Synthetic Biology

from a New Zealand perspective

Physicians and Scientists for Global Responsibility

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"Never doubt that a small group of thoughtful,
committed citizens can change the world.
Indeed, it is the only thing that ever has."

Margaret Mead.

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Physicians and Scientists for Global Responsibility Charitable Trust New Zealand
PO Box 16164
Bethlehem
Tauranga 3147
New Zealand

Synthetic Biology
from a New Zealand perspective

Synthetic biology refers to the design, fabrication and engineering of biological components and systems that do not exist in the natural world, and to the re-design, fabrication and engineering of existing biological systems. Developments could have huge scientific, technological and economic impacts. Synthetic biology is in its infancy and substantive knowledge is scarce.

Synthetic biologists aim to build from scratch cellular components, compartments, and cells to create living devices using the bottom-up approach. For example, they propose using these to:

- Build molecular-scale factories
- Detect chemical weapons
- Clean up pollutants
- Make simple computations
- Diagnose disease
- Deliver vaccines
- Create new, hybrid materials.

Keeping the same goals using top-down approaches, synthetic biologists aim to focus on simplifying and genetically reprogramming existing cells with simple genomes.

Systems biology studies complex biological systems as integrated wholes. It uses modelling tools, simulation and comparison. It tends to focus on natural systems, often with some medical significance, at least in the long term. Synthetic biology uses tools from systems biology. It is engineering biological science directed to biotechnology: gene expression, gene networks, metabolic engineering and genetic circuits, synthetic genes and synthetic networks. Synthetic biology is also strongly associated with protein engineering, genetic engineering and nanotechnology. Many of the risks in genetic engineering[1] and nanotechnology[2] also apply to synthetic biology.

The discipline of synthetic biology faces serious technological, scientific and societal challenges.

Biologists see synthetic biology as a means of providing a complementary perspective from which to consider, analyze, and ultimately understand the living world. They see designing and building a synthetic system as a practical measure to achieve that understanding.

Scientists see synthetic biology as a means to explore the behaviour of molecules and their activity inside living cells. Observing the design of a synthetic system and seeing how it behaves can draw attention to relevant intracellular physics.

[1] See PSGR Publication Frequently Asked Questions.
[2] PSGR Nanotechnology from a New Zealand perspective (2014)

Engineers see the living world as providing a largely unexplored medium for controlling and processing information, materials, and energy. They see learning how to effectively harness the power of the living world to be a major engineering undertaking. Synthetic biology may aid in this.

Synthetic biology focuses on creating a general scientific and technical infrastructure to support the design and synthesis of biological systems. More specifically, for example:

- To specify standard parts with well-defined performance characteristics, to be used and re-used in building biological systems;
- To develop and incorporate design methodology and tools in an integrated engineering environment;
- To reverse engineer and redesign pre-existing biological parts and devices to expand the accessible functions and to programme these;
- To reverse engineer and re-design a simple naturally occurring bacterium.

Bacteria are the least complicated organisms in the natural world that are capable of replicating given the right environmental components. This is a basic environment in which synthetic biological systems can exist and act.

By re-designing and refactoring a simple living system, synthetic biologists and systems biologists aim to learn how to better couple and decouple design systems from the environment of a selected new host.

Synthetic biologists are researching what they see as many potential applications. For example:

- In the medical field and for biopharmaceutical applications
- In biofuel and microbial fuel production
- A synthetic platform organism for biotechnological functions and biodegradation pathways
- For epigenetic inheritance in bacteria
- For bioremediation
- For metabolic engineering
- In software and bioinformatics
- For gene circuits
- For mutagenesis, the study of metagenomes (genetic material recovered directly from environmental samples)

All new technologies pose some unknowns and thus potential dangers, some by direct application, some by relying on their continuous operation without re-evaluation and/or adequate monitoring, and some when their use continues in order to recover research and development costs despite the risks becoming known. Potentially, hazards could arise with synthetic biology:

- By the accidental release of an organism or system that becomes harmful;
- By the deliberate design and release of an intentionally harmful organism or system;
- By over-reliance on and over-confidence in science’s ability to design and maintain engineered biological systems in the natural world.

Proponents say:

- Experiments are being carried out only with Biosafety Level 1 organisms and components in approved research facilities;
- They are working to educate and train a responsible generation of biological engineers and scientists;
- They are learning what is possible and at what cost using simple test systems;
- Understanding synthetic biology and its potential gains justifies responsible research and development;
- Interacting with the natural, living world should be at a level of resolution; that is, at the molecular level which allows for precise actions and applications.

In the laboratory

Synthetic biologists see low-cost, exponentially scalable products and medical health solutions in the form of self-replicating organisms. These have been coined ‘living devices’. As proof comes that these conceived systems work, development and production will move from tightly regulated laboratories to less secure, private spaces; thus increasing risk factors.

Proponents claim they aim to develop innovative tools to mitigate risks. For example, there are reports that software designers are working with synthetic biology concepts to develop safeguard tools that help scientists design safe synthetic systems before the system is actually built and prevent unintentional creation of dangerous organisms.

In the environment

Synthetic biologists aim to create living systems they perceive will meet human needs. Reverse-engineered organisms aim at producing fuels, generating renewable chemicals, and reducing the cost of producing pharmaceuticals. Scientists say preventing the risk of accidental release of these is reasonably straightforward:

- They are carried out in closed physical containment;
- Appropriate waste management can be monitored;
- Enforcement of regulations can be carried out by appropriate authorities;
- Containment mechanisms can be built into synthetic organisms.

On the other hand, open systems such as bioremediation, and agricultural and medical applications that distribute synthetic organisms in open areas or the human body pose risks that may not be predictable. These require built-in containment mechanisms; e.g. in engineered microbes used to treat human illnesses.[3]

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[3] See ‘Preparing synthetic biology for the world’ Gerd et al, Front Microbiol. 2013; 4: 5. Pub. online 25 January 2013. doi: 10.3389/fmicb.2013.00005PMCID: PMC3554958 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3554958/

Safety, responsibility and dangers

One of the risks of synthetic biology is the potential for the technology to be used irresponsibly, as in the creation of bio-weapons. An obvious and real danger comes from organisms that already exist; for example, bacteria and viruses.

Viruses are relatively simple to make and control, including the most lethal.[4] 4 The smallpox virus is very potent. [5] Its sequence is published and it is relatively simple to obtain appropriate DNA sequences to create the virus. [6] [7] [8] [9]

Such easy availability increases the risk of the development of bio-weapons or other irresponsible products. Biological weapons have been used for centuries, culminating in sophisticated research and testing programmes run in several countries. Details of potential human biological pathogens can be found in a North Atlantic Treaty Organization handbook[10] which deals with biological warfare defence. It lists agents that can do harm, including bacteria, viruses, rickettsiae[11], and toxins.

Synthetic biology is claimed as unique because of its aim to use nature's design principles for the design and construction of molecular systems with novel, reliable functions. In fact, synthetic biology uses the same molecular biology practices as genetic engineering. Critics say synthetic biology is an extreme form of genetic engineering.

With genetic engineering genes are transferred from one organism to another, even into a different species, or specific target genes are "edited" at the single nucleotide level. Synthetic biology goes further. It digitises information about such processes and the molecular machinery for carrying them out, holding the potential to use the digital database to assemble an entire genome from scratch.

If the products of synthetic biology are, as some predict, to become as common as electronic devices, the precautionary principle must be upheld. Synthetic biologists must address the responsible and safe use of synthetic biological practices and systems. Intrinsic bio-containment protocols and protocols on how synthetic biology can accomplish best practices for biosafety are essential.

Public perception of new developments usually approves of applications that address societal,

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[4] 'The Dangers of Synthetic Biology', an interview with Dr David Baltimore, by Emily Singer, Biomedicine News, 30 May 2006. David Baltimore was winner of the 1975 Nobel Prize in physiology or medicine, and is president of the California Institute of Technology. http://www.technologyreview.com/news/405882/the-dangers-of-synthetic-biology/

[5] Smallpox killed over 300 million people in the 20th century. Those who contracted it and did not die were potentially left scarred and blind. The disease was eradicated by 1980. The US and Russia still maintain stocks of the virus, and the US continues with research and development.

[6] http://www.sinobiological.com/?gclid=CIr1j7irsrcCFQISpQod6gEAJQ

[7] http://www.invitrogen.com/site/us/en/ home/Products-and-Services/Applications/Cloning/ Clone-Collections/Ultimate-RF-Clone-Collection.html

[8] http://www.naturalnews.com/032641_smallpox_bioweapons.html#ixzz2UM4H70HY

[9] 'Extreme Genetic Engineering: An Introduction to Synthetic Biology' The ETC Group, January 2007 https://www.cbd.int/doc/emerging-issues/etcgroup-introduction-synthetic-biology-2011-013-en.pdf

[10] http://www.nato.int/docu/handbook/2006/hb-en-2006.pdf

[11] rickettsiae is the plural of rick·ett·si·a; any of a group of bacteria (genus Rickettsia, order Rickettsiales) carried as parasites by ticks, fleas, and lice that includes the causative agents of typhus, scrub typhus, and Rocky Mountain spotted fever in humans. http://www.thefreedictionary.com/rickettsiae

medical, and sustainability needs. However, engineering biology - transgenic or synthetic – raises public concerns. There is a call for oversight priorities for transparency and accountability and for appropriate governance

PSGR maintains:

- It is essential synthetic biology has substantive, specific oversight and regulations
- The implications for the technology need to be balanced against the fundamental importance of biological diversity to human welfare and the health of planet Earth.
- There must be discussion in the scientific community, with interested parties and scientists working in overlapping disciplines, and public education, debate and consultation.
- There should also be independent scientific assessment of the actual and potential risks to biological diversity posed by synthetic biology.

If a moratorium is established, it merits providing for regular periodic review to allow for the continued development and testing in containment of the products of synthetic biology, and for the testing and improvement of containment and control protocols.

Overseeing on-going development of synthetic biology

Synthetic biologists may initially focus on how their science can address food, energy and medical needs, as they did with genetic engineering and nanotechnology, but other questions are being raised.

A New York Times article[12] asks could synthetic biology impact on conservation, on improving agricultural yields and in reducing the demand for wood and thus reduce deforestation. Could it allow species to adapt to climate change? Could it control an invasive species, change the biology of an organism to be more productive, or enable an organism to grow in a new environment? Could it lead to the manufacture in a laboratory of wildlife products like ivory or bring back species that have gone extinct? What if there is an unintentional release or unintentional effects of a synthetic organism that destroy all the fauna in an ecosystem?

As the article said, the scenarios are endless.[13] Oversight is essential.

Oversight of Synthetic biology in New Zealand

Synthetic biology oversight and research on safety comes under the Ministry of Business, Innovation and Employment Science and Innovation. Their website can be monitored (www.msi.govt.nz/) and enquiries directed to them from the site. Other websites that can be monitored for up-to-date information on developments include:

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[12] 'Will Synthetic Biology Benefit or Threaten Wild Things?' Andrew C. Revkin, 12 April 2013, New York Times, http://dotearth.blogs.nytimes.com/2013/04/12/will-synthetic-biology-benefit-or-threaten-wild-things/.
[13] Over at the loom http://phenomena.nationalgeographic.com/2013/03/28/rewiring-life-learning-about-synthetic-biology-in-debates-videos-and-comic-books/; 'A Comic Book Guide to Rewiring Life' http://www.downloadtheuniverse.com/dtu/2013/03/a-comic-book-guide-to-rewiring-life.html; 'Can We Save the World by Remixing Life?' National Geographic http://phenomena.nationalgeographic.com/2013/04/11/can-we-save-the-world-by-remixing-life/; 'Synthetic Biology and Conservation of Nature: Wicked Problems and Wicked Solutions' http://www.plosbiology.org/article/info%3Adoi%2F10.1371%2Fjournal.pbio.1001530

- MacDiarmid Institute http://macdiarmid.ac.nz/search/content/synthetic%20biology;
- Maurice Wilkins Centre for Molecular Biodiscovery http://www.mauricewilkinscentre.org/ See end
- Auckland Bioengineering Institute http://sites.bioeng.auckland.ac.nz/mcoo001/researchoutputs.html
- Science Media Centre http://www.sciencemediacentre.co.nz/2012/03/09/synthetic-biologys-future/

In conclusion

If genetic sequencing is about reading DNA - and genetic engineering as we know it is about copying, cutting and pasting it - synthetic biology is about writing and programming new DNA with two main goals, to create genetic machines from scratch and gain new insights about how life works.

While transgenic crops generally contain a single or small number of engineered gene/s, synthetic biology allows for the generation of larger clusters of genes and gene parts, which can subsequentlybe engineered into plants or microbes. The products may be tomorrow's generation of genetically engineered organisms.

Some see synthesized DNA as a frightening prospect. The environmental organization, Friends of the Earth, calls synthetic biology an "extreme form" of genetic engineering. Some have called it GE on E.

It is acknowledged that assessing the risks is complex and we do not know how synthetic organisms will interact with pollinators, soil systems, and other organisms. Released into the environment – human or physical - self-replicating organisms with synthetic DNA could potentially transfer to wild counterparts as have genetically engineered organisms.

Existing regulation of transgenic plants is generally the responsibility in the US of the EPA, FDA, and USDA and the rest of the world take those decisions with little or any further testing. Minimum vital requirements for responsible use of synthetic biology are transparency and international regulations specific to the new technologies.

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