Scientific Evidence for the [Biological Security Strategy] call for evidence

Title: Synthetic Biology Policy Recommendations

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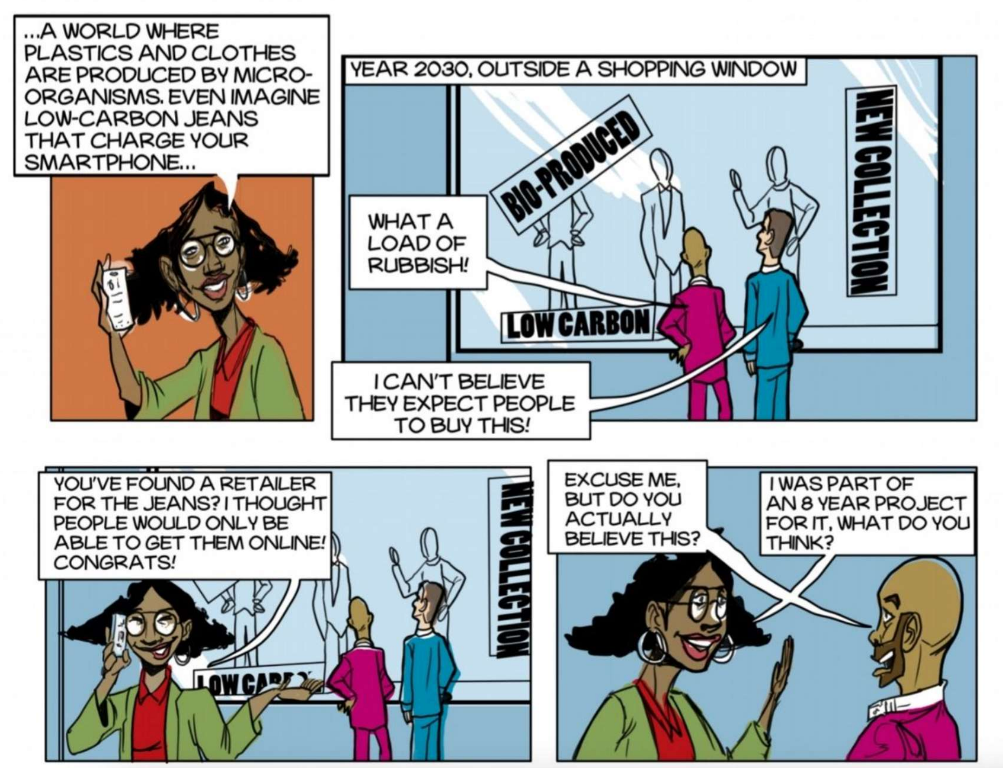
Reason for submitting evidence:

This submission of evidence aims to address some aspects of the following questions:

- What are the key biological security opportunities, challenges, threats and vulnerabilities facing the UK (now and in 5 years)?
- How should the government prioritise its efforts to identify and respond to these?



https://www.cser.ac.uk/news/comic-bioengineering/

<u>Evidence</u>

Introduction

Synthetic biology attempts to design new types of artificial life according to human needs by using genetic engineering[1] to alter the genetic composition (DNA) of organisms or biomolecules[2] to design and engineer biologically inspired parts and systems (that do not exist in nature) conferring them novel functions for specific purposes. Some examples of synthetic biology are:

1. Creation of a bacterial cell that contains a synthetic genome within a bacteria that had its own genetic code (DNA) removed (Gibson et al. 2010).
2. The use of "gene drive" tools to modify mosquito populations by introducing genetic modifications that can eliminate the malaria parasite transmission or the mosquito populations themselves (Carballar-Lejarazú, 2018).
3. Design of a “cyberplasm” which is a biohybrid that integrates engineered bacteria, yeast, and mammalian cells into a micro-scale robot designed to be capable of sensing environmental chemicals for remediating purposes (Prindle, 2011).

Since synthetic biology is an emerging field, its definition and its boundaries are still debatable. Synthetic biology uses tools, techniques an approaches from genetic engineering is based on recombinant DNA technology[3] and all organisms developed by synthetic biology are considered to be genetically modified. However, only organisms that had their genome re-engineered can be referred to as synthetic biology organisms since their creation includes many large scale interventions and different cycles of standardisation, abstraction, and design-build test-learn to optimise their production.

The rise of Synthetic Biology research

In 2018 alone, a group of 98 companies raised 3.8 billion dollars in investment to build engineered biological products, more than double in comparison to what it raised in 2017 (US$1.7 billion) and 2009 (US$175 million) (Synbiobeta, 2018). Governments across the world also invested over $50 million into synthetic biology companies in 2018 which may be due to the policies introduced by various governments, including:

- The UK identified synthetic biology as one of the eight great technologies of the future spending over £90 million on advanced synthetic biology research and commercialisation with an additional £50 million to be invested in support of the implementation of key recommendations from the UK Synthetic Biology roadmap (UK government, 2013). Moreover, the UK government

[1] Genetic engineering: Genetic engineering is the act of modifying the genetic makeup of an organism (virus, bacteria, plant, animal, etc). Selective breeding is not a form of genetic engineering.
[2] Biomolecules: molecules produced by a living organism (such as proteins, carbohydrates, lipids, and nucleic acids)
[3] Recombinant DNA technology: is the process to join DNA molecules from two different species which is later introduced into a host organism to produce novel genetic combinations.

decided to establish a Synthetic Biology Leadership Council[4] to provide leadership for the UK's interests in this rapidly developing field.

- China has largely invested in synthetic biology projects through its basic research funding scheme and on its strategic emerging industry for development in China's 2016 Five-Year Plan (Schmid. 2021)
- Singapore's government launched in 2018 a Synthetic Biology Research and Development Programme which participates with 19 million dollars of funding for over five years (Ong, 2018).

The potential of Synthetic Biology

In health:

- Creation of biosensors (such as genetically-engineered microbes) that produce electrical signals for direct detection of biochemicals[5] associated with diseases.
- Through "DNA origami" is possible to design and build DNA based devices that are used as carriers for delivering drugs (medicine) to specific parts of the body (Amir, 2014). They are more efficient and have fewer side effects when in comparison to current treatments.
- Disease dissemination can be reduced by the use of synthetic gene drives (explained in the introduction) which will allow the control of specific disease-carrier species such as mosquitoes.

In conservation:

- By using synthetic gene drives it is possible to reduce wildlife diseases such as avian malaria that threaten endangered species.
- In addition, there are proposals to reduce problematic invasive species that feed upon or outcompete native species (Faber, 2021).
- Bioremediation, using modified microorganisms or enzymes[6] for cleaning up certain pollutants from the environment.
- There are rather speculative proposals to recreate extinct species. These include proposals for mammoths and Passenger pigeons.

In agriculture:

- By regulating pests that damage agricultural productivity and competitiveness.
- Biosensors that are able to detect, integrate, and respond dynamically to a wide range of environmental conditions is used for studying environmental and Earth sciences (Del Valle, 2021).

In energy consumption:

- Creating biofuels produced by bio-engineered organisms could be a more sustainable alternative to fossil fuels, as they can be produced without using land suitable for growing crops.

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[4] https://www.ktn-uk.co.uk/programmes/synthetic-biology-leadership-council

[5] Biochemicals: substances (molecules) produced by chemical reactions in living organisms.

[6] Enzyme: is a chemical substance that is found in living creatures which produces changes in other substances without being changed itself (https://www.collinsdictionary.com/dictionary/english/enzyme)

The risks of Synthetic Biology:

<u>In health:</u>

- Perpetrators could use synthetic biology to deliberately produce harmful organisms that can damage humans or the environment. For example, a virus that targets a defined population is created (biological weapons).

<u>In conservation:</u>

- Synthetic biology solutions to global challenges may distract policymakers from the deeper underlying causes of biodiversity loss. This is a particular concern with restoring extinct species.
- There is a long history of species being introduced that were thought to be benign and beneficial but had problematic and sometimes catastrophic consequences. Synthetic biology could be a way of creating new unanticipated problems.
- Large scale removal of locally abundant species such as some disease-carrying mosquitos might have important unintended consequences in the trophic chain.
- Microbial systems are very poorly understood. Interfering with them might have unexpected consequences.

<u>In culture:</u>

- The construction of 'life' by synthetic biology may raise questions about what 'life' really means, thus affecting people's perception of nature and our relationship with the natural world.
- If governments decide to use "gene drives" to purposely decimate some pests, who will decide which species will get extinct? Would the citizens accept these policies or would they be considered unethical?

<u>In agriculture:</u>

- The release of organisms with substantial genetic modifications may detrimentally impact humans and the environment if they become (new) types of pests.

<u>In the global economy:</u>

- Shifting towards biotechnology-based economies based on the use of biological resources may have particularly significant impacts on the rural economy and low-income tropical countries which could be sources of biomass.

Policy Recommendations

<u>Concerning synthetic biology research:</u>

- When assessing synthetic biology projects or funding applications establish that bio-containment must be part of the research proposal. Example 1: use of 'kill switches" to cause the death of the engineered organism by a particular signal, such as the introduction of a chemical. Example 2: making engineering organisms to be dependent on nutrients. Example 3: include self-destruct mechanisms that are triggered once the population density exceeds a certain threshold. Example

4: a further possibility is the inclusion of nucleic acids containing elements not found in nature (xeno-nucleic acids), which cannot mix with naturally occurring organisms

- Governments should also promote/fund the research of the following topics: physiological differences between natural and synthetic organisms; investigate how engineered microorganisms might alter ecosystems (food chain and biodiversity), determine if synthetic organisms can survive if released in the environment, if they can evolve (and at which rate) and how it can be stopped in scenarios of threat.

Concerning policies already implemented:

- The government should assess which of its established laws, acts, regulations or directives can capture the risks coming from synthetic biology. For example, in the USA, the laws implemented to chemicals are used for regulating synthetic biology whereas the European Union uses GMO directives to regulate it.
- Use an expert panel composed of a variety of professionals (from basic sciences to social sciences) to provide information about a specific synthetic biology topic. These discussions will allow getting greater depth of insight into its potential policy impacts and if there is a need to create new policies.

Concerning biosecurity:

- The government should put in place cautionary monitoring and take small steps if introducing synthetic biology organisms. Moreover, governments should develop a system that can manage unexpected events related to biosecurity in a resilient, flexible, and immediate way.
- Risk management should be always part of the process when monitoring Synthetic Biology organisms and should include: close supervising, the foresight of potential hazards, strict containment measurements and systems that can react to surprises in a resilient, flexible, and adaptive way.
- Set up a group of biosecurity regulations for each type of synthetic biology organism: from generation, transport to release.
- Create a plan of action in case of accidental release or leak of the Synthetic Biology organism.

Concerning foresight:

- Analyze the impact of gene drives release in public health in a short and long-term manner to foresee if the implementation of gene drives do not create new problems (Example #1: Removing one population of species by the use of gene drives could allow another potentially dangerous species to take its place. Example #2: by eradicating a species using gene drives in a geographical region could generate a new problem to a neighbouring country if the species spreads overseas)

Concerning citizen engagement:

- Responsible Research and Innovation is a European approach to the application of new technologies and is based on the consideration of the social, cultural and ethical risks and benefits of innovation that includes new technologies. Therefore, citizen engagement during the policy cycle will reduce public distrust as opposed as we have seen in the case of GMOs and research on human embryos.

- Incorporate external peer review and public participation for early communication and empowerment of all potentially affected parties in regards to synthetic biology implementation and monitoring.