Systems biology

bbsrc
biotechnology and biological sciences research council

"Since 2004, BBSRC has committed over £85M for research, training, infrastructure and resources for systems biology. This has helped the UK to become a major international force in this science and its applications."

Professor Nigel Brown
Director of Science and Technology

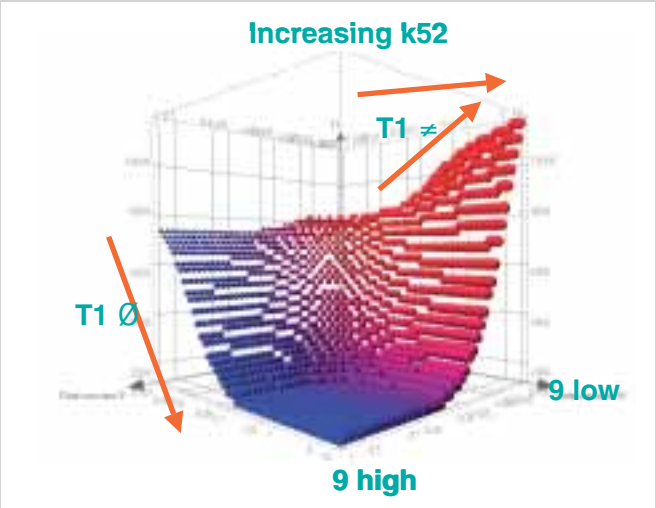
- Dedicated research centres
- Focused postdoctoral training
- Collaborative research with industry
- International partnerships
- Funding for mathematical resources
- £25M for large grants and networks

Systems biology – a definition

Systems biology is an approach by which biological questions are addressed through integrating experiments with computational modelling and theory, in re-enforcing cycles.

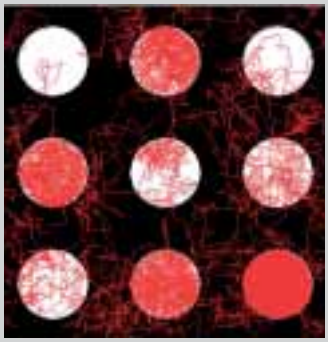
In practice it works like this. Researchers use mathematical models and current data to develop ideas and hypotheses, which they test experimentally. They then use the results of the experiments to refine and expand the models, making them as encompassing and systems-wide as possible. The refined models are then tested by further rounds of experiments, each time being developed further. In its fullest expression, systems biology integrates information across different levels of organisation to explain **biological function at all levels**: from molecules and cells to whole organisms and populations.

Systems biology depends on high-powered computation to construct **predictive models**. Typically these draw upon the large amounts of quantitative data generated by high-throughput techniques such as genomics (DNA content of cells), transcriptomics (the messenger RNA produced from active genes) proteomics (the proteins produced from the messenger RNA) and metabolomics (small compounds in cells). The models relate these data to research on metabolic and other functions in cells and tissues, and to the physiology and behaviour of whole organisms.



Manchester Centre for Integrative Systems Biology (MCISB)

The dynamics and reorganisation of cell surface receptors that occur on white blood cells during development of an immune response are being studied by imaging techniques as part of an experiment-theory programme at **Warwick Systems Biology Centre**. One aim is to develop and verify a model of signalling and receptor dynamics in this process.



Applications

Systems biology enables an holistic analysis of individual systems and processes as well as investigation of how different processes interact in complex living systems. For example, it offers a powerful way to identify: critical steps in metabolic pathways that trigger particular responses; genetic variations that exert the most impact on commercially important traits in crops and livestock, and key gene-environment combinations that affect ageing and immune responses.

Expected benefits from systems biology research include:

- faster routes to 'lead' candidates for new drugs and bioprocesses for the pharmaceutical and biotech sectors
- better forecasting and diagnostics for diseases of plants and animals (including humans)
- increased ability to 'design' products such as bio-compatible materials for surgery, bio-fuels, healthier foods and renewable feedstocks for manufacturing.

BBSRC Centres for Integrative Systems Biology

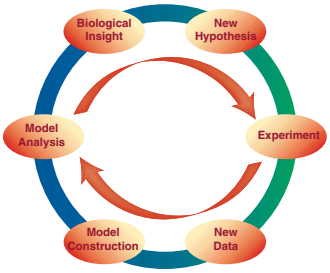
BBSRC is investing over £45M in dedicated centres for systems biology in universities across the UK.

Established in 2005, representing an investment of £20M (including £3M from EPSRC)

Imperial College London

Focus: Host/pathogen interactions

Key technologies include: high-throughput genomics, proteomics, transcriptomics and glycomics; cutting-edge imaging facilities; data integration; machine learning; dynamic systems modelling



Imperial College Centre for Integrative Systems Biology (CISBIC)

Targets include: prediction of glycan expression from pathogen genomes; recognition and signalling mechanisms in innate immune responses; predictive models for vaccine design; robust methods of integrating data sets; new tools for multi-scale modelling

www.imperial.ac.uk/cisbic

Centre for Integrated Systems Biology of Ageing and Nutrition (CISBAN)

Newcastle University

Focus: ageing and nutrition

Key technologies include: quantitative high-throughput 'omics technologies, stochastic modelling, distributed bioinformatics workflows, high-throughput automated yeast genetics screening, cell biology including stem cell biology, *in vivo* studies, cell imaging, data archival and integration, statistical methods for calibration of biological models against experimental data

Targets include: cell maintenance networks and their vulnerability to damage, identification of targets for interventions to secure healthy ageing, interactions between nutrition and intrinsic mechanisms of biological ageing

www.cisban.ac.uk

University of Manchester

Focus: quantitative modelling of yeast and mammalian cell biology; training the next generation of systems biologists

Key technologies include: quantitative high-throughput omics technologies, especially proteomics and metabolomics; high-throughput protein purification and enzyme kinetics; distributed bioinformatics workflows; automated literature mining and kinetic model building; visualisation and system identification

Targets include: quantitative and predictive models of large-scale biochemical systems; distributed integrated toolboxes for systems biology

www.mcisb.org

Manchester Centre for Integrative Systems Biology (MCISB)


Courtesy of CISBIC

Established in 2006, representing an investment of £27M (including £4.8M from EPSRC)

University of Edinburgh


Centre for Systems Biology at Edinburgh (CSBE)

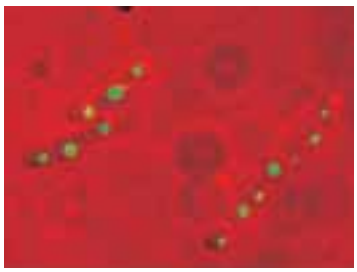
Focus: RNA metabolism, interferon pathway and circadian rhythms

Key technologies include: modelling, advanced computation

Targets include: identification of general principles of biological organisation in dynamic systems and opportunities for manipulation

http://csbe.bio.ed.ac.uk

University of Oxford

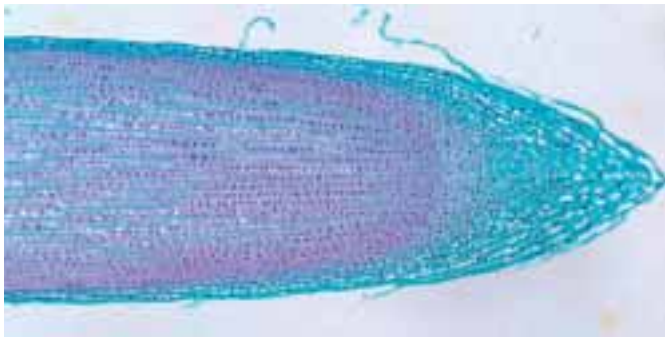

Oxford Centre for Integrative Systems Biology (OCISB)

Focus: signalling networks in bacteria and eukaryotic microbes

Key technologies include: cutting-edge microscopy including fluorescence microscopy to track the dynamics of single molecules and their interactions in living cells under different conditions, and to correlate these with in vitro measurements

Targets include: a predictive model of how single-cell organisms sense, respond and adapt to their environment

www.bioch.ox.ac.uk/sysbio


Centre for Plant Integrative Biology

University of Nottingham

Focus: integrative biology applied to the control of plant root growth

Key technologies include: *Arabidopsis* genetics, genomics, proteomics and metabolomics, plant biophysics, mechanical engineering, adaptive finite element analysis, cell and whole-organ imaging, computer vision, multiscale modelling from molecular to whole-organ level

Targets include: develop a multi-scale, predictive 'virtual root' of *Arabidopsis* which can be integrated with other organ models; translate this approach to crop species for sustainable agriculture; develop plant strains and antibodies for use by the plant-science community

www.cpib.info

In addition, many scientists supported by BBSRC grant funding now work in multidisciplinary groupings and centres, which have been established by UK universities to take forward systems biology.

Support for systems biology

BBSRC supports research and training in system biology through a range of mechanisms.

Dedicated research centres

These bring together researchers from diverse disciplines, including biosciences, engineering, mathematics, statistics, physics, chemistry and computation, around specific biological themes. They provide training in specialist and cutting-edge technologies (see centre pages).

Targeted collaboration with industry

To help UK bioindustry harness the new information provided by systems biology, we are encouraging joint academic-industry projects, 50:50 funded schemes through EBS-LINK and support for collaborative research between our six Centres and industrial partners.

Focused postgraduate training

In partnership with the Engineering and Physical Sciences Research Council (EPSRC) we have established three Doctoral Training Centres in Systems Biology (at a total cost of £11M) at the universities of Manchester, Oxford and Warwick. BBSRC is supporting a total of 30 studentships.

We have also announced plans for a further 20 studentship awards specifically in systems biology (see below).

Grant awards

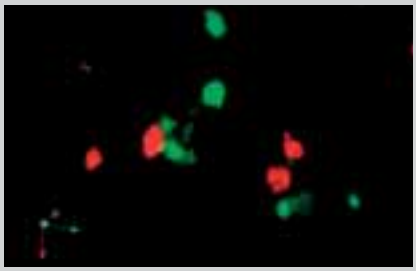
BBSRC supports systems biology research through standard grants, with an overall spend of approximately £30M since 2005. We are also contributing up to £25M in a new funding partnership with EPSRC to increase capability in systems biology. This will support large projects (£2M-£6M) that include private sector involvement. Twenty BBSRC studentships will also be made available through this scheme.

BBSRC also supports systems biology research indirectly in many ways. These include funding for e-science, bioinformatics and biological resources and for the development of new research tools and resources.

BBSRC has introduced a policy to establish a culture of data sharing in the biosciences, facilitating the development of standards and providing tools for data mining, curation and annotation.

Mathematical resources and networks

We are fostering a new inter-disciplinary community of mathematicians and bioscientists by supporting new networks for collaboration. These are expected to generate innovative new mathematical tools for analysing and understanding biological processes. Initial awards have been made for networks in genetics (Edinburgh); immunology and imaging (Leeds); cell signalling (Nottingham); plant biology (University of East Anglia) and gene networks (Roslin Institute).



International partnerships

We support research and networking with scientists around the world, to build on respective strengths and to help keep UK research at the forefront (see back page).

International partnerships

BBSRC supports international collaboration to develop and deliver systems approaches in the biosciences. This includes joint funding and support for networking.

We have contributed £5M to a £7.5M initiative with the **Agence Nationale de la Recherche**, France, to support high quality joint proposals in systems biology of microbes, plants and animals. Ten projects are being supported in areas including neurobiology, organelle function, plant development, insect biology, pathogen evolution and animal metabolism.

Several BBSRC **Partnering Awards** for collaborative research between UK scientists and researchers in China, India and Japan respectively are supporting systems biology projects. Examples include:

- **A 'virtual laboratory' for systems biology of membrane function**
  This brings together a total of over 40 research leaders from the University of Leeds and seven research centres in China, in disciplines including biophysics, engineering, cell biology and medicine.
- **Heart cell modelling**
  Integrated models, from single cells to whole heart function, are being explored by scientists at the University of Oxford and Kyota University, Nara Medical University and Okayama University in Japan.
- **Plant and crop science**
  Researchers at the University of Leeds and the Indian Agricultural Research Institute are harnessing expertise in mathematics and rice genomics to extract information about gene function and to develop models of more complex crop genomes.

European Research Area Network (ERA Net)

SysMO is a transnational initiative on Systems Biology in Micro-organisms, which focuses on organisms relevant to bio-energy, health, biotechnology, nutrition and environmental protection. This pilot programme is a joint activity within the **Systems Biology ERA-Net**. It was set up by six European agencies: BBSRC contributed £7.4M to the £18M programme, with funding partners in Germany, Austria, the Netherlands, Norway and Spain. Of the 11 projects, 10 involve UK partners.

Professor Phillip Wright from the University of Sheffield is part of a Sysmo-funded consortium that is using the 'thermophilic' microbe *Sulfolobus solfataricus* as a model to help understand how and why metabolic networks could fail to adapt to different temperature conditions. Increased understanding of how microorganisms can withstand such extreme environments is vital for product novel bioproducts, such as industrial enzymes, that can function at elevated temperatures.

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For further details email **iru@bbsrc.ac.uk** (international) or see **www.bbsrc.ac.uk** (general enquiries)

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