

Using supervised learning algorithms to search metabolomics and preoteomics information about genetic make-up and gene function in order to identify genes that control the stability of enzymic catalysis in bacterial cells – and using these to define the criteria for making artificial 'minimal host cells'. The idea is that these simple cells would be dedicated to carrying out specific enzymic reactions and would be much more efficient than current industrial biocatalysis, which relies on using modified conventional cells. (University of Manchester)

Constructing novel biomolecules that act as switches by inserting new functional sites into protein molecules so that they have the capacity to respond to an external signal. The construction of such proteins will allow a specific activity to be switched on and off by the signal. Protein switches of this sort have potential for use as sensors and modulators in systems ranging from the cell to components in diagnostic devices. (Cardiff University)

Ethical and other societal issues

It is very important that ethical and other social issues are identified at this early stage in the development of Synthetic Biology, before new products and processes are made, so that research funders and researchers can take these into consideration.

In 2007, BBSRC's Bioscience for Society Strategy Panel established a working group to consider the societal issues raised by Synthetic Biology. The group commissioned an independent review of UK Synthetic Biology and its broader social context, Synthetic Biology: Social and Ethical Challenges by Dr Paul Martin and Andrew Balmer of the Institute for Science and Society, University of Nottingham.

We are using the findings of this review (www.bbsrc.ac.uk/ syntheticbiology.html) to inform our policy and funding decisions and to help us to raise public awareness and stimulate constructive public debate. We are working closely with EPSRC, AHRC, ESRC and other bodies; with BBSRC focusing initially on working with Government advisory committees and others to ensure that the UK's regulatory framework can provide robust safeguards for taking Synthetic Biology forward safely and responsibly.

The review by Martin and Balmer drew attention to several issues, including:

- intentional or accidental release of synthetic organisms into the environment
- misuse of synthetic organisms e.g. to create biological weapons
- a need to employ the precautionary principle
- commercial race to synthesise and privatise synthetic life forms
- current patent law may stifle collaboration and development, and overcomplicate the patent process
- perceptions of scientists 'playing God'

Each Network in Synthetic Biology (see overleaf) is required to address ethical, legal and social issues (ELSI) as an integral part of its research; drawing upon expertise from the humanities and social sciences as appropriate.

ELSI considerations are also embedded in Europewide policy development activities that include:

- Towards a European Strategy for Synthetic Biology (TESSY), providing a research roadmap in Europe
- SYNBIOSAFE, to identify the commercial prospects for EU research and frameworks for funding, ethical oversight, safety and public engagement
- EMERGENCE, looking at education, infrastructural needs and to standardise various aspects of the research.

Potential applications

Some of the earliest applications of Synthetic Biology are likely to be in 'second generation' biosensors and diagnostics for use in biomedicine and environmental monitoring and protection. In these cases, Synthetic Biology will be providing an expanded 'tool box' that enables existing genetic or protein synthesis and manipulation at the level of individual molecules to be conducted more quickly, and across a wider range of applications than currently possible.

Projected areas of application include:

- Novel and improved diagnostics, vaccines and biopharmaceutical drugs
- Biosensors
- Hydrogen fuel cells
- New cell-biofactories
- Microbial communities for environmental clean-up
- New biomaterials
- Programmable cells for use in gene therapy
- New biofuels
- New food ingredients

At the level of individual cells, Synthetic Biology will provide new capability for scientists to ramp up what can be done at the moment in terms of the profile of products produced, and to increase the efficiency of producing high-value compounds. This is expected to improve existing processes for manufacturing biopharmaceuticals. Longer-term researchers might be able to add their own building blocks to core materials such as nucleic acids and proteins to produce novel products. Advances in understanding and manipulating cell-to-cell signalling will offer new opportunities to use synthetic biology to build simple communities of cells, for example, to make scaffolds and biofilms, for example for use in new materials, for environmental clean-up and filters, and to make cell cultures as feedstocks for production of biopharmaceuticals, other high-value bioproducts and energy.

Longer-term possibilities include artificial 'cells' ie. entities, packages that provide the essential components to manufacture bioproducts and technologies to produce tissues of 'defined' architecture and structure eg. in medical tissue engineering or plant breeding, to control the direction of growth of cells and cell interactions.

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Synthetic biology

Linking bioscience, engineering and computer sciences to develop rationally designed biological parts, devices and systems.





"Synthetic Biology offers new tools for research and a new framework for biotechnologies. Until now, biotechnological and biomanufacturing processes have been confined largely to the use of single genes or proteins in bespoke applications, each requiring its own specific set of tools and reagents. Synthetic Biology holds out the prospect of universal tool kits and interchangeable components that may be deployed in combinations to construct biological pathways and more complex systems, including artificial cells. An example is the potential to design and produce biological fermentation processes that can convert non-edible parts of food crops and wastes into energy – so-called 'second-generation biofuels." Professor Nigel Brown

BBSRC Director of Science and Technology

The Biotechnology and Biological Sciences Research Council (BBSRC) is leading national efforts to increase the UK's capacity and competitiveness in the emerging field of Synthetic Biology – where the research market is predicted to rise to £1.8Bn in the next 10 years.

In partnership with the Engineering and Physical Sciences Research Council (EPSRC), we have established new 'networks' for synthetic biology around research groups at the universities of Bristol, Durham, Edinburgh, University College London and Birkbeck College, Nottingham and Oxford. These take forward both the science and ethical and social issues surrounding its applications, the latter supported by funding from the Arts and Humanities Research Council (AHRC) and the Economic and Social Research Council (ESRC).

BBSRC is also leading the UK in Europe through TESSY (Towards a European Strategy for Synthetic Biology), a collaborative activity that will produce a roadmap for developing Synthetic Biology across the EU.

Early career scientists supported by BBSRC participate in the International Genetically Engineered Machine (IGEM) competition, an initiative of the MIT iCampus programme, in the USA funded by Microsoft Corp. (http://igem.org).



As with other new developments in bioscience, such as bionanotechnology and systems biology with which it is closely associated, Synthetic Biology is an approach rather a discrete set of activities with defined boundaries.

At its core is the application of the principles of engineering to bioscience. In essence, this means being able to: define individual components; standardise them; and reconfigure them to produce novel products, which can then be modelled, tested and validated.

One defining feature of Synthetic Biology is the drive towards a 'universal currency' that will allow scientists to assemble and interchange biological components rationally to make new systems – at the level of molecules, cells and tissues. Two approaches are being pursued to provide the fundamental information and understanding about core biological processes. In top-down approaches, elements are systematically removed, with the aim of identifying a minimal core of processes that can be studied and manipulated. In bottom-up approaches, individual components are put together with the aim of constructing functioning entities.

As with other innovations in the biosciences, Synthetic Biology encompasses some activities that are extensions of natural processes and/or existing technologies, and some that are completely new. Examples of the former include developing multi-component kits of molecular 'building bricks', 'switches' or 'motors', rather than single one-off components as currently. These kits would enable procedures for regulating gene activity or transferring genes between organisms to be standardised and accelerated. An example of the latter, novel technology, is the synthesis of an artificial sequence of DNA designed to exhibit novel properties or the design of wholly artificial chemical cells (chells).

BBSRC's focus is at the fundamental level of exploring

the potential of synthetic biology approaches to create technology platforms on which researchers funded by BBSRC or by other agencies may create new products.

BBSRC funding and support

BBSRC established a Working Group on Synthetic Biology in 2006, under the chairmanship of Professor Rob Beynon of the University of Liverpool. This has advised BBSRC's strategy in this area and led to a seminal workshop in 2007

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- Research community Networks led by seven universities
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- Core related research in areas such as systems biology, bioengineering and bionanotechnology.

BBSRC currently spends around £19M a year on projects in synthetic biology and core related research areas.

The new Networks

Research Councils funding to the Networks is aimed at facilitating multidisciplinary working and development of a 'common language' between bioscience and engineering research groups, as well as supporting the development of new research tools.

"By developing this emerging science, the UK will continue to keep its leading edge and increase its international competitiveness for the future. This initiative is aimed at raising UK profile and capability in this area to put the country at the forefront of the field."

Ian Pearson, Minister for Science and Innovation speaking in May 2008

Some Networks are addressing generic approaches, focusing on multidisciplinarity and the development of basic 'tool kits'. Others are exploring specific technical challenges and specific potential applications.



XXXXXX XXXXX XXXXXX Credit: Alistair Gentry (artist-inresidence at the ESRC Genomics Forum, from a video installation called Three Times True.)

Edinburgh - Standards for the Design and Engineering of Modular **Biological Devices** Leader: Dr Alistair Elfick

This Network brings together a group of researchers who will meet in the UK and in the USA with invited experts in the field to address standardisation issues around parts-based synthetic biology. A particular aim is to produce resources,

such as validated protocols, for use by synthetic biologists.



Bristol - Synthetic Components Network: Towards Synthetic Biology from the Bottom Up Leader: Professor Derek Woolfson

The Synthetic Components Network is a Bristol-led consortium involving the Universities of Durham, Leeds, Oxford, Sheffield and Sussex, together with NIMR London and Unilever. Its aims are: to consider 'bottom-up' approaches to assemble



Biomolecular toolkit approach at Bristol.

systems from their component parts - producing biomolecular toolkits based on natural components and processes will be a key part; to help develop and define this biomoleculardesign approach; and to consider specific and broader ethical, legal and social issues with ethicists and the public.

Nottingham - A Synthetic Biology Network for Modelling and Programming Cell-Chell Interactions Leader: Dr Natalio Krasnogor

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Simulated self-assembled lipid vesicle - a protocell membrane with pores.

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Sheffield - Microbial Applications to Tissue Engineering: An Exemplar of Synthetic Biology Leader: Professor Phillip Wright)



Image of metabolic networks Courtesy of Phillip Wright and Josselin Noirel, University of Sheffield.

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