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SYNTHETIC BIOLOGY IN AUSTRALIA

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At a glance

- Synthetic biology holds great potential to solve global challenges, and create social and economic benefits across the medical, environmental and industrial sectors.
- Synthetic biology combines engineering with biology to assemble new biological systems. These may be non-living component systems or new microbes and plants. Its sphere of impact spans medical, environmental, agricultural and industrial applications.
- Advances in biotechnology, automation, artificial intelligence and data analysis have opened the door to the mass manufacture of these bioengineered components and products. Synthetic biology at scale could in future provide economically viable alternatives to unsustainable production methods for useful chemicals, and new solutions to pollution, changing climates and disease.
- Researchers are conscious that these techniques raise ethical questions and come with social, economic and environmental risks, requiring careful regulation and proactive engagement with government and the community.
- Strategic investment in infrastructure and skills development by government, in partnership with industry, will allow Australia to capitalise on our research expertise, industry strengths and record of responsible regulation to develop new products and industries.

BIOLOGY BY DESIGN

Synthetic biology is an applied science. Its focus is on developing designer biological systems and unique microbes and plants for defined purposes.

The field merges engineering principles with genetic engineering techniques to develop and test biological processes and unique microbes and plants.

Synthetic biology sits on a continuum of genetic technologies. Traditionally, classical genetic engineering introduces one or a few genetic components, making adjustments to existing systems. Synthetic biology uses standardised DNA encoded parts to facilitate the planned assembly of DNA components, and more complete engineering of unique microbes and plants.

Synthetic biologists use tools like protein engineering to improve enzymes, and CRISPR to make specific changes to DNA sequences.

Recent advances in technology and knowledge have vastly improved the potential of synthetic biology.

These advances include:

- increased standardisation of synthetic biology parts;
- decreases in the cost of key technologies by a million-fold, including genome and DNA sequencing and synthesis; and
- increased computational power, software design and automation.

Box 1: Key terms explained

Genome - the entire genetic material of an organism.

DNA - A double stranded structure in cells that contains the hereditary genetic material in most organisms. This material is duplicated from one generation to the next.

CRISPR - a tool that allows the introduction of specific changes into the DNA of an organism.[1]

Microbe - a microscopic organism, such as yeast, mammalian cells, bacteria or viruses.

Biosensor - a device that uses a microbe or biological molecules to detect the presence of specific chemicals.

Biofoundry - an automated DNA assembly and testing facility.

Synthetic biology products - products that synthetically engineered microbes create, such as biofuel or medical compounds.

Synthetic biology components - parts (genes), devices and modules (biosynthetic pathways) that can be combined in predictable and reliable ways.

Biobrick - a compatible standard part consisting of a DNA fragment that encodes information or a functional property.[2]

CUSTOM SOLUTIONS TO COMPLEX PROBLEMS: OPPORTUNITIES FOR AUSTRALIA

The potential applications of synthetic biology are broad. Developments in the field could control environmental and agricultural pests, help fight major diseases including cancer and diabetes, and increase food production and stability (Table 1). Australia has already made progress in applying synthetic biology solutions in medical, environmental, industrial and agricultural fields.

Consequently, Australia has the potential to benefit economically both as a supplier and as a consumer of synthetic biology products. Economically viable applications are already in play, and markets for products and services based on synthetic biology are growing.[4]

As a relatively new market segment, commercial estimates vary widely. In 2018, the global market for synthetic biology was valued at almost US$5 billion, with North America accounting for the largest share at US$2.2 billion.[5] The Asia Pacific region accounted for a quarter of the market in 2018, and is expected to be the highest growth region over the next five years. Private investment in the field is also growing: in 2017, top synthetic biology companies raised US$1.7 billion in capital in the USA for technology development; in 2018 it was US$3.8 billion.[6]

Table 1: Examples of short and long term applications of synthetic biology, by field

	Medical	Environmental	Industrial	Agricultural
Short term (10 years)	Engineered viruses to target antibiotic-resistant bacteria[3, 7-8]	Cheap biosensors to detect environmental pollutants[3, 8]	Microorganisms that assist in the manufacture of high value chemicals, acids and alcohols[3, 8]	Plant based production of omega 3 fatty acids to replace fish-based fatty acids at large scale[3,8-9]
Long term (10 + years)	Nanodevices for vaccines and molecular diagnostics[3,8]	Unique microbes and plants for environmental remediation[3, 10-11]	Artificial photosynthesis for biofuel and chemical synthesis[3,8]	Agrochemicals to increase crop productivity and reduce fertiliser use[3,8,12]

Medical applications

Australia's medical research community is already making significant progress towards the use of synthetic biology to improve health outcomes, including revolutionising the way biological tools are developed and used to advance human wellbeing, manage human and animal health, and enhance commercial opportunity in biomedicine.

Human trials have been completed or are underway for several products, such as human cancer immunotherapy, and clinical trials to treat chronic rhinosinusitis (inflammation of the nasal cavity and sinus caused by bacteria) using engineered viruses that attack the disease causing bacteria.[3]

Australia also has access to unique bacteria and fungi, a largely untapped resource for researching new antimicrobial and antibiotic agents.[3]

Case Study: Targeted cancer therapy using Synthetic Biology

Immune cells can be programmed via synthetic biology to recognise and attack cancer. These programmed cells are known as Chimeric Antigen Receptor T (CAR T) cells, and have already shown high rates of targeted response to blood cancers in particular.

In a clinical trial of children with acute lymphocytic leukaemia, 83 percent of children were in remission within three months of treatment with CAR T cells. Other trials have shown similar results.[14-16] In Australia 300 people are diagnosed with acute lymphocytic leukaemia each year, with this disease responsible for 19 percent of deaths in children between the ages of one and 14.

Programmed cells could likewise be used in the treatment of autoimmune diseases, for example lupus or multiple sclerosis. Autoimmune diseases affect five percent of Australians, and cost the community billions of dollars each year.[17] Currently there are limited effective treatment options for advanced cases of autoimmune disease.

The market for CAR T cell type therapy is estimated to reach US$1.1 billion by 2026.[16]

Environmental applications

Invasive species cost Australia an estimated $13.6 billion per year,[18] while soil contamination from industry and agriculture is believed to affect some 160,000 sites.[19] These issues cause enormous damage to both the natural environment and to agricultural industries. Synthetic biology can provide Australia with cost-effective and environmentally friendly methods to manage the impact of pests, clean up contaminated land, and solve other environmental issues.

Synthetic biology can also be used to create replacements for certain animal products that may be unsustainable – for example plant derived omega 3 oils or replacements for horseshoe crab blood (used in the biomedical industry).[20]

Australia has a history of developing synthetic biology-based approaches for cleaning up insecticides and pesticides in the environment and for engineering resilience into ecosystems.[21-23] For example, Landguard™,[21] launched in 2006, is used in agricultural areas for the rapid treatment of pesticide residues in water. Australia's experience in this area is now the foundation for current research and innovation.

Case study: Artificial sentinels to clean up environmental pollution

Pesticides, insecticides, fertilisers and other toxic chemicals entering Australia's rivers and ocean cause environmental damage and have human health implications. Synthetic biology can be used to create cellular systems that can identify and destroy contaminants in the environment.

In Australia, research is underway to create self-propelled 'sentinels' that can clean up environmental pollution, specifically organophosphates.[8, 10-11] Organophosphates are common toxic pesticides that are found in agricultural runoff, and cause damage to human and animal health. The aim of this long term project is to create a small 'sentinel' organism that can detect a contaminant, move through a body of water towards it and then destroy it.

Agricultural applications

Synthetic biology can increase crop yields, create drought and disease resistant crops, develop alternate proteins, and improve the quality of food products. Australia is well placed to be competitive in this area, with a strong agricultural and food production industry that is known for its innovation and research capabilities.[3] The demand for high quality Australian produce for Asian markets affords promising opportunities for synthetic biology applications in Australian agriculture.

Three Australian Research Council (ARC) Centres of Excellence relevant to agriculture with strong synthetic biology programs have already been established. These are the ARC Centre for Excellence in Synthetic Biology, the ARC Centre of Excellence for Translational Photosynthesis (with a focus on engineering improvements to photosynthetic processes) and the ARC Centre of Excellence in Plant Energy Biology (with a focus on energy acquisition in plants). These centres can support the research levels needed for commercial scale agricultural applications.

Case Study: Reducing costs and improving ethics of the egg industry

Globally, the poultry industry culls 6 billion one-day old male chicks each year.[3] To address the ethical and economic implications of this practice, the US egg industry has announced its commitment to new synthetic biology technology that will stop the need for male chick culling by 2020.[24]

Synthetic biology could be used to identify male chicks prior to hatching and divert those eggs to be used for other purposes (e.g. in the production of vaccines and other biological products). To achieve this, a marker would be introduced onto male sex chromosomes.[25] The gene would produce a protein that fluoresces when eggs are exposed to laser light. This would allow male eggs to be cheaply identified and separated at an early stage, reducing production costs and waste for the farmer.[25]

Industrial and manufacturing applications

Using synthetic biology, microorganisms including yeast or E. coli can be reengineered to produce high value compounds, including pharmaceuticals, industrial chemicals and biofuel components. CSIRO and Australian industries are already focused on developing the next round of chemical producing microorganisms.

In order to manufacture novel products using yeast or bacteria, a reliable food source for the microorganisms is needed; for example, sugar. Australia's sugar industry is well established, with current export earnings of $2 billion annually and capacity for expansion in Northern Australia.[26] This reliable feedstock is one of the reasons why Australia is capable of becoming a commercial leader in industrial synthetic biology.

Applications in advanced materials and for the circular economy are also important opportunities.

Case Study: Manufacturing synthetic biology products as a renewable alternative to petrochemicals

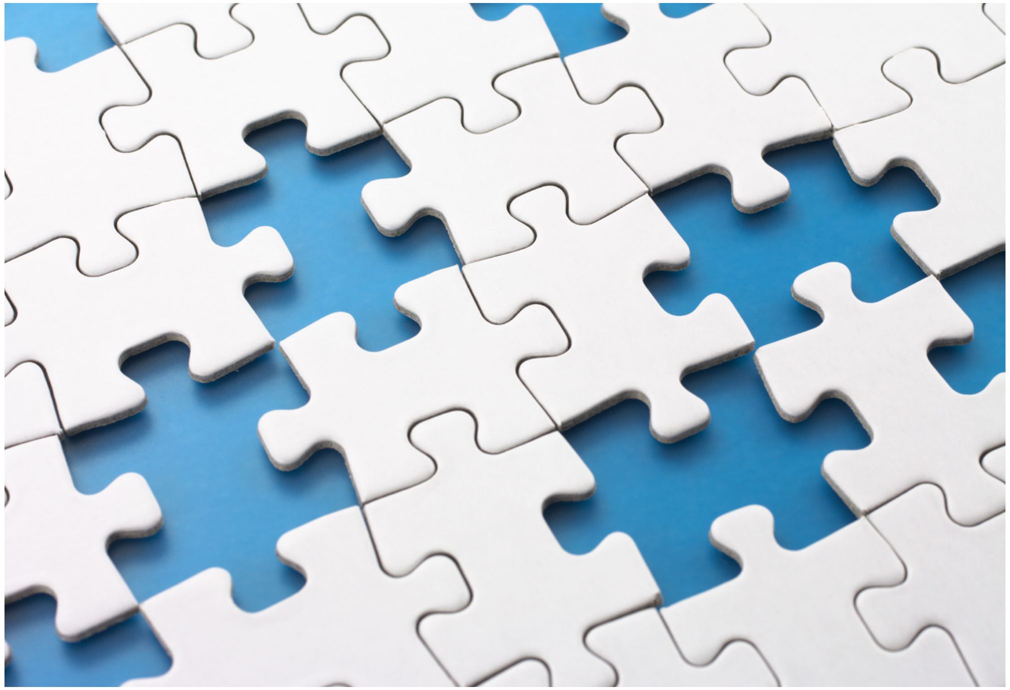
Renewable energy and alternatives to fossil fuels are a target area for synthetic biology. Fossil fuels have historically been used as energy sources and in chemical and plastic production due to their low cost and availability. However, the dramatic advances in synthetic biology in the past twenty years means that microbes can now be used as chemical producing factories instead.

Farnesene, a hydrocarbon, is a renewable alternative to petrochemicals. Made from sugar by an engineered strain of yeast, this chemical can be used to make a variety of high value products including cosmetics, plastics and lubricants. The global market for farnesene is expected to reach US$485 million by 2023.[27] The Queensland Government is in discussions with the renewable products company Amyris to construct a yeast-produced farnesene facility, which has the potential to generate $60-80 million in annual revenue.[28]

Biofuels can also be made from farnesene and can reduce greenhouse gases by more than 50 percent when used as an aviation fuel.[29] Although it is not currently a cost effective alternative to aviation fuel, farnasene-derived aviation fuel has been approved for use by the global authority for aviation fuel standards. In the future, farnesene could play an important role as a renewable source of fuel.

ADDRESSING THE CHALLENGES

Researchers are conscious that synthetic biology techniques raise ethical questions and come with social, economic and environmental risks. Addressing these challenges will require careful regulation, parallel research on responsible innovation, and proactive engagement with government and with the community. Some of the challenges that must be addressed in order for this research to fulfil its promise are discussed in this section.



Filling in the science gaps

There are still scientific challenges that must be addressed to achieve the full potential of synthetic biology. For example, scientists are not yet able to accurately and repeatedly predict the outcome of circuits constructed from multiple synthetic parts using current synthetic biology tools. This is because the way a part functions may be context dependent, and because nature itself is inherently variable.

One approach to solving this problem is 'directed evolution'. This method imitates the process of natural selection to engineer nucleic acids or proteins with improved properties, by mutating existing genes and screening the resulting variants.[30] In 2018, the Nobel Prize in Chemistry was co-awarded to Frances Arnold, George Smith and Sir Gregory Winter for their independent works on directed evolution and phage display, which have resulted in enzymes and antibodies with numerous applications in manufacturing and medicine.[31]

Standardisation of synthetic biology parts also has a long way to go. One of the key aspects of synthetic biology is modularity, and having a range of interchangeable parts is essential – like LEGO® bricks that all snap together. Compatible parts with designated standards are increasingly being developed (e.g. BioBricks). CSIRO has identified the development of a BioBricks library as a priority for Australia, and has established a Synthetic Biology Future Science Platform to develop capability and build SynBio-based industries.[8]

Developing skills and knowledge

Synthetic biology is inherently interdisciplinary – drawing from biology, chemistry, modelling, engineering, computer science, mechatronics and the humanities (including science communication, social science, law and ethics). Consequently, an educated, multidisciplinary workforce is required to maximise opportunities in synthetic biology.

Australia is well placed to provide this. Australia's research capability in the field is ranked highly (14th in the world, ISI Web of Science) and Australian universities and industry are especially strong in tool construction, circuit design, protein engineering and biological engineering. A strong education system is also vital to building Australia's future capacity, and Australia has a robust tertiary education sector in relevant fields.[32]

However, Australia needs to increase its skills base in genome design and artificial gene construction to compete globally. Computational and programming skills as well as expertise in artificial intelligence, engineering, robotics and machine learning will be needed to support the design, test and manufacture at scale of biological components.[3]

Investing in and building the infrastructure

Commercial production facilities will be required to translate laboratory findings into large scale production of synthetic biology derived products and components. In the past decade, synthetic biology in Australia has received increased funding and investment.[3] This has led to the building of synthetic biology-related research infrastructure under the National Collaborative Research Infrastructure Strategy, including the National Biologics Facility and the Mackay Renewable Biocommodities Pilot Plant.

Access to a bio-foundry (also known as a genome foundry), an automated DNA assembly and testing facility, would also accelerate the development of economically viable projects, and help make Australia internationally competitive in this space. With this is mind, the NSW government recently invested $2.5 million towards the establishment of a bio-foundry at Macquarie University. CSIRO and the University of Queensland have also partnered to establish a bio-foundry in Queensland. The CSIRO facility is already available to researchers and industry.

Regulatory systems to manage risk

It is vital that any potential risks to human health, biosecurity, and the environment posed by synthetic biology components and systems are well-understood. A well-developed regulatory system is needed to anticipate the risks of both unforeseen consequences and deliberate misuse, weigh these risks against the risks of inaction, and provide a framework with accountability mechanisms for responsible decision-making.[33]

Australia's risk frameworks and current regulatory regime governing genetic engineering and technology is highly regarded and is sufficient for current synthetic biology applications.[34] The review of Australia's Gene Technology Scheme recommended that future advancements in the field should be carefully monitored and regulatory agencies are already in the process of identifying potential areas of legislation change to support new developments.[34]

Australia's intellectual property protection is viewed internationally as rigorous, and this will give investors confidence to support the industry.

Community engagement

A responsible research framework will recognise and respond to community perspectives. To support progress that aligns with community values, ethical, legal and social research should be incorporated from the outset into technical synthetic biology research activities. This approach is already underway, with the Responsible Research and Innovation program adopted by leading Australian institutes emphasising upstream social engagement and early consultation.

CONCLUSION

Synthetic biology holds great potential to solve global challenges, and create social and economic benefits across the medical, environmental and industrial sectors.

Australia's research capability and expertise in synthetic biology fields, regulatory environment, access to Asian markets, and strong agricultural industry makes it well placed to take advantage of the opportunities synthetic biology provides.

Significant progress will require strategic national investment in infrastructure and research, an appropriately skilled work force and a supportive regulatory environment.

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