**FET Consultation - template FET Flagships**

*-* ***please limit proposals to at most five pages*** *-*

**About you**

* What is your background? Are you submitting this proposal as an individual, or do you represent a community or institution?

I’m a professor in systems and cell biophysics, and Chair of the Department of Bionanoscience, Faculty of Applied Sciences at the Technical University Delft. I submit this proposal on behalf of my Department, as one of the pioneers in the reconstitution of minimal biological systems in the Netherlands and Europe, and as the leader of a large multi-disciplinary Dutch initiative to Build a Synthetic Cell (the BaSyC consortium), that includes researchers with backgrounds in physics, chemistry, modelling, and microbiology from the Universities of Groningen, Nijmegen, Wageningen, VU Amsterdam, Delft, and the NWO-FOM Institute AMOLF in Amsterdam. I’m also one of three researchers who recently took the initiative to gather a group of top-scientist to formulate a joint roadmap towards the bottom-up engineering of minimal life.

**What is the challenge and the vision?**

* What is the grand S&T challenge and its underlying vision and what are the main objectives your initiative would address? Why is this a grand S&T challenge and what makes it a "game-changer"?

**The challenge: Building a Synthetic Cell**

Building a synthetic cell is one of *the* grand scientific and intellectual challenges of the 21st century. While we now have extensive knowledge about the molecular building blocks that form the basis of modern life, we currently *do not understand* how these building blocks collectively operate to define life. Cellular life, which provides the fundament of most organisms, appears to be the result of a collection of highly controlled, energy consuming, dynamic self-assembly and self-organization processes that lead to autonomous entities that can reproduce, transfer information, interact, and evolve.

Building a synthetic cell is the most fundamental approach towards elucidating the cell’s intricate working and the basic life-defining principles. Truly understanding life will bring huge intellectual, scientific, and technological rewards. At the same time it will raise fascinating philosophical and ethical questions, as it impacts on our fundamental understanding of ‘who we are’.

* What are the main technologies, including digital technologies[[1]](#footnote-1), which your initiative will advance?

The path towards a synthetic cell involves the development of numerous methods and tools with important spin-off possibilities in the form of test beds for synthetic biology applications, advanced drug delivery systems, drug-screening methods, and bionanodevices for multiplex detection of molecules. Examples include:

1. The development of a robust cell-free expression system with precisely tunable protein production rates. This could become an in vitro ‘test bed’ for complex genetic networks with applications in synthetic biology (i.e. engineering of bacteria or yeast to produce valuable molecules). Ultimately, we could even envision a self-synthesizing biocatalyst with engineered control over its growth and biosynthesis. Whereas current techniques focus on the use of genetically modified organisms, the synthetic cell would add a new chapter to these developments, opening up new opportunities for knowledge utilization and with targeted functionality only to the desired characteristics. In this way, it would also lead to the development of personalized, protein-based medicines – low scale, with high efficiency and tunability.

2. Liposomes are recognized as important vehicles for programmed delivery of drugs to specific locations in the human body. The generic use of liposomes is currently prohibited due to (in) stability of the membrane scaffold, unspecific targeting of the vesicles to body tissue, uncontrolled release of (pro) drugs or other cargo at the site of disease, and immunogenicity and toxicity of the component molecules. The biochemistry and microfluidics technology developed with the synthetic cell will allow more advanced drug delivery systems to be developed, for instance pro-drug activation in the vesicles in the context anticancer drugs en route to the malignant tissue and controlled release via functionalized membrane components.

3. Equally important will be the development of confined systems for DNA transcription and protein synthesis in the high-throughput screening of novel antibiotics and drugs, e.g. through protein-synthesizing liposomes immobilized in a microfluidic-based device. In addition, the analytic tools originating from the BaSyC programme may find application in the multiplex detection of specific analytes in bionanodevices.

These are merely a few examples. The lipid-based reactor in which sustained cell-free protein synthesis can be achieved is an enabling ‘device’. Unanticipated applications will surface once such a synthetic cell is realized and next-generation synthetic cells will emerge or evolve from the initial prototypes. Designer synthetic cell systems undoubtedly will find their use as mini-reactors in biotechnology (fine chemicals, bioactive compounds, complex chirality, platform chemicals), nanotechnology (devices, sensors), biorefinery (materials, platform chemicals, polymers), environmental remediation (water, soil, mineral recovery), and health (e.g. drug delivery, biosensors).

**Why is it good for Europe?**

* Is your initiative relevant for the European industry and what is its innovation potential that would benefit Europe's economy and/or society?

Clearly, building a Synthetic Cell and the fundamental insights that will come with this achievement will have impact beyond scientific discoveries. We foresee impact on a broad reach of industries in the areas of Health, Food, and (Bio-based) Materials.

Industry is already demonstrating awareness of potential applications of synthetic biology. Examples of companies linked to synthetic biology research in the Netherlands include DSM, Crucell, and Corbion. Additionally, the potential impact on biomaterial applications has raised the interest of companies in food and regenerative medicine, including Unilever and Fibriant. Many other companies may be named in Europe and worldwide, and we are confident that the interest of companies will grow even more as the realization of a synthetic cell comes closer.

* Are there existing international research initiatives linked to this proposal? How would this initiative position Europe with respect to other regions in the world?

There are several national and European initiatives relevant to this topic (see below). By joining these activities in a coordinated program, Europe has the opportunity to become leading in this effort, and complementary to strong research initiative in the US and Japan.

**What would it take to do it?**

* What is the scale of the effort required to reach the objectives and how long will it take to do so?

The time-scale to reach the final objectives is 10-20 years. It would require a large-scale effort that unites the experimental research activities of various disciplines, physics, chemistry, synthetic biology (and brings in additional expertise from engineering and modelling) and focus the scattered networks in Europe that are currently working on different aspects of minimal life rather independently (see below).

* Why is Europe well positioned in terms of skills/expertise and capabilities, including industrial capabilities, to address the challenge and exploit the results? Which are the research communities to be involved?

There is a strong presence of bottom-up approaches to biology in the physics and chemistry research community in Europa, more so than in the US, where traditional cell biology and top-down approaches to minimal life (e.g. the Venter group) are very strong. Pharmaceutical and food industries are well-represented in Europe (including Switzerland) to benefit from the generated knowledge in this initiative.

* Are there existing national or European research initiatives linked to this proposal? What is the added value for such an effort at the European level?

Recently a group of European top researchers from the physics and chemistry communities have taken the initiative to establish a dedicated European community with a common ambition to engineer synthetic life using a bottom-up approach. This initiative for the moment includes researchers from a multi-disciplinary consortium in the Netherlands, researchers supported by the MaxSynBio programma on synthetic biology that was initiated in Germany by the Max Planck Gesellshaft in 2013, as well as researchers from other European countries (most notably the UK). The scope of this consortium includes efforts that focus on the construction of synthetic cells based on natural components, artificial cells based on a combination of natural and non-natural components, as well protocells that aim to elucidate the chemistry that was relevant for the first form of life on earth. Jointly, we aim to provide an alternative bottom-up route to synthetic life, complementary to the top-down approach that aims to strip down the genome of existing life to a minimal size. A large European effort should furthermore benefit from strong research groups in Scandinavia, Italy, and France who are active in these topics.

The following existing national European synthetic biology initiatives (not-exhaustive) are relevant to this initiative:

National:

* BaSyC Consortium in the Netherlands.
* MaxSynBio program started in 2013 by the MPG in Germany.
* BriSynBio research centre in UK.
* OLIM in Munchen, <http://www.biosystems.physik.lmu.de/olim/>.

European:

* The ERASynBio initiative, <https://www.erasynbio.eu>.
* The COST action Emergence and Evolution of Complex Chemical Systems, <http://www.systemschemistry.com/cm1304/>

|  |
| --- |
| ***How to submit your idea to our "Digital4Science" Platform?*** *[Register to our "DIgital4Science Platform](https://ec.europa.eu/futurium/en/user/register?flavour=digital4science" \t "_blank) and* [*Submit your idea (completed template)*](https://ec.europa.eu/futurium/en/digital4science/add/document?field_tags=1035)  *Once your idea is submitted we will publish it on our [Digital4Science discussion forum](https://ec.europa.eu/futurium/en/digital4science/discussions/FET%20flagships" \t "_blank) and it will be open for comments.* |

1. See in particular the EU's Digital Single Market Strategy (<http://ec.europa.eu/atwork/pdf/cwp_2016_en.pdf>)?  [↑](#footnote-ref-1)