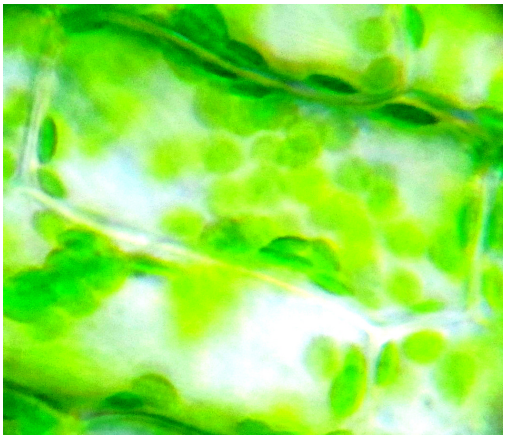
Canadian Friends Service Committee
(QUAKERS)

SYNTHETIC BIOLOGY: 2016 UPDATE #2

By combining biology, computer science, and engineering, synthetic biologists are creating novel life forms. Canadian Friends Service Committee is the peace and social justice agency of Quakers in Canada. Grounded in our values of peace, integrity, equality, simplicity, and respect for all creation, we are led to respond to the rapidly advancing field of synthetic biology. CFSC's mandate regarding synthetic biology is listed in the Appendix. It includes sharing updates about synthetic biology (previous updates at http://quakerservice.ca/SyntheticBiology).



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As you read each piece of news, we invite you to consider three queries:

1. How do we address the ecological dimension of synthetic biology, e.g. impacts on biodiversity?

2. How do we address the social dimension of synthetic biology, e.g. distribution of risks? and

3. How can we address the spiritual dimension of synthetic biology, e.g. the sacred in living beings?

Please share your thoughts or feedback (however brief or detailed):
Email matt@quakerservice.ca or call 416-920-5213

We will start this issue again with quotes from two very different perspectives:

"The entire electronics industry is based on a plug-and-play mentality. Get a transistor, plug it in, and off you go. What works in one cell phone or laptop should work in another. That is true for almost everything we build: when you go to Home Depot, you don't think about the thread size on the bolts you buy, because they're all made to the same standard. Why shouldn't we use biological parts in the same way?" - Jay Keasling[1]

"But how do you govern living things, which, unlike chemical compounds, are apt to be so unpredictable and so different from one case to the next? How to capture all the potential risks when new biological entities are introduced to the wider environmental milieu, or when they pass down variations of their genes from one generation to the next? And can regulation itself — notoriously immovable — ever keep up with biology or the blur of human innovation?" - Brooke Borel[2]

Our last update discussed gene drives. To refresh you, these aim to overcome evolution by forcing a trait through an entire population (or even an entire species). Gene drives haven't been tested in the field. The intention is to pass on a trait, or its absence, to all offspring. It appears to be one of the most powerful applications of synthetic biology to date, so in this issue we'll start again with gene drives.

Benevolent motives for gene drives have dominated headlines. The potential power to wipe out diseases like Zika and malaria, by eradicating mosquitoes that transmit these diseases, has attracted major donors like Bill Gates.[3] *Scientific American* says gene drives are 5 to 10 years from being usable in the field,[4] and several articles have detailed the many challenges, including natural genetic variations in wild populations, and the tendency for resistance to gene drives to evolve.[5] Others have claimed that local mosquito populations can be eradicated through releasing mosquitoes that will produce sterile offspring without any synthetic biology involved.[6]

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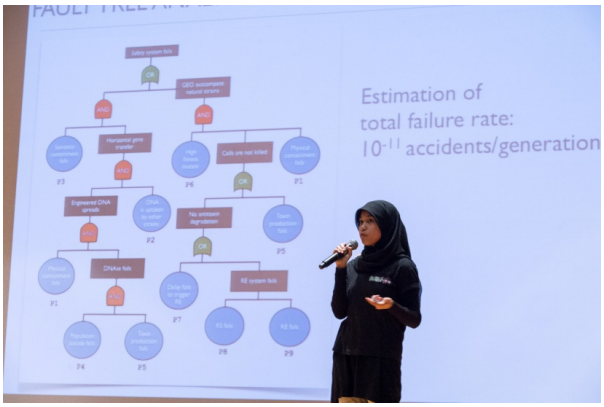
Some conservationists have written positively about using synthetic biology gene drives to eradicate invasive species, like mice introduced to islands.[7] On the other side of the debate, prominent scientists like Jane Goodall and David Suzuki have stated their strong opposition to the use of gene drives in conservation work.[8]

Some articles have dealt with the subject in a cavalier way (e.g. *Mosquitoes are deadly, so why not kill them all?*[9]). However media coverage has often raised potential problems as well as potential benefits. For example, the *Washington Post* notes there is, "a growing concern among both scientists and environmentalists about the technology's potential power to irrevocably alter species and reshape ecosystems."[10]

It was particularly encouraging to see one article that considered the complexity and interdependence of ecosystems, and also explored non-technical issues, including how gender-based power differences and financial inequality play into the spread of the Zika virus. “The Zika epidemic has exposed deep societal inequalities, which differentially affect women in particular, including their rights and ability to control their reproduction.”[11] This level of reflection on ethical and social issues is encouraging.



CC-BY International Genetically Engineered Machines Foundation/ Justin Knight

Jennifer Kuzma of North Carolina State University recently explained how new applications of synthetic biology are "challenging regulatory definitions, highlighting inadequacies in health and environmental assessments, and revealing gaps in agency jurisdiction."[12] Her article details these challenges in the US, but the insights are broadly applicable elsewhere. Increasingly, we are even seeing advocates of the benefits of synthetic biology express hopes for new regulations. For example, the J. Craig Venter Institute recently organized a conference and published a report about policy and regulation of gene drives.[13]

The National Geographic succinctly states a common feeling in the industry: "Without regulation, the tremendous potential of this revolution could be overshadowed by fear."[14]

The United States' National Institute of Health (NIH) has lifted a previous moratorium on funding of human-animal embryos ("chimaeras"). National Public Radio notes:

"One issue is that scientists might inadvertently create animals that have partly human brains, endowing them with some semblance of human consciousness or human thinking abilities. Another is that they could develop into animals with human sperm and eggs and breed, producing human embryos or fetuses inside animals or hybrid creatures."

As in so many uses of SB, the main argument offered in favour of chimaera research is that it will lead to new understanding of medical conditions from cancers to Alzheimer's, with the hope of future treatments.[15]

Bioethics professor Insoo Hyun wrote an opinion piece in which he argued that even if a chimaera has been "biologically humanized", it doesn't have the same moral status as humans, who become moral only through engagement in society. Hyun further states that scientists must know "the right and wrong ways to treat sentient beings according to the complexities of their attributes" and contends that chimaeras are no different here from other sentient animals.

Hyun suggests that scientists have found the right ways to treat research animals through existing regulations, and would therefore be able to appropriately treat chimaeras, whatever their changes in characteristics like intelligence/consciousness.

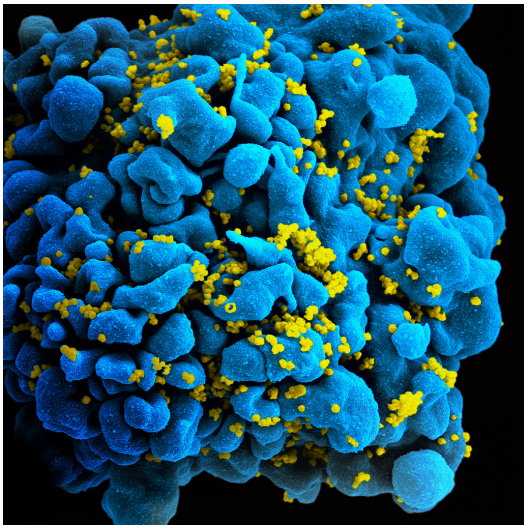
He notes that the NIH is proposing additional steps like reviewing "the characteristics of the host animal, the physical and behavioural changes likely to be caused by human-cell transfers, and incremental research monitored to determine the effects of chimaerism". This will include euthanizing chimaeras showing "deviation from normal behaviours". He also invokes the idea mentioned above, that an irrationally fearful public may shut down this research, even though it is in the public interest.[16]

We previously reported[17] on a start-up that, in 2013, raised nearly half a million dollars on the crowd-funding website Kickstarter, promising to give backers seeds to glowing plants made via synthetic biology. To date the company has failed to produce any bioluminescent plants, despite having spent more than $900,000 trying.

The company, now named Taxa, is selling shares via Wefunder (a site which facilitates investment in startup companies), and using the new income to work on a moss that smells like patchouli oil. They believe the synthetic biology moss is less technically challenging than the bioluminescent plant.

The case of the failed bioluminescent plant raises the question of how much of the buzz around synthetic biology applications is just hype. It is also noteworthy that the company would have been able to ship glowing plant seeds without passing any assessment of risks, due to loopholes they found in US laws.[18]

Companies, including Editas Medicine, Intellia Therapeutics, and Crispr Therapeutics are working on synthetic biology applications to try to cure genetic defects in humans.[19] Additionally, much has been made about the potential uses of synthetic biology technique CRISPR/Cas-9 to prevent or cure disease. One experiment attempted to use synthetic biology to edit the genes of the HIV virus. Scientists said, "this approach seemed simple and efficient."



T-Cell infected with the HIV virus CC-BY National Institute of Allergy and Infectious Diseases

Initially this appeared to have succeeded, however, two weeks after editing, the virus returned. Researchers admitted being surprised by the speed at which HIV had adapted. They concluded that, "the very act of editing — involving snipping at the virus's genome — may introduce mutations that help it to resist attack." Scientists remain confident that they can find ways to overcome HIV using synthetic biology, though the sheer amount of a patient's cells that would need to be edited for synthetic biology to offer a cure has caused others to reject the notion that this technique could ever be viable.[20] For now, HIV's rapid

adaptation serves as another reminder that even in something as "simple" as a virus, the use of synthetic biology may not be clean and predictable.

Chinese scientists have started using synthetic biology in clinical trials with humans to mobilize patients' immune response to lung cancer. The trial has identified 10 participants and plans to treat them one by one to assess the risks of treatment. After two months of monitoring a participant, if nothing has gone wrong, synthetic biology will be used on another participant. The hope is to remove a gene that "encodes a protein named PD-1, which normally keeps the immune cells in check but is also used by cancer cells to hide from the immune system. The [synthetic biology] engineering is intended to switch on the immune response to attack cancer." Scientists acknowledge the possibility of the patients' immune systems attacking healthy cells as well as cancerous ones, and of synthetic biology creating unwanted mutations.[21]

Scientists in Europe have identified genetically modified enzymes in a range of products from foods to cleaning products as "potent allergens". How the enzymes in these products are made is kept secret as the intellectual property of the manufacturers, which has made the researchers efforts to study their effects difficult. 813 people who were regularly exposed to these enzymes while working in a range of industries took part in the study. 23% showed specific antibodies, leading investigators to state, "Genetically engineered enzymes are potent allergens eliciting immediate-type sensitisation... Enzymes should be tested like any other potentially hazardous chemical."[22]

CC-BY US Department of Defense

We mentioned previously[23] that US intelligence officials had listed synthetic biology as a possible weapon of mass destruction. Several stories since then have suggested that the US Department of Defense is increasingly investing in synthetic biology research and development. The U.S. Defense Advanced Research Projects Agency (DARPA) is spending an estimated minimum of $50 million on the research program "Safe Genes", seeking to develop synthetic biology techniques to "turn off" gene editors in organisms, drugs to block or reduce the action of synthetic biology gene editors, and tools to cleanup genetic contamination in the environment.[24]

The US Department of Defense has also posted online, seeking 10 to 12 experts to form a committee to study "the changing nature of the biodefense threat in the age of synthetic biology."[25]

Some experts have called for The Biological Weapons Convention (established in 1972 it is formally reviewed every five years) to take SB as a more urgent priority.[26]

A recent article in New Scientist explains the belief that the survival of humanity will depend on "engineering ecosystems using synthetic life."

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Ricard Sole's *Let's Harness Synthetic Biology to Fix our Broken Planet* provides an enthusiastic embrace of synthetic biology for much of what ails the earth: synthetic biology bacteria to help soil retain water so it doesn't succumb to desertification as global temperatures increase (Sole says his team is working on such a bacteria which it plans to start testing in "controlled outdoor plots"), bacteria to break down toxic chemicals, and bacteria to capture carbon dioxide. A research project, Synterra, is planning to examine the uses of synthetic biology to reshape ecosystems, relying on computer simulations to model impacts. Sole's article does not mention any need to change human behaviours like consumption patterns that cause problems to ecosystems, focusing exclusively on synthetic biology fixes.

Sole says, "There is good reason to be cautious about unintended consequences, but remember how high the stakes are." He makes the case for a synthetic biology "kill switch" to "ensure" that organisms will only survive in the environments they are planned to live in (we've previously explained why "kill switches" may not be viable[27]). There is no mention in the article of uncertainty about how such synthetic biology bacteria may evolve, or what their actual impacts on ecosystems would be. Sole contends, "Geoengineering with synthetic life is relatively safe and essentially free."[28]

If the geoengineering fails, others are thinking about ways synthetic biology can be used to make more moral human populations who can colonize mars.[29]

Unintended changes produced by the synthetic biology technique CRISPR/Cas-9 may be more significant than often acknowledged. Algorithms used to predict such "off-target" effects appear to be far less accurate than originally thought. According to *Stat News*, scientists use these algorithms to predict which off-target regions of the genome might be edited by CRISPR/Cas-9. However many more regions may be affected. These edits, because they were not predicted, may be less frequently detected.

"One reason for concern about off-target effects is that genome-editing might disable a tumor-suppressor gene or activate a cancer-causing one. It might also allow pieces of two different chromosomes to get together, a phenomenon called translocation, which is the cause of chronic myeloid leukemia, among other problems."[30]

APPENDIX

Canadian Yearly Meeting of the Religious Society of Friends (Quakers) recommends that Friends work on this concern in the following ways:

1. That CYM affirm the seven principles identified in Principles for the Oversight of Synthetic Biology, a document that makes many important recommendations, and continue to work with the Biotechnology Reference Group of the Canadian Council of Churches (BRG) on discerning ways to implement the seven principles:
    i. Employ the Precautionary Principle;
    ii. Require mandatory synthetic biology-specific regulations;
    iii. Protect public health and worker safety;
    iv. Protect the environment;
    v. Guarantee the right-to-know and democratic participation;
    vi. Require corporate accountability and manufacturer liability; and
    vii. Protect economic and environmental justice.
2. That CYM request that Canadian Friends Service Committee (CFSC), with the help of concerned groups such as the ETC Group and the BRG, provide Canadian Quakers with an annual, easily understandable update on synthetic biology;
3. That CYM request CFSC, and encourage Monthly Meetings, to find opportunities to link with other faith and community groups, and with Indigenous peoples, to share insights and discernment about synthetic biology; and
4. That CYM encourage CFSC and Quaker Meetings in Canada to engage with other faith groups and interested parties, including organizations involved in research and/or manufacture in synthetic biology, to hold and/or participate in conferences that address ethical, spiritual, social, and economic aspects of synthetic biology.

Find out more about synthetic biology, including background of how this concern of Friends has developed and what Meetings from across Canada have said:
http://www.quakerservice.ca/syntheticbiology
416-920-5213 matt@quakerservice.ca

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