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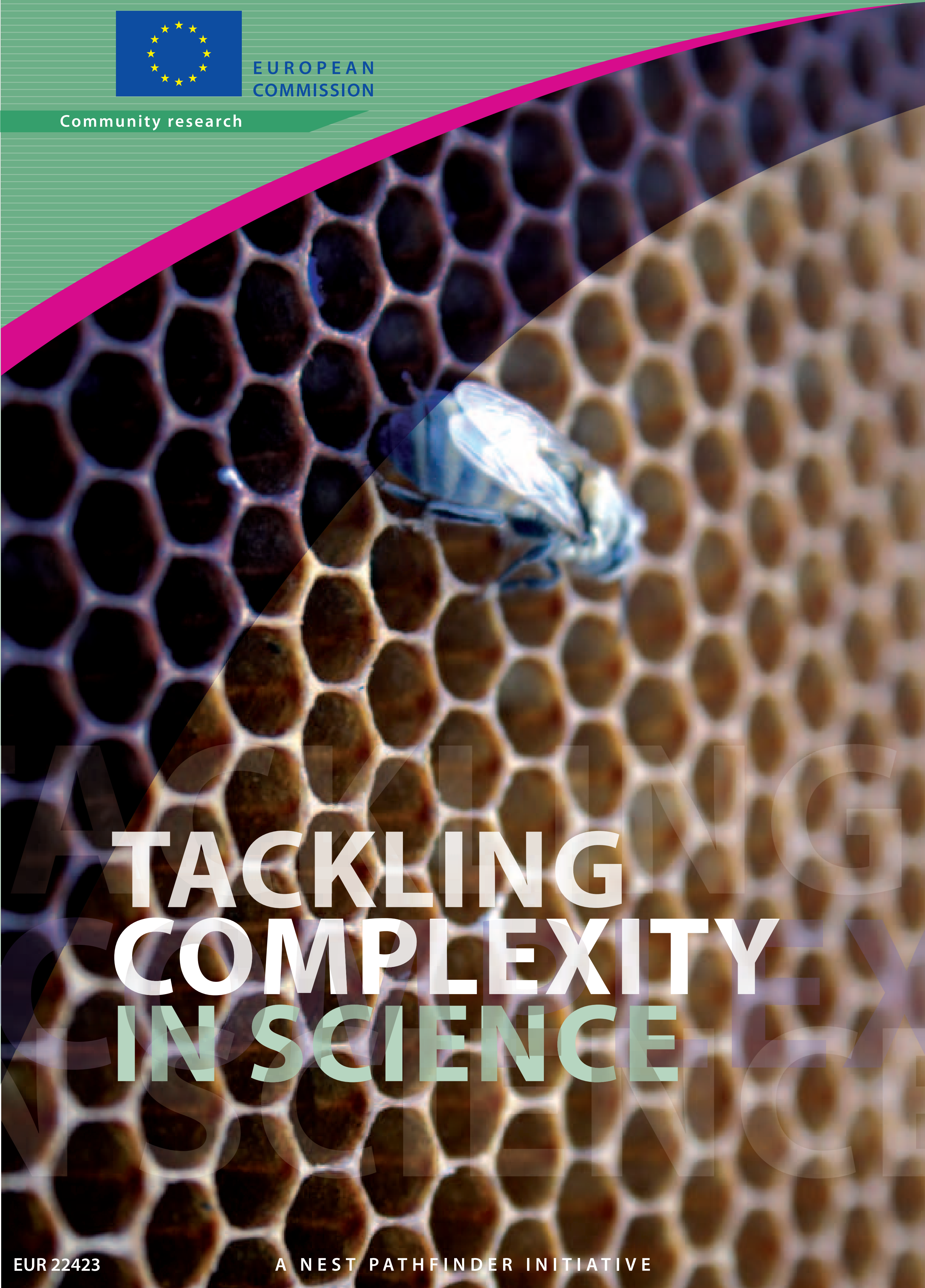

TACKLING COMPLEXITY IN SCIENCE

EUR 22423

A NEST PATHFINDER INITIATIVE

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TACKLING COMPLEXITY IN SCIENCE

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Directorate-General for Research

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COMPLEXITY IS SIMPLY SCIENCE AT ITS LIMITS

The world in which we interact is becoming ever more complex. The number and types of interactions amongst people have greatly multiplied due to modern technology and its consequences on society.

Nevertheless, no commonly accepted scientific definition of 'complexity' exists. It is understood that widely different systems, composed of many interacting units, generate (under certain conditions) a characteristic, common phenomenology. The most prominent signature of this is the 'emergence' of new patterns transcending the characteristics of the individual units. Such systems are ubiquitous in many branches of natural and human sciences as well as in technology.

The promise of the science of complexity is to provide, if not a completely unified approach, at least common tools for tackling complex problems in various scientific domains.

Tackling Complexity in Science aims to encourage the development and transfer of solutions and approaches to concrete, complex real-world problems from one area of science to another. It also aims to help identify, coordinate and consolidate the European community working on such problems by providing the means to facilitate the exchange of ideas and information.

As required by the overall NEST mandate, the research supported in this initiative is highly interdisciplinary, innovative and holds the promise of high long-term impact, both scientific and otherwise.

The research projects offer real prospects of bridging the gap between the physical sciences, and the social and other natural sciences. They take a practical, problem-solving approach to research, grounded in observation and experimental data. At the same time, the problems are tackled from a complexity-inspired approach, which takes into account issues such as emergence, robustness and predictability. Typically, it considers complex problems from the perspective of networks or even networks of networks.

This NEST Pathfinder initiative has assembled an impressive portfolio of ambitious beacon projects which seek interdisciplinary opportunities at the very edge of scientific knowledge. They are expected to maintain a degree of cooperation and interaction throughout their lifetime by means of the common Coordination Action (GIACS) in order to optimise their collective outcome.

PROJECTS

NEST
Pathfinder

NATURAL NANO-DESIGN IS A BEAUTY TO BEHOLD

BIOPHOT

The natural world shows a huge diversity of colour and form. Elucidating the mechanisms by which these colours and contrasts are achieved through the interaction of light with an organism's bio-structure and how these structures have evolved over time is an extremely complex task. However, success would significantly enhance our understanding of nature and behaviour, as well as offering us design models for new materials with novel properties that have been 'tested and approved' by nature.

The kaleidoscope of colours, shapes and sizes that is found in the natural world is clear evidence of the complexity of living organisms. This complexity has been driven by evolution over millions of years and many creatures show extraordinary adaptations that have given their species a competitive edge in the game of life.

The BIOPHOT project aims to study this natural complexity in the specific case of how creatures interact with the electro-magnetic spectrum, particularly visible light but also the neighbouring infra-red and ultraviolet regions, to enhance their survival and reproduction chances. A vast range of optimised natural optical devices and materials have evolved that are used by various organisms in a wide variety of complex tasks ranging from sexual signalling to thermal management.

The project team from Belgium, Hungary, France and the United Kingdom will investigate these natural designs, using a broad perspective and a number of complementary disciplines. This complex, multidisciplinary approach will involve high-resolution structural and physical characterisation, evolutionary data in terms of both time and geography, significant modelling activities and the study of the behaviour of living organisms.

Evolutionary design

The combination of techniques will give a deep and detailed insight both of the evolutionary processes that have optimised a certain structure for a particular task and also the manner in which different but related structures exhibit altered properties.
The physical characterisation will focus around a combination of optical and electron microscopy techniques that will give new knowledge of the micro- and nano-morphology of specific bio-organisms which display unique and remarkable lightscattering ability. This structural information will be related to precise

> **"Significant 'technology transfer' from natural biology to synthetic materials science can be achieved."**

measurements of the light-filtering function using micrometer resolved spectrophoto-metric and thermal measurements.

Extensive measurements of the reflection, absorption and polarisation changes as a function of the frequency and angle of incidence of electromagnetic radiation will be made. Extensive numerical simulation will also be employed using the parallel computing system at the University of Namur. As a bonus, this will provide an opportunity to test the 'grid-computing' model that is an essential issue for a number of European initiatives.

The target organisms will also be studied in terms of their ecological and phonological (the timing of various biological phases) history and closely related or competing species will be identified for future examination. Cross-disciplinary discussions, including the use of paleontological data where available, will help to determine whether an organism's optical scattering mechanisms give an evolutionary advantage that can explain the survival of the species in its ecosystem.

Complex interactions

The study of the bio-organism in its environment at different evolutionary epochs requires analysis of a very large number of interactions and dependencies. Similarly, the experimental and theoretical aspects of the organism's interaction with light will also address complexity.

Complexity is not an easy phenomenon to explain, however one of its characteristics is the emergence of new patterns or behaviours that transcend the individual characteristics of component units. The NEST PATHFINDER initiative on understanding human complexity, of which BIOPHOT is part, looks to develop and transfer solutions and understanding of real-world complexity from one area of science to another. This builds both crossnational and cross-disciplinary links that enhance European research ability.

The greater understanding that BIOPHOT will bring to the hierarchical assemblies of natural structural elements over length-scales of varying orders of magnitude will provide guidance for the design of new synthetic structures. The improvement of simulation and modelling tools can significantly reduce the development costs for man-made nanostructured materials with novel photonic properties. The hope is that a significant 'technology transfer' from natural biology to synthetic materials science can be achieved.

AT A GLANCE

Official Title
Complexity and Evolution of Photonic Nanostructures in Bio-organisms: Templates for Material Sciences

Coordinator
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- Research Institute for Technical Physics and Materials Science, Budapest (Hungary)
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Project Cost
€ 2 047 675

EU Funding
€ 1 493 993

Project reference
Contract No 12915 (NEST)

The kaleidoscope of colours, shapes and sizes that is found in the natural world is clear evidence of the complexity of living organisms.

The study of the bio-organism in its environment at different evolutionary epochs requires analysis of a very large number of interactions and dependencies.

NEST
Pathfinder

UNDERSTANDING ANAESTHESIA COULD HELP US ALL

BRACCIA

The Braccia project is studying the complex interactions between electrical activity in the brain, and oscillations in heart and breathing activity during anaesthesia. The findings may reveal new ways to monitor the depth of anaesthesia. The research could be of much wider relevance, however, because coupled oscillatory systems are all around us, in the natural world and in modern technology. Investigating anaesthesia could therefore also help us to understand and control many other complex systems.

Anaesthesia is a subtle and imperfect science, with the level of anaesthesia needing to be very carefully controlled to avoid awareness and pain while minimising the risk of complications. The Braccia project is exploring ways in which the brain's electrical activity, especially delta and gamma brain waves, and their interactions with heart and breathing activity, vary with the depth of anaesthesia. This work looking into the complexities of human physiology is part of the NEST PATHFINDER initiative on 'Tackling complexity in science'.

The project will use measurements on humans and rats to explore the causal relationships between oscillations in the brain, heart and respiratory system. It asks the fundamental question: 'Which oscillations are the drivers of others and which are being driven by others?'

The first step is to develop a methodology to test for causal relationships between interacting complex systems. Human subjects will be monitored while awake and under anaesthesia. The results will then be used to develop systems that can model the oscillatory behaviour of human, and more generally mammalian, physiology.

From the specific to the general

The need for a better understanding of anaesthesia is driven by the enormous medical and societal importance of this technique, without which most modern complex surgical procedures would be impossible. The physiology of anaesthesia is not well understood, however, and the mechanisms causing loss of consciousness remain mysterious. Complications due to inadequate control of anaesthesia range from a patient experiencing pain and some unwanted level of awareness, to rare extreme reactions that can lead to brain damage or even death. The most common problem is some awareness during surgery, which affects approximately 1 in every 900 patients. This is particularly undesirable in

> “The Braccia project will greatly enhance our knowledge about what is going on in the body during surgery.”

those procedures in which a patient is unable to indicate that they have become aware and can feel pain, as can happen when a muscle relaxant is used, for example during *Caesarean* section.

Greater understanding of how the body is behaving during anaesthesia, and how consciousness and the sensation of pain can be better monitored, would clearly be of enormous benefit in improving general practice in the operating theatre.

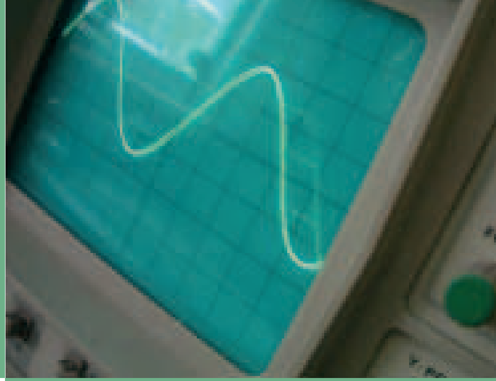
Complex oscillating systems are found everywhere, however. They are involved in many other aspects of physiology, but also occur in industrial and engineering settings, within the operation of computer software, and in the many chemical and physical interactions of the natural environment. Insights gained by studying the complexities of anaesthesia could be relevant to such varied fields as software development, aeronautical engineering and environmental management.

The project is a collaboration between physicists, electrical engineers, information theorists, medical scientists and clinicians. This wide multidisciplinarity reflects the fact that, although directly focused on anaesthesia, it is exploring aspects of complex science that are important in a huge range of situations

Significant possibilities

The most immediate aim of the Braccia project is to develop the methods and the understanding needed to create a new and improved kind of anaesthetic monitor.
If the results of the project are as useful as the partners hope, the next step will be to prepare the ground for a large-scale study that would refine and test such a monitoring system. The Braccia project may be the first step towards building a simple but highly effective anaesthesia control system that will be found in every operating theatre, and used to provide precise management of anaesthesia in a way that is completely impossible today.

Even if that dream is not fulfilled, however, the project will greatly enhance our knowledge about what is going on in the body during surgery, and our understanding of the many interactions within complex systems in general.



AT A GLANCE

Official Title
Brain, Respiration and Cardiac Causalities in Anaesthesia

Coordinator
Lancaster University, Department of Physics (UK)

Partners
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- University of Potsdam, Institute of Complex Systems (Germany)
- University of Oslo, Ulleval Hospital (Norway)
- University of Ljubljana, Faculty of Medicine (Slovenia)
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Project Cost
€ 1 417 200

EU Funding
€ 1 417 200

Project reference
Contract No 517133 (NEST)

Levels of anaesthetic need to be carefully calculated for each patient.

NEST
Pathfinder

COMPLEXITY SCIENCE IN THE SERVICE OF SOCIAL POLICY

CAVES

It can be hard to predict how social policy will affect land-use patterns and social networks. This is because uncertainty arises from the complexity inherent in such systems. Complexity science facilitates the modelling of complex realworld networks involving human activity and environmental change. These models can help us understand how change in the past has impacted on land use and human populations. Generalised models may have wide application in formulating policy under conditions of uncertainty.

Complexity science is revealing the function and behaviour of complex networks in the real world, including information-technology networks, power grids and transport networks. However, the benefits of this deeper understanding are only slowly being felt by policy-makers, with those working with financial markets slightly ahead.

The CAVES project aims to provide a link between complexity science and social policy. Land use is being modelled to determine how it might change, for instance, in response to policy initiatives such as revision of the EU's common agricultural policy (CAP). The project forms part of the NEST PATHFINDER initiative on 'Tackling complexity in science'. In line with this, CAVES is a highly interdisciplinary project that: a) helps answer important scientific questions involving complexity, and b) encourages the transfer of knowledge and techniques to new areas of application.

Modelling land use

The analysis of land use using complexity science differs from traditional analytical methods, because no central organising principle is assumed. The behaviour of a complex network instead emerges through the interaction of individual quasi- autonomous software programs called agents. The agents in land-use networks typically represent stakeholders such as farmers and industrial decision-makers. A complex network changes in response to internal stress or external shock. A large external shock, for instance, causes an episode of volatility. In a resilient network, land use will remain largely unchanged as a consequence of this, although dramatic changes in land use may occur in less resilient networks.

The CAVES project incorporates three case studies, involving complex networks of differing resilience. The scientific aim is to identify reasons why some complex networks are more resilient. Models are

"Models are run forwards in time, so that past evidence provides the basis for predicting the impact of future shocks."

being constructed retrospectively for each case study, using datasets of land use over time to determine the impact of previous episodes of stress and shock. The models are then run forwards in time, so that past evidence provides the basis for exploring possible impacts of future shocks.

Case studies

Two of the case studies are from Europe, while the third from South Africa demonstrates the relevance of the methodology beyond Europe. A dataset from the Grampian region in Scotland shows that land tenure and social structures have not changed greatly, despite a series of external shocks that include entry to the EU, changes in agricultural subsidies and epidemics of livestock disease. This resilience arises through the social structure of family farms, flexible land use, and other factors.

A case study from the Oder River Valley in Poland, on the other hand, reveals a high rate of change in land use since the end of the Second World War. This shock arose from political events and a large-scale shift in population. Water-management systems went into decline and agricultural diversity was reduced, with crops becoming more vulnerable to flooding. The prospective part of this study will address how farmers in the region might respond to fresh challenges posed by EU membership. The third case study, from the Limpopo Province in South Africa, encompasses the large-scale landuse and demographic changes that occurred after the fall of the apartheid regime.

Aiding policy development

The CAVES project aims to demonstrate how models of complexity can help to formulate social policy. The two European case studies, for instance, are being used to inform discussions on CAP reform. The models obtained from all the case studies are being analysed for common features, to produce clusters of generalised models that can be applied to all complex networks involving land use.

Both coarse and finegrained models are being constructed to investigate the process of scaling up. Models should be sensitive to scale, but be amenable to forming parts of larger models. This will be important when constructing global models, such as those for land use and climate change. The identification of networks susceptible to change will enable social policy to be refined in order to reduce the impact of future shocks.

AT A GLANCE

Official Title
Complexity: Agents, Volatility, Evidence and Scale

Coordinator
UK: Centre for Policy Modelling

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- Universität Kassel (Germany)
- Politechnika Wroclawska (Poland)
- International Institute for Applied Systems Analysis (Austria)
- Macaulay Land Use Research Institute (UK)
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Project Cost
€ 1 722 202

EU Funding
€ 1 292 650

Project reference
Contract No 12816 (NEST)

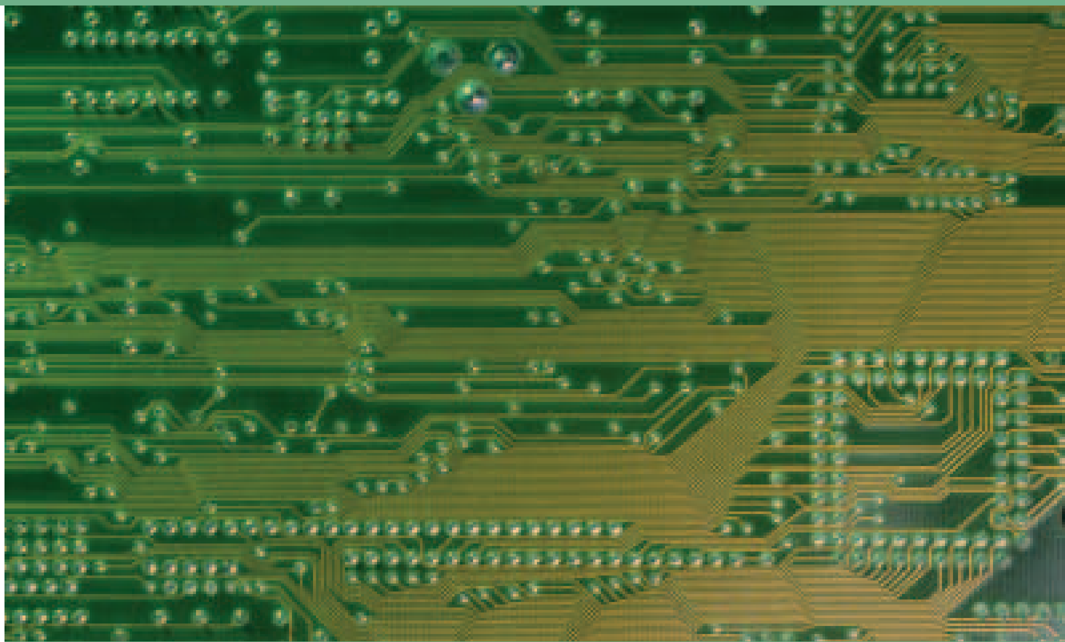
Land-use patterns develop within a complex network of actors.

Complex models can help develop social policy which affects land use.

NEST
Pathfinder

THE IMPORTANCE OF RARE EVENTS

CO3



Mathematical models have long been used to simulate complex biological, social and economic systems. The CO3 project argues that such models fail to take account of rare events that can grow to change the behaviour of the system as a whole. The project team will apply a new type of model to understand the development of private enterprise in Poland, the spread of technological innovation, the location of high-tech businesses and the development of auto-immune disease. The results could change the way we think about social, health and economic problems.

Physicists have a complete understanding of atoms, but that does not mean that we understand everything that atoms can do. Atoms come together to form molecules, molecules form cells, cells form people, and people form a society. Yet we are far from understanding how societies work. Each step up the ladder sees a huge increase in complexity. There have been many attempts to model complex systems in terms of their component parts but with only partial success.

It is commonly believed that such failings are due to a lack of knowledge about the components and how they interact. If we knew more about chemical reactions or human behaviour we might do better. But according to the proposers of the NEST CO3 project, these approaches fail not because of insufficient information but because the models do not take proper account of the discrete nature of the components. Conventional modelling tools use differential equations which treat the properties of the system (such as the economy) as smooth and continuous, like a fluid, rather than a collection of freely acting individuals. The proposers will use a new type of model, the 'AB' model, which recognises this difference.

Rare events drive change

A key outcome is that random fluctuations, or 'noise', can, in some cases, grow to change the collective behaviour of the whole system. The proposers argue that such rare events are, in fact, the main motor driving changes in collective behaviour. It is a rather abstract concept, and the CO3 team intend to put it to practical use in a number of socio-economic and biological applications.

For example, a group led by the University of Warsaw will create an AB model of the macro-level economic, cultural, and political mechanisms relevant for social and economic change. They will test it on the changes in Poland since 1989 from a central to a market

> **"A key outcome is that random fluctuations can, in some cases, grow to change the collective behaviour of the whole system."**

economy, where private businesses have become more clustered than they were before, with prosperous areas alongside areas of economic decay. The University of Paris 2 will lead another study looking at how and where businesses start up and grow. Industry has traditionally located in places favourable for natural resources and transport links. But many had predicted that the 'new' industries based on intellectual capital, such as biotechnology, software and media, would not be so constrained and would be distributed more evenly – location should matter less in the connected age. This has not happened, and the partners will apply the AB model to understand why the new industries have concentrated in places such as San Francisco, San Diego, New York and London. They hope to discover what lessons we can learn about supporting start-ups.

Auto-immune disease

A third study, led by the two Italian partners, will examine the conditions under which technological innovation can spread through a large region, and why innovation will tend to cluster in certain areas. This model will be tested on the pharmaceutical sector.

A completely different application will be led by Bar Ilan University. They will use the AB model to study the development of B lymphocytes, a type of white blood cell important in the body's immune system. Current models are not satisfactory and the CO3 work may help to understand the emergence of auto-immune diseases such as diabetes and multiple sclerosis.

The Bar Ilan researchers will also underpin all these studies by developing tools to handle more realistic biological and socio-economic models which will then be used by the other groups.

The partners expect that the methods developed in CO3, part of a wider NEST PATHFINDER initiative on complexity in science, will lead to a better understanding of how the behaviour of complex systems emerges from the cumulative effect of numerous individual agents. In the longer term, they hope that their findings will be applied by many other workers in economics, social sciences and biology and will have a very practical impact on economic planning, health and capital investment.

AT A GLANCE

Official Title
Common Complex Collective Phenomena in Statistical Mechanics, Society, Economics, and Biology

Coordinator
Fondazione ISI (Italy)

Partners
- Scuola Superiore Sant'Anna (Italy)
- Université de Paris 2 (France)
- University of Warsaw (Poland)
- Bar Ilan University (Israel)
- Università di Roma 'La Sapienza' (Italy)

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Project Cost
€ 1 499 830

EU Funding
€ 1 499 830

Project reference
Contract No 12410 (NEST)

Advances in computer power make complex models easier to develop.

Complex models may help develop understanding of auto-immune diseases.

NEST
Pathfinder

HANDLING INTER-ORGANISATIONAL COMPLEXITY

COLL-PLEXITY

Companies lacking the flair for crafting and managing inter-organisational networks are at a disadvantage in the modern business environment. Such is the complexity of these networks that managing them is no easy task. The Coll-plexity consortium's ambition is twofold – to leverage fundamental insights from the new discipline of complexity science for managers in industry and to advance complexity science itself by applying it to the social world in which network management takes place.

Shifting alliances of natural scientists have tried for several decades to forge a new science by unifying insights from an unlikely assortment of disciplines – ecology, biology, physics, geology, mathematics, information science and more. If the COLL-PLEXITY partners are on solid ground, science in-the-making – the science of complexity – has come of age. It is now mature enough, they believe, to justify the launch of a project with the potential for a great pragmatic pay-off.

The project's name is COLL-PLEXITY. Its objective is to fashion practical tools for industrial managers as a support to improve their decision-making for building and managing inter-organisational networks. For an increasing number of contemporary businesses, the ability to manage inter-organisational networks is nothing less than vital.

The importance of networking is nothing new, of course, but it has increased with the emergence of outsourcing, e-marketplaces and virtual enterprises. One of the COLL-PLEXITY partners, the Virtuelle Fabrik AG, exemplifies the trend – a network of 72 diverse SMEs organised via three virtual factories. By pooling the resources and coordinating the efforts of its member companies, each 'factory' is able to manufacture products which none of those SMEs could have taken on in the past. Projects involving SMEs from two or more factories are possible, too. However, these require a better understanding of the often complex dynamics of inter-organisational collaboration.

Paradigm shift

Being one of the fastest growing scientific disciplines, complexity science has been identified within NEST as a field with substantial longer-term promise – a field worth strengthening in Europe. Hence, the PATHFINDER initiative on understanding complexity, of which COLL-PLEXITY is a part,

> **"Improved understanding of the management of complexity will accrue from a thorough understanding, description and modelling of complexity in inter-organisational enterprise networks."**

provides a promising approach to meet the modern challenge of intricate, interrelated processes.

The disciplines from which it has emerged are all natural sciences and the complex systems its scientists grapple with are physical ones. Nevertheless, with others in the field, the COLL-PLEXITY consortium acts on the assumption that there are fundamental regularities underlying the complexity of the systems that the latter share with social systems. In respect of this, complexity science may hold the key to a new way of tackling the problems of industrial networks. Moreover, tackling such problems could contribute to the further advance of complexity theory.

By means of the availabletools, management scientists usually ascribe the success or failure of inter-organisational collaboration efforts to stock causes. Culture or resistance to change is one example. COLL-PLEXITY's researchers from institutes in Germany, The Netherlands, Israel, Switzerland and Hungary hope that their theories, although originating in the natural sciences, can help to find causes and alternatives that may suggest new solutions. What the consortium is looking for, in its own words, is 'a true paradigm shift'.

Generic model of complexity

Creating a toolkit for ordinary managers from the methods and theories of an unfamiliar science is no easy task. When the environments in which their companies operate are social by nature and the science in question is a science of physical phenomena, it is a very tall order. The teams have acknowledged this and orient their perception towards this understanding. What they expect to achieve at the end of their work is one powerful tool for the kit – a unique framework for managers that helps to match the complexity of the networks they need to build with the complexity of the problems they intend to solve.

The scientists characterise it as a framework of thought, a first step towards eventual implementation of integrated complexity management systems. As a result, these might occupy the same capacity in future organisations as enterprise-resource-planning (ERP) and customer-relationship management (CRM) systems do in present-day organisations. On the way to success, first of all, the partners need to devise a classification scheme for complex problems and complex systems in manufacturing.

Beyond that, they will fashion a generic model of complexity for system coordination in collaborative production networks. Schiesser AG – a COLL-PLEXITY partner that designs, manufactures and sells underwear – and the Virtuelle Fabrik AG will be among the organisations in which the prototype framework will be piloted. Ultimately the project's practical findings will be brought together in a managers' manual presenting guidelines for setting up and coordinating collaborative networks.

AT A GLANCE

Official Title
Collaborative Complexity, Collaborations as Complex Systems

Coordinator
Rheinisch-Westfälische Technische Hochschule Aachen (RWTH) – Laboratory for Machine Tools and Production Engineering (WZL) (Germany)

Partners
- TU Delft – Faculty of Technology, Policy and Management (TPM) (The Netherlands)
- Global Research and Financing (Israel)
- Universität St. Gallen, ITEM-HSG (Switzerland)
- The Computer and Automation Research Institute - Hungarian Academy of Sciences (SZTAKI) (Hungary)
- Schiesser AG (Germany)
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Project Cost
€ 2 494 631

EU Funding
€ 1 800 000

Project reference
Contract No 12781 (NEST)

The project partners will fashion a generic model of complexity for system coordination in collaborative production networks.

To an increasing population of contemporary businesses, an ability to manage inter-organi-sational networks is nothing less than vital.

NEST Pathfinder

DEVELOPING ALLERGIC RESPONSES

COMPLEXDIS

Common diseases are complex. This means that they are caused by an altered balance between multiple genes, rather than single causal genes. As such, they can be modelled using complexity theory, which offers the opportunity to predict the reversal of the pathogenic progress of disease. This could lead not just to personalised medical regimes, but also to a radical rethink in the way we approach serious illnesses such as multiple sclerosis, and even certain cancers.

The illness could be as minor as a few irritating sneezes when the pollen count is high. Allergic reactions to nuts can be more serious, even fatal. Or it could be cancer, the probability of contracting the disease currently stands at approximately one in every three of us. The quest to conquer diseases (be they minor or major) is never ending, and the scientists and doctors involved in the ComplexDis project are playing their part.

ComplexDis involves the study of the complex nature of diseases. More specifically, the project partners are looking at the use of complexity theory in understanding the complex gene and protein interactions that underlie disease.

So, what is complexity theory? In broad terms, it aims to gain predictive understanding of how altered interactions between multiple components in complex systems alter the behaviour of that system. For example, a complex disease may be caused and reversed by altered interactions between multiple genes and their products.

Changing the picture of disease

Since all genes and their products can be studied in common diseases, complexity theory could be a useful and productive tool in their analysis. The ComplexDis consortium believes that this approach has been somewhat under-utilised in the past.

It proposes that the theory can be used to develop useful tools capable of predicting complex diseases. The team's immediate goal is to validate such models in the clinical environment, and to identify relevant biological markers, which will pave the way towards personalised medication.

The team has set itself a challenging set of short-term and long-term objectives. In the near future, the partners aim to develop biological markers for the production of personalised treatment of allergies and

“The ability to predict and prevent targeted diseases, as well as the availability of personalised treatment, is expected to become a reality over the next five to ten years.”

multiple sclerosis. They will also ensure that their results are widely disseminated to the relevant audiences. Looking further ahead, targets include using experimental models to simulate the reversal of pathogenic changes occurring in disease progression.

Pooling resources from Europe and beyond

The project partners comprise an impressive group of experts in a number of specialist fields. The eight-member consortium includes specialist clinicians, computer scientists, molecular biologists, immunologists, geneticists, bio-informaticians, as well as experts in complexity theory.

Collaboration at the European (and indeed intercontinental) level to implement the ComplexDis proposal was necessary, since the required expertise is not available at any single location, or indeed within any individual country.

Coordinated by Sweden's Göteborg University, each consortium member has a specific contribution to make: the University of Tennessee (United States) will provide super-computing and other high-performance computing platforms; the University of Oslo (Hungary) will offer facilities at its cancer research institute; and the Free University of Brussels (Belgium) will adapt its expertise in complexity theory derived from the study of language development.

Additionally, the Universitat Pompeu Fabra (Spain) is to produce models and simulations of disease development; the Institute for Computing Applications (Italy) will research complexity tools suitable for clinical application; the University of Padua (Italy) will share its expertise in the field of allergies; the Hungarian National Institute for Paediatrics aims to promote complexity science in medical research in Central and Eastern Europe; and the University of Navarra (Spain) brings mathematical modelling, network analysis and system biology studies to the table.

Cutting to the bottom line

The ability to predict and prevent targeted diseases, as well as the availability of personalised treatment, is expected to become a reality over the next five to ten years. In the case of the 30 to 40 percent of the population that suffers from allergies, this will contribute both to reducing the cost of treatment, and increasing its efficacy.

Similarly, the partners are confident that they will be able to identify potential new drugs to treat a variety of diseases, including cancers and multiple sclerosis, and to define the reversibility of disease.

ComplexDis will benefit from interactions with other EU-funded projects, such as Exystence, UniNet and ImmunoGrid. Combined, these endeavours may contribute significantly to healthcare in Europe, both on an academic and clinical level.

AT A GLANCE

Official Title
Unravelling Complex Diseases with Complexity Theory: from Networks to the Bedside

Coordinator
Göteborg University (Sweden)

Partners
- Rikshospitalet-Radiumhospitalet (Norway)
- Svabhegy National Institute of Paediatrics (Hungary)
- Consiglio Nazionale delle Ricerche (Italy)
- University of Tennessee (United States)
- Azienda Ospedaliera di Padova (Italy)
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Project cost
€ 2 015 446

EU funding
€ 1 813 046

Project reference
Contract No 043241 (NEST)

NEST
Pathfinder

FINANCIAL TRADING IS A COMPLEX BUSINESS

COMPLEX MARKETS

Research in the area of heterogeneous agents and interaction in the modelling of financial markets has made rapid progress since the 1990s. Advances in theoretical tools and computational capacity to analyse and simulate large systems have given new insight into market behaviour. The Complex Markets project brings together an interdisciplinary team to explore these developments in depth. A more comprehensive understanding of market behaviour will enable more effective management and produce greater stability

The prime function of financial markets is to bear risk, enabling the transfer of resources from suppliers of liquidity to entrepreneurs and risk-takers. In order to do that efficiently, they must ensure a proper return on capital, coupled with market stability so that long-term planning may proceed with confidence and resources can be allocated efficiently. But the operation of markets is often accompanied by periods of instability and excessive volatility, including speculative 'bubbles' and crashes.

Complex Markets, part of the NEST PATHFINDER initiative on 'tackling complexity in science', aims to explore an alternative to the classical theory of rational behaviour of a single agent. The alternative proposes a large number of heterogeneous agents within markets – each of which can employ rational behaviour – but the interaction between these agents allows collective effects to arise. In this way, the financial market behaves as a complex system. Within such a heterogeneous system, traders can either base their investment decisions on the market fundamentals (dividends, earnings, interest rates) or go by patterns and trends in recent prices. Irregular switching between these two strategies can occur, resulting in irregular price fluctuations.

Unravelling the strands

Complex Markets brings together leading researchers in numerical simulation, experimental economics, mathematical analysis, finance, econometrics and psychology. It ill build in high-level contact with the financial industry and the Bundesbank, the Bank of England and the European Central Bank, and specialist advisers in the US.

The team plans to collect and analyse data on behaviour in specific markets, including markets for wholesale fish, fruit and vegetables and internet auctions. Complex Markets will also study the structure of foreign-exchange markets and stock

> **"The project will use mathematical, psychological and economic insights to develop an understanding of the observed characteristics of financial markets."**

markets, evaluating the extent and effects of behavioural networks. The prices in markets where traders interact and trade within a small group of other traders, rather than take the apparently best deals on their screens, appear to be much more volatile than in markets with an electronically organised order book. These studies should form the basis for understanding the processes that lead to bubbles and crashes. The basic data will also enable the project team to derive the general principles of the evolutionary approach to the behaviour of financial markets, ranging from simple models of a rational agent forecasting on the basis of unknown parameters, to complex models with interacting traders with co-evolving strategies. Estimation of such complex systems is still very new, but evidence suggests that such an evolutionary system could account for the volatility we see in markets. It will also show whether international trade and long-term capital movements are distorted by short-term speculation – an important outcome for policy-makers

Risk and uncertainty

Complex Markets will use psychological and economic insights to develop a deeper understanding of decision-making in complex environments exploiting the concepts of risk and uncertainty. Risk refers to individuals being able to evaluate the prob-ability of the unknown elements of their environment for decision-making. Uncertainty acknowledges that in many cases they cannot rely on this probability, because of the possibility of 'one-off' events of which they have no experience, and therefore no basis for a riskbased analysis based on a known probability.

Complex Markets will use its varied expertise to take uncertainty into account in studies of how individuals react in a complex environment which is only partially understood, and therefore its effect on individual financial decision-making and on the collective market outcome.

Stock markets, exchange, commodity and derivative markets all share the same properties, so the Complex Markets project should reveal whether these human multiagent systems work according to common principles in the same way as physical and biological systems.

AT A GLANCE

Official Title
Financial Markets and Complexity: Uncertainty, Heterogeneous Micro Agents and Aggregate Outcomes

Coordinator
University of Warwick (UK)

Partners
- Université Aix-Marseille III (France)
- University of Kiel (Germany)
- Abdus Salam International Centre for Theoretical Physics (Italy)
- University of Cagliari (Italy)
- University of Amsterdam (The Netherlands)

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Project Cost
€ 1 500 000

EU Funding
€ 1 500 000

Project reference
Contract No 516446 (NEST)

Access to information is critical to well-functioning financial markets.

The project will develop greater understanding of market behaviour.

NEST
Pathfinder

SCIENTIFIC AVALANCHES

CREEN

Research breakthroughs, controversies and fashions in science can emerge unexpectedly, sometimes with unwelcome political and economic effects. What triggers these so-called 'scientific avalanches'? An interdisciplinary team from five countries will apply insights from physics, mathematics and the social sciences to the complex social networks of science and the media. Why do such critical events occur and can their probability be estimated? The results will be of interest not only to scientists and journalists but also to science policy-makers.

Why did stem-cell research suddenly become such an issue in the 2004 US presidential election? What is fuelling the simmering controversy about genetically modified foods? How are the research choices of scientists influenced by what appears to be fashionable at the time? In short, why do scientific research topics like these suddenly erupt from the labs and saturate the media?

The partners in the CREEN (Critical events in evolving networks) project call these phenomena 'scientific avalanches'. Just as an avalanche of snow can be forecast by careful modelling and study of environmental conditions, it may one day be possible to predict under what circumstances scientific avalanches will happen. And could we even trigger an avalanche in a constructive and desirable direction?

Such questions can only be answered by a truly interdisciplinary effort from many branches of the natural and social sciences. This project, part of a wider NESTPATHFINDER initiative on complexity inscience, will draw on many strands of research on how information spreads within social networks. Scientists, like journalists, are individuals, but the collective behaviour of science or the media can be unpredictable, related in a complex way to the actions of individuals within them.

Linking social science and physics

The proposers, from five countries, are theoretical and statistical physicists, specialists in socio-physics, computer scientists, mathematicians, information and communication scientists and sociologists.

Prof. Janusz Holyst, from the Warsaw University of Technology, is coordinating the project. His group will apply the principles of statistical physics to social networks. For example, thermodynamics predicts how liquids boil or freeze – can we learn something about sudden social changes

“Scientists, like journalists, are individuals, but the collective behaviour of science or the media can be unpredictable.”

from such analogies? Another approach will look at what happens when a network of scientists interacts with a network of journalists, which in turn interacts with a network of newspaper readers or TV viewers. The second topic, led by the University of Liège, will deal with how scientists and other people organise themselves into formal and informal networks and how individual decisions can affect collective behaviour. Researchers will look at how ideas spread through the scientific community, leading to an avalanche when topics suddenly become fashionable.

The project will create natural links between physics and social-science methodology. One of these links points to a group led by the Royal Netherlands Academy that will look at the influence of ‘media hype’, and seek ways to model and measure avalanches, applying their methods to such real-life controversies as BSE, foot-andmouth disease, genetically modified foods and stem-cell research.

Influence of ‘bloggers’

Meanwhile, the University of Wolverhampton will lead a study into how the world-wide web is being used asmedium for scientific debate. They will analyse the content of on-line newspapers, personal web pages and especially ‘blogs’, to track how the web has influenced recent avalanches and also to spot new avalanches as they take place.

Finally, a group led by the University of Karlsruhe, will develop methods of visualising complex information, based on the results of a previous EU-funded project (COSIN),and applying it to the results from the other groups in CREEN.

The proposers freely admit that what they are trying to achieve is well ahead of the state of the art but the risk of failure is offset, they say, by the promise of major advances leading to social and economic benefits. When the project is complete in three years time, the proposers hope not only to have gained a deeper understanding of how science and society interact, but also to be able to help policy-makers anticipate where avalanches are likely to happen and to deal with them effectively. They even speculate that their findings may have applications in other multidisciplinary studies such as river flooding, protection of species in food webs and trade-network crashes. They will disseminate their findings to policy-makers, journalists and other experts through meetings, brochures and a website.

AT A GLANCE

Official Title
Critical Events in Evolving Networks

Coordinator
Faculty of Physics and the Centre of Excellence for Complex Systems Research, Warsaw University of Technology (Poland)

Partners
- SUPRATECS group, University of Liège (Belgium)
- Netherlands Institute for Scientific Information Services, Royal Netherlands Academy of Arts and Sciences (The Netherlands)
- Research Institute for Advanced Technologies and School of Computing and Information Technology, University of Wolverhampton (UK)
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Project Cost
€ 1 241 640

EU Funding
€1 241 640

Project reference
Contract No 012864 (NEST)

When science makes headlines scientists themselves may be unprepared for the controversy.

The different interactions between science and society make up a complex relationship.

NEST
Pathfinder

UNDERSTANDING THE DYNAMICS OF HUMAN BEHAVIOUR

DYSONET

In recent years it has become clear that common principles underlie the behaviour of many systems in the real world, which are composed of units connected into complex networks. Such networks occur in nature, physics and in many aspects of human social behaviour. DYSONET is applying mathematical principles to understand the dynamics of social networks. Study of real examples will improve understanding of how to optimise real-world networks, for example in limiting the spread of epidemics.

The Dysonet project is looking at a range of complex social networks. Its interdisciplinary team aims to develop techniques for specific problems, like the dynamics of crowd behaviour, which can then be tested in other more general systems. There are many unanswered questions about the structure of networks and about flows through them (e.g. of information). Ultimately the methods will be made available to researchers in all fields of study through the internet. Dysonet is part of the NEST PATHFINDER initiative on 'Tackling complexity in science'.

Real data analysis

Dysonet participants will first (with permission) collect real-world data from social networks in Sweden, covering networks of people who share the same household, work at the same workplace, live in the same building, attend the same hospitals, or are part of networks of sexual partners. It will also collect financial data for study of the dynamics of different types of portfolios traded in financial markets.

Most of the individuals in social networks (nodes) have a small number of connections, but a few have a very large number. Network models will be developed by Dysonet to allow study of robustness (the number of nodes which must be removed before connectivity of a network is destroyed) and the capability for network flow (the features of the optimal flow path, using the least time, energy or cost). To do this, the team will make use of large-scale computer simulations and grid computing, and develop new analytical, numerical and simulation techniques. The information gained will be used to identify designs of network models showing the best robustness and flow. The network analysis will then be applied to the realworld data, and should make large advances in understanding complex human systems.

> "The analysis will make major advances in understanding complex human networks involving spread, for example of information or disease."

Practical applications

Dysonet addresses five areas of collective human behaviour. The first will look at the spread of information and rumours across networks which, enhanced by mobile communications, can escalate out of control. Knowledge of this phenomenon will prevent further rumours like the one in Hungary in June 2003, which caused nationwide panic about a nuclear explosion. Understanding the relay of information through a crowd in panic will help develop more efficient evacuation methods, for example from football crowds, earthquakes or terrorist attacks. The behaviour of networks can contribute to organised search strategies, e.g. for missing persons. In a random search, a new direction and distance are selected by the searcher every time the target is not found; better understanding of this behaviour will help to design more effective collective search methods.

Traffic flow is an example of crowd behaviour where enhancing flow is important. If a large number of drivers are heading in the same direction, their choice of route will be influenced by the same information, from their observations and traffic reports. Collective behaviour emerges, making the bottlenecks worse. This study will contribute to more effective distribution such as of food and medical aid.

An area where the aim is to minimise flow, is that of epidemics. The epidemic spread of disease is almost inevitable if individuals are immunised randomly, but if the most-connected individuals are targeted, immunisation is much more effective. However these key individuals are very hard to identify. Dysonet studies will improve the efficiency of such targeting.

In finance, collective behaviour is shown by adaptation to market changes, and in extreme cases to response to unexpected events, leading to changes in stock prices and even public hysteria. Such responses depend on the structures underlying information flow. Better understanding of the behaviour of this information flow would inform market regulatory policies. To be able to do so, Dysonet is investigating the structure of portfolios from leading and emerging financial markets. Later, the findings and methods will be applied to a commodity market, to examine common features of the two systems, so that the methods can then be applied to other types of networks.

AT A GLANCE

Official Title
Human Behaviour Through Dynamics of Complex Social Networks: an Interdisciplinary Approach

Coordinator
Aristotle University of Thessaloniki (Greece)

Partners
- Justus-Liebig-Universitaet Giessen (Germany)
- Bar-Ilan University (Israel)
- Instituto Nazionale per la Fisica della Materia (Italy)
- Universidade de Aveiro (Portugal)
- Stockholm University (Sweden)
- Boston University (USA)

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Project Cost
€ 1 578 798

EU Funding
€ 1 420 000

Project reference
Contract No 012911 (NEST)

Human behaviour depends on a range of networks with different networks coming into play in given situations.

Crowd behaviour may contribute to deteriorating situations such as traffic jams.

NEST
Pathfinder

MAKING SENSE OF EXTREME EVENTS

E2-C2

Earthquakes, floods, storms, riots and stock-market crashes have one thing in common: they cannot be successfully described by conventional statistical methods. Such 'extreme events' are the focus of E2-C2, a 17-partner NEST project trying to understand, and perhaps predict, some of these unexpected and damaging occurrences. Among other things, the project will look at the social and economic effects of impending climate change and even attempt to forecast crime waves in major urban centres.

The earthquake and tsunami that ravaged many communities around the Indian Ocean in December 2004 were typical of what are called extreme events. They came as a complete surprise, even though the area was well known as an earthquake zone and the underlying geophysical mechanisms were well understood. Other extreme events include floods, storms, droughts and landslides. Not all such events have natural causes: stock-market crashes, bridge collapses, crime waves and terrorist attacks are of human origin but share many of the same characteristics. A third group of events – possible catastrophic effects of climate change on the economy – have both natural and human origins.

What they have in common is that they are not well described by conventional statistical methods. Mathematical models of geophysical, climatic or socio-economic systems may have some success in describing their normal state or gradual changes but are not able to predict sudden, extreme events. And, what is more, these events do seem to be more common than conventional statistical analyses would suggest.

Interconnected hazards

The E2-C2 project, part of a wider NEST PATHFINDER initiative on complexity in science, will take a new look at both natural and socio-economic hazards and the connections between them. The 17 partners from nine countries will attempt to predict extreme events and also examine their consequences.

The first task will be to improve the statistical theories used to model extreme events. Conventional statistical methods are very poor at describing events that happen infrequently, so a team will devise new methods of analysis and prediction, and test them against a variety of historical records.

"All these extreme events share a common characteristic: the bigger the event the less likely it is to happen, but the greater the social and economic costs if it does."

The second line of research will look at extreme climatic events in Europe that arise from the way in which greenhousegas emissions and volcanic eruptions interact with natural climate variability. Partners will use atmospheric models to simulate the effects of global warming on the North Atlantic and Western Europe, and historical and geological records from the Campania region of Italy to investigate connections between volcanic eruptions and climatic extremes.

Can a climatic extreme cause a reversal in the economic cycle? This is one of several questions on the relationship between climate and the economy that will be addressed by the third research group. Conventional long-term economic models are unable to cope with short-lived events such as the winter storms of 1999 or even the summer heat-wave of 2003. Therefore this group will aim at developing novel, fully integrated, dynamic models of the coupled climateeconomy system.

Emergency planning

One reason why we need to understand extreme events is so that we can prepare for them in the design of buildings, control of land use and emergency planning. In each case, we need to know how often and how big any events are likely to be.

Another task will be to look for evidence that extreme events are not random, but that one event may increase the likelihood of another. The team will look at records of strong winds, rogue waves, forest fires, hydrological extremes and landslides. They will attempt to simulate such events and develop methods for forecasting them.

The Carpathian Mountains in Romania are known for their major earthquakes, and another group will take on the goal of developing an earthquake prediction system for the Vrancea region, one of the world's best natural laboratories for studying earthquakes and landslides.

Finally, in perhaps the most ambitious activity in the E2-C2 project, a group will attempt to create a 'socio-economic barometer' to monitor conditions in major urban centres and provide dayby- day forecasts for impending crises such as crime waves, outbreaks of mass violence and surges in terrorist activity.

All these extreme events share a common characteristic: the bigger the event the less likely it is to happen, but the greater the social and economic costs if it does. It is too soon to say how successful the E2-C2 project will be, but any progress towards under-standing and anticipating the unexpected is bound to pay off in the long run.

AT A GLANCE

Official Title
Extreme Events: Causes and Consequences

Coordinator
France: Ecole Normale Supérieure (ENS)

Partners
- LSCE, joint institute of Centre National de la Recherche Scientifique (CNRS) (France) and Comissariat à l'Energie Atomique (CEA)
- Société de Mathématiques Appliquées et de Sciences Humaines(France)
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- Meteorological Institute, Universität Hamburg (Germany)
- DYKOS (Germany)
- King's College London (UK)
- Physics Department, Università degli Studi di Roma "La Sapienza" (Italy)
- Physics Department, Université de Liège (Belgium)
- Institut Royal Météorologique de Belgique (Belgium)
- MITPAN (Russia)
- IRPI-CNR (Italy)
- Dipartimento di Fisica Generale, Università degli Studi di Torino (Italy)
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- IGPP, University of California at Los Angeles (USA)
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Project Cost
€ 2 070 000

EU Funding
€ 1 500 000

Project reference
Contract No 12975 (NEST)

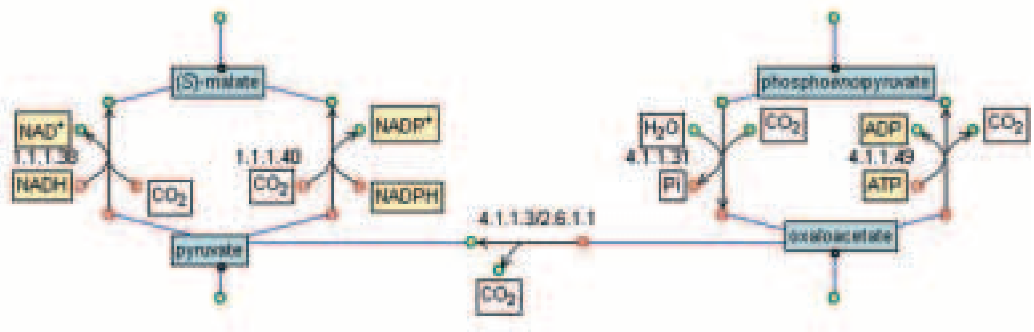
Extreme events can't be predicted with traditional statistical methods.

Better understanding of extreme events will help prepare communities better to deal with them.

NEST
Pathfinder

MODELLING THE MECHANISMS OF CELLULAR RESPONSE

EC-MOAN



A new generation of antimicrobial drugs is one of the benefits of new research into living cells. In an attempt to learn the underlying behaviour of complex living systems, the EC-MOAN project will break new ground in producing a model integrating two response systems in the bacterium E. coli. The novel tools developed will enable life scientists to better simulate cellular behaviour, and will consequently allow for applications in industrial control systems and software. Applications of these tools in other complex areas are also foreseen, such as improving safety critical systems in railways.

Studies of cells *in silico* can greatly reduce the need for expensive and prolonged laboratory experimentation. However, current mathematical modelling methods are unable to cope with the complexity of cells' interwoven regulatory systems.
The molecular mechanisms that make a cell react to its ever-changing environment are incredibly complex. Its movement towards a rich nutrient source, for example, may seem like an obvious response. But it is actually the net result of many interwoven regulatory systems that control genetic, metabolic and signalling pathways within a cell.

The sheer complexity of these interdependent response systems effectively forces researchers to simplify their studies; they generally look at single regulatory 'modules' in isolation. However, studies of single modules or signalling pathways do not allow for the myriad of positive and negative feedback loops that link the different modules within a cell.

One way to better understand the global behaviour of a cell is to consider all the modules working together as a single regulatory network. This is too complicated for experimental studies, so researchers try to build mathematical models of the regulatory modules instead. Unfortunately, even the simplest cells are still too complex; values for numerous parameters in numerical simulations are frequently unavailable, and whilst grid computing can harness sufficient computing power to perform the necessary calculations, there is a lack of tools for analysing the output of distributed modelling.

Predicting a cell's response

Given these major bottlenecks in our understanding of cellular response systems, the EC-MOAN project starts off small – with the classic and well understood bacterium E. coli – but its aims are big. The consortium will develop new methods for modelling and analysis that are scalable, and capable of integrating a cell's entire regulatory network. The project's long-term goal is to develop the tools and techniques that will enable scientists to predict a cell's response to a range of stimuli or environmental changes.

"The EC-MOAN project starts off small – with the classic and well-understood bacterium E. coli – but its aims are big."

The project partners are initially focusing their attention on E. coli's stress responses, through the regulation of carbon use and nitrogen assimilation. As carbon and nitrogen are essential elements for all living organisms, their metabolism is tightly regulated, and also intrinsically linked.

E. coli is an appropriate focus for this project as the mechanisms of genetic, metabolic and environmental regulation are shared by many bacteria, making the results of this modelling exercise readily transferable to other organisms. Moreover, E. coli is one of the best understood laboratory organisms, with vast amounts of data on the individual genes, proteins, metabolites and reactions involved in its stress response pathways.

Three EC-MOAN partners have worked extensively on E. coli and have complementary expertise and capabilities for experimental studies of the carbon and nitrogen modules. The other partners bring to the project significant knowledge in mathematical modelling and computer science. Working together, they will translate all the known experimental knowledge into an accurate model of E. coli's regulatory network, with tools to query the model and predict experimental outcomes.

Simplifying the networks

The trick to modelling such vast and complex networks is to simplify them without affecting their reliability. To this end, novel mathematical techniques for system reduction will be applied. Various general methods exist, but the EC-MOAN partners will attempt to develop more specific techniques that take account of the specific properties of cells. These novel techniques should make it easier to build more complex models of cells.

Another bottleneck in 'whole cell' modelling is that the standard 'model-checking' (verification) tools are cumbersome, and slow to run for complex models of this nature. Three of the project partners will combine and adapt existing verification algorithms to the E. coli model, and develop analysis tools that can be configured for models running on distributed grid computers.

Despite the many strands to this project, the immediate success of EC-MOAN will be relatively easy to measure; predictions of cellular behaviour should reflect experimental results. However, the impact of the project will reach far beyond E. coli experimentation and could have a significant impact on computational biology, especially for the development of so-called silicon cells.

By modelling the emergent behaviour of cells as they respond to many different stimuli, silicon cells are particularly useful in helping researchers test hypotheses and prioritise which expensive (and slow) laboratory experiments to conduct. They could also help in the rational design of new drugs that can act sequentially to shift cells into different states, to make them less pathogenic or more prone to disruption.

EC-MOAN's novel modelling methods could extend beyond the life sciences too. Non-linear modelling techniques have many applications in industrial control systems, and the project's verification algorithms could be applied to analysing critical safety software and hardware. Indeed, the wide ranging consequences of EC-MOAN's success appear almost as inter-linked as the cell response mechanisms that the project hopes to model.

AT A GLANCE

Official Title
Scalable Modeling and Analysis Techniques to Study Emergent Cell Behaviour

Coordinator
CWI (The Netherlands)

Partners
- INRIA (France)
- Vrije Universiteit (The Netherlands)
- Université Joseph Fourier (France)
- Masaryk University (Czech Republic)
- University of Edinburgh (United Kingdom)

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Project cost
€ 2 318 409

EU funding
€ 1 498 718

Project reference
Contract No 043235 (NEST)

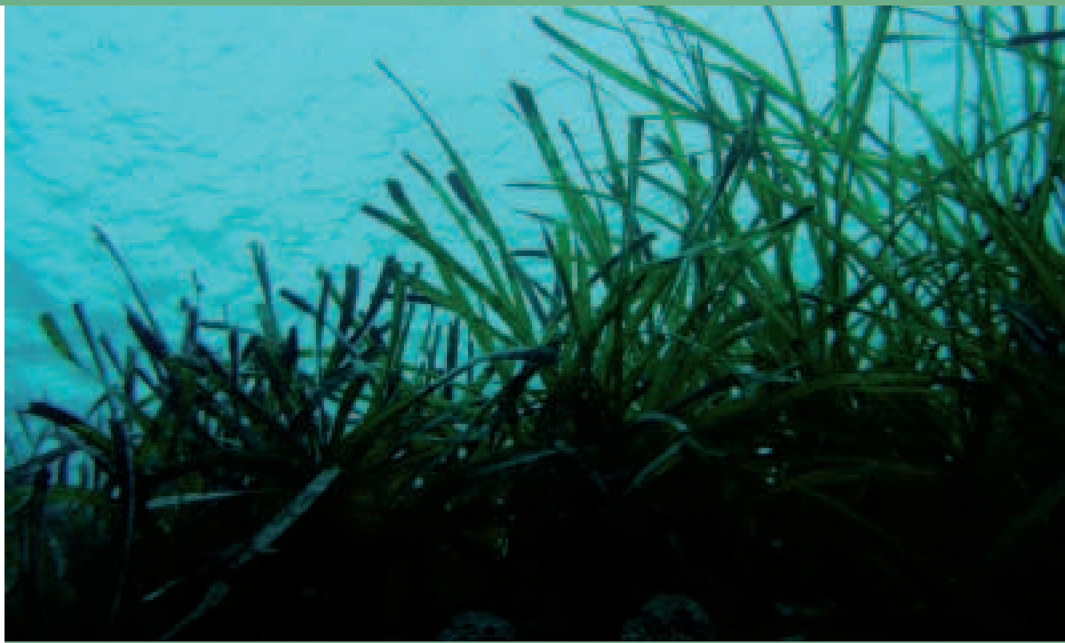
E. coli pathway for 'Anapleurotic reactions.'

Escherichia Coli, the most studied organism in biology (2µm).

NEST
Pathfinder

DETERMINING COMMON PATTERNS IN COMPLEX NATURAL SYSTEMS

EDEN



Many properties of natural biological systems – from plants to microbes – are connected. EDEN is developing tools to determine patterns of connections in different natural systems, to see both how individual species differ and how different species have evolved from common ancestors. These networking methodologies will make it possible to identify which biological populations should be protected to maintain a species. A particular focus will be preserving biodiversity in the Mediterranean.

Biological systems are highly complex, with evolutionary relationships between species generally represented as phylogenies or evolutionary trees. However, many properties of natural systems are related to the way they are interconnected. Complex science projects are now attempting to apply modern network theory to natural or manmade systems to characterise such interactions and understand their development.

This new scientific paradigm is being applied in EDEN – not looking directly at how things are connected but rather at the global pattern of connections involved, and at developing suitable analytical tools. The project will work on methods to analyse the structure of biological populations and identify key points that influence the distribution of these populations.

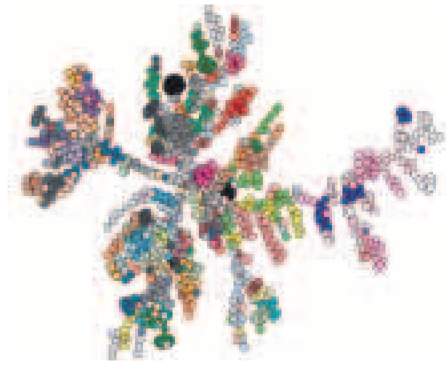
Using large samples of genetic data, EDEN will apply highly innovative cross-disciplinary network methods to examine population structure, gene flow, evolution and biogeography. This will make it possible to replace the 'tree of life' concept with a much more flexible 'network of trees' to gain biological insight into the evolution of life.

Dual-prong approach

Two dimensions are involved: the ecological and the evolutionary. On the ecological side, EDEN is seeking to characterise interactions between different species and between different populations inside a species. This approach involves understanding how they interchange genes, how they meet each other and what kind of connections they maintain.

On the evolutionary side, the same kind of ideas can be applied on a larger scale using similar methods to analyse how some of the species studied have developed: when they differentiated from a common ancestor; which species descend from which other species; and what kind of relationships develop between species.

"A key goal of EDEN is to ascertain which important biological populations should be protected to maintain a species."



AT A GLANCE

Official Title
Ecological Diversity and Evolutionary Networks

Coordinator
University of the Balearic Islands (Spain)

Partners
- Center of Marine Sciences (Portugal)
- Leipzig University (Germany)
- Helsinki University of Technology, Laboratory of Computational Engineering (Finland)

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Project cost
€ 1 427 574

EU funding
€ 1 176 271

Project reference
Contract No 043251 (NEST)

A multidisciplinary approach at European level, involving biologists, mathematicians and bioinformaticians, is essential to carry out this task. Despite the focus on biological populations, the approaches being developed come from other fields. The methodologies were first developed in the context of both physical and social systems requiring complex network analysis. The intention is to bring the methods developed in these other disciplines to bear on biological networks.

Europe's north and south join forces on EDEN. The project team hails from four different institutions, team members who have previously developed bilateral contacts in other contexts. For example, the Spanish coordinators from the University of the Balearic Islands have worked with members of Portugal's Center of Marine Sciences in projects on the biology of plants, as well as with personnel from the Helsinki University of Technology on communications networks. And there has been collaboration between the Finnish group and Germany's Leipzig University. These earlier experiences made it possible to assemble a team that combined good working relationships with relevant expertise in all the fields concerned.

Preserving biodiversity

Work has begun using a mass of genetic data already collected on many Mediterranean sea plants. During the development of the project, the intention is to expand the data to cover not only marine plants but also some marine animals. In practice, there is not a lot of difference genetically between plants and fish, for example. Much more important differences are expected to be found with bacteria and microbes. EDEN is particularly keen to study microbes as there is a strong difference in their genomes and in the way they reproduce. The intention is to find patterns of evolution and patterns of ecological relationships in all the areas covered.

A key goal is to ascertain which important biological populations should be protected to maintain a species. This activity will focus particularly on *Posidona oceanica*, a long-living clonal sea grass that provides an ecologically rich natural habitat that is crucial in maintaining biodiversity in coastal ecosystems in Southern Europe. Despite being protected under the Habitats Directive and the Convention for Biological Diversity, this sea grass is in drastic decline through the Mediterranean – a source of both ecological and economic concern, since local fisheries are also dependent on the marine plant.

Using network characterisation tools developed in EDEN, new diagnoses can be designed to evaluate global Mediterranean sea grass health, to estimate habitat extinction probabilities, and to design conservation and management strategies.

The approach being developed is, therefore, highly relevant to improving the understanding of population dynamics, evaluating the consequences of habitat fragmentation and local extinctions on the fate of species, as well as to improving the level of information on the spread of invasive species. Results will be shared with other groups involved in European complex systems research, particularly through NEST Pathfinder's GIACS action.

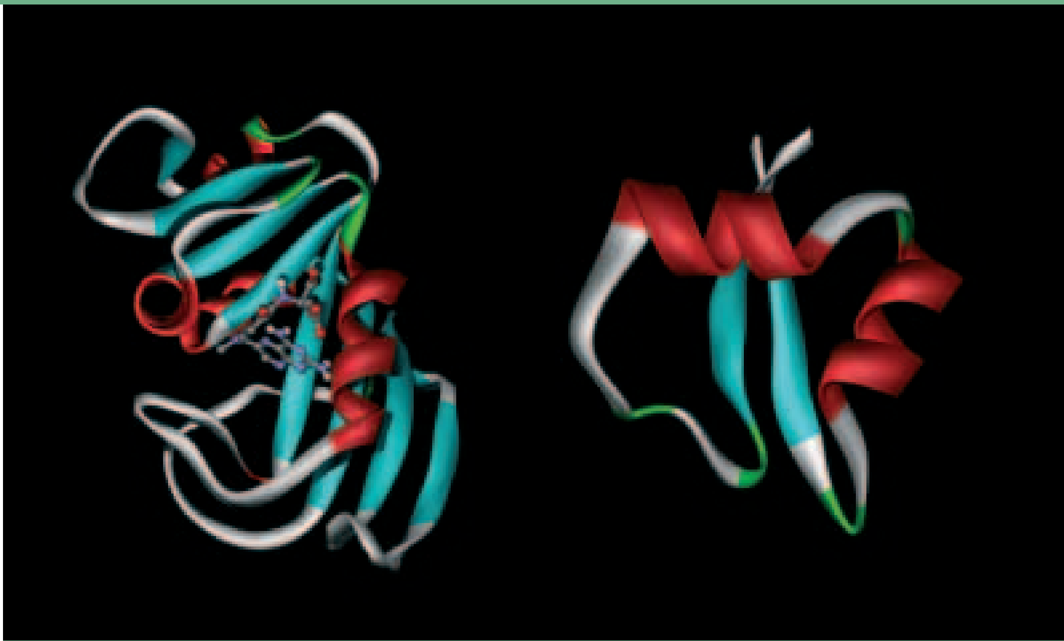
The marine plant Posidonia oceanica, one of the organisms for which EDEN will develop extensive network-based genetic analysis.

A Minimum Spanning Tree representing genetic diversity of samples of a marine seagrass (each of the circles) across the Mediterranean.

NEST
Pathfinder

EMERGING COMPLEXITY IN PROTEIN FOLDING

EMBIO



Complexity has a key role to play in biology yet is still poorly understood. A European project, EMBIO, aims to provide the research community with new methodologies based on innovative mathematics and software to help make sense of the dynamics of self-organisation. By focusing on the emergence of complexity in protein folding, the project team will be addressing one of the major problems in modern biology, and their results will have important implications for drug discovery.

Complexity and self-organisation are critical to many biological systems, yet many questions about how complexity emerges from simpler starting states remain unanswered. Current computer simulations of complex systems in biology take many hours to achieve a rather poor copy of what Nature manages perfectly in a split second. The EMBIO project, part of the NESTPATHFINDER initiative on 'Tackling complexity in science', aims to provide new tools and approaches to help answer some of these questions. By focusing on one of the major challenges in modern biology – protein folding – they hope to identify the fundamental principles governing the emergence of complexity in self-organising biomolecular systems.

The interdisciplinary research consortium, comprising eight European laboratories with expertise in mathematics, statistical physics, chemistry, information theory, biology and computing, will develop highly innovative mathematical and computational approaches to characterise the dynamics of self-organisation and apply these to protein structure.

Because of its focus on protein folding, EMBIO will have a particular impact in molecular and structural biology, but its innovative approach to analysing complexity will be relevant to many other systems that give rise to self-organisation.

From chaos to calm

Protein folding is a striking example of emergent complex behaviour and, being well defined, it is an ideal system in which to study complexity. Most proteins spontaneously and reproducibly fold from an arbitrary chain of amino acids to a specific 3D structure adapted to their biological function. But although data exists on the chemical compositions and structures of thousands of proteins, it is still not possible to predict accurately or to explain how and why this transition to a folded structure takes

“Advances in understanding protein folding will bring much needed innovation to the drug discovery business.”

place, partly because it is a non-linear, dynamic process influenced by many factors.

As the protein’s final 3D structure is considered the most thermodynamically stable one, scientists currently use a ‘folding funnel’ model to explain the dynamics of the transition. Initially, the chaotic motions of the atoms have high levels of free energy and occupy large areas of potential folding space. As the protein molecule folds and its free energy decreases, the available space is reduced to the point where the molecule is ‘forced’ into its final structure, corresponding to its minimum energy.

Whilst this model is now generally accepted, it does not explain many aspects of protein folding, notably the speed at which it takes place. The EMBIO consortium will develop a new computational approach which will provide a more accurate description of the dynamics involved, taking into account temporal, topological, statistical and dynamic properties. Powerful state-of-the-art computing facilities available within the consortium will enable sophisticated ‘all atom’ simulations of folding and the generation of new data on which to base novel methods and algorithms.

An alternative view

The new methodologies developed by EMBIO, underpinned by innovative mathematical approaches and applications software, will open the door to an alternative view on protein folding. A greater understanding of how proteins fold is likely to bring strategic benefits and much needed innovation to drug discovery. Most new drugs target specific proteins in the body. In addition, misfolded proteins are directly implicated in a number of debilitating conditions such as Alzheimer’s and Creutzfeldt-Jakob disease.

The consortium also expects its work on complexity estimation to impact on areas of study involving complicated chaotic dynamics. Examples of these are heart rhythms, where a better understanding of their chaotic nature could lead to new diagnostic tools for heart disease, and electromagnetic signals, which are generated in photonic devices used for optical communication.

More generally, if EMBIO succeeds in identifying the generic features which characterise dynamic complexity, their results will be widely applicable by the scientific community for the study of complexity in areas as diverse as social science or forest fires.

AT A GLANCE

Official Title
Emergent Organisation in Complex Biomolecular Systems

Coordinator
University of Cambridge (UK)

Partners
- University of Vienna (Austria)
- Friedrich-Schiller-University Jena (Germany)
- University of Heidelberg (Germany)
- University of Leipzig (Germany)
- University of Florence (Italy)
- Chalmers University of Technology (Sweden)
- University of Groningen (The Netherlands)

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Project Cost
€ 1 999 964

EU Funding
€1 999 964

Project reference
Contract No 12835 (NEST)

The project will focus on protein folding.
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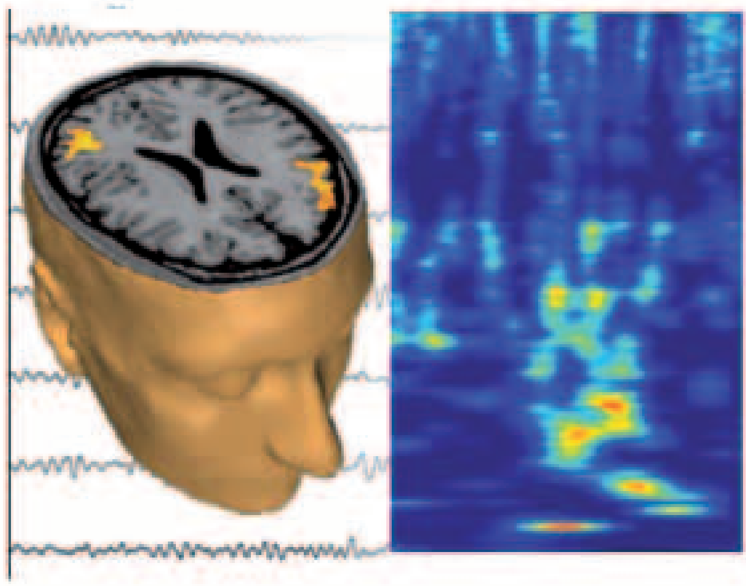
Improved understanding of protein folding is vital to the pharmaceutical industry.

NEST
Pathfinder

MAPPING BRAIN FUNCTIONS TO TREAT NEUROLOGICAL DISORDERS

GABA



Lack of synchronisation at different levels in our brain plays a fundamental role in many degenerative and socially-debilitating neurological illnesses. GABA will improve understanding of how the collective organisation of the brain emerges from the local behaviour of neurons. It will study the organisation in healthy brains compared with that of patients with neurological problems, contributing to early diagnosis of diseases such as Alzheimer's and prevention of epileptic fits. It will also increase knowledge of higher level brain activity.

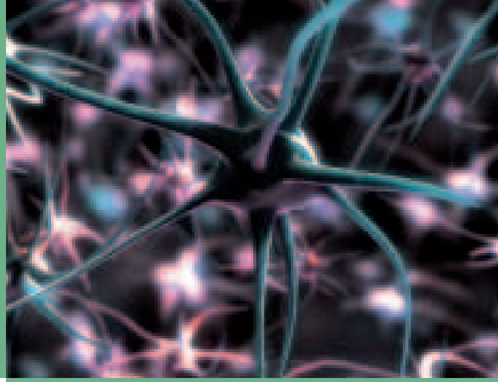
The cortex of the human brain is one of the most complex systems in nature. It consists of some 10^{11} dynamic neurons, coupled through a complex network of around 10^{14} links, mainly chemical synapses. This system is self-organising and able to perform a wide variety of physiological functions ranging from controlling our heart rates and our body environments to determining emotion and consciousness.

Disruption of the synchronised dynamics of the brain can lead to severe neurological problems. The GABA project intends to characterise mathematically the dynamics involved in higher cognitive functions and in neurological diseases. The results will provide a better understanding of how consciousness emerges and how the brain functions in healthy and diseased subjects – areas of major interest both scientifically and in terms of health care and improving quality of life.

Synchronisation: an engine of life

Found throughout nature, synchronisation can be considered one of the engines of life in complex biological systems. Its study has provided fundamental new insights and analytical tools in both locally- and globally-coupled dynamic models stemming from divergent disciplines. By providing a complete and consistent framework for the study of normal and abnormal synchronisation processes in the brain, GABA offers the possibility of early detection and treatment of a range of neurological disorders.

For example, disruption of synchronisation during ageing can lead to memory loss. According to recent World Health Organisation reports, some 37 million people suffer from dementia in developing countries, with 5% of men and 6% of women over the age of 60 having being diagnosed with Alzheimer's. And between three and six percent of the total health system resources in developed countries are dedicated to dementia – a cost that is bound to increase in Europe with our rapidly ageing population.



> **“Enabling the delay of onset and reduction in symptoms, and thus providing a better quality of life to sufferers.”**

GABA will compare brain activity in healthy people with others of the same age who have cognitive impairments – a large percentage of whom will develop Alzheimer’s. This study should show up significant changes in synchronisation activity between different areas in healthy brains and in those with memory problems.

These correlations will be studied for three years as the Alzheimer’s progresses and should make possible the development of techniques that allow for its early diagnosis – enabling the delay of onset and reduction in symptoms, and thus providing a better quality of life to sufferers for longer.

Improved awareness of brain functions resulting from GABA will also help treatment at the other extreme where there seems to be an excess of synchronisation, such as in epilepsy. Understanding of epilepsy and its associated brain dysfunctions has come on in leaps and bounds over the past 100 years, with the wide availability of new anti-seizure medications. But the unpredictability of seizures is still a major danger to sufferers. GABA should make possible the development of a system able to predict seizures far enough in advance to allow preventive action that will, again, greatly improve the quality of life and safety of those affected.

Higher cerebral functions

Using tools from nonlinear dynamics and complexity theory, GABA will also determine the functional role of normal and aberrant mechanisms in the emergence of higher cerebral functions in the brain. Such studies do not fit easily into traditional fields as they involve theoretical and experimental researchers from biomedical, physical and mathematical fields working together to gain a better understanding of the neural processes underlying both normal and pathological states.

The GABA project will collect and analyse brain responses using multi-channel electro-encephalograms (EEG), intracranial EEGs, magneto-encephalographic recordings and local field potentials, as well as observing single-neuron activity. These studies will cover physiological conditions from cognitive performance to pathological mechanisms underlying neurological disorders.

Traditional studies of the brain involve visual examination of raw EEG recordings, with pathologies showing up as unexpected graphical features such as spikes or oscillations. However, such interactions are difficult to quantify and the analysis of relationships between neuroelectronic signals shows that strong non-linear dynamics characterise couplings in neural networks. Neural activity also reflects consecutive changes of the global dynamics that depend on the topology of the neural network.

GABA will then apply linear and non-linear analysis, as well as tools from stochastic analysis and from the theories of complex networks and delayed dynamic systems. Complex systems theory will be used to see how the global dynamics affect local interactions.

By using the framework for the study of brain processes, the results will provide for early detection and treatment of neurological disorders. These results, ultimately, have the potential to enhance the wellbeing of millions of people around the world.

AT A GLANCE

Official Title
Global Approach to Brain Activity: from Cognition to Disease

Coordinator
Universitat Politècnica de Catalunya (Spain)

Partners
- Consiglio Nazionale delle Ricerche (Italy)
- Universidad Pablo de Olavide (Spain)
- Centre National de la Recherche Scientifique (France)
- Tampereen Teknillinen Yliopisto (Finland)
- Max-Plank-Institut für Hirnforschung (Germany)
- Institut National de la Santé et Recherche Médicale (France)

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Project cost
€ 2 410 993.66

EU funding
€ 1 599 989.53

Project reference
Contract No 043309 (NEST)

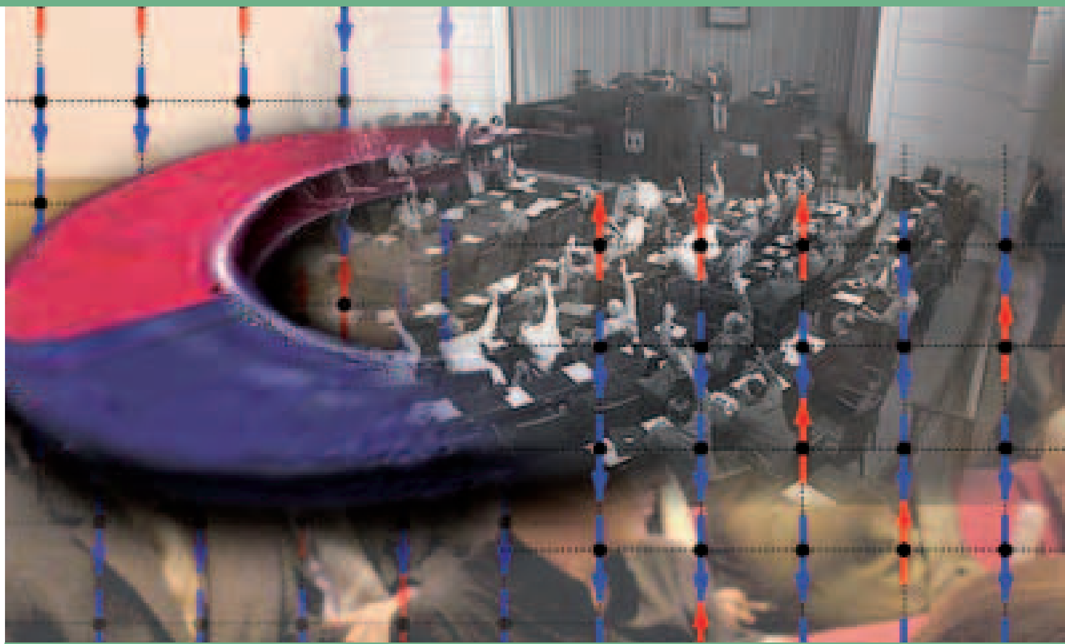
© Laboratorio de Neurociencia Funcional, Universidad Pablo de Olavide, Sevilla

Combining neurophysiological and neuroimaging techniques to shed light on cerebral mechanisms underlying higher cognitive functions in humans.

NEST
Pathfinder

UNCOVERING THE ROOTS OF COMPLEXITY

GIACS



Complexity in science embraces the application of diverse disciplines, techniques and concepts. The study determines whether seemingly unrelated complex objects, systems and events can be explained on the basis of common generic causal agents. The GIACS initiative will coordinate the activities of NEST Pathfinder projects in this field, creating optimal synergy and encouraging a new generation of researchers to think beyond traditional scientific boundaries. This could provide breakthrough answers to many fundamental questions about life and the world we live in.

Today, society faces many unprecedented difficulties – climate change, globalisation of the economy and healthcare for an ageing population – all of which demand a fresh approach to the design, planning and management of very complex socio-technical systems. Complexity arises as the result of interactions between numerous individual elements, inducing collective phenomena that can spread with fortuitous or disastrous consequences.

This concept is well illustrated by the process of Darwinian evolution, which is driven by a host of influences that cause mutations in the genome of organisms. Since random mutation is usually harmful, the average effect is actually negative. But the mechanism is successful because good mutations multiply faster, enabling the populations associated with them to grow exponentially and dominate the species. Such effects are described as autocatalytic.

The economy is another domain in which complexity is a key issue. Economic systems comprise a large number of interacting co-adapting agents that display surprising self-organising features and macroscopic order, despite the underlying disorder among their constituents.

The fact that the dynamics of such scenarios are governed by exceptional individuals or random events has profound implications for the rationale of scientific explanation. It invalidates 'reasonable' arguments based on typical or representative cases.

A universal principle?

Moreover, these generic effects appear to be common to the emergence of complex collective objects in widely differing fields. They are now recognised as central to understanding and predicting the behaviour of many, more natural and manmade systems – from ecology and social networks, to communications, transport and politics.

"Complexity brings a new synthesis between theoretical and applied science."

AT A GLANCE

Official Title
General Integration of the Applications of Complexity in Science

Coordinator
Fondazione ISI

Partners
- Technische Universität Dresden (Germany)
- Centre National de la Recherche Scientifique (France)
- Université de Liège (Belgium)
- Consorzio Nazionale Interuniversitario per le Scienze Fisiche della Materia (Italy)
- Bar-Ilan University (Israel)
- The Open University (United Kingdom)
- GENOPOLE® (France)
- Universitaet zu Koeln (Germany)
- Ente per le Nuove tecnologie, l'Energia e l'Ambiente (Italy)
- Hadassah Medical Organization (Israel)
- University of Warsaw (Poland)
- Academy of Economic Studies Bucharest (Romania)
- University of Wroclaw (Poland)
- University of Salerno (Italy)
- Hebrew University of Jerusalem (Israel)
- University College London (United Kingdom)
- Weizmann Institute of Science (Israel)
- Ecole Normale Supérieure (France)
- Manchester Metropolitan University (United Kingdom)
- Aachen University (Germany)
- Aristotle University Thessaloniki (Greece)
- The chancelor, masters, and scholars of the University of Oxford (United Kingdom)
- Lancaster University (Britain)
- Facultés Universitaires Notre-Dame de la Paix (Belgium)
- University of Warwick (United Kingdom)
- The chancelor, masters, and scholars of the University of Cambridge (United Kingdom)
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Project cost	**EU funding**
€ 1 399 964	€ 1 379 954

Project reference Contract No 012380 (NEST)

Complex economic models use the 'de-localisation' phase transition: growth is driven by the sites with higher education. Complex social phenomena (e.g. parties) emerge from individual autocatalytic interactions as magnetism results from particles interactions.

The challenge for researchers is, therefore, to understand basic objects from one science in terms of the collective dynamics of objects belonging to another science. This requires new ways of thinking and a readiness to cross traditional disciplinary frontiers. It also demands recognition that the study of complexity has a sound experimental basis, and that the formal tools available for this purpose are as valid as those for the conventional 'exact' sciences.

Complexity brings a new synthesis between theoretical and applied science. Traditional disciplines apply the results of experimental science to material/physical reality. Modern complexity, on the other hand, applies theoretical concepts to issues such as, social and economic change or individual and collective creativity, which form the information flow underlying life.

These approaches are not material/hardware-related, but rather relational and theoretical. They could be described in terms of 'theoretical applied science', a concept with the potential to deliver practical rewards.

Within the NEST Pathfinder programme, 13 individual Strategic Targeted Research Projects (STREPs) are addressing specific aspects of complexity. Four deal with physiology and molecular biology; a further group is exploring agent-based modelling in various social and economic fields; four more are concerned with networks and social self-organisation; while a final stand-alone initiative will test the ability of agent-based and networking approaches to cope with extreme self-organising phenomena.

GIACS fields an impressive consortium of institutes from the EU and Israel. Members from the STREP will lead by Italy's Fondazione also assist by serving on a special advisory board and contribute directly to some of the work packages.

The mission is not simply to build bridges between the STREPs, but also to find and contact individuals or groups that may help them to succeed, and to inform potential end-users who can profit by turning the results and ideas into real-life applications.

Education and diffusion

Since complex systems dynamics is hardly taught in university curricula, a special educational effort will be needed in the next few years. Cultivating the kind of scientists that the STREPs will create and employ will not be achieved with the current PhD course concept. Researchers will need to become more self-reliant and mobile in order to gather the pieces of expertise they need to make the next breakthrough.

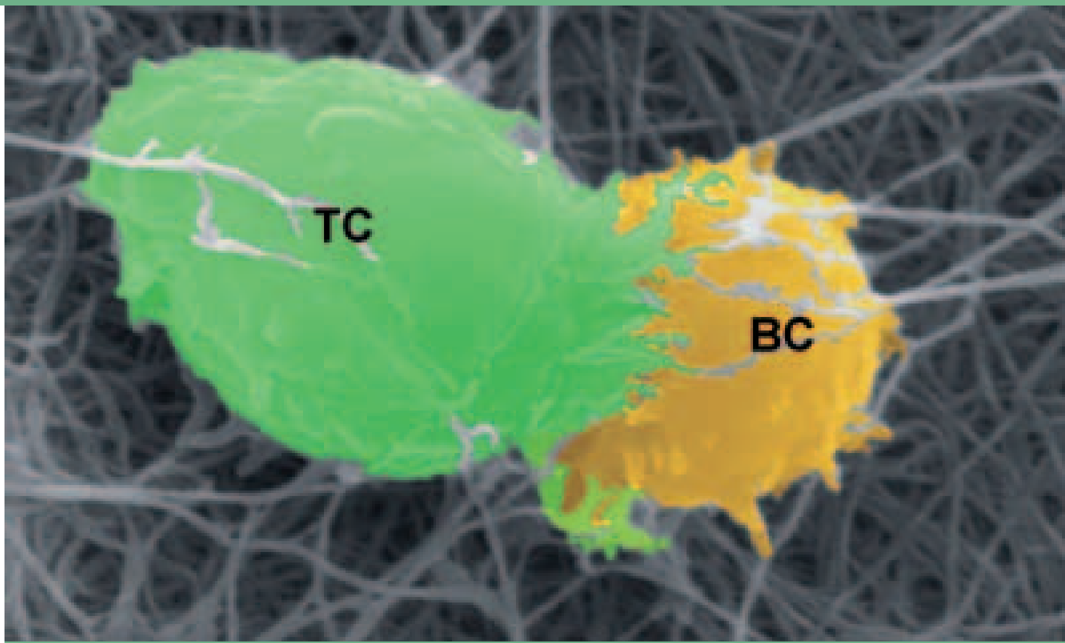
Through GIACS, people from various complexity application areas will be put in touch with the appropriate STREPs. Events will be staged whereby scientists from different projects can meet, share experiences and grow together into a more unified community.

One aspect of this will be to organise a series of seasonal schools, which have in the past proven to be an extremely efficient way of educating young researchers in new or trans-disciplinary fields. Most of these will be conducted together with ONCE-CS, funded as part of the EU's Information Society Technology programme.

NEST
Pathfinder

INJECTING MATHS INTO IMMUNOLOGY

MAMOCELL



In Europe, vaccination is taken for granted. We receive various injections throughout childhood, knowing that they will protect us from unpleasant diseases like tetanus, measles and diphtheria. However, even though immunisation techniques have been around for hundreds of years, scientists do not fully understand the biological mechanisms that induce protection. The MAMOCELL project will help solve one of the great mysteries of medicine and immunology: what actually happens following inoculation in the special structures called germinal centres?

These centres play a crucial role in the development of long-term immune 'memory'. MAMOCELL combines cutting-edge microscopy and mathematical modelling techniques to better understand the complex cellular migration and interactions that occur in these structures. The project aims to explain the mechanisms that lead to the emergent properties of germinal centres. It will create vital tools for studying biological complexity, and offers the possibility of *in silico* experimentation in immunological research.

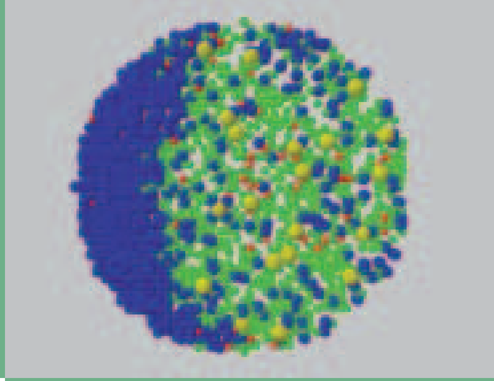
Germinal centres appear in lymph nodes following the activation of B lymphocytes, the white blood cells that produce and secrete antibodies against infectious agents. For the first three days after infection, the B cells in the germinal centre proliferate, contained within a network of specialised follicular dendritic cells. The mass of B cells begin to mutate their antibody-encoding DNA, leading to a huge array of different antibodies.

However, only the cells with 'improved' antibodies that strongly bind to antigen from the infectious agent are able to survive, the others self-destruct. Further differentiation takes place in a sub-zone of the germinal centre; interactions with T lymphocytes trigger the B cells to become either memory B cells (which maintain immunity) or antibody-secreting plasma cells (which fight off immediate infection).

New targets for new treatments

The germinal centre is home to a complex array of specialised cells and cellular interactions that induce cell migration, proliferation, hyper-mutation, cell death and differentiation. All these processes are tightly controlled but researchers have been unable to build satisfactory mathematical models or to unravel the dynamics of germinal centres *in vivo*. Yet the activity of the germinal centre is key in many diseases, including infection, autoimmune diseases and cancer.

> **"A novel combination of techniques promises breakthroughs in fundamental understanding and industrial applications."**



The MAMOCELL project provides an opportunity for Europe to make a significant contribution to the limited knowledge of this complex immune function and, in doing so, pave the way for major improvements in the treatment of several diseases.

The project aims to break new ground by combining novel mathematical modelling techniques, *in silico* simulations and laboratory studies that will visualise cellular movement and interactions in the germinal centre *in vivo* using a technique called two-photon imaging.

Currently, the field of theoretical biology and cell modelling is largely based on methods using differential equations. However, these methods are unable to cope with the complexity of some systems, especially those that involve a wide range of different, individual units. As the germinal centre is packed with possibly millions of unique variations of B cells (plus the follicular dendritic cells and T cells), standard models break down.

European germinal centre expertise

The MAMOCELL partners believe that so-called 'agent-based' models are more appropriate for this work. The MAMOCELL models will treat cells individually, allow for their physical characteristics, as well as incorporate rare or random events that might shift the balance of the germinal centre and play an important role in its global activity. The two-photon imaging, meanwhile, will allow the scientists to observe cell migration and interactions in the germinal centre in real-time, providing important data for the mathematical modelling, and enabling model predictions to be tested *in situ*.

The project involves four experienced partners from Germany, Switzerland and the United Kingdom. Whilst all the techniques used in this project have existed for some time, this is the first time they have been combined to explore the emergent behaviour of the germinal centre.

Europe already has an excellent reputation for germinal centre research, but MAMOCELL could secure its leadership in the field and provide a boost to the under-developed discipline of mathematical immunology.

MAMOCELL will also provide important tools for medical research and pharmaceutical investigations into immune-related diseases and vaccination. The development of a reliable computer simulation of the germinal centre with predictive power is particularly important as it will permit researchers to test hypotheses, plan experiments, and limit expensive and time-consuming animal studies.

In addition, the methods developed by MAMOCELL could be adapted and used to evaluate complexity in other areas of biology that involve cell migration, differentiation and death (such as wound healing and tumour growth). Outside of biology, similar models could be adopted for research into polymer gels, such as those found in disposable nappies. Indeed, one nappy manufacturer has already expressed interest in working with the project in its later stages.

MAMOCELL demonstrates how a novel combination of techniques promises break-throughs in fundamental understanding and industrial applications – whether in the form of more effective vaccinations or safer, drier nappies.

AT A GLANCE

Official Title
Mathematical Modelling of In Vivo Cell Dynamics in Germinal Centres

Coordinator
Frankfurt Institute for Advanced Studies (Germany)

Partners
- Helmholtz Centre for Infection Research (Germany)
- NovImmune SA (Switzerland)
- MRC Centre for Immune Regulation (United Kingdom)

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Project cost
€ 1 201 083

EU funding
€ 999 719.50

Project reference
Contract No 043243 (NEST)

Scanning electron micrographs of the interaction of T cells (TC, green) and B cells (BC, orange) on a background of collagen fibres /in vitro/. Similar interactions are observed in the simulation. Previously published in Gunzer et al. Blood 104 (2004) 2801.

A simulation of a germinal centre at day 5 after immunisation. Proliferating B cells (medium sized blue) build the dark zone (to the left). The light zone contains FDCs (large yellow) and B cells (small green). Several B cells are in functional contact to FDCs and T cells (small red). See also Meyer-Hermann et al Math Med Biol 23 (2006) 255.

NEST Pathfinder

PROTECTING INFRASTRUCTURE

MANMADE

Modern life could hardly survive without the transport, communication and energy supply infrastructures that everyone takes for granted. And yet, despite their importance, there has never been a rigorous theoretical framework available to characterise the behaviour and vulnerabilities of such systems. The MANMADE project responds to this knowledge gap with its proposal to build advanced analysis tools. By applying complex systems analysis and related mathematical theories to these vital resources, as well as committed expertise, the project will offer better functions, improved methods and a safer place in which to live.

Manmade, and often interdependent, infrastructures are vital strategic assets. Their robust and affordable functioning is essential to Europe's socio-economic development and stability. But many of these systems are now being destabilised by radical change – the result of market deregulation, the unbundling of the energy and utilities sectors and the increasing dependence on imported resources. Importantly, the risk of disaster is further increased by the current threat of terrorist attacks.

However, while malicious actions are always possible, records indicate that major regional or nation-wide disruptions are often the result of chance events affecting systems operating at the limits of their capacities. The causes may be natural or of human origin, occurring over long and short time scales. Dangers include shifting supply-side geopolitics, natural processes and calamities (such as extreme weather, seismic activity and flooding) as well as the effects of climate change.

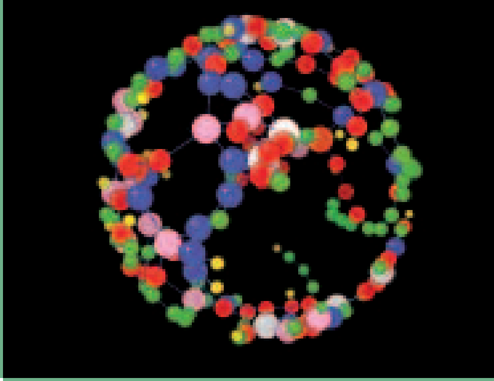
Technological factors such as ageing equipment, accidental damage and complex grid interconnections pose more threats and hazards, which often transcend the interests of individual Member States. For example, undamped frequency oscillations initiated at one point in an electricity grid can quickly propagate over thousands of kilometres, crossing national borders without restraint.

Long-term planning strategies for infrastructure development and risk containment are the subject of vigorous debate between utility owners, governments and the public at large. Yet, despite the magnitude of the problems, there remains a lack of knowledge and understanding of the macroscopic behaviour of Europe's essential networks.

Safeguarding vital systems

The aim of MANMADE is to assemble, develop and apply complementary mathematical methods for analysis of the so-called 'complex behaviour' of such large, manmade multi-

“Blend the blue-sky visions of scientists with the practical needs of the network professionals.”



element infrastructures. This initiative focuses primarily on energy supply, emergency response systems and the key subsidiary structures that either depend directly on them or are relied upon in times of crisis.

While differing greatly, these systems share a need for qualitative and quantitative methods to provide insight into the processes that generate complex behaviour. The functioning of individual network components is well understood, but their interdependencies, key vulnerabilities and the consequences of a major disruption at some critical nodes remain unclear. Resolving these issues will assist not only in the development of civil emergency preparedness strategies but also in the general long-term planning of operating programmes and supply-chain relationships.

The MANMADE consortium assembled for this breakthrough project includes academic institutes from four EU Member States and one target country (Macedonia), whose role will be to provide expertise in pure and applied mathematics. They are joined by two stakeholder agencies – the National Emergency Supply Agency (Finland) and Gestore Mercato Elettrico (Italy) – which will direct the project towards real-world issues.

Although the project will make use of standard mathematical concepts of complex systems theory, new methods based on the spectral representation of weighted connectivity matrices will be introduced and tested on actual networks. MANMADE will also examine the role of feedback and scaling as the drivers for emergent phenomena, and to correlate volatility/persistence in coupled systems.

The MANMADE partners will map specific physical and service networks that make up the main elements of functional inter-connected networks. A prime motivating principle is that, although network owners and managing authorities may be aware of the underlying concepts of complex systems analysis, mathematicians have not yet fully proved its worth in this context.

Problem-solving, yet visionary

As well as conforming to the NEST philosophy of applying a practical problem-solving approach grounded on the observation of experimental data, the project strategy will also embrace direct liaison with industry and governments to develop specific case studies.

By fielding interdisciplinary teams, MANMADE will encourage the transfer of techniques for solving complexity problems from one area of science to another. It will blend the blue-sky visions of scientists with the practical needs of the network professionals. The project will bring together both the researchers and the technologists from the networked utilities, as well as the social entities responsible for maintaining and monitoring the systems being investigated.

The strong theoretical content of the proposed research will lead to a long-term educational endeavour. And, while driven by real application-oriented questions, it is possible that the new mathematical techniques developed will lead to applications beyond those envisaged within the project itself – potentially inspiring fresh ideas of immeasurable value.

AT A GLANCE

Official Title
Diagnosing Vulnerability, Emergent Phenomena, and Volatility in Manmade Networks

Coordinator
Queen Mary College London University (United Kingdom)

Partners
- JRC-IPSC (Italy)
- Collegium Budapest (Hungary)
- Macedonian Academy of Sciences and Arts (Macedonia)
- Universita Carlo Cattaneo LIUC (Italy)
- National Emergency Supply Agency (Finland)
- Gestore Mercato Elettrico (Italy)

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Project cost
€ 1 382 260

EU funding
€ 1 099 999

Project reference
Contract No 043363 (NEST)

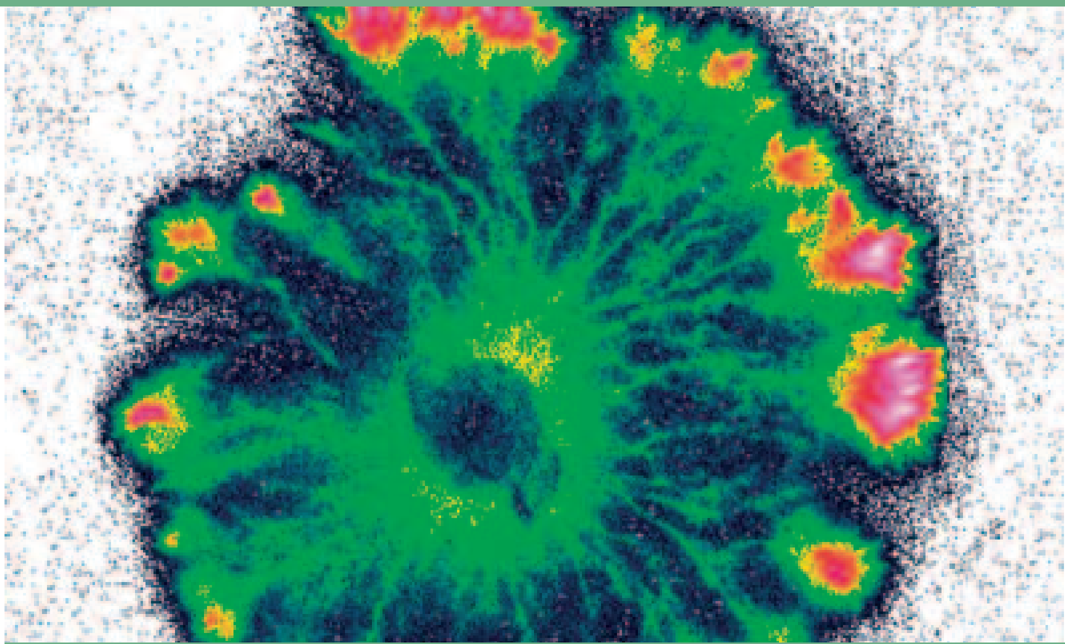
Electricity supply and relay systems now depend on the interconnections of the pan-European network which makes them vulnerable and less stable.

NEST Pathfinder

NETWORK NEWS

MMCOMNET

Recent advances in the science of complexity facilitate the measurement of networks. Certain classes of complex networks seem to share common structural characteristics, and more importantly may also exhibit analogous functional properties. The quantification and modelling of networks enables general rules to be formulated concerning their dynamic and functional behaviour. The MMCOMNET project uses a multidisciplinary approach to measure and model biological, socioeconomic and business datasets, with the aim of predicting, managing and designing behaviour in a wide range of real-world networks.



Fungal growth, supermarket supply chains and the clustering of biotech companies may sound like disparate areas of study. However, an understanding of each can be obtained by analysing them as networks. Biological networks share common features with other complex networks, in terms of their overall structure and dynamics. Once the general principles governing different kinds of complex networks are understood, steps can be taken to improve real-world networks.

The MMCOMNET project has set out to measure and model complex networks from different domains, with the goal of understanding their structure, function and behaviour. The multidisciplinary consortium forms part of the NEST PATHFINDER initiative on 'Tackling complexity in science'. This aims to encourage the study of complex systems and the transfer of knowledge between different disciplines.

Measuring networks

Networks can be studied using macroscopic or top-down approaches, or using bottom-up approaches utilising recent findings from the science of complexity. The MMCOMNET project seeks to integrate these approaches, in order to develop statistical techniques and software tools to analyse complex networks. Methods for measuring local (individual nodes) and global behaviour are also being assessed using existing datasets.

Data from three domains, representing biological, socio-economic and innovation networks, are being measured. The specific examples were chosen for ease of data collection, and their promise as generic models. The biological system is a fungal network: one of the simplest living systems to show adaptive behaviour. The main socio-economic system is a supply-chain network, involving the flow of information, money and goods from manufacturing, distribution and retail organisations across Europe. Datasets on public transport in Poland and

> **"Once the general principles governing complex networks are understood, steps can be taken to improve real-world networks."**

traffic networks in Germany are also being analysed. The innovation system involves datasets showing the clustering of high-tech businesses, as occurs in California's Silicon Valley. In particular, a comprehensive dataset of the population and businesses in Stockholm over a 10-year period is being used.

Bottom-up analysis

The three types of system consist of multiple interconnected layers, comprising autonomous agents which allocate resources within the network. Agents distribute resources on the basis of incomplete or noisy information. They typically act without a central control mechanism. The characteristic behaviour of networks emerges through the interactions of agents. Agents may be cells, people, or companies, in the case of biological, socio-economic and business networks, respectively.

The project exploits advances in complexity science to elucidate the individual and collective behaviour of agents.
The participants are developing models which simulate the different combinations of agents and network dynamics that can account for desirable behaviour. Criteria for choosing between alternative combinations provide insights into how agents and networks adapt, and the trade-offs that occur between different network functions. In the case of the supply-chain model, for example, the conditions that enable networks to retain their integrity in the face of local disruptions are being investigated.

Manipulating networks

Model networks can be used to identify ways of altering the structure or behaviour of real-world networks to enhance desirable properties, such as robustness, persistence, flexibility, responsiveness and efficiency. Adjustments in the local decision-making behaviour of agents, for example, may be effective in achieving desirable global stability.

The overall aim of the project is to generate modelling approaches and formulate universal principles to aid in the management of complex networks in real-world situations. The desirable properties observed in model networks can potentially be transferred, for example, to networks involving computers, information, business and enterprise, power grids, and railway and other transport systems. The potential long-term benefits from this project are therefore great, and could improve the quality of life of almost everybody in the EU.

AT A GLANCE

Official Title
Measuring and Modelling Complex Networks across Domains

Coordinator
University of Oxford (UK)

Partners
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- Politechnika Warszawska (Poland)
- INSEAD Business School (France)
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Project Cost
€ 1 712 352

EU Funding
€ 1 499 226

Project reference
Contract No 12999 (NEST)

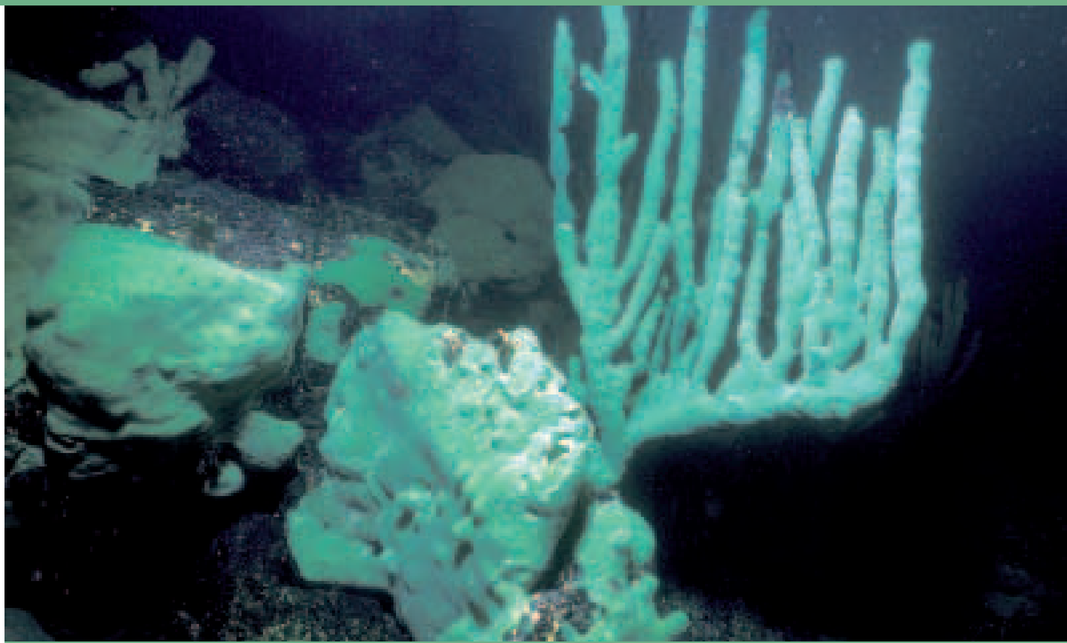
Fungal growths show common features with commercial networks.

Traffic-network modelling provides insight into understanding complex networks.

NEST
Pathfinder

VIRTUAL EXPERIMENTATION

MORPHEX



Growth of biological organisms is influenced by genes in individual cells and by interactions between cells. MORPHEX seeks to understand how interactions between genes cause cells to differentiate, grow and divide, and how exchanges between cells contribute to this process. The results should improve understanding of why the growing process sometimes fails, and how to overcome this. It will also lead to the expansion of computer-based experimentation on virtual organisms, and to the development of a generic platform for model-driven experimentation.

Biological organisms consist of complex systems involving genes and cells. Growth in plants or animals is governed by what happens inside the cell – regulated by genes and their interactions – and by the exchanges between cells. The goal of the MORPHEX project is to understand how these two levels of complexity combine to create the form of the final organism.

This shape-forming or morphogenesis is influenced by both internal and external environmental factors. So it is necessary not only to carry out experiments to see what is happening, but also to model the overall growing process mathematically, and then in the computer. This involves modelling cells, gene regulatory networks and, more difficultly, their interactions and what will emerge from these interactions.

Plant and sponge development

MORPHEX will focus on the development of the reproductive organs in the flowering plant *Arabidopsis thaliana* and that of two sponges, *Suberites domuncula* and *Lubomirskia baikalensis*. Sexual organs in flowering plants are formed from populations of dividing undifferentiated stem cells known as shoot apical meristems at the tips and branches of the plant, a process that continues throughout the life of the plant.

A great deal of data has been collected about the regulatory networks involved in the development of these organs but its analysis – without the use of modelling and simulation methods – is very difficult. This project will synthesise and expand existing gene-expression studies to determine the mechanics of morphogenesis in the plant, and so improve overall understanding of floral architecture.

On the animal side, major advances have been made in modelling quantitative and dynamic pattern formation in sea urchins. Currently, the interest is linking the quantitative model of gene expression in such models to

> "The project should enable us to understand
> why the growing process sometimes does not work."

a biomechanical representation, and determining the influence of the environment on the morphogenetic process.

The two sponges offer simpler structures than sea urchins for such a study. MORPHEX will model early development before growth in the adult sponge. Optimisation techniques will be applied to determine causal relations between genes in the regulatory networks, as well as the dynamics involved. Spatial and temporal expression patterns in the developmental processes will be simulated and compared with observed patterns. Attempts will also be made to understand the physical coupling between cells and shape formation.

Shape creation in the sponges and the plant share many common elements, justifying tackling their morphogenesis in the same complex systems framework. The total number of genes, for example, is around 30 000 for the sponges and about 25 000 for the plant. However, there are sufficient differences in the number of cells involved, the levels of emergence, and the development time scales, to be able to guarantee a generic approach to the design of the modelling and simulation tools.

The MORPHEX project will focus on establishing a general model to describe the underlying complex systems, developing tools to extract concrete models based on experimental data provided by biologists, and then determining how to describe, execute and analyse relevant protocols for computer simulation. All this will involve a highly interdisciplinary team bringing together biological development experts, mathematicians, physicists, computer scientists specialised in modelisation, as well as software specialists and engineers from across Europe.

Such an approach makes it possible to construct models of complex systems from incomplete, missing or inconsistent data. It also allows prediction and control of the models and the overall systems. As a result, although the focus will be on biological questions, with concrete results expected on how the sexual organs in the flower and the form of sponges develop, the concepts and software tools developed will be sufficiently generic for reuse in other biological or even non-biological domains. Moreover, the ability to model and validate such simulations will bring more rigour to the verification of results in parallel fields.

Global benefits foreseen

The results should enable us to understand why the growing process sometimes does not work, and how to overcome the problem of a missing gene by manipulating the interaction of surrounding cells. The software and procedures developed in the project will enable the development of model-driven experimentation, markedly cutting the cost of studies on genes, gene interactions and relations with cells.

MORPHEX should also lead to the creation of virtual plants or animals, allowing a large part of experimentation to be carried out on the computer rather than on real plants or animals – reducing risks and avoiding ethical dilemmas. This could, for example, enable crop yields and quality to be improved, and make it possible to optimise farming methods to enable us to feed an ever-growing population.

AT A GLANCE

Official Title
Morphogenesis and Gene Regulatory Networks in Plants and Animals: a Complex Systems Modelling Approach

Coordinator
Centre National de la Recherche Scientifique – Délégation Rhône Auvergne (France)

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- Chalmers University of Technology (Sweden)
- Corporacion de Ciencias y de la Educacion – Instituto de Sistemas Complejos de Valparaiso (Chile)
- Johannes Gutenberg Univesity Mainz (Germany)
- Unversität Stuttgart (Germany)
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Project cost
€ 2 222 961.60

EU funding
€ 1 599 990.40

Project reference
Contract No 043322 (NEST)

The freshwater sponge Lubomirskia baicalensis represents one of the most structured sponge species. The green colour of the specimens originates from the green algae which live in symbiosis with this animal.

An x-ray image of the freshwater sponge Lubomirskia baicalensis demonstrates the complex architectural structure of the hard skeleton of this animal.

NEST
Pathfinder

COMPLEXITY RESEARCH GETS MORE ROBUST

PATRES

The sight of new growth following a devastating forest fire shows nature's inherent ability to withstand major disturbances and rebuild itself when necessary. Understanding how such complex systems demonstrate resilience by absorbing or recovering from major external perturbations allows scientists to learn valuable lessons. The multidisciplinary PATRES team will develop new methods defining the actions favouring the recovery from perturbations – applicable from ecology to cognitive sciences and sociology – in a project that will bridge the divide between the physical and social sciences.

Complex systems are often capable of showing remarkable robustness. Despite major changes in their surrounding environment they are somehow able to adapt and survive by overcoming negative effects. Examples include bacterial colonies developing resistance to antibiotics, beaches recovering from oil spills, and human societies remaining intact even in the face of natural disasters and economic pressures.

Scientists and mathematicians have studied this type of resilience for over 30 years. After all, the ability of a system to recover from disruption is just as important as its performance under more favourable conditions.

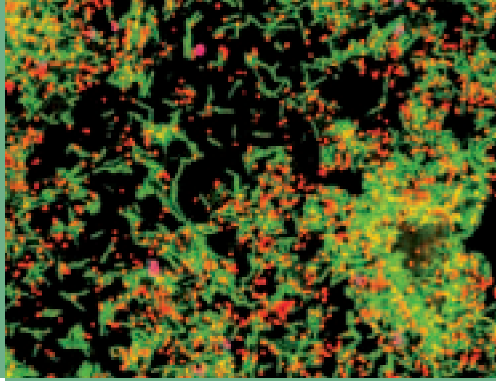
Methods for modelling such resilience are far too simplistic, making it difficult to discover the key to this robustness. By uniquely combining viability theory and the mathematics of pattern dynamics, the PATRES project will develop new modelling techniques. The team will demonstrate that abstract maths has many practical applications, ranging from the sustainable use of African savannah to improved business networks.

Currently, models of resilience in complex systems presume that such systems will eventually reach a state of equilibrium following a perturbation. This focus on maintenance and recovery is a long way from reality, however, as occasional changes in the environment can cause a dramatic shift to another state resulting in entirely new behaviour patterns.

A viable approach

Work recently undertaken at Cemagref (France) suggests that drawbacks to the current models may be overcome by employing viability theory. By ignoring the mechanisms behind a system's resilience, this approach is able to look at the effort or 'cost' required for maintaining or restoring particular functions of a system during disruption. The cost can be translated as a quantitative measure of a system's robustness.

"To stimulate and predict outcomes for real-world situations."



Unfortunately, this method has one major drawback; the intricate viability calculations need significant computer resources. In practice, therefore, this promising approach can only cope with relatively small systems, certainly not the levels of complexity found in most ecological, biological or societal systems.

The PATRES project is seeking ways to overcome these limitations and establish viability modelling as an effective way to study resilience. The consortium will develop methods to 'simplify' the complex systems, construct viability models, and test their ability to simulate and predict outcomes for real-world situations.

Patterns for partnership

Several of the project partners have a particular interest in the mathematics formation and recognition. It is impossible for viability models to work for systems with a large number of interconnected agents. But where the interconnections have statistical regularity or 'patterns', the complexity can be diminished. Rather than trying to describe the agents and their interactions, you describe the patterns they make instead.

The partners will apply their collective knowledge and experience to develop two complementary software types. The first is a tool for identifying and modelling patterns and their dynamics in complex models. The second will compute the resilience properties of a system and determine what kinds of action are required to maintain or restore the patterns within it.

The team will use the software tools to explore resilience in very different complex real-world systems. The tools will also help to solve practical problems in a number of other areas such as bacterial dispersion biofilms (to improve water treatment technology), and the sustainable management of trees and grass in savannah landscapes (to conserve biodiversity and identify sustainable stocking rates).

These tools can also be used to study the emergence and demise of language in human societies, thus aiding the identification of policies that can help preserve languages that are under the threat of extinction. The work can also be applied in business to study the strength of networking structures between biotechnology firms, and how successful networks are cushioned or recover from major economic upsets.

The wide-ranging applications of the novel modelling techniques and software highlight the importance of this project to Europe's capabilities in resilience research. The project involves researchers specialised in physics, ecology, social sciences, cognitive sciences, computer sciences and applied mathematics, making the new tools and techniques potentially highly flexible and easily adopted by scientists from many other disciplines.

Moreover, the work to test PATRES' methods in five specific case studies will disseminate the results of the project to a much wider research community. Clearly, the PATRES project is set to make Europe's expertise in this field substantially more robust.

AT A GLANCE

Official Title
Pattern Resilience

Coordinator
Cemagref (France)

Partners
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- Universitat Illes Balear (Spain)
- Centre for Environmental Research (Germany)
- Centre de Recherches en Epistémologie Appliquée (France)

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Project cost
€ 2 088 554.38

EU funding
€ 1 199 427.79

Project reference
Contract No 043268 (NEST)

View of African savannah.
© Jula Zimmermann, UFZ

The project will apply similar methods to detect ecological patterns in the African savannah, and use them to define more sustainable policies of land-use.

Bacteria colony
© Theodore Bouchez, Cemagref

PATRES will develop methods to detect dynamical patterns in bacteria ecosystems, and use them to define politics of control actions for more efficient processes.

NEST
Pathfinder

HOW STARLING FLOCKS CAN HELP PREVENT FINANCIAL PANIC

STARFLAG

The study of biological systems can provide insights into the behaviour of complex socioeconomic systems. Flocking in birds is a complex system that is amenable to study. Advances in techniques for visualising and analysing the movement of flying birds in 3-D are leading to a better understanding of flocking and other animal group behaviours. The techniques developed can be applied to more complex systems that are harder to observe directly, including the behaviour that drives financial markets.

Starling (Sturnus vulgaris) flocks contain many autonomous individuals. However, the behaviour of the flock cannot simply be explained by deducing the behaviour of individuals. The system is said to be complex, because its behaviour emerges through the interaction of individuals or agents that are following relatively simple rules.

Bird behaviour

The findings of this project will be of immense interest to those working in ornithology, animal behaviour and ethology. Once airborne, consistent patterns quickly appear in a group, or murmation, of starlings. Innovative data recording and 3-Dmodelling techniques are being deployed to study the movements of individuals and the shape of the overall flock. A key technical challenge has been to identify individual birds over time, in images recorded from three directions. There have been many previous studies on flocking behaviour, but none with the precise and accurate data collection or the 3-D modelling capabilities of this project.

One of the forces driving the evolution of grouping in animals is predation. Flocking behaviour in this study will be recorded with and without the presence of a 'predator' to observe changes in collective behaviour. In addition to field recordings, experiments are being conducted in aviaries. Bird behaviour changes seasonally, and this is being correlated with an analysis of hormone levels and social bonding. This will be a step towards understanding the endocrine control of flocking. The project will provide general insights into migration, navigation and animal-group movement.

> **"The project will use collective animal movement models to gain insights into human behaviour in the social sciences and economics."**

Modelling collective behaviour

The models start with the idea that individual agents are responsive to the behaviour of others nearest them. Flocks of starlings exhibit anti-predator responses, for instance, which take the form of 'terror waves' that are propagated through the flock. The behaviour of individuals at the sides and front of the flock are of particular interest in initiating changes in collective behaviour.

The statistical methods, software tools and visualisation techniques developed to study starlings are all easily transferable to other domains of study. A range of measurements, for instance, to quantify the population level or density of agents necessary for emergent behaviour, can be applied generally to complex systems. In particular, the project will use collective animalmovement models to gain insights into human behaviour in the social sciences and economics.

Money matters

At the end of the Starflag project, a simulation package will be delivered, for application to complex systems such as financial markets. In essence, it will predict the interaction between individual opinion and collective group behaviour. In cases where individual opinion causes a rapid change in collective opinion, a system can either change detrimentally (with a crash) or favourably (with rapid adaptation to a changing environment).

One area where general models of complex systems can be applied is to the problem encountered in financial systems when collective frenzy overrides the rationality needed for market efficiency. In strictly modelling terms, collective frenzy shares common features with the 'terror waves' observed in starling flocks. The models could suggest ways for regulators to act to stabilise markets. A range of other insights into human herding and collective decision-making are likely to arise from advances made in this project.

AT A GLANCE

Official Title
Starlings in Flight: Understanding Patterns of Animal Group Movements

Coordinator
Istituto Nazionale per la Fisica della Materia (Italy)

Partners
- Commissariat a l'Energie Atomique, Centre d'Etudes de Saclay (France)
- Max Planck Society (Germany)
- Eötvös Loránd Science University (Hungary)
- Istituto Superiore di Sanità (Italy)
- Scuola Normale Superiore (Italy)
- Centre of Ecological and Evolutionary Studies of Rijksuniversiteit Groningen (The Netherlands)

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Project Cost
€ 1 293 025

EU Funding
€ 1 160 000

Project reference
Contract No 12682 (NEST)

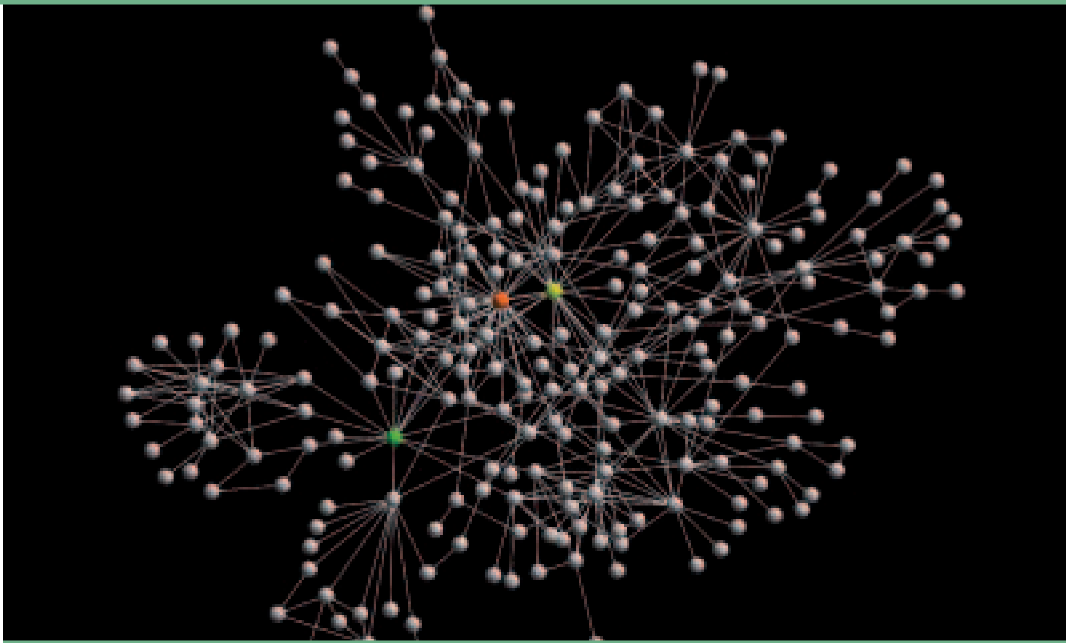
A flock of starlings…

…or a floor of traders?

NEST
Pathfinder

BOOSTING THE PERFORMANCE OF CANCER DRUGS

SYNLET



Cancer is the second most prevalent cause of death in developed countries. Some 2.9 million cases are diagnosed annually in Europe, with over 1.7 million deaths attributed to cancer each year. Chemotherapy regimes currently used show limited effectiveness, with chemoresistance a major therapeutic shortcoming. SYNLET's novel approach to this key drawback will not only improve our understanding of cancer cell chemoresistance but propose combination drug treatment regimes for fighting cancer.

As the statistics clearly indicate, there is a vital need to improve cancer survival rates as well as the quality of life for those affected, while also reducing the overall social and economic consequences of cancer-related illnesses. Yet, despite decades of cancer research, only limited fundamental knowledge has been gained about the central aspects of cellular malignancy at different stages of the disease. Cancer treatment regimes tend to be designed for obtaining a specific effect in a particular stage of the disease.
The consequence of this lack of understanding is rapid resistance to chemotherapeutics, in the worst case leaving only palliative care.

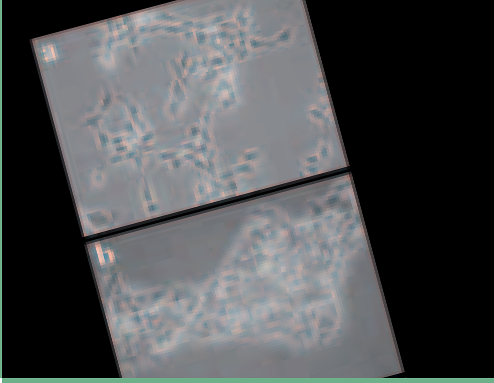
SYNLET aims at obtaining a greater understanding of the complex processes involved in malignant transformation by combining theoretical, computational and experimental approaches. An interdisciplinary consortium involving theoretical biologists, complex systems scientists and experimental oncologists will integrate this knowledge towards improving the effectiveness of cancer drugs.

Killing cancerous and healthy cells

Current chemotherapy treatment regimes apply drugs to kill rapidly dividing cancer cells. However, such drugs can also be lethal to normal cells, which restrict the types of drugs that can be used and the treatment duration. Chemotherapy resistance is particularly complex, as robustness and viability of drug-resistant cancer cells depends on a variety of molecular changes that are difficult to interpret.

Survival and malignancy of chemotherapy-resistant cancer cells appears to depend on gene expression and protein-interaction networks that differ markedly from those of chemotherapy-sensitive cells. Furthermore, the acquisition of chemotherapy resistance is commonly associated with a more malignant phenotype, indicating increased robustness of chemoresistant cancer cells.

Genes, their expression and the cellular function of encoded proteins, can be seen as a complex interaction network defining the phenotype of a cell – being 'healthy' or malignant and, as a consequence, being chemosensitive or chemoresistant.



"Towards solving the phenomenon of chemoresistance."

SYNLET is developing a complex systems analysis approach for identifying the key proteins that enable cells to overcome drug toxicity resulting in chemoresistance. Blocking these proteins in their functional context may result in synthetic lethality, leading to re-sensitising chemotherapy-resistant cancer cells to conventional drug treatment. However, simultaneous inhibition of two or more genes/proteins rather than any single gene/protein may be needed to realise synthetic lethality on this level.

While this general concept has been discussed in scientific literature, the practical implementation has been limited due to a lack of understanding of key cellular mechanisms involved. Availability of broad experimental data sets from chemoresistant cancer cells, combined with mathematical modelling of the cellular dynamic system on the level of interaction networks, now allows for qualitative and quantitative analyses. This provides novel hypotheses for overcoming chemoresistance mechanisms. Such hypotheses can now also be directly tested in an experimental setting.

Systems analysis and biology

Complex systems science has provided pivotal concepts, theories and insight towards an understanding of dynamic systems both at a general level and in the practical context of cellular processes.

SYNLET unites leading European experts in complex systems science and computational biology with clinical oncologists to create an alternative procedure towards solving the phenomenon of chemoresistance. This work is focused on a unique collection of drug-resistant cancer cell lines.

A broad experimental profile characterising chemoresistant cancer cells will trigger computational analysis procedures using complex systems science methodologies. These results will feed into experimental verification. Small interfering RNA (siRNA) molecules directed against synthetically lethal hubs in the cellular control network will be tested for overcoming chemoresistance in conjunction with current cancer drugs.

Merging algorithmic approaches in complex systems analysis with state-of-the-art computational simulation of biological processes is one of the major innovative procedures involved in this project. SYNLET will also focus on deepening our understanding of cellular interaction network dynamics in terms of stability, robustness and the prevalence of 'escape routes' used by cancer cells towards overcoming external selection pressure actuated by cancer drugs.

Once functional protein hubs enabling cellular drug resistance escape routes have been identified, experimental efforts will be applied towards blocking these processes, followed by *in vitro* analysis of effects on chemoresistance. As a result, novel strategies for improving the effectiveness of cancer drug treatment may emerge.

SYNLET will strengthen Europe's position on the broader scale of the global research community. The research organisations and small and medium-size enterprises involved will ensure that the results are clinically tested and that the subsequent commercial avenues for the new combinational cancer drug treatment regimes are explored.

AT A GLANCE

Official Title
Regulatory Control Networks of Synthetic Lethality

Coordinator
blue-drugs Gmbh (Germany)

Partners
- emergentec biodevelopment (Austria)
- Universitat Pompeu Fabra (Spain)
- Weizmann Institute of Science (Israel)
- University of Leipzig (Germany)
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Project cost
€ 2 208 924

EU funding
€ 1 725 161

Project reference
Contract No 043312 (NEST)

NEST Pathfinder

FROM BREAKDOWNS TO EARTHQUAKES: IT'S A QUESTION OF SCALE

TRIGS

Natural catastrophes such as earthquakes, landslides and avalanches are triggered by perturbations. These perturbations have much in common with the disturbances that cause the failure of engineered structures. TRIGS is the first project to use the tools of complex systems analysis to explore triggering mechanisms across this wide scale range. As well as paving the way for improved geohazard forecasting, it will provide new methods for identifying weaknesses and mitigating breakdown of the infrastructures and devices that are essential to everyday life.

A landslide can be started by an earthquake; fatigue failure in an engine component can be induced by increased stress levels. While such effects occur over vastly differing spatial and temporal scales, the underlying causes are fundamentally similar. They, nevertheless, remain extremely difficult to explain and predict.

Natural disasters may also result from specific events: from precipitation and pore pressure variations; or from endogenous defects, ranging from chemomechanical deterioration and creep deformation to microcracking and microplasticity. Similarly, failure in engineering materials can be triggered by external environmental conditions: by mechanical, chemical or electromagnetic perturbations; or by internal causes related to relaxation of the structure through creep deformation, fracture or plastic flow.

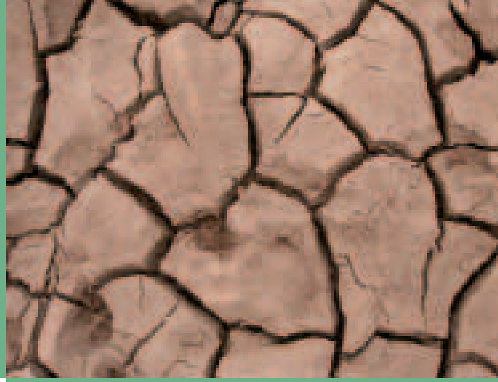
Multiscale phenomena

The processes extend down to the atomic level, where the arrangement of atoms and the ensuing defects such as dislocations and microcracks are of crucial importance. And up to geological magnitude, where deformation instabilities manifest themselves in the form of extreme events, such as rockfalls, landslides, avalanches and earthquakes. But the response is invariably complex and non-linear.

One example of internal perturbation acting as a trigger is in wet snow avalanches, where surface warming and melt water production cause percolating water to be caught at capillary barriers, leading to a loss of shear support. Due to the complexity of the percolation in stratified snow cover, wet snow avalanches are notoriously difficult to forecast.

The aftershocks and landslides initiated by major earthquakes are among the many instances that can be cited of natural hazards triggered by external perturbations.

> **"TRIGS will develop more realistic modelling and allow greater accuracy in the forecasting of potential disasters than has so far been possible."**



A further complication is that, in most cases, several triggering mechanisms act simultaneously. This makes it necessary to address the interplay between different phenomena, adding further to the difficulty in understanding and predicting material failures and natural hazards.

New theoretical basis needed

Gaining a better insight will depend on the development of new theories that give the ability to bridge the scale ranges. This entails integrating methodologies from materials and earth sciences into the more general perspective of complexity. This requires a transfer of knowledge across traditionally separate disciplines.

Complex systems methodologies – from statistical characterisation of time series and spatial patterns to agent-based models, cellular automata and non-linear equations – have been applied over the past two decades to the modelling as well as assessment of natural hazards in geosystems. While several of the resultant models reproduce most properties of seismicity, the limited quality of the data, and limited knowledge of the Earth's crust rheology, have so far prevented the formulation of an 'optimal' seismic hazard model. Statistical tools and complex systems theory are now also used in materials science to understand fracture and plasticity, although this work is progressing at a slower pace than in the earth sciences.

The six institutes that make up the TRIGS consortium provide a balance of expertise that will facilitate cross-fertilisation between the two fields. The present need is to shift attention from the abstract, general thinking that is typical of complexity research, to a more quantitative, experimentally-based analysis.

The partners are approaching this issue by combining the statistical analysis of catalogued data and field measurements with laboratory experiments, multiscale materials simulations and non-equilibrium statistical modelling.

This European initiative draws on progress made in the different fields towards detailed modelling of materials and geosystems. Yet, at the same time, it will avoid the danger of neglecting system scale complexity because of an unwarranted attention to detail.

Instead of performing a global analysis of natural hazards, the team is using the basic framework of complexity theory and its associated models to study specific responses to well defined triggers.

From these findings, they will derive experimental strategies that allow for a quantitative assessment of system-specific parameters. The study of cross-scale interactions will enable new types of laboratory tests to be devised, delivering results that are more useful in understanding the triggering of instabilities in materials, devices and complete geosystems.

TRIGS will develop more realistic modelling and allow greater accuracy in the forecasting of potential disasters than has so far been possible. It will also contribute to better assessment and avoidance of the unforeseen consequences of human interference with the environment.

AT A GLANCE

Official Title
Triggering of Instabilities in Materials and Geosystems

Coordinator
Consiglio Nazionale delle Ricerche (Italy)

Partners
- Istituto Nazionale di Geofisica e Vulcanologia (Italy)
- Center for Materials Science and Engineering, the University of Edinburgh (Scotland)
- Helsinki University of Technology (Finland)
- Laboratoire de Géophysique Interne et Technophysique, Université Joseph Fourier (France)
- WSL/Swiss Federal Institute for Snow and Avalanche Research (Switzerland)

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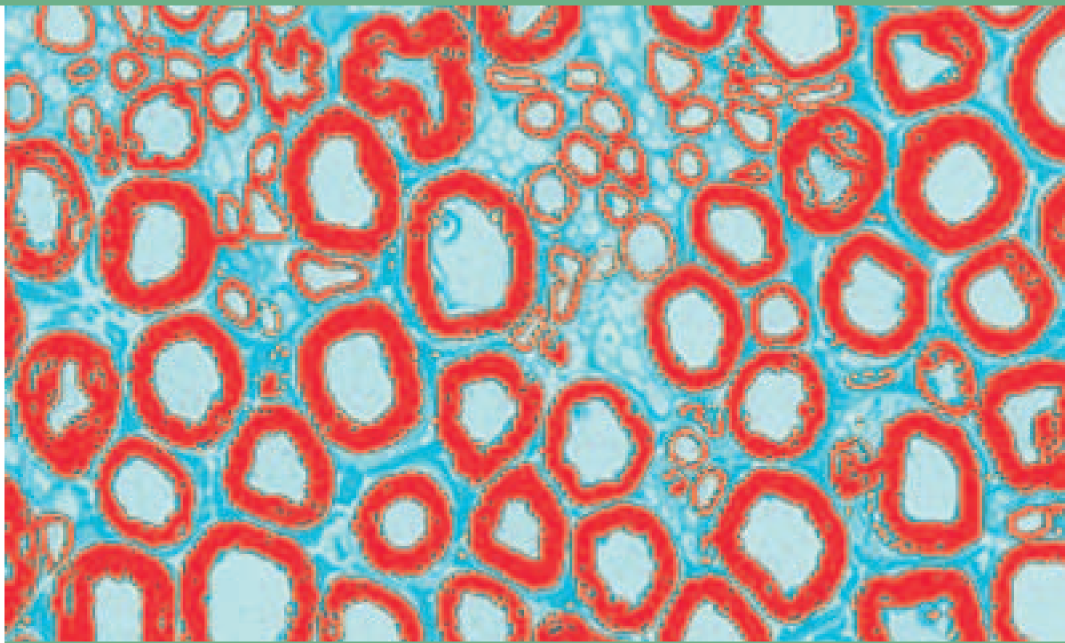
NEST
Pathfinder

A UNIFIED APPROACH TO INTERPRET COMPLEX NETWORKS

UNINET



The growth of studies of complex systems has revealed that they exist on many scales, from the molecular to the global, and in many different fields of science. Uninet is attempting to unify the variety of network theories which have been proposed for these varied systems. Applying mathematical techniques to analyse complex networks in five very different areas, Uninet should enable re-interpretation of the original theories in new applications, so that major improvements of insight are expected.

It is now well established that many features of the physical, biological, and sociological world – like molecular structures, neural transmission, crowd behaviour – are organised in systems or networks. They exist on an infinite range of levels of size and complexity, but all are characterised by the ability of the network to respond collectively to external conditions or stimuli. Many different theories have been developed in parallel to analyse and model these systems. The current stage of scientific understanding presents an unrivalled opportunity to develop a more unified network theory. This is the intention of Uninet, part of the NEST PATHFINDER initiative on 'Tackling complexity in science'.

The consortium includes leading research workers in five widely differing areas: genetics, metabolism, neurobiology, ecology and economics. Within each area, the leading group will first review the existing network theories which attempt to describe it. Later, each group will study, model and simulate up to three topics of particular impact in that area, which should also yield methodologies useful in some of the other subjects. Mathematical analysis of the network theories will be provided by the coordinating group. Finally the project will examine their potential applications in technology and industry.

A world of networks

Understanding complex networks is a science in its infancy, as computers have only recently made it possible to analyse the huge amounts of data needed. For example, the explosion of data generated by genomics still leaves a very long way to go before its implications are unravelled. Similarly, analysis of the behaviour of individual animal species, or of functional groups like a food web reveals only a fraction of the complexity of the whole ecosystem and its dynamics. And we all live in a variety of social networks, with different levels and scales of interaction from individuals to nations, involving many different flows,

"The project's work will bring out common aspects so that models can be reduced in complexity to the simplest mathematical abstraction."

of traffic, of people or of information, for example.

Uninet's five areas for study will be linked by annual workshops throughout the project. These will give participants the opportunity to explore aspects of network modelling, including data, dynamics and robustness. It will also bring out common aspects so that models can be reduced in complexity to the simplest mathematical abstraction. The work packages to be undertaken in each of the individual areas will examine the methods that have been used to derive networks and their dynamics, which include clustering algorithms and Bayesian network approaches. Graphoriented search algorithms have been used to understand the structure of networks, e.g. triangles in a network topology. Other methods relate to dynamic systems theory, e.g. stability of components, and also mathematical methods relating to observable features like robustness. Biological systems are often extremely robust, that is they are self-maintaining under external pressure.

Uninet's expected influence

Because of its interdisciplinary approach, Uninet expects to be able to offer insights into significant new areas of research. In pharmaceuticals, for example, analysis of genetic and metabolic networks should contribute to optimising drug effects. Studies of enzyme behaviour may offer enhanced yield in biotechnological production. In the area of biological diversity, principles derived from ecosystem analysis will enable Uninet to advise on conservation strategies, especially for problems linked with loss of diversity through disturbance of food webs. Neural system research in Uninet will advance understanding of impulse transmission and brain function. And in the rather different but comparable area of economic networks, Uninet research on world markets and major auctions (like privatisation) will provide valuable guidance for policy-makers concerned with improving the efficiency of market structures. By completion, Uninet will have created new and improved algorithms for solving network-related problems, with wide-ranging potential applications.

AT A GLANCE

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Complex networks exist at all scales of nature.
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Biological systems are robust enough to maintain themselves under outside pressure.

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