Parliamentary Office of Science and Technology

postnote

January 2008 Number 298

SYNTHETIC BIOLOGY

Synthetic biology aims to design and build new biological parts and systems or to modify existing ones to carry out novel tasks. It is an emerging research area, described by one researcher as "moving from reading the genetic code to writing it."[1] Prospects include new therapeutics, environmental biosensors and novel methods to produce food, drugs, chemicals or energy. This POSTnote outlines recent developments, the possible applications and risks of synthetic biology and examines policy options for the development and governance of the research.

Background

In the US, where most of the research takes place, the term 'synthetic biology' describes research that combines biology with the principles of engineering to design and build standardised, interchangeable biological DNA building-blocks. These have specific functions and can be joined to create engineered biological parts, systems and, potentially, organisms.[2] It may also involve modifying naturally occurring genomes (an organism's entire hereditary information usually encoded in DNA) to make new systems or by using them in new contexts. There is sometimes confusion about the definition of synthetic biology amongst those outside the research community, reflecting its position as a complex, new and rapidly developing field.

What's new about synthetic biology?

Established DNA research methods involve using genetic material from existing organisms. Synthetic biology is free of this constraint. DNA sequences can now be designed using computers and chemically synthesised in the laboratory: from a single gene to an entire genome. In some cases this is either impossible or impracticable using existing biotechnological methods. Natural genetic components may also be used to design novel genetic sequences, biological pathways, parts and devices. Synthetic biology is also a multidisciplinary science where biologists and engineers work together to design and build biological systems from scratch, in the same way that engineers design and assemble complex devices from discrete constituent parts, with specific functions.

Advances in biotechnology

Improvements to two technologies used to study and manipulate DNA are opening the door to cheap, large-scale genome engineering, design and assembly:

- **DNA sequencing** reveals organisms' genetic make-up. Sequencing advances were instrumental in the success of the Human Genome Project and have allowed complete and large-scale DNA sequencing of many bacterial, and several plant and animal genomes.
- **DNA synthesis** chemically synthesises DNA's building blocks. For example, the genome of a medium-sized virus can now be constructed in weeks.[3]

The productivity and reliability of both methods has increased markedly in the last decade, while costs have fallen. A study for the US Department of Energy estimated that the global market for DNA sequencing technology and services exceeded $7bn in 2006. The current research market for synthetic biology is assessed at £300m but could rise to £1.8bn in the next decade.

Applications of the technology

Potential applications of synthetic biology research are diverse. Scientists speculate that the technology will offer societal, environmental and medical benefits and improve knowledge of biological processes. Box 1 highlights examples of recent research developments (from some synthetic biology research groups) with potential applications of synthetic biology including:[3]

- new biological production techniques for existing or novel biological materials and chemicals, including food ingredients and biofuels;
- new and improved diagnostics, drugs and vaccines;
- biosensors;
- bioremediation tools to process contaminants.

It is suggested that synthetic biology might provide an environmentally effective way to produce raw materials that are currently petroleum-based. However there are concerns about risks associated with synthetic biology

Box 1. Recent developments in synthetic biology: New processes for producing chemicals and drugs

Organisms can now be engineered to produce small molecules. Du Pont and Tate & Lyle produce a chemical commonly used in textiles from corn sugar using a synthetic biology process. Artemisinin is a naturally occurring, effective anti-malarial drug. It is currently obtained through extraction from a plant at high cost and with low efficiency. A $43m project at the University of California at Berkeley funded by the Gates Foundation has extensively engineered new pathways in yeast which produce a precursor to the active drug. It is hoped that this potentially high-yield method will mean that the drug will become cheaper, of consistent quality and more widely available.

Biosensors

A team at the University of Edinburgh designed and engineered bacteria as biological sensors for arsenic in water. A sequence of genes in the bacteria stimulates them to produce acid if arsenic is present above the safe level for human consumption. The resulting change in acidity can be read cheaply and simply using existing pH test devices.

Biofuels

Engineering organisms to produce hydrocarbons has received considerable interest as a possible outcome of synthetic biology. A major focus is to examine the potential for using synthetic or modified organisms to generate ethanol from plant matter. The University of California recently received $600m from BP and the US Department of Energy for bioenergy research. Several biotech companies are researching industrial applications to produce biofuels using bioengineered organisms. They speculate that fuels could be on the market within five years.

Bioremediation

Bioremediation is the use of biological systems to treat environmental contaminants. Researchers are using knowledge of natural processes to develop micro-organisms that can accumulate and/or degrade substances such as heavy metals and pesticides. For example, a team at Berkley has engineered a strain of *Pseudomonas* to degrade an organophosphate (commonly used as a pesticide).

and the scope for malicious use. For example it could be used to produce new pathogenic organisms or dangerous chemicals. Some NGOs cite possible negative economic impacts in developing countries where naturally occurring commodities may be devalued if synthetic production occurs elsewhere. The promise of the technology is also tempered by the reality that many of the more complex technologies may be a decade or more away.[3]

Government funded research

Synthetic biology in the US

The US dominates this research area, based on numbers of scientific publications, scientists involved and funding, as well as by provision of post-graduate courses for students.[4] As the research is already established there, other, related issues are also more well-defined. Existing US funding streams come from the National Institutes of Health, plus substantial contributions from the government defence and energy agencies. A recently opened multi-institution synthetic biology research facility - the Synthetic Biology Engineering Research Center (SynBERC) - further strengthens the US position in the field. It brings together scientists from life, social and computer sciences plus mathematicians and engineers. Its researchers run an undergraduate synthetic biology competition (Box 2) in which some UK universities participate.

Box 2. The international Genetically Engineered Machines competition (iGEM)

This project - co-ordinated at the Massachusetts Institute of Technology - is for undergraduates to learn about synthetic biology by designing and building a ‘genetically engineered machine’ during the summer break. University teams include students from different disciplines (science, engineering, maths and computer science) who are mentored by senior academics. Since the first project in 2003, the scheme has grown rapidly in popularity and standing. Last year it included participants from 56 university or national teams from 20 countries. The UK had four teams in the 2007 competition - from the Universities of Cambridge, Edinburgh, Glasgow and Imperial College London. Students attend the November iGEM conference in the US (at MIT) to present their work, often leading to scientific publications. Biological parts created by the students are entered into a parts library - the Registry of Standard Biological Parts. Several functional biological machines have already been created by students, including arsenic and infection biosensors, bacterially-produced red blood cell substitutes and biological photographic film.

Synthetic biology activities in Europe

The EU funds research via the Framework Programmes for Research and Technological Development (FP). The Sixth FP funded NEST (New and Emerging Science and Technology), mandated to boost promising novel scientific areas. In 2003 synthetic biology was identified as one of several targeted research areas, even though there was no identifiable European synthetic biology community. The first call for proposals led to such a community growing quickly and to a NEST High-Level Expert Group report on the subject.[5]

Research activities

This report, in turn, led to FP6 funding for 18 synthetic biology research and policy projects. Researchers at the University of Southampton are leading one European research consortium and found that the unusual flexibility of the research funding compared with other grant sources, has benefited their research programme.

European policy development activities

Five current EU-funded projects (expected to run until 2009) intend to stimulate and co-ordinate further European synthetic biology. These projects are viewed as important to keep the subject high on the research agenda, to improve competitiveness in the field and to maximise any economic benefits. They include:

- **Towards a European Strategy for Synthetic Biology (TESSY),** providing a research roadmap by looking at the broader framework for synthetic biology in Europe, bringing together dispersed research groups and scientists of different specialisms through workshops.
- **SYNBIOSAFE,** examining the ethics, perception and safety and security of the research. It will identify the commercial prospects for EU research and the frameworks for funding, ethical oversight, safety and public engagement.
- **EMERGENCE,** looking at education, infrastructural needs and attempts to standardise various aspects of the research.

The UK's position in synthetic biology research
In contrast with the US, the UK has a very small number of scientists involved, only one commercial DNA synthesis company compared with 24 in the US[4], no well-defined funding streams from the Research Councils and limited teaching. Funding is, however, becoming available: the Biotechnology and Biological Sciences Research Council and the Engineering and Physical Sciences Research Council - prompted by the EC NEST synthetic biology report - have awarded new funding (£800K) for inter-disciplinary synthetic biology networks to build the research community and to stimulate research proposals. Additional social science funding targets research on social, ethical and economic impacts.

Other than undergraduate participation in the iGEM project, the only formal teaching in synthetic biology is offered by Imperial College London's Institute of Systems Biology and Synthetic Biology (a final year undergraduate course and from October 2008, a Research Masters). Most other teaching relevant to synthetic biology is done as part of courses in systems biology: an allied subject that studies complex interactions in biological systems. Scientists involved in iGEM see it as an excellent educational programme, encouraging students to learn and share skills, defining areas for postgraduate research interests, producing high quality scientific results and seeding the next generation of synthetic biologists.

Policy issues

The main policy questions raised by synthetic biology are whether current regulation allows scientific and technical development whilst reducing potential risks sufficiently. There are also questions of the UK's capacity in this area and how this could be developed.

Biosecurity and biosafety
In the US biosecurity (such as use of the technology for malicious purposes) is a major focus for concern. In contrast, the emphasis in Europe is on biosafety (safe research conduct) as well on practical applications for the technology and on public engagement with the subject. Newly created or modified organisms might behave in unexpected ways if they are released into the environment. The main concerns include:

- unknown risks to the environment and public health;
- whether existing risk management policies are adequate for the products of synthetic biology;
- accidental release or intentional malicious use.

There is widespread recognition of the potential for negative outcomes and so the major synthetic biology conference includes sessions on biosecurity and safety every year. One response is to engineer failsafe self-destruct mechanisms into new organisms, which are triggered if they are accidentally released into the environment.

The Health and Safety Executive and the Environment Agency are monitoring developments. They suggest that risks to the environment and human health are not well-defined.[6] Assessing the risks of synthetic organisms may be difficult since there may be no natural equivalent from which to draw comparisons. For those based on natural pathogens or with pathogenic mechanisms, associated risk may be easier to assess. Although it is considered unlikely that synthetic organisms could survive outside a laboratory environment and would pose lower risks than naturally occurring micro-organisms, it is unclear whether they could become self-sustaining and able to evolve. Research is subject to existing regulation for genetically modified organisms but this will be kept under review.

Defence: threats and opportunities
It is possible that new or modified organisms could be developed for use as offensive weapons. The Ministry of Defence's 2006 Defence Technology Strategy highlighted synthetic biology as one of several technologies that might impact on future defence capability. In 2006, the department held a synthetic biology workshop and the Defence Science Advisory Council agreed to examine the military opportunities and threats that may be presented.

Patenting synthetic biology
Some view existing intellectual property (IP) law as inappropriate for rapidly developing biotechnologies. The main challenge is providing a framework to encourage investment without stifling research/restricting benefits. For synthetic biology, patent protection can be applied:

- to methods, techniques or technologies;
- to specified sequences of DNA.

For example, a pared-down version of *E.coli*, a bacterium commonly used in biological research, has been patented. Patents may be speculative and broad in scope. For instance, the J. Craig Venter Institute in the US has applied for rights to a gene sequence representing the 'minimal requirements for life' for a synthetic, self-replicating version of a bacterial species. While it has yet to produce a functional version, it has applied for broad patents to cover the creation of any synthetic genome. Some scientists and NGOs argue that synthetic biology is at an early stage and that inappropriate patenting of basic research could stifle progress and limit competition if proprietary products or technologies cannot be easily accessed.

An alternative to patenting gene sequences is the 'open-source' approach. An example of this is the Massachusetts Institute of Technology's (MIT) Registry of Standard Biological Parts (Box 3).[6] Researchers can use any of the biological building blocks (called BioBrick parts) and data held in the Registry, but must report any improvements and modifications and register new parts on the same terms. However, problems with IP have arisen even with this open-source approach. For instance, it has emerged that some of the standard parts in the Registry have been patented. This may restrict researchers' access to parts and raises questions about IP ownership of devices that may incorporate patented parts. Registry users may be reluctant to find out which parts are patented since this may expose infringements by unlicensed users. Some speculate that as DNA synthesis costs decrease, it would be easier for companies to synthesise their own parts rather than to access those held in open repositories.

Box 3. A Registry of Standard Biological Parts
The MIT has developed a repository of over 2000 standardised biological building blocks (BioBrick parts) which anyone can use. These parts are designed, standardised and indexed so that they can be easily assembled with others into integrated parts, devices and systems. At present the registry holds the physical DNA but it is expected that this will change to just a specification or set of instructions as DNA synthesis technologies become more accessible. The MIT group believes that such repositories are a critical step towards the design and construction of integrated biological systems and will encourage an open community of biological engineers and scientists. It is unclear how well-aligned repositories designed by different institutions or countries might be, and what consequences for research progress this might have.

Some groups oppose patenting of DNA sequences and organisms and see this as the first step in 'privatising' synthetic life forms.[7] Others do not support wholesale prohibition of genomic patents, but prefer to see them granted only if standard patent criteria of novelty, usefulness and non-obviousness are apparent.

Governance of synthetic biology research
Several international projects are monitoring research progress and developing models to oversee its development and to characterise the risks and benefits. A 2007 review in the US proposed several governance options for the development of synthetic biology to maximise potential benefits and to reduce risks.[3] These focus on laboratory safety, biosecurity and the protection of the environment and human health. It proposed policy intervention points by oversight of:
- companies selling synthetic DNA and synthesisers;
- owners of DNA synthesis technologies (licensing);
- end-users of synthetic genomics (individuals and institutions).

Some comment that such regulatory frameworks are unlikely to be successful without international agreement.

Scientists are keen for active dialogue about safety and other issues that the research presents. The Royal Academy of Engineering is undertaking an inquiry into the field, following previous work on a related area.[8] The Royal Society has set up an expert synthetic biology policy co-ordination group. Members come from government departments, research funders, policy organisations, NGOs and the science community. The group will exchange information on national and international developments, identify gaps in current policy and co-ordinate the responsible and responsive development of synthetic biology. It also aims to minimise duplication of work and to promote collaboration. NGOs are campaigning for more inclusive decision making processes about such research rather than leaving it to scientists, expert groups and funders.

Some scientists believe research council investment in synthetic biology should fund research and schemes like iGEM, rather than setting up networks. The research councils expect the networks to encourage growth of the community. They already offer flexible responsive funding to scientists with proposals in synthetic biology. Without clear consensus on a definition of synthetic biology defining research for funding purposes is difficult. Some argue that it does not constitute a new area of science at all and is simply an extension of genetic engineering. Scientists also comment that they find raising funding for inter-disciplinary research very difficult despite cross-council funding arrangements. This could be detrimental to the development of synthetic biology in the UK.

Social and ethical considerations
Some groups have ethical objections to creating DNA sequences that do not occur naturally and to experiments that involve new or mixed-species organisms. Other concerns relate to ownership and control of the technology and to research safety. NGOs concerned with the impacts of science and technology want regulatory oversight, public engagement and broad debate to raise awareness of synthetic biology in the UK and globally. Others believe that the science is at too early a stage and that such activities could be counter-productive.

Overview
- Synthetic biology is an immature but rapidly developing area involved with research into novel, engineered purpose-built biological parts, devices and organisms.
- Several high level policy projects - many involving the scientific community - in the US and Europe are assessing the potential risks and benefits involved and formulating governance strategies.
- UK government departments are beginning to assess the relevance of the technology.
- The UK's synthetic biology community is small and funding for this type of multidisciplinary research falls within the remits of several research councils.
- There is concern that the research should be developed with a global, open dialogue about the scientific, social, economic and ethical implications.

Endnotes

1 Next Dream for Venter: Create Entire Set of Genes From Scratch (quoting Dr Venter), *The Wall Street Journal*, 29 June 2005
2 http://parts.mit.edu/
3 *Synthetic Genomics - Options for Governance*, The J. Craig Venter Institute, Massachusetts Institute of Technology & Center for Strategic and International Studies
4 *Constructing Life - Early Social Reflections on the Emerging Field of Synthetic Biology*, Huib De Vriend, The Hague: Rathenau Institute, Working Document 97, 2006
5 www.cordis.lu/nest/home.html
6 *Horizon Scanning Group Report - Synthetic Biology*, SR010, March 2007, Health and Safety Executive
7 *Extreme Genetic Engineering – An Introduction to Synthetic Biology*, January 2007, etc Group, www.etcgroup.org
8 *Systems Biology: A Vision for Engineering and Medicine*, February 2007, Academy of Medical Sciences and The Royal Academy of Engineering

POST is an office of both Houses of Parliament, charged with providing independent and balanced analysis of public policy issues that have a basis in science and technology.

POST is grateful to all contributors and reviewers. For further information on this subject please contact the author, Dr Sarah Bunn, at POST.

The Parliamentary Office of Science and Technology, 7 Millbank, London, SW1P 3JA; Tel: 020 7219 2840; email: post@parliament.uk

www.parliament.uk/parliamentary_offices/post/pubs.cfm