

Synthetic biology

– opportunities and challenges for the total defence

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Imagine a total defence where plants change colour to warn against toxic gases, where civilian and military emergency service vehicles are powered by fuels produced from micro-organisms, where crops are designed to cope with a changing climate. With protective substances circulating in the body, chemical warfare agents are broken down before they have time to cause injury. These concepts are not science fiction but have already been demonstrated in laboratories. The development in synthetic biology is rapid and has the potential to have a revolutionary impact on the capabilities of the total defence. But the development also leads to new risks because the enemy can use synthetic biology for its own purposes, for attacks against agriculture, genetic assassinations, and more.

THE SIGNIFICANCE OF SYNTHETIC BIOLOGY FOR THE TOTAL DEFENCE

Development and applications in synthetic biology already affect important parts of civil society, and the potential for the total defence of the future is considerable. The production of important medicinal products, as well as advanced antidotes against chemical warfare agents, is already a reality. Crops designed with an inherent climate and pathogen resistance, i.e. resistance to harmful viruses and bacteria, amongst other things, can contribute to Sweden's food security and forestry in the event of a warmer climate. Organisms can be designed to indicate the release of toxic substances, to purify drinking water, and to clean soil from toxins and environmental pollutants. Genetically modified algae and cyanobacteria are already used for small-scale production of

biodiesel and other fuels from locally available raw materials, such as forestry residues. In the longer term, the development will provide new materials with completely new properties. A more speculative outcome in the long term is that development may include genetically modified soldiers that withstand chemical and biological warfare agents or with improved physical strength and endurance.

An intrinsic problem with development is that the same technologies used to do good can also be used for illicit purposes. Despite the opportunities for abuse being to some extent limited by international regimes through legislation and control bodies, the methods and knowledge for modifying or moving genes between species, for example, are universal, regardless of the properties added. Designed, highly contagious, micro-organisms that evade both detection and medical treatment are an obvious threat. A hostile attack with a designed micro-organism is likely to require a rapid response, such as in the form of an advanced antidote. There is a legitimate concern about genetic assassinations and targeted genetic weapons designed to knock out specific parts of the genome. However, it is important to note that antagonistic applications of synthetic biology do not necessarily have to be directed against the Swedish population, even agriculture and forestry are potential targets for an attack. A high level of knowledge is required by the Swedish authorities affected to understand the nature of the threat, but also an infrastructure, including laboratories and specialist expertise, designed to quickly use the knowledge of the threat and implement effective countermeasures.

EXAMPLES OF THE CURRENT USE OF SYNTHETIC BIOLOGY

It is likely that synthetic biology will have a profound effect throughout most of our society. The applications are found in many areas, making it difficult to provide a comprehensive picture. To illustrate the potential, some of the areas where synthetic biology has already made big impressions are described below.

Provision of medicinal products. Enzymes are substances of biological origin that increase the rate of chemical reactions; they are involved in almost all of the processes that occur in living organisms and are therefore a prerequisite for all life. Enzymes convert sugar into energy, allowing plants to absorb carbon dioxide from the atmosphere and giving bacteria resistance to antibiotics. Transferring the gene that encodes an enzyme between different organisms is nowadays routine practice. As early as a decade ago, genetic material was transferred from summer wormwood to baker's yeast. The new genome gave the yeast cells the ability to produce a substance that can be easily modified to Artemisin, a medicinal product recommended by the World Health Organisation (WHO) for the treatment of malaria. More recently, chemical processes have similarly been created by combining genetic material from widely different organisms. One striking example is yeast cells modified with over 20 genes from mammals, plants and bacteria to produce opioids, which are medicinal products used for analgesic treatment and palliative care.

An excellent illustration of the possibilities of synthetic biology for the total defence is the development of enzymes capable of breaking down chemical warfare agents. The development of these enzymes has largely been realised by directed evolution in a laboratory environment. The modified enzyme breaks down some nerve agents more than 17,000 times faster than the natural enzyme, and experiments show that animals treated with the modified enzyme have significantly improved tolerance to nerve agents. Directed evolution today is a technique widely used in various applications, something that was acknowledged by the 2018 Nobel Prize in Chemistry.

Living sensors. Sensors that detect chemicals are important in many contexts, ranging from detecting emissions from industries to preventing import of

illicit substances. Using plants as living sensors is an attractive proposition because they can live in a variety of environments if they are provided with sunlight and water. A research team recently managed to utilise the thale cress plant to create a highly sensitive biosensor for the detection of fentanyl. Fentanyl is a very potent analgesic that is also produced illegally and has caused several deaths among drug users.

The detection of fentanyl is complicated since the molecule exists in many different three-dimensional structures. With the help of computer modelling, the researchers first designed a number of proteins that should theoretically bind to the most common forms of fentanyl. This can be compared to designing locks to fit specific keys. The genes of these proteins were synthesised and then introduced into plants, along with a signalling system that made the plant luminous when in contact with fentanyl, in the form of a solution. There are many other projects underway that attempt to utilise plants and other organisms as sensors for the detection of everything from emissions of chemicals into the environment to early detection of human diseases. One example of the latter is a project where researchers are trying to create bacteria that can detect cancer, or infections of the gut. If necessary, the bacteria could potentially release pharmaceuticals that they carry themselves.

Food security. The supply of food to the population during a protracted crisis could be a significant challenge, especially if Sweden is simultaneously exposed to adverse operations targeting agriculture, or if import trading routes have been affected. Perhaps the most obvious use of synthetic biology is to modify existing crops so that they have improved resistance to plant pests or can be cultivated despite changing climates. It is also possible to modify crops to improve nutritional value or productivity. There is ongoing development to use cells as factories to produce special nutrients or completely new foodstuffs. In the long term, perhaps it will be possible to develop micro-organisms that produce foodstuffs that have their natural origin in the plant or animal kingdom.

Human modification. With today's technology, it is not only possible to change specific parts of the genome, but also to remove or add whole genes. For example, there are medicinal products used to treat different types of blood cancer that are based on the patient's own immune cells being genetically

modified so that they target and kill the cancer cells. The modification takes place using a virus that delivers new genetic material to the immune cells.

INVESTMENTS IN SYNTHETIC BIOLOGY

Globally, a considerable amount of money is being invested into synthetic biology and the development could lead to a new industrial revolution. Influential nations such as the United Kingdom and the United States are also investing a significant proportion of their defence research budgets into synthetic biology. One concrete example is the US Defence Advanced Projects Agency (DARPA), which increased its investment into synthetic biology by \$100 million between 2010 and 2014.

Sweden is a nation that is investing a significant proportion of its GDP on research. However, compared with other countries, it does not invest as much into biotechnology, the field in which synthetic biology lies.

In Sweden there are no investments being made to exploit synthetic biology and utilise its potential in order to increase the Swedish total defence capability. The consequences are potentially serious, and also limit Sweden's readiness to face antagonistic use of synthetic biology. Global differences are not just found within funding; legislation also varies considerably. For example, China has more permissive legislation in this area, which, amongst other things, enabled genetic modifications of human embryos. The United States also has far more permissive legislation than the EU.

THE WAY FORWARD

Today, synthetic biology largely focuses on modifying biological systems which already exists in nature. For example, an existing enzyme can be modified to withstand a higher temperature, which is required in many industrial processes. Designing a new enzyme with completely new properties is much more

difficult. To do so, very many so-called 'design-build-test' cycles are often required, which becomes very resource intensive. In order for synthetic biology to mature and fulfil its full potential, increased knowledge of complex biological and chemical systems is required. Academic research is therefore important for the future development of synthetic biology. In addition, authorities and other actors, such as the biotech industry, must increase their expertise in synthetic biology in order for Sweden to be able to take advantage of the opportunities in this field. Another fundamental prerequisite for fulfilling the potential from a total defence perspective is effective interaction between academia and the total

defence authorities. The step from a basic understanding of synthetic biology to a use that is relevant to the total defence is significant. One challenge, for example, is to adapt concepts that work on a laboratory scale into industrial production, which requires a close collaboration with industrial partners.

What should be prioritised today is research that links the progress in basic research with the needs of the total defence. In defence-related research, the focus should be on developing methods, knowledge and infrastructure in synthetic biology. Only when these conditions are in place can products and solutions directly aimed at Sweden's total defence needs be developed. Well-balanced investments with clear objectives provide opportunities to tailor the research to Swedish needs, and make Sweden an attractive partner in the international arena.

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