ESIGNET
NEST ADVENTURE

The project could have applications in investigations into quite different networks – traffic, telecommunications, even business-communication networks.

Evolutionary cell signalling

A multi-disciplinary team of four research groups plans to create new computer simulations of cell-signalling networks (CSNs) in the ESIGNET project. Through mathematical modelling and software development, they aim to investigate biological CSNs and computational methods for evolving artificial CSNs. One practical outcome will be open-source code for 'filling in' the unknown parts of partially characterised CSNs. Researchers in the life sciences and in drug discovery could be among the beneficiaries.

Cell signalling is a key area in biology which deals with how cellular processes in biological organisms may be regulated by signals from other cells or cues from the environment. Investigating how cell signalling is carried out in the human body and what happens if components of the signalling pathway are defective is critical in understanding how diseases such as cancer develop and spread through the body. Abnormalities in cell-signalling pathways have been implicated in the progress of many other diseases and illnesses, such as cholera, rheumatoid arthritis and diabetes. This is one reason why pharmaceutical companies have concentrated a lot of resources on the development of drugs that target key components of signal pathways, and kits and assays for detection of diseases.

CSNs contain molecules with which they respond to and transduce signals. As input-output systems, CSNs may be likened to computers – their biochemical reactions to appropriate electronic circuits. The aim of the ambitious ESIGNET project is to develop software to simulate biological CSNs. The work involved demands a combination of expertise in biology, computer science and control engineering which is not found in any single Member State. Bringing together researchers from the United Kingdom, Germany, the Netherlands and Ireland, this is a project with clear European added value.

Artificial CSNs

To achieve their aims, the team will first have to develop languages for data entry and for representing the computational properties of CSNs. They will implement fast evolutionary algorithms for subjecting artificial CSNs to a computational evolutionary process as a means of generating descendants that behave just like biological CSNs. The resulting software will take as an input a desired computational task and calculate for its output a CSN capable of carrying out that task. In a parallel effort, the partners will use existing simulation software to investigate real CSNs and mathematical modelling to describe their properties so that artificial CSNs can be developed with matching properties.

In real life, CSNs often share components – in this way one signal-transduction pathway may regulate another. The consortium will create software to mimic this 'cross-talking' in artificial counterparts. To validate the evolved CSNs, the team will develop software to transfer them to

➔

Evolutionary computation techniques are already used in industry for optimising jobs.

ESIGNET
NEST ADVENTURE

AT A GLANCE

Official title
Evolving cell signalling networks in silico

Coordinator
United Kingdom: University of Birmingham, School of Computer Science

Partners
- *The Netherlands: Technical University Eindhoven*
- *Germany: Friedrich Schiller University*
- *Ireland: Dublin City University*

Further information
Dr Jonathan Rowe
School of Computer Science
University of Birmingham
Birmingham, B15 2TT, United Kingdom
Fax: +44 121 414 4281
E-mail: jer@cs.bham.ac.uk

Duration
36 months

Project costs
€ 1 599 999

EU funding
€ 1 599 999

Project reference
Contract No. 12789 (NEST)

Web: http://www.cordis.lu/nest

existing molecular-dynamic and artificial-chemistry packages. They can then test them in realistic molecular simulations.

CSN 'predictor' and other applications

In addition to providing useful insights for biologists into the workings of CSNs, software developed during the project's three-year duration has the potential to improve productivity in several industry sectors. The team will develop a 'predictor', for example, to allow unknown components of partially known pathways to be identified. The input for this software module will be a description of an incompletely identified CSN and a specific computation; the output will enumerate possible candidates. Experimental *in vitro* methods for analysis of real CSNs are time-consuming and costly, so this could be useful in the pharmaceutical industry for drug development as well as for scientific research.

Within biology, ESIGNET will give a completely new perspective on the properties of real CSNs and new ways to study them.

Looking to the future, members of the ESIGNET team believe that findings from the project could well have applications in investigations into quite different networks – traffic networks, telecommunications networks, even business-communication networks, for example. Evolutionary computation techniques are already used in industry for optimising jobs. As this project will increase experience in this field of computing, there may be benefits too for human resource management in Europe.

The possibilities do not end there. 'Closure' occurs when cross-talking CSNs self-regulate and thereby maintain homeostasis in the system. A question the partners are looking for answers to is: "How well can CSNs maintain closure in the face of abrupt changes in their environment?" If answers are found, they may hold lessons in the design of more resilient control systems in engineering.

SIXTH FRAMEWORK PROGRAMME