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New life from reprogrammable cells

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Scientists at The University of Nottingham are leading an ambitious research project to develop an in vivo biological cell-equivalent of a computer operating system, or CellOS for short. If successful, the project to create a 're-programmable cell' could revolutionise synthetic biology and pave the way for scientists to create completely new, useful life forms.

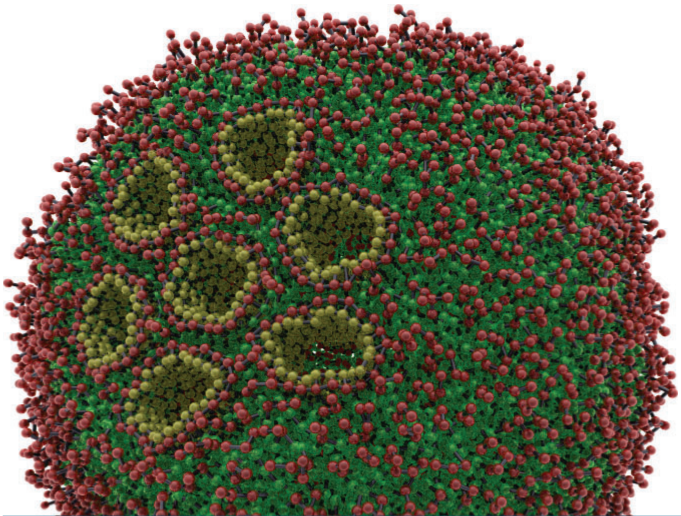
Towards a Biological Cell Operating System

A multidisciplinary team of researchers led by Professor Nat Krasnogor is pursuing a fundamental breakthrough that will — ultimately — enable scientists to prototype rapidly, implement and deploy living entities that are completely new and do not appear in nature, adapting them so they perform new useful functions.

The project — Towards a Biological Cell Operating System (AUdACiOuS) — is attempting to go beyond systems biology, the science behind understanding how living organisms work, to give scientists the power to create biological systems. The team will start the work by attempting to make e.coli bacteria much more easy to program. This technology could substantially accelerate Synthetic Biology research and development, which has been linked to myriad applications — from the creation of new sources of food, biofuels and environmental solutions to a host of new medical breakthroughs such as drugs tailored to individual patients and the growth of new organs for transplant patients.

AUdACiOuS is a substantial collaborative effort involving computer scientists, biologists and chemists from Nottingham as well as academic colleagues at other universities in Scotland, the US, Spain and Israel. Importantly, the project includes robust collaborations with experts in Ethical, Legal and Societal matters who will help shepherd the project through any delicate issues that this research might uncovered during its execution. It is funded with a Leadership fellowship for Professor Krasnogor worth more than £1m from the **Engineering and Physical Sciences Research Council** (EPSRC).

Among the most fundamental challenges facing the scientists will be developing new computer models that more accurately predict the behaviour of cells in the laboratory. Scientists can already program individual cells to complete certain tasks but scaling up to create a desired, more complex, biological functionality remains a challenge.



Reprogramming E.coli

- A bacterium is an information-processing machine.
- Each bacterium has sub-systems that work in concert by sensing external stimuli, assessing internal states and making decisions through a network of complex and interlinked biological regulatory network (BRN) motifs that act as the bacterium neural network.
- Its decision-making processes often result in various outputs: more cells, chemotaxis, bio-film formation, etc.
- Research shows cells not only react to their environment but even predict environmental change.
- Synthetic Biology (SB), considers the cell a machine which can be built from parts in ways similar to electronic circuits and airplanes.
- This research aims to make E.coli bacteria easier to program and to harness for useful purposes.
- Using tools, methodologies and resources computer science created for computer programs, researchers will find ways of making them useful in the microbiology lab.

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From computers to programmable cells

This EPSRC Leadership Fellowship will allow Professor Krasnogor and his fellow researchers to transfer their expertise in computer science and informatics into the wet lab, while simultaneously creating a new platform for next generation computing, namely, living cells. Currently, each time a cell is needed that will perform a certain new function, scientists have to employ a long and laborious process to recreate it from scratch. "Most people think all we have to do to modify behaviour is to modify a cell's DNA," said Professor Krasnogor, "but it's not as simple as that — we often find we get the wrong behaviour and then we're back to square one."

"If we succeed with this AUdACiOuS project, in five years time, we will be programming bacterial cells in the computer and compiling and storing its program into these new cells so they can readily execute them. Like for computers, we are trying to create a basic operating system for a biological cell."

The technology could be used in a whole range of applications where being able to modify the behaviour of organisms could be advantageous. In the long run, this includes the creation of new microorganisms that could help to clean the environment for example by capturing carbon from the burning of fossil fuel or removing contaminants, eg arsenic from water sources. The efficacy of medicine could be improved by tailoring it to specific patients to maximise the effect of drugs and reduce harmful side effects.

Professor Natalio Krasnogor

> We are looking at creating a cell's equivalent of a computer operating system in such a way that a given group of cells could be seamlessly re-programmed to perform any function without needing to modifying its hardware.

About the author

Professor Natalio Krasnogor is an EPSRC Leadership Fellow in Synthetic Biology and Professor of Applied Interdisciplinary Computing in the School of Computer Science at The University of Nottingham. He leads the **Interdisciplinary Computing and Complex Systems (ICOS) Research Group** and works collaboratively with other groups across the University and at other institutions.

His research activities lie at the interface of computer science and the natural sciences – including biology, physics and chemistry. He has applied his expertise to bioinformatics, systems biology, synthetic biology, nanoscience and chemistry. In particular, he focuses upon developing innovative and competitive search methodologies and intelligent decision support systems with an emphasis on transdisciplinary optimisation, modelling of complex systems and very-large datasets processing.
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About ICOS

The mission of the **Interdisciplinary Computing and Complex Systems research group (ICOS)** is to derive new knowledge and provide innovative solutions to problems arising in natural complex systems such as in biology, chemistry and physics and man-made ones including socio-technical organisations, infrastructure in healthcare and logistics. To accomplish its mission, the group leverages its interdisciplinary expertise in advanced information processing (eg image analysis, machine learning, data mining), process modelling (eg optimisation under uncertainty), and high-performance computation (eg distributed, cloud and GPU computing).

ICOS three main research areas are:

- Bioinformatics, Systems and Synthetic Biology
- Information Processing in Complex Systems
- Machine Intelligence

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