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Why the Synthetic Cell Needs Democratic Governance

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Engineering synthetic cells from the bottom up is expected to revolutionize biotechnology. How can synthetic cells support societal transitions necessary to tackle our current global challenges in a socially equitable and sustainable manner? To answer this question, we need to assess socioeconomic considerations and engage in early constructive public dialogue.

Half a century ago, Hannah Arendt warned that our technologies might leave us unable to think and speak about the things we are nevertheless able to do. The engineering of an autonomous, self-reproducing synthetic cell by integrating molecular building blocks would fulfill this prophecy. It would require us to rethink some of the most fundamental categories of our thinking, such as life and matter, technology, and biology. A synthetic cell will be all of those, a living technology. This blurring of boundaries may in turn change our views and values towards life. How this will influence our relationships, our social practices and production methods, and our attitude towards life is, to a large extent, unpredictable but too important not to anticipate.

From Organic Molecules to Synthetic Cells

Ever since the acceptance of Darwin's theory of natural selection, biologists have been interested in how life emerged on earth. Following the famous Miller–Urey experiment in the 1950s [1] that demonstrated the formation of common organic molecules from a chemical environment (primordial soup), simple structures that resembled life have been constructed in the laboratory [2]. Modern studies of simple protocells started in the 1980s in the context of origin-of-life research and artificial life, but advances in synthetic biology at the beginning of the twenty-first century, along with developments in genomics, computing, materials science, and nanotechnology, accelerated the pace of synthetic cell research. Recently, a new sense of optimism has emerged in the field, which is reflected in an increase in publications and reports on using engineering principles to reconstruct biological processes from the bottom up [3] as well as in the convergence of an international scientific community [4]. In October 2019, for instance, various European research networks joined the 'Syncell2019: Defining the Challenges' meeting in Madrid, a symposium organized to develop a European roadmap towards building a synthetic cell.

Promises and Caution

Currently, this converging research field of engineering synthetic cells is in the midst of creating visions, expectations, and imaginative speculation in order to attract international support and funding. Most scientists involved in this field of research position it as being driven by curiosity with the goal of understanding life. Others, however, emphasize the enormous potential of so-called living technologies, as they possess properties such as autonomy, sustainability, self-repair, and self-replication. Indeed, funding agencies are interested in economic and societal benefits that this bottom-up research itself will provide, including valuable information and data, patents, spin-off technologies, and improved research tools. Revolutionizing medicine through drug delivery systems [5] and sustainable solutions to address the energy problem and the environmental crisis are mentioned as possible outcomes of synthetic cell research [4,6].

Engineering synthetic cells from the bottom up, like creating minimal cells in the top-down synthetic biology approach, entails stripping down the complexity of the cell to gain technical control over the building blocks of life. It is exactly this ambition to control nature via objectification, compartmentalization, and commodification that others caution against [7].

Biosafety Concerns

Similar to Faust, who in the scene entitled 'Laboratory' (Part II Act II Scene 2; 6819 ff.) stressed that the fragile and vulnerable homunculus created by his disciple Wagner could only survive inside his tube, synthetic cell researchers believe that the system they are creating will not be able to survive outside controlled laboratory environments [8]. Moreover, because of the reduced complexity and the increased control over bottom-up synthetic cells when compared to micro-organisms, most scientists we have interviewed believe their work carries fewer risks than genetic engineering. Furthermore, biological control mechanisms can be incorporated into synthetic cells to make them safer, such as induced lethality and gene flow prevention. However, even the simplest forms of life have unpredictable, emergent properties, and in the long run, these synthetic cells could pose potential danger because of their ability to proliferate and evolve [6].

At the moment, several major gaps in knowledge exist, limiting the ability to perform a reliable environmental risk assessment for introduction into the environment [9]. It is therefore important that, parallel to the engineering effort to build a synthetic cell, integrated risk research takes place to gain knowledge on the evolutionary and ecological consequences of both current, non-living protocells and future, living, autonomous synthetic cells.

How future synthetic cells will be regulated and governed is complicated by the fact that there is no common idea and no clear definition of what a synthetic cell is, as became evident during discussions at the European SynCell2019 symposium; diverging views exist on whether synthetic cells are alive, whether they will be able to replicate, and whether they are able to evolve. It is likely that many different synthetic cells will be developed.

Limits of Current Innovation Policy to Maximize Social Value

Whether bottom-up synthetic biology and the engineering of a synthetic cell will indeed provide us with socially beneficial products will depend on whether it will be possible to align scientific and commercial interests with the public good. Science and innovation policy often start from the naïve belief that innovation will necessarily contribute to economic growth and therefore the growth of prosperity and well-being [10,11]. But, even if science and innovation policy result in economic growth, an increase in well-being does not automatically follow. Indeed, our current pattern of economic growth has led to rising inequalities and severe environmental degradation 'undermining our capacity to maintain current standards of living' [11]. We need to analyze how a new technology can benefit society and not assume that benefits will be demonstrated by market success.

The Need for Democratic Governance

Technologies are intrinsically political, with certain interest groups having a higher influence on the development of technologies, shaping the technology within the existing context of asymmetrical power relations [12]. In our current society, owning information constitutes having power; see, for example, the economic and political power of big tech companies such as Google and Facebook in the current internet age. Reformulating life as chemical and physical information inevitably raises the question who is going to control this 'vital' information? Despite the political choices in designing technologies, public intervention is still limited compared to a steadily growing role of experts and technocracy. At the same time, not surprisingly, promising innovations, predominantly those shaped by the technological paradigm of biotechnology, have met with considerable social and political resistance, especially genetically modified foods.

In general, public opposition and concerns over technological innovation are often dismissed as ignorant and emotional, resulting in the belief that the public needs to be educated in science [13]. The valid worry of the public about the lack of legitimate democratic control over science and the fact that science has become the culture of policy is overlooked. It is therefore important that knowledge deficits on the part of natural scientists are addressed; understanding science is not itself a sufficient basis for knowing how to best govern it. Yet, as Jasanoff writes: not often calls run the other, that scientists need to be educated in democratic theory [7].

At the onset of this new wave of biotechnology, we can learn from past 'mistakes' in the biotechnology field and attempt to address the mentioned issues with the public early on to develop a technology guided by values such as equity, solidarity, sustainability [10], and well-being. It is important that we do not delay analyzing to what extent synthetic cells can become catalysts for supporting societal transformations towards socially equitable and sustainable developments. In Box 1, we suggest three actions that are vital to initiate this analysis.

Building Our Future Together

In various research groups, ethical, societal, and philosophical aspects of synthetic cells are addressed by social scientists (Box 2). Also, within the Dutch Building-a-Cell (BaSyC) consortium, the societal significance of building synthetic cells is examined in order to discuss this foundational technology and its possibly disruptive impact on society. The involvement and knowledge of natural scientists is important but not sufficient; we need a broader range of perspectives. To convincingly explore the future, we must crowdsource the insights and experiences of many voices, which so far have not been involved in the synthetic cell endeavor at all. For this reason, we initiated a Future Panel on Synthetic Life, consisting of natural and societal scientists as well as artists and experts in policymaking and media, to discuss challenges, priorities, and public values necessary for value-driven innovation. What values and interests are currently guiding these evolving research practices? What are the conditions under which building a synthetic cell has value for society, and how plausible are these conditions in real-world circumstances? One lesson we have learned from previous

Box 1. Three Important Steps Towards the Future

We advocate that the following three actions should be taken without delay:

(i) Give social science and humanities research an integral place in current and future synthetic cell research so as to increase the social–ethical reflexivity of scientists and better integrate ethical and socioeconomic concerns into the practices and strategy of scientists and companies.
(ii) Initiate a broad, international, constructive public dialogue on how synthetic cell technology can be developed in a socially responsible manner.
(iii) Engage scientific, corporate, civil society, public, and government actors in this international dialogue.

We applaud the significant efforts the international scientific community has made to include social science and humanities in synthetic cell research programs. The Future Panel on Synthetic Life is set up as a social laboratory that will give us the rough contours of a social agenda for the international dialogue on current and future synthetic cell research. The international dialogue will in turn provide insight into the roles and responsibilities of government, industry, science, and society and will define the important challenges, priorities, and public values necessary for value-driven development of synthetic cells.

Box 2. Worldwide Efforts to Engineer Synthetic Cells

Worldwide, there are various consortia and research institutions involved in synthetic cell research and its ethical, sociological, and philosophical aspects. Besides the Dutch BaSyC program, the German MaxSynBio program and BrissynBio research center of the University of Bristol have focused their research in part towards engineering a synthetic cell. In the USA, where the top-down synthetic biology approach has been predominantly present, the bottom-up approach has received an increasing amount of attention from scientists and funders. An informal network 'Build-a-cell' supports open collaboration among scientists. In addition, in 2019, the National Science Foundation invested $36 million in the first projects under its Understanding the Rules of Life portfolio. These awards are aimed at accelerating development in building a synthetic cell and epigenetics. In Israel and Japan, researchers have been working towards building a synthetic cell for many years, although we are not aware of any large consortia here. Indeed, many scientists are, or can be seen as, working under the umbrella of creating a synthetic cell, because it encompasses integrating many different aspects of cells, such as compartmentalization, replication, and metabolism.

technoscientific endeavors is that these questions have to be taken into consideration from the very outset.

Launching the Future Panel is a first step to timely engage with social and ethical issues and to stimulate wider societal involvement so as to develop the synthetic cell in a socially responsive and equitable form.

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Author Contributions

M.G.J.L.H., H.A.E.Z., and R.v.E. jointly planned the paper. M.G.J.L.H. took the lead on writing the paper, and H.A.E.Z. and R.v.E. substantially revised the paper.

Disclaimer Statement

The authors declare no competing interest.

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