INTERVIEW: SYNTHETIC BIOLOGY

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What does the term 'synthetic biology' mean to you? How is it different from 'traditional' bio-engineering?

Markus: Of all the definitions out there I prefer to use the one elaborated by the EC SCENIHR working group on synthetic biology[1] in 2014: „*Synthetic biology is the application of science, technology and engineering to facilitate and accelerate the design, manufacture and/or modification of genetic materials in living organisms.*"

The advantage of this definition is that it is broad enough to encompass the different activities under the label "synthetic biology", such as

- Genetic parts, devices and systems,
- Minimal cells and designer chassis
- Protocells
- Xenobiology
- DNA synthesis and genome editing

Also the term „genetic" is not strictly limited to information encoded on the DNA but includes all information carrying molecular systems that compose the organism.

If you look at the way how a genetically modified organism (GMO) is defined in Europe, then there is (in most cases) no qualitative difference to traditional genetic engineering. In Europe a GMO is an organism that has been modified by introducing genetic elements from outside the organism, a definition that applies also to synthetic biology. The major difference lies in the attempt to make this process more accurate, by better understanding biological systems, by using standardized elements that are modular and well described. The whole process of modifying an organism is said to be more precise, faster and more predictable. Altogether synthetic biology is different to traditional genetic engineering on a quantitative but not so much on a qualitative level. See figure (SCENIHR 2014)

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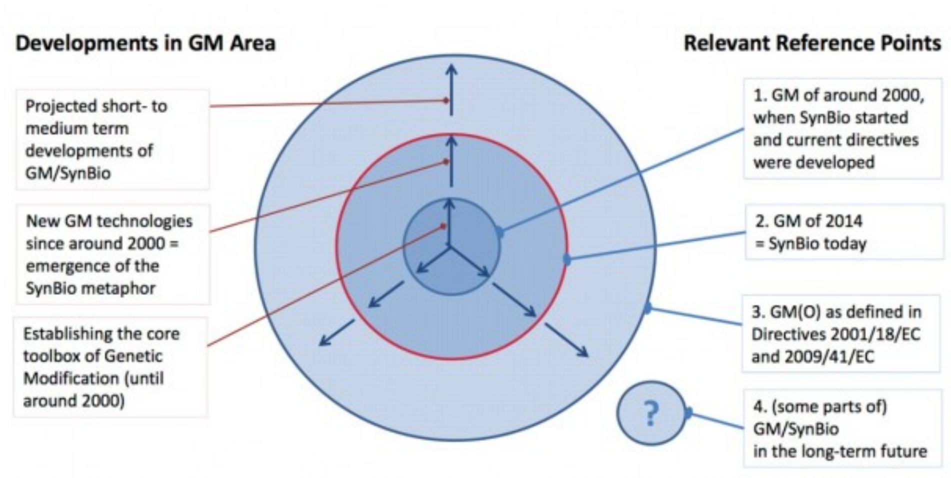


Oron: As an artist I am more interested in the mindsets that drive our relationship to life, more than the actual technology that enables it. So I think that SB represent a significant moment, in the sense that the mindset that drives it is the engineering paradigm; a mindset of control. As an umbrella term that covers many modes of intervention into, and simulation of, living processes, it seems that the only unifying and "revolutionary" aspect of SB (beside it being a hot catchphrase for funding agencies) is that it is mainly driven by engineers. This is why I find the field so interesting as there is an inherent tension between the "irrational" ever-changing messiness of life, and the SB rhetoric; such as that of optimising and standardisation.

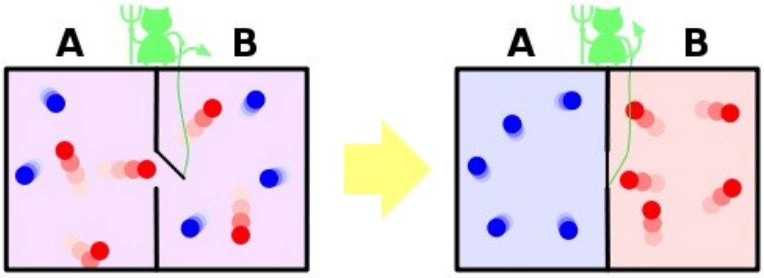
Another interesting aspect of SB is that it is one of a very few technological fields that seems to employ PR strategies form it's very inception to try and engineer public acceptance for its yet unknown outcomes, this is a reason why there seems to be some funding for artists and designers to work in this field.

In his 1944 publication 'what is life', Erwin Schrödinger asked "how can the events in space and time which take place within the spatial boundary of a living organism be accounted for by physics and chemistry?" with genetic engineering we began to be able to answer his question and even alter its parameters. with the advent of synthetic biology how might we revisit Schrödinger's question?

Markus: Fellow Austrian Erwin Schrödinger looked at biology from the point of view of physics, wondering if life does obey the laws of thermodynamics. Schrödinger identified/defined life as being able to apparently counteract the second law of thermodynamics, that relates to the ever (statistic) increase of entropy (disorder) in a closed system.

Living organisms are, however, not closed systems. Even the smallest entities of life, a single cell organism, is an enclosed space but its boundaries are semi-permeable membranes, meaning that it can exchange chemicals (and radiation) from and to the environment. The "decision" of the cell to take up nutrients, protons etc. from the environment is mediated by molecular pumps, channels, and receptors that try to be very selective in what they allow into the cell and what not. Spatial boundary and selective exchange with the environment are among the reasons the cell can, for a certain time, keep up a higher order than in the non-living world. A certain class of antibiotics, for example, punches wholes into the cell membrane thus allowing for an indiscriminate flow between the in- and outside of the cell, which leads to the immediate death.

Another famous physicist, James C. Maxwell, presented a thought experiment now known under the term "Maxwell's demon"[2] that also allegedly violates the second law of thermodynamics. The demon opens and closes a gate allowing only certain particles (hot and cold) to go from left to right in a container, until after some time achieving a nice orderly separation of the hot and cold particles. The solution is that the demon, when measuring particles and opening and closing the gate (applying information to the system), needs to consume energy, thus the system is (a) not closed, and (b) only able to achieve a higher degree of order if energy is transformed to an information heavy operation. Life, and its apparent violation to increasing entropy is comparable to the Maxwell demon, as it needs to consume energy to create more information/order.



I don't think, however, that genetic engineering holds the key to answer Schrödinger's question as it was already answered before the 1970's (when genetic engineering first was done).

The development and design of protocells, however, could help us to measure and better understand the informational needs of a living entity as it goes from non-living to living, from the inanimate to animate.

Oron: This is the long lasting debate between the vitalists and the materialists. The term synthetic biology was coined by Stéphane Leduc back in 1911 in his book The Mechanism of Life. What's interesting with his argument then (which we see repeated now) is that we know enough about life for biology to become, in his word *Synthetical*; as charming as this proposition might be, in the time that Leduc wrote it the knowledge about life was quite limited, for example, the role of DNA in biological processes was unknown. So even though we know now much more about the Mechanism of Life this kind of hubris seems to persist, while we are still lacking quite a lot of knowledge about many aspects of life.

While I tend to be on the materialist side, I still believe that there is something special about life, something that requires us to allow for some special consideration that goes beyond the engineering and reductionist mindset of SB. This special thing might only be the fact that we are living beings ourselves, and ultimately, what we choose to do to life, we do to ourselves.

We have seen that through the application of synthetic biology we can influence the path of our biological future. What are the implied ethical issues, if any?

Markus: Although the current capabilities of synthetic biology are still limited, it is not unreasonable to think of a future where the magnitude and depth of the changes we exert on living organisms is going to increase significantly. The higher the options to modify biology, the less will the modification be dictated by technical constraints but more by (socio-)economic pressure and to some degree by ethical considerations. The first applications are directed to make currently inefficient, expensive and unsustainable production processes more efficient, cheaper and more sustainable. Examples are the production of pharmaceuticals (e.g. the anti-malaria compound artimisinin, antibiotics), other fine chemicals of interest (e.g. colour, aromas, skin lotion) or biofuels by microorganisms. In most of these cases the ethical issues are confined to socio-economic questions (access and benefit sharing, consumer rights, land use change) and environmental issues (biosafety of unintended release).

Over the long term, of course, ethical issues will pick up speed as we might speculate on designer animals and maybe even genetically improved humans. In any case we need to stay ethically vigilant on developments in synthetic biology, observing the developments and be as considerate and responsible as possible. But we also need to discuss again what it is that we want to achieve, what should be off-limits and conserved, and what should be OK to be modified.

Oron: This is a question of perception, scale, and intention. We should acknowledge that every action we take has a potential to "influence the path of our biological future". The cascading nature of biological processes through the time scale of the complex web of planetary life means that there is no way we can ever determine the long term impact of our actions; be it a construction of a dam, tinkering with molecular biology or urinating in the forest. So in the big scheme of things, we should accept that through our actions we will indeed have an impact. As our knowhow of processes increases so does the scale of that impact. But claiming that we can control as to what kind of influence our intentional action might have is a false one. I would go farther and argue that with our increased powers we are just becoming a more impactful random mutagenic agent. I like to use this argument as the starting point of the conversation, as it requires us to be more humble in regard to the idea of rational, intentional, controllable outcomes, which is an ethical stance.When we talk about shorter temporal scale, we can have somewhat of a different posture, and we can talk about who is going to benefit from the indented impact. This discussion tend to be more of political than ethical.

What could synthetic biology tell us about the origin of life, or the possibility of life elsewhere in the universe?

Markus: A lot, with Synbio, scientists can go to their labs and design experiments recapitulating the steps that led to origin of life, or at least help us to better understand the principles and different pathways that might have been the successful routes to life.

Obviously we will never know what exactly happened at the origin of life about 4 billion years ago (for that we would have to invent a time machine) but we could set up experiments that help to give us plausible answers.

The same holds true for life elsewhere in the universe. In a way the early Earth can be seen as an exoplanet, with a different atmosphere and physical parameters than the current Earth and then ask how life could have evolved there. The more we learn about exoplanets the better should we be able to understand about the physical and chemical constraints for life there.

On the other hand, I suspect that instead of some national space agency detecting life elsewhere in the Universe, scientists will be faster in designing and creating alien life (i.e. life as we don't know it by now) in laboratories here on Earth.

Oron: The experimental approach of some aspects of basic research that might fall under the banner of biological life – such as protolife and protocell research, can shed light, and present potential mechanisms that lead to development of life.

What role can DIY biologists, hackers or artists have in the direction and practice of synthetic biology and its applications?

Markus: DIYBio can have many practical effects, e.g. there is an educational component that allows non-biologist to get their hands "wet" in the lab and learn about the technology. But there is also a diverse set of societal and entrepreneurial goals that sets DIYBio apart from regular academic and business activities. DIYBio brings up projects that, for example, aim to help people in the developing world even if this doesn't make the inventors rich. DIYBio is also a vehicle for the biocommons, or creative commons in biology, something that was previously only known from the digital world where some people are happily sharing their work.

DIYBio, by not having to follow the specific rationale of academia (advance knowledge, publish papers) or industry (make money) they should be able to ask other kinds of questions and realize other projects. So I think they are enriching the biotech scene and also help to democratize the technology, both in terms of making the tools and methods accessible, but also in allowing regular people to come up with a biotech project of their interest (as long as biosafety guidelines are followed).

Oron: First I would like to state that I find this question offensive; clustering artists with DIY biologists and hackers is extremely problematic. Artists are professionals that have a very different set of concerns than DIY biologists and hackers. What is interesting with synthetic biology is that many of its drivers are not professional biologists – often they are engineers and physicists of different areas of specialisation. So maybe the question could have been better formulated as "What role can non-biologists have in the direction and practice of synthetic biology and its applications?" and the answer would be "a very big one".

What current application or research in synthetic biology has the most potential to have an impact and how could it affect us?

Markus: Depends what is meant by impact and by which time frame? Societal impact, economic, ethical, environmental impact? Next 10, 20, 50 or 100 years? The answer is different according to the specific focus.

Over the short term, I suppose the production of high value fine chemicals will have the highest economic impact. Over the short and midterm the development of novel synthetic antibiotics will have a huge positive impact on public health, as multi-resistant pathogens are at the moment increasing rapidly, threatening to put us back to the era before Fleming discovered Penicillin.

Over the long term I could even imagine the onset of new forms of life that are incompatible with life as we know it, representing a radical diversification.

All these measures do represent an emancipation and liberation of many constraints we now face with biology. In the future we will probably be less likely to accept nature as it is but demand that this or that should be changed to fit our needs (whatever they are). So over the long term (20, 50 years maybe even earlier), for better or worse, we will get used and familiar with the possibility to modify organisms as the technology matures (such as today hardly nobody has issues with making fire, wearing clothes, boarding an airplane, use contact lenses or using a smart phone).

Oron: See answer to the second question.

[1] See: http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_044.pdf

[2] http://en.wikipedia.org/wiki/Maxwell%27s_demon

Posted in Media on 21st May 2015 by sarah.

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