks for critical reflection on the technology itself. It might be helpful to consider ‘safety of the synthetic cell technology’ instead of ‘safety of the synthetic cell’ as a product.

A product, not yet characterised and resulting from a technology can be assessed for safety concerns based on knowledge regarding its components and production process (a process-based assessment). At that stage, knowledge on its functionality and interaction with the natural world is unknown and needs to be studied. After that, when data are available on these aspects, a product-based assessment of safety concerns can be implemented. This emphasises a need for iteration between design and assessment, which should begin early and continue for the duration of the lifecycle of the innovation. This also gives the opportunity to include societal considerations, for instance coming from the Sustainable Development Goals, to design choices.



6.2 Addressing the challenges

Risk research needs to be developed in parallel to and integrated with the developments in engineering synthetic cells to collect data on potential concerns. Next to this technocratic process, an understanding of the socio-economic and political context of the development of the synthetic cell is required.

There are well-known examples of professionals working with new technologies that show awareness of safety concerns: companies that sell synthetic DNA developed a Code of Conduct on DNA synthesis[10] in order to prevent the synthesis and selling of hazardous DNA sequences. This has resulted in a lot of outreach and openness by these communities. There are also opportunities to improve educational programmes with regard to safety issues, in ways that provide more specialist knowledge, and also big picture and long-term thinking skills.

A code of conduct for transparency about issues, related to the development of the synthetic cell, presents some control about what is going on in the specific field. Awareness, education, and early involvement of relevant stakeholders might result in broadening horizons of concerns of synthetic cell technology in a still unknown future.

10 Harmonized Screening Protocol. https://genesynthesisconsortium.org/wp-ontent/uploads/IGSCHarmonizedProtocol11-21-17.pdf

7 Intellectual property

The BaSyC consortium aims to build a synthetic cell from molecular components, to gain knowledge of how cells work and how we can use this information to, for example, engineer and build artificial cells.

Bottom-up synthetic biology raises issues in relation to property rights. If you create something – drawings, algorithms, even kinetic schemes[11] – or invent something new – such as lifesaving medication or ‘patentable’ plants – then our legal system grants the creator or inventor property rights, provided certain legal conditions are met. For example, in Europe patents are available for inventions that have a technical character, are novel, inventive, have an industrial application and are sufficiently described in the patent application.[12] In such cases the inventions are protected by intellectual property rights (IP-rights), namely patent rights.

In current deliberations about IP-rights, multiple legal issues are at stake, but the starting point is a more fundamental question. To the extent that synthetic cells will mimic or plagiarise living systems, the question emerges: can we (or should we want to) own or patent the life-like systems? Can we appropriate living technologies, which are actually copied from nature? Many contributors to the debate start from the conviction that fundamental knowledge about life should belong to everybody and should be a common heritage. Is life patentable at all? Life as such can certainly not be patented, but the products and properties (e.g. biosensing) of life-like systems will likely be patentable. Within the context of the BaSyC project, we cannot answer this daunting question. Nonetheless, in an effort to anticipate IP discussions, this broader question must be addressed first and foremost. Fundamental knowledge concerning life is not patentable, but where does legitimate patentability begin? The discussion whether we want to patent synthetic cells as such will inevitably arise, but the answer to this question is far from pre-determined. Rather, it is one of the challenges that must be addressed.

Patent rights and copyrights are examples of IP-rights. In some cases, IP-rights are granted by virtue of law, for example by creating a work protected by copyright or a

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[11] “A kinetic scheme is a network of states and connections between them representing the scheme of a dynamical process”, see: https://en.wikipedia.org/wiki/Kinetic_scheme. In 2006, the Dutch Supreme Court did not rule out that a schematic representation of the production process of ethylene and propylene may qualify as a work protected by copyright. See: https://www.ie-forum.nl/artikelen/technip-vs-goossens-copyright-on-scientific-work-1.

[12] For an overview of the general patent law framework, see: European Commission, *Trends and developments in artificial intelligence - Challenges to the intellectual property rights framework : final report*, Luxembourg: Publications Office of the European Union, 2020, paragraph 4.2, available at: https://op.europa.eu/s/oFhJ.

collection of data which sometimes can be protected by a *sui generis* database right. In other cases, IP-rights are granted as a result of a successful application filing. Think of patents, trademarks, or plant variety rights. Application filings can be time-consuming affairs. It takes years from application to a granted patent and most applications will not make it. IP-rights are not infinitely valid, but last for a certain period of time. Patent rights can have a lifespan of 20 years, while copyrights in the European Union are valid 70 years *post mortem auctoris*. Patents are only valid in countries where fees have been paid. The system of IP-rights is designed to support its creators and inventors for a limited time, after which the invention becomes part of the public domain, which allows follow-up innovations.

Holders of IP-rights may exclude others from using their creation or invention in order to make a profit by licensing. Consequently, they decide who may enjoy their work and which licensing terms apply. IP-rights such as patents represent a financial value in economic transactions. They can be used to trade, negotiate, collaborate, etc. Legislation may vary throughout the world, although EU Member States share to a certain degree harmonised IP laws.

Creations or inventions by (members of) the BaSyC consortium may be protected by IP-rights. This could mean that BaSyC and its participants can prohibit anyone to use its IP-protected works, databases, and patentable inventions, such as the synthetic cell or parts thereof. Is this a desirable situation, in light of BaSyC's goals that aim to provide insight for the general public? Again, this fundamental question should be addressed first. Decisions can be recorded in public–private partnership (PPP) arrangements about governance or IP. Based on such arrangements it may be considered in the public interest to valorise new scientific insights in IP applications when relevant.

In the upcoming section, we first address the developments and challenges of IP-rights in general. Then we focus on three key challenges and formulate our positions on these matters. We conclude with a proposal on how the challenges should be approached.

7.1 Developments and challenges

Complex systems like chemical compounds or formulae, synthetic versions of genes (e.g. for breast cancer screening) or nanotechnologies are to a certain extent patentable. (Parts of) the synthetic cell may therefore be protected by IP-rights such as patents, or may involve technologies protected by IP-rights. The patent system is in principle open to such technological developments.

The normative debate concerning the desirability of the IP system has a long history. For example, the incentivizing effect of patents in the pharmaceutical industry is a matter of debate (Palombi 2009). Also the immense costs of the patent system have been critiqued (Sterckx, 2006). The price for patented products and processes is deemed artificially high and there is a risk of delaying wide-spread use, thus delaying the realization of possible socially beneficial products. For instance, questions have been raised whether or not pharmaceutical companies should give up patent protection regarding the COVID-19 vaccines, so anyone could apply this technology unrestricted. In the pharmaceutical industry, some patents use resources that could have been directed towards better purposes, some argue. There are a number of justifications for patents such as legal and economic arguments. However, according to some these can be contested (Sterckx, 2006).

Another development concerns the effect of the patenting system on social justice. This is particularly significant for foundational technologies such as bottom-up synthetic biology. Although patents do not necessarily delay access to the technology – because the licensor can provide others with a license – it of course depends on the strategy of the licensor (Feeney et al., 2018). For example, Stanford University's licensing strategy regarding its foundational biotechnological recombinant DNA (rDNA) technique provided non-exclusive licenses to non-profit organisations. However, Stanford is not legally obliged to maintain such non-exclusive licensing practices. Other holders of IP-rights may demand others to apply for a license, which the IP-right holders may or may not grant. This will cause a risk of delaying the realization of possible socially beneficial inventions, although the significance of this risk may vary since the patent system can also act as enabler of creativity. The patent system prevents the status quo of single solutions, promoting different approaches to the same problem. This can be observed in the challenge to develop a COVID-19 vaccine, which leads to a wide range of solutions by different inventors. How should we deal with this when regarding synthetic cell development?

Different approaches may reflect cultural differences between disciplines that have converged into synthetic biology: fields like software design and engineering embrace open source innovation, while molecular biology and biotechnology tend to patent discoveries. An open source approach may also be based on economic reasons (e.g. when a patent would not contribute to a return on investment), rather than cultural or altruistic reasons. Synthetic biology is facing a tug of war over patenting versus open source as its access-to-knowledge framework (Nelson, 2014). How this will be resolved will be of significant influence on the distribution of possible benefits to society considering the revolutionary nature of emerging technologies such as synthetic cells.

7.2 Three key challenges

We observe three key challenges. These challenges arise due to tensions within the current legal framework, rooted in international and European legal agreements such as treaties.[13] In addition, we set forth possible positions.

7.2.1 Who may own what?

Certain parts of the synthetic cell may be eligible for protection by IP-rights. Who may own which part of the technologies involved? Researchers tend to make their work openly accessible. At the same time, companies, incubators, or other organisations may become involved with their own (commercial) motives. They may want to keep the technology to themselves. To them, publishing may not be the default *modus operandi*.

The BaSyC consortium aims to create technology that can lead to a more just and sustainable society. For instance, the technology bears the promise to produce fuels, plastics or medicine by using artificial cells instead of chemical processes, making industry more sustainable.[14] IP-rights may relate to particular objects (e.g. software, algorithms or patentable inventions) that are crucial to building the synthetic cell. In that case there should be a shared understanding whether IP-rights will be invoked. For example, if third-parties use the technology for less beneficial purposes (dual use), it is conceivable that BaSyC or its participants try to prevent that by invoking IP-rights.

7.2.2 Who should own what?

Another challenge emerged regarding the question ‘are we patenting life’? Some argue that life should not be patented, others argue that bottom-up synthetic biology is not about creating life; it *mimics* life, while a third view stresses that it is impossible to specify the boundary between ‘life’ and ‘mimicking life’ due to the lack of a clear answer to the bigger question of what ‘life’ is. Some aspects of living systems are de facto patentable, for instance, if they are technologically reformulated.

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[13] For a non-exhaustive overview of international and European legal sources regarding IP-rights, see: https://www.ivir.nl/about-us/legislation/intellectual-property/ (i.a. copyright and database rights law) and https://www.ivir.nl/about-us/legislation/industrial-property/ (i.a. patent law). See also: https://www.wipo.int/wipolex/en/index.html.

[14] TU Delft, 'TU Delft - Charlotte Koster PhD Building a Synthetic Cell (BaSyC)', 20 February 2020, https://www.youtube.com/watch?v=JWbIs16NvOY.

Technically speaking, certain elements involved in bottom-up synthetic biology are, to some extent, patentable. The fundamental question whether it is morally commendable to move in this direction, however, should be raised as well. Yes, even though some argue that patenting a technology like the synthetic cell should not be possible, right now it is. The question arises: if the BaSyC members can claim IP-rights, *should* they claim such rights? Or should they revert from making such claims? If certain elements of the synthetic cell are considered patentable, then BaSyC-members should actively file a patent application. If they refrain to do so, and they are not able to keep their inventions a secret, then BaSyC risks losing legal control on how the inventions may be used or distributed.

In conclusion, yes: BaSyC's members could claim IP-rights, provided there is a clear understanding among the consortium's participants in which cases these rights will be invoked and in which cases licenses will be granted to others.[15] First and foremost, however, as part of this anticipation, the more fundamental question must be posed: is it morally commendable to claim ownership at all, or should we opt to make these technologies freely accessible? It is important to start asking this question now. Postponing may imply facing these developments unprepared, as happened in the CRISPR-Cas9 case.

7.2.3 In need of systemic changes?

Inventions concerning bottom-up synthetic biology may be of great societal interest. One could even argue that these developments are so new that we should consider changing the patent system, in order to ensure that bottom-up synthetic biology technology can be used by anyone. An IP-rights system especially created for bottom-up synthetic biology technology? Such an alternative system could draw inspiration from the plant variety rights system, which allows innovation based on the seeds created by others (Kamperman et al., 2016). When examining this, we should keep in mind that the current IP system is the result of decades of debate in which a certain balance has been struck between private and societal interests.

[15] Inspiration for such IP model may be drawn from the current CRISPR-Cas9 patent and license model, see: https://www.broadinstitute.org/partnerships/office-strategic-alliances-and-partnering/information-about-licensing-crispr-genome-edi.

7.3 How should the challenges be addressed?

The first two challenges (who can/should own what?) can be addressed by formulating a clear IP strategy and formulate agreements on IP rights where needed. The IP strategy should at least address the following questions and provide answers where appropriate:

- Under which circumstances will licenses be granted concerning the use of the synthetic cell's technology? For instance, is it needed to maintain an open-source, access and/or data licensing structure? If so, how can these open structures be inscribed in the socio-technological development of synthetic life in society?
- The synthetic cell in itself is a new frontier in science, and yet part of the long history of scientific developments since the early 2000s. BaSyC needs to use existing technologies from other parties. In some cases, their permission

(license) would be needed. How should BaSyC and its participants deal with IP-rights of other parties who are not directly involved in the consortium? This may pose a challenge when the right holders do not share the same goals and beliefs as the consortium concerning the distribution of technology.

The third challenge (systemic change) can be addressed by organizing debates around this topic, by engaging the general public, experts, and legislators. These debates can be conducted in parallel with the IP strategy track since changing the legal system can take years if not decades. These efforts should not be undertaken by BaSyC alone. There are plenty of other consortia or collaborative efforts that are facing the same issues.

8 Conclusions and recommendations

The ambition of BaSyC is to create a functioning, self-reproducing synthetic cell bottom-up, by integrating biomolecular building blocks. This Future Panel was established for the purpose of creating an agenda for future academic, public and political debate concerning synthetic cell research.

The design of this concluding chapter is as follows. First, the basic questions raised by BaSyC are summarised. Next, we summarise the key challenges the Future Panel encountered during its deliberations. Subsequently, we present a number of dilemmas that have to be addressed. Finally, we present the Future Panel's main recommendations for addressing the challenges and dealing with the dilemmas.

8.1 Guiding questions

Once heralded as a driver of progress and emancipation, technology now often emerges as a disruptive threat. This inevitably raises the question whether technology (or more generally technoscience) can change its profile once again and can contribute to a more just and sustainable global culture. What transformations are needed to create a society in which it is possible to organise the development of the synthetic cell in the context of a more responsible, just and sustainable development? How to involve public deliberation as an inherent dimension of the project's work?

Rather than framing the question in terms of possible benefits and risks involved for society, we want to ask the question how projects such as BaSyC can become part of a broader transition, which not only entails technological, but also societal and normative developments? Besides zooming in on specific aspects, we also want to consider the broader landscape, by asking how the synthetic cell may disrupt or contribute to sustainability as an open, responsive and deliberative process.

What is needed to make the building of a synthetic cell support a more fair and sustainable society and how to take this on board in the further development of the research agenda? What societal challenges and concerns are involved in (living with) synthetic cells? Which worldviews are implicitly represented by the scientists who contribute to the development of a synthetic cell? What kind of values and norms should guide the development of synthetic life? What kinds of governance arrangements need to be put in place to navigate synthetic cells through society? How will the synthetic cell transform the social world we live in?

8.2 Key challenges

In the course of our deliberations, the future panel concluded that multiple challenges are involved in this.

8.2.1 The challenge of novelty

It is a challenge to devise a methodology capable of anticipating public concerns in a domain where overt public attitudes as yet do not exist.

To be able to consider opportunities and concerns for a synthetic cell, it is important to understand what the synthetic cell is. The synthetic cell will be very different from the natural cell. Because the synthetic cell is obviously still a work in progress, these explorations and deliberations have to be conducted along the way, as a flanking pursuit, preferably in close interaction with the technoscientific work.

8.2.2 The challenge of addressing existing power structures

Developments in science and technology take shape in specific social, economic and political contexts that include specific power structures. As long as these power structures are not explicitly addressed, the development of a synthetic cell will inevitably reproduce and may even strengthen existing power inequalities between academics and society, large and small companies, and rich and poor countries.

Over the last decades public participation in science often emerged as a way to inform and engage members of the public on scientific developments. These efforts often had the explicit objective to convince the public of the relevance and necessity of a particular line of research and to strengthen public support. How to change this into a genuine dialogue, where a diversity of views, concerns, and intelligence of the public is not seen as a potential obstacle to innovation, but as an important source of insight, knowledge, and inspiration?

The conventional approach to public participation is supply-driven: starting point is not the societal challenges that need to be addressed, but the expected results and outcomes of technoscientific research (presented as a solution looking for a problem). Civil society neither has the power nor the resources to voice its multiple views. Therefore, an important challenge is to find new research methods and practices that make the future of synthetic cell research a participatory, inclusive and interactive process for various publics. Such a process should be preceded by a diagnostic of what is actually happening (socially, politically, economically, culturally) in the developing phase of synthetic cell technology.

Another challenge involves collaborations with commercial partners. Endeavours such as building a synthetic cell often entail a tension between short-term and long-term time scales. For academic scientists, it is clear that the building of a synthetic cell will be a matter of hard work and patience. Governments, industries and companies may in principle be interested in these developments, but the current technology readiness level (TRL) of the research is too low for making committed investments. Challenge: How to develop long-term partnerships between academia, industry, and society that are value-driven, impact-driven and responsive to societal questions and concerns?

Another challenge pertains to academia as such. It is desirable that the building of a synthetic cell requires trans-disciplinary collaboration, which means: involving voices from multiple disciplines, but from society as well. Although convergence has a long history and is increasingly stimulated, academia is still mainly organised along disciplinary lines. Organizing convergence is therefore necessary, but still challenging, because the issues and concepts with which scientists are involved from their discipline are clearly and structurally prominent for them, while issues and concepts of other disciplines form a kind of unstructured presence in the background (Elias, 1971).The challenge is to find a way to communicate in such a way that different meanings, interests and values become explicit and different perspectives are allowed to collide (Serres, 1982).

Governments stimulate technological innovation. At the same time, new technologies will need innovative governance structures. Will governments have attained the required vision and level of preparedness: how to timely anticipate the responsible governance and to identify preconditions for a societally and ethically sound embedding of synthetic cells in society?

8.2.3 The challenge of preparing the ground

In order to involve civil society and allow citizens to articulate their views and concerns, besides factual information, the synthetic cell has to be positioned in a proper context: how to develop a responsible narrative that allows the public to actively relate to these developments?

Sooner or later, to the extent that the synthetic cell becomes increasingly real, issues concerning intellectual property rights have to be addressed, in an anticipatory manner rather than post-hoc. The patentability of fundamental knowledge concerning life is not a given. Besides the challenge of clarifying who may and should own what in synthetic cell research, a more fundamental question arises. The discussion of whether we want to patent synthetic cells as such will inevitably arise, but the answer to this question is far from pre-determined.

We see the Future Panel as part of a broader movement, which moves away from technocratic approaches to biosafety, biosecurity and risk assessment, towards a more interactive, inclusive and responsible form of assessment and deliberation. The methodologies for such an approach are not ready made, but are rather being developed along the way.

8.2.4 The current challenge of the BaSyC programme

BaSyC's ambition to create an autonomous, self-reproducing synthetic cell bottom-up, i.e. by integrating molecular building blocks, is currently in a decisive, mid-project moment. From the start, the aim was to further our basic understanding of the structure and functioning of a living cell by technically reconstructing life-like systems. Thus, from the very start, BaSyC combined basic research with an engineering approach, combining scientific with technological ambitions. Now that researchers within BaSyC have gained more insight during the first stage of the project, they assume that the engineering dimension should be given more emphasis, in order to achieve a concrete result. At the same time, it is clear that there are still many unknowns, even unknown unknowns, so that a purely engineering approach will not be feasible. Moreover, although during the second stage BaSyC wants to work towards a concrete result (a convincing synthetic model of a living cell), it is nonetheless clear that the ideal of a fully autonomous cell will not be realised. Some external support will be required.

It seems perfect timing that precisely now the Future Panel is about to present its recommendations. For on a societal level there are many unknowns as well. The panel explored the possible implications of a synthetic cell, when the research is still in full swing. This means that the recommendations of the Future Panel can be incorporated into the design of the work during the upcoming years. Thus, a key challenge of the Future Panel is how to connect social, ethical, and science perspectives, and dilemmas, ambitions, and uncertainties related to the building of a synthetic cell.

8.3 Dilemma's

Many reasons have arisen, from different perspectives, for involving the general public, governments, industry, and NGOs in an anticipatory way. However, the Future Panel has identified fundamental dilemmas and tensions as well. Here is an incomplete overview:

The BaSyC project is curiosity-driven, aspiring to deepen our understanding of life. At the same time, our desire to know is driven by an impetus to control. It fosters admiration for the complexity of nature, but at the same time, technoscience aims to enhance our power over life.

> Dilemma 1: how to practice synthetic cell research as a dialogue with nature rather than as an appropriation and instrumentalization of the living cell?

Many aspects of synthetic cell research are as yet unknown.

> Dilemma 2: how to allow space for the unknown while at the same time opt for an anticipatory and imaginative approach to take the future social and ethical implications and concerns into account?

BaSyC combines fundamental (curiosity-driven) research with an engineering approach (understanding by making).

> Dilemma 3: to what extent is the wish to involve the public in fundamental research that may have important consequences for society as a whole at odds with the wish of scientists to freely carry out fundamental research? How to make research more inclusive by involving public, politics and policy in such a way that it is fostering and inspirational rather than detrimental for curiosity-driven experimentation and exploration?

As a rule, technology (application of what is known) can more easily be opened-up to societal input than basic science (discovery of what is unknown). Curiosity-driven science requires a great deal of specialism, thrives on serendipity and is not a democratic process.

> Dilemma 4: how to achieve convergence in science, involving multiple stakeholders and taking into account societal expectations and concerns without frustrating the process of discovery?

Deliberation requires a dialogue across disciplines, languages, and levels of information.

> Dilemma 5: how to combine different vocabularies, perspectives, socio-cultural and time horizons in a meaningful way?

Within science and technology, and in particular biotechnology, there has long been a discussion about how to deal with knowledge and intellectual property rights. Various public issues arise there.

> Dilemma 6: should life be considered patentable (or appropriate living technologies which are actually copied from nature) or should life be seen as a common heritage that belongs to everybody?

What about the need for various disciplines (e.g. software design and engineering) to embrace open-source innovation versus disciplines (e.g. molecular biology and biotechnology) that tend to protect inventions or other materials with intellectual property rights?

> Dilemma 7: how to deal with researchers who need to make their work openly accessible and companies, incubators, and organisations that want to protect their inventions?

Researchers, especially PhDs and post-docs, find themselves in a precarious position. First, they are under pressure to focus on and deliver scientific publications in their own field of expertise. And besides, they are encouraged to actively reflect on and engage with the potential societal impact of their work. Both tasks require a lot of time and effort and can be at the expense of each other if they are not properly coordinated. Also, the time-line of individual researchers (notably PhDs, both in terms of research and in terms of training components) is short-term (four or five years) compared to the long-term vision of synthetic cell research as such.

> Dilemma 8: how to balance conflicting expectations related to different time horizons?

8.4 Recommendations

The development of a synthetic cell that contributes to a more sustainable and fairer society requires scientific and technical innovation, but also societal involvement, governance, and regulation. This implies building bridges between science and society on multiple levels, fostering public awareness of the possibilities and impossibilities of synthetic cell research, combining a fascination for discovery with an understanding of how this type of research may contribute to a sustainable and inclusive future. Below, the Future Panel presents four recommendations for fostering a socially responsible development of the synthetic cell.

1. Ensure that the synthetic cell contributes to a fair and sustainable future

The synthetic cell may contribute to the development of technologies that are sustainable and bio-compatible rather than disruptive, provided this type of research becomes part of a broader development that involves cultural, political, and normative dimensions as well. This will result in research programmes and technologies that are value-driven and guided by respect for nature and people.

To foster sustainable synthetic cells, we need co-constructed narratives that allow us to explore how synthetic cells may contribute to a sustainable future. A comparative exploration of future scenarios will help us make informed decisions, by addressing scientific prospects as well as societal concerns, expectations and needs. Including for instance the question how synthetic cell research can contribute to achieving SDGs. To contribute to a more sustainable future, it is not enough to stimulate technoscientific innovation as such. Governments must simultaneously stimulate social innovation, and promote broad stakeholder involvement in synthetic cell research.

2. Organise participation of civil society in synthetic cell research

Establishing, regaining, and maintaining public trust in science requires genuine participation of civil society in scientific research in such a way that it may have important consequences for future developments in research and society.

In order to ensure that synthetic cell research contributes to a fair and sustainable society, an inclusive and participatory process of reflection is required, open to public intelligence, and sensitive to societal expectations and concerns. This requires innovative methods to engage the wisdom of the crowd. This can, for instance, be achieved by organising a platform for formal and informal communication, in which researchers and societal stakeholders participate right from the start of the research process. Meetings with societal stakeholders should be organised on relevant issues at different moments of the project. These meetings should be designed as in-between spaces in which different meanings, interests, and societal values come together and are made explicit. Such interspaces should provide safety for free talk and joint exploration as a process which leads to mutual understanding and careful decision-making about scientific and related social and ethical issues and developments. Use dialogue principles for conversations between stakeholders from different backgrounds. This implies that the right and the space to speak should be equal for scientists, governments, civil society, lawyers, human rights organizations, environmental activists, and so on.

3. Foster a socially responsive academic ecosystem

Rather than endorsing the status quo, synthetic cell research emphasises the importance of rethinking the university of the 21st century. Research and education must become more inclusive and interactive, bent on developing long-term partnerships with companies and governmental organisations, but first and foremost with society at large. Encouraging societal responsiveness and interaction requires adjustment of how science is organised and researchers are rewarded, for otherwise, it runs the risk of becoming an extra burden, rather than an integrated task.

This includes empowering researchers to engage with society. Societal reflection and interaction with society should be an integral part of academic research and education. Sustainable synthetic cell technology requires societal anticipation, imaginative deliberation, and mutual learning. Therefore, researchers must be empowered to engage with society in such a way that dialogue and interaction become an inherent part of their work, from design to publication. This includes an understanding of the power dynamics in the development of emerging technologies. Thus, the training of future scientists should include societal, governance, ethical aspects of research, as well as the art of public dialogue. Top-down control structures and approaches will estrange researchers and discourage rather than foster genuine interaction.

4. Design social governance experiments aimed at renewing the regulatory landscape for new biotechnologies, including the synthetic cell

Ensuring that the synthetic cell will be able to contribute to a more sustainable and socially equitable world requires an adequate social understanding of governance and regulatory systems. The current regulatory system is not prepared for that task, and needs to be developed parallel to synthetic cell research. This is in line with recent discussions within the European Commission, which called for a thorough revision of current regulations. These regulations are for a large part still informed by past debates concerning GMO debates and recombinant DNA research.

The current risk-based regulatory system has been developed over the last 40 years and has recently led to much discussion and dissatisfaction. We should start building a new system, which does not reproduce previous polemics. Besides looking at risks, a more comprehensive regulatory regime would integrate questions concerning sustainability, human rights, ethics and societal desirability. Governance experiments co-designed with societal actors are needed to gain insight into the contours of such a new regulatory landscape on synthetic biology or new biotechnologies, including the synthetic cell.

In summary, the panel advises that social and ethical issues should be addressed proactively and throughout the research process.

The development of synthetic cell research raises multiple social and ethical issues. These issues vary from questions about the technical feasibility of mimicking life, to questions about safety, intellectual property rights, and data management issues, e.g. data sharing and open science. Synthetic cell research also raises multiple governance questions, such as how to align synthetic cell technology with societal needs, how to ensure that the government has the capacity to properly embed emerging technology in society, and how to organise the interaction between science and society. These types of social, legal, and ethical issue should be addressed proactively and throughout the development process.

Glossary

Artificial cell	An engineered entity that mimics one or more functions of a biological cell. An artificial cell uses a repertoire of naturally existing biomolecules, complemented with non-natural components.
Biomimetics / Biomimicry	The design and production of materials, structures, and systems that are modelled on biological entities and processes, seeking sustainable solutions by emulating nature’s tools and strategies. Biomimetic approaches are more biocompatible, sustainable and nature-like than previous technologies. Rather than seeing nature as a resource for raw materials to be transformed into sophisticated products and devices by human technology, biomimetics mimic the technologies which evolved in nature.
Biosafety	Containment principles, technologies and practices that are implemented to prevent unintentional exposure to pathogens and toxins, or their accidental release that could lead to large-scale loss of biological integrity, focusing both on ecology, animal and human health. Preventive mechanisms include the development of biosafety guidelines as well as the conduction of regular reviews of biosafety in laboratory settings.
Biosecurity	Institutional and personal security measures designed to prevent the loss, theft, misuse, diversion or intentional release of pathogens and toxins.
Bottom-up approach	In the bottom-up (or constructive) synthetic biology approach, cells are constructed from molecular components, which can be natural or non-natural. The bottom-up approach assembles biomolecular building blocks with the aim of creating autonomous self-sustaining systems that can grow and replicate, exploring the boundaries zones of physics, chemistry and biology.
Civil society	The aggregate of non-governmental organizations and institutions that give voice to the interests and will of citizens and their organizations, independent from government and companies, and endorsing democratic principles such as freedom of speech, freedom of assembly and civic values.
Dual use	Indicates that, in principle, technologies can be used to satisfy more than one goal at any given time, for instance in

	the sense that they can be used both for both civilian and military purposes (e.g. nuclear energy). More generally, dual use indicates that technologies can be used for multiple purposes: intended and unintended, moral and immoral, beneficial and nefarious.
Globalisation	The processes of interaction and integration among people, companies, and governments worldwide. Globalization has accelerated due to advances in transportation and communication technologies. This increase in global interactions has caused a growth in international trade and stimulated the rapid spread of ideas, beliefs, cultural trends and technologies.
Governance	All processes of governing, not only by the government of a state, but also by other institutions and organisations, via legislature, the production and reinforcement of laws, norms, codes of conduct, decision-making procedures, formal and informal leadership practices, etc. In short: all the processes that exist within and between formal institutions to guide and manage them.
Innovation	The introduction of new technological, organisational or social ideas, products, tools or methods that prove successful in practice, notably in areas where they have not been used before. Carriers of innovation may be governments, enterprises, universities and non-governmental organisations.
Intellectual property rights	Protection of, for example, drawn up ideas or techniques developed by inventors, designers and authors, for instance by means of copyright or patents.
Life	Life is what distinguishes living (biological) from non-living entities. Although the concept is hard to define, important characteristics are confinement, metabolism, homeostasis, growth, adaptation and reproduction.
Minimal cell	A minimal cell is a cell whose genome has been reduced by deleting as many genes as possible, yet still being able to grow and reproduce. This should ultimately lead to a cell with only essential genes and more room for introducing new functionalities.
Protocell	A protocell is any model that involves a self-assembled compartment allowing chemical processes to take place within, aimed at explaining the functioning of more complex biological systems.

Synthetic cell	A synthetic cell is built from molecular components, provided to us by evolution or recombinant biology techniques, to provide mechanistic insight in the principles by which modern cellular life operates and to harness this for new functionalities and production of useful compounds.
Sustainability	Sustainability refers to the capacity for planet Earth's global biosphere and human civilization to co-exist by containing change and maintaining a balanced environment, in which the exploitation of resources and the orientation of technological development become embedded rather than disruptive. Besides an environmental (ecological) dimension, there are economic, technical, social, cultural and political dimensions to sustainability.
Sustainable development goals	A collection of 17 interlinked global goals designed to provide a blueprint to achieve a better and more sustainable future. The SDGs were determined in 2015 by the United Nations General Assembly and are intended to be achieved by the year 2030. Increasingly, universities and companies are using SDGs as a benchmark to assess and compare their societal impact.
Technoscience	While we usually distinguish between science (basic research, curiosity-driven research) and technology (application-driven research), technoscience emphasises the technicity of research, e.g. the impact of emerging and enabling technologies on how research is conducted (for instance: the impact of high-throughput screening technologies in genomics and life sciences research; the large-scale genome sequencing for medical discoveries).
Top-down approach	In the top-down approach, living cells are genetically and metabolically engineered with the aim to impart new functions, taking advantage of large-scale recombinant DNA technology. This can involve the engineering of minimal cells and the introduction of synthetic genomes.

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Appendix 1: the Future Panel on Synthetic Life

Fourteen experts accepted the invitation to be part of the Future Panel on Synthetic Life and participated during the panel meetings. A short resume of each panel member can be found below in alphabetical order.

Noelle Aarts
Noelle Aarts is a professor Socio-Ecological Interactions and director of the Institute for Science in Society (ISiS) at Radboud University in Nijmegen. Her research focusses on interactional processes for creating space for change towards socio-ecological transformations, developing insights into the interplay between everyday conversations and the wider structures and developments in society. ORCID ID: 0000-0001-5134-4004.

Saurabh Arora
Saurabh Arora works on the politics of sustainability at the Science Policy Research Unit of the University of Sussex (UK). ORCID ID: 0000-0003-1073-5564.

Roel Bovenberg
Roel Bovenberg is Senior Science Fellow Biotechnology at Royal DSM and honorary professor Synthetic Biology and Cell Engineering at the University of Groningen, with a special interest in the design and evolution of microbes for the fermentative production of bioproducts.

Marileen Dogterom
Marileen Dogterom is a university professor at the TU Delft and Medical Delta professor at Leiden University. She is internationally renowned expert in experimental cell biophysics with a pioneering track record in biophysical research of the microtubule cytoskeleton. Over the years, her group has systematically worked on increasing functional biological complexity in reconstitution experiments, which paved the way for her current and future ambition to build synthetic cells. She published ~100 papers in high-ranking physics and biology journals. Dogterom actively and frequently collaborates with leading national and international researchers in both physics and biology. Since 2017, she leads the Dutch Consortium BaSyC (Building a Synthetic Cell) and is one of the initiators of the European Synthetic Cell Initiative. ORCID ID: 0000-0002-8803-5261.

Joost Gerritsen
Joost Gerritsen is a privacy and data lawyer at Legal Beetle, The Netherlands. His legal expertise is primarily focused on the legal aspects of (emerging) technologies, such as AI, robotics and big data.

Phil Macnaghten
Phil Macnaghten is a Professor in the Knowledge, Technology and Innovation (KTI) group at Wageningen University. His PhD is from Exeter and he has held appointments at Lancaster, Durham and Campinas before joining Wageningen in 2015. His research background is in science and technology studies (STS) and sociology. His current research focus is on responsible innovation, gene editing and the governance of science.

Bert Poolman
Bert Poolman is a biochemist that is active in the field of synthetic biology, in particular the construction from molecular building blocks of complex cell-like systems. His research focuses on three central questions: what tasks should a living cell minimally perform and how this can be accomplished with a minimal set of components? How do molecules permeate biological membranes? How can one control the volume and physicochemistry of the cell? ORCID ID: 0000-0002-1455-531X

Zoë Robaey
Zoë Robaey is Assistant Professor in Ethics of Technology at the Philosophy Group of Wageningen University. Her work investigates moral responsibility under conditions of uncertainty in the field of biotechnology in agriculture. In 2019, she received a VENI grant from the Dutch Research Organization for her research on the virtues for innovation in practice. In this work, she combines conceptual and empirical investigations to develop a notion of responsibility under uncertainty that builds on the practices of both scientists and farmers. ORCID ID: 0000-0002-0501-2030

Steen Rasmussen
Steen Rasmussen, professor in physics and center director, works on creating minimal life from nonliving materials, as well as on how new technologies change what it means to be human. He spent 20 years at Los Alamos National Laboratory, USA. In Denmark he founded the FLinT and ISSP centers in 2008 and 2009 respectively. He co-founded the European Center for Living Technology in Venice, Italy, 2004, and he has been part of the Santa Fe Institute, USA, for 33 years. He has consulted on science and technology issues for the European Commission, the Danish Parliament, the German Bundestag, the US Congress, as well as private companies. ORCID ID: 0000-0002-3336-843X.

Guido Ruivenkamp
Emeritus Professor Guido Ruivenkamp investigates the interaction of societal transformations and biotech/genomics developments. He focuses on disconnecting contemporary agri/food biotech products from the asymmetric power relations inscribed in those products, aiming instead at a redesign that empowers communities striving for a more equitable and sustainable world. His critical re-constructivist approach to biopolitics emphasises commons-based knowledge practices.

Esther Thole
Esther Thole is a freelance science journalist and moderator based in The Netherlands and author of the 2018 book *Makers van leven: hoe wetenschappers leven bouwen in het lab* (*Making life: how scientists build life in the lab*). She mainly writes about the interface between chemistry and (synthetic) biology.

Georg Tremmel
Georg Tremmel has a background in Media Art and Bioinformatics, he is currently pursuing a PhD in Artistic Research at the University of Applied Arts in Vienna. His artistic work focuses on the ethical, legal and societal implications of emerging biotechnologies and the relationships between human and non-human agencies.
ORCID ID: 0000-0001-5706-8442

Cécile van der Vlugt
Cécile van der Vlugt is appointed as senior risk assessor at the National Institute for Public Health and the Environment (RIVM). In that function she works on risk assessment and risk management issues concerning genetically modified organisms applied in contained use. As an expert on new biotechnological developments she advises the Dutch Ministry of Infrastructure and Water Management on emerging risks and safety measures of these new developments.

Tom Wakeford
Tom Wakeford works at ETC Group, which supports social movements to steer technologies towards the common good. ORCID ID: 0000-0002-4721-3658

Please note, two members of the Future Panel, Arora and Wakeford, contributed to the activities of the Future Panel, but disagreed with the way their contributions were combined with those of others in the final position paper to the extent that they asked to withdraw their names from the list of co-authors. This request was accepted. In Arora’s view, the paper's final version lacks substantive engagement with issues of pluralism and power, particularly from Southern and decolonial perspectives. Wakeford experienced a culture of scientism during the Panel meetings, and a lack of acknowledgement of people's right to free, prior and informed consent.

Appendix 2: the project team

The project team consists of 5 people from the Rathenau Instituut and Radboud University. A short resume of each team member can be found below in alphabetical order.

Kyra Delsing
Kyra Delsing works as a researcher at the Rathenau Instituut. She has a background in Interdisciplinary Social Sciences (Utrecht University) and New Media and Digital Culture (University of Amsterdam). Within the Rathenau Institute she specialises in the societal aspects of biotechnology and leads the T-TRIPP (Tools for Translation of Risk Research into Policies and Practices) project on safety in biotechnology and the BaSyC project on the synthetic cell. She also co-developed a podcast series on the synthetic cell called *Herschept* (or Recreated in English).

Rinie van Est
Rinie van Est works as a research coordinator for the Rathenau Instituut. He has a background in physics, public administration and political science and is a global expert in technology assessment, governance and public participation. He is concerned with the politics of innovation: from augmented reality and synthetic cells to energy technologies. He is professor of Technology Assessment and Governance at Eindhoven University of Technology. ORCID ID: 0000-0002-3990-3042.

Bettina Graupe
Bettina Graupe is a PhD candidate in the BaSyC project at the Institute for Science in Society (Radboud University) where her research is dedicated to the societal impact of synthetic cells. Bettina obtained her BSc and MSc in Medical Biology at the Radboud University with a Master's specialisation in Science and Society focussing on the responsible innovation of synthetic biology.

Michelle Habets
Michelle Habets' research focuses on the socially relevant aspects of various developments in the field of synthetic biology, agricultural biotechnology, and medical biotechnology. She has been working at the Rathenau Instituut since 2017. Michelle studied biology, philosophy, and Healthcare Ethics and Law. She received a PhD in evolutionary biology at the Lab of Genetics at Wageningen University, and a PhD in medical ethics at the University Medical Center Utrecht.

Hub Zwart

Hub Zwart (1960) studied philosophy and psychology at Radboud University and defended his thesis in 1993 (cum laude). In 2000 he became full Professor of Philosophy at the Faculty of Science at Raboud University. In 2018 he was appointed as Dean of Erasmus School of Philosophy (Erasmus University Rotterdam). He is editor-in-chief of the Library for Ethics and Applied Philosophy (Springer). His research develops a philosophical (dialectical) assessment of contemporary technoscience. Special attention is devoted to the dialectical relationship between science and genres of the imagination (drama, poetry, cinema, novels, music). He published 20 books (7 in English), 150 international peer-reviewed articles as first or single author and presented more than 200 international academic lectures, most of them invited. His open-access monograph entitled Continental Philosophy of Technoscience has just been published (Springer; 2021). ORCID ID: 0000-0001-8846-5213.

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