University of BRISTOL

re: search

University of Bristol • Research Review • Issue 10 • October 2005

research themes issue

Brain science, addiction and drugs

Delivering public services

A burning issue

I would like to welcome you to this special issue of *re:*search, highlighting the University's research themes.

Most of our research here at the University of Bristol is carried out in departments that were rated 5 or 5★ (the highest grades achievable) in the last Research Assessment Exercise – an independent review of research done in all UK universities. But, despite this, our external stakeholders are sometimes frustrated by the lack of available information about the precise areas of our expertise. Being a 5 or 5★ department is excellent but the rating doesn't exactly describe what research we are engaged in!

As a world-class, research-intensive university, we want to offer something that is distinctive and exciting in this highly competitive and under-funded environment. Bristol engages in the full range of discipline-based academic research, but while the breadth of that research is a strength, we recognise that we cannot do everything to the same standard and must focus on what we are best at. Excellent discipline-based research is absolutely essential, but our distinctiveness will be reflected in our ability to work across the breadth of disciplines and use our research to answer 'real world' questions, engaging in agenda-setting research.

The University's Research Strategy for 2003-08 charged the research committee with identifying a core group of interdisciplinary research 'themes' that cut across departmental and faculty boundaries, and in which the University already has, or can attain, world-class excellence. The faculties, working with their research directors, have now identified the current research themes and these are listed on the opposite page. This issue of *re:*search highlights examples of research being done within some of the themes: there are five articles from established themes; three from areas of research that we think have the potential to become themes; and one from an emergent area.

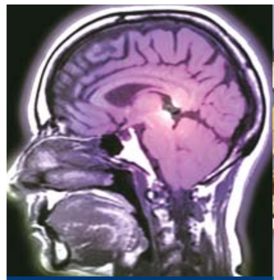
While the research themes will allow us to articulate our interests and strengths better, the concept of themes must be dynamic to reflect the reality of doing research in a challenging and ever-changing world. Themes will come and go. But with a vibrant, progressive research base we will continue to review what we are best at and to tell our external stakeholders about our strengths, as well as to identify those areas that we want to nurture. Of course, internationally excellent research outside the scope of the themes will continue to be fostered as an important component of the University's research activity, complementing our interdisciplinary research.

So, what next? We will focus our efforts on effectively building on our world-class research (whether thematic or otherwise) and on providing support for the potential themes and emergent areas to ensure that they all realise their full potential.

Dr Siân Thomas
Director of Research and Enterprise Development

Research themes 2005

Established research themes



Theme: Neuroscience
Brain science, addiction and drugs
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Theme: Reception
The long chain of reception
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Theme: Communications
Designing your future
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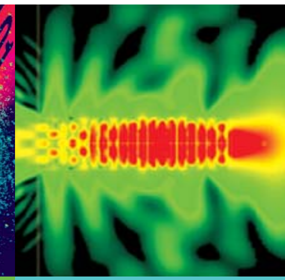

Theme: Nanoscience and Quantum Information
Exchanging keys in the Canaries
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Theme: Applied Quantitive and Social Science
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Other established research themes:
- Cardiovascular Science
- Colonialism
- Epidemiology and Human Services Research
- Ethnicity and Migration
- Medieval Cultures

Potential research themes

Theme: Exabyte Informatics
The exabyte challenge
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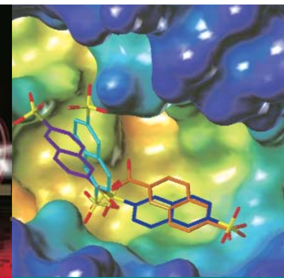

Theme: Structural Biology
The building blocks of life
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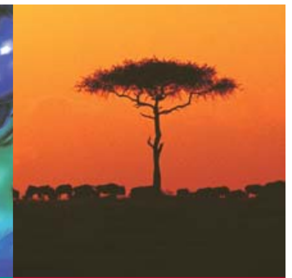

Theme: Global Change
A burning issue
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Other potential research themes:
- Advanced Composites and Intelligent Structures
- Animal Welfare and Behaviour
- Cell Signalling and Cell Biology
- Children and Childhood
- Gender
- Governance and Regulation
- Infection and Immunology
- Information Processing in Biological Systems
- Neighbourhoods
- Performativity, Place, Space
- Science, Knowledge and Reality

Emergent research areas

Theme: Human Rights
Human rights for the 21st century
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Other emergent research areas:
- Dynamics Engineering
- Robotics and Autonomous Systems

Brain science, addiction and drugs

***David Nutt*, Professor of Psychopharmacology, was one of three key advisers recently appointed to provide detailed scientific input into the Government's Foresight programme on Brain Science, Addiction and Drugs. The project was led by Sir David King, the Government's Chief Scientific Adviser. Some of their findings are reported here.**

An important role played by many researchers at the University is to inform Government about new reasearch in order to help it develop appropriate policies. Not only does the University have two members on the Government's Council of Science and Technology that advises the Prime Minister on issues of strategic importance in those fields, but others are frequently asked to advise the Government because of their exceptional expertise in a certain area.

The DTI's Foresight programme exists to produce challenging visions of the future to ensure that we develop effective strategies. The Brain Science, Addiction and Drugs project aimed to provide information on how scientific and technological advancement may impact on our understanding of addiction and the use of psychoactive substances over the next 20 years. Based on currently available scientific evidence, it looked at scenarios for possible future change. To do this it asked one key question: how can we manage the use of psychoactive substances in the future to best advantage for the individual, the community and society?

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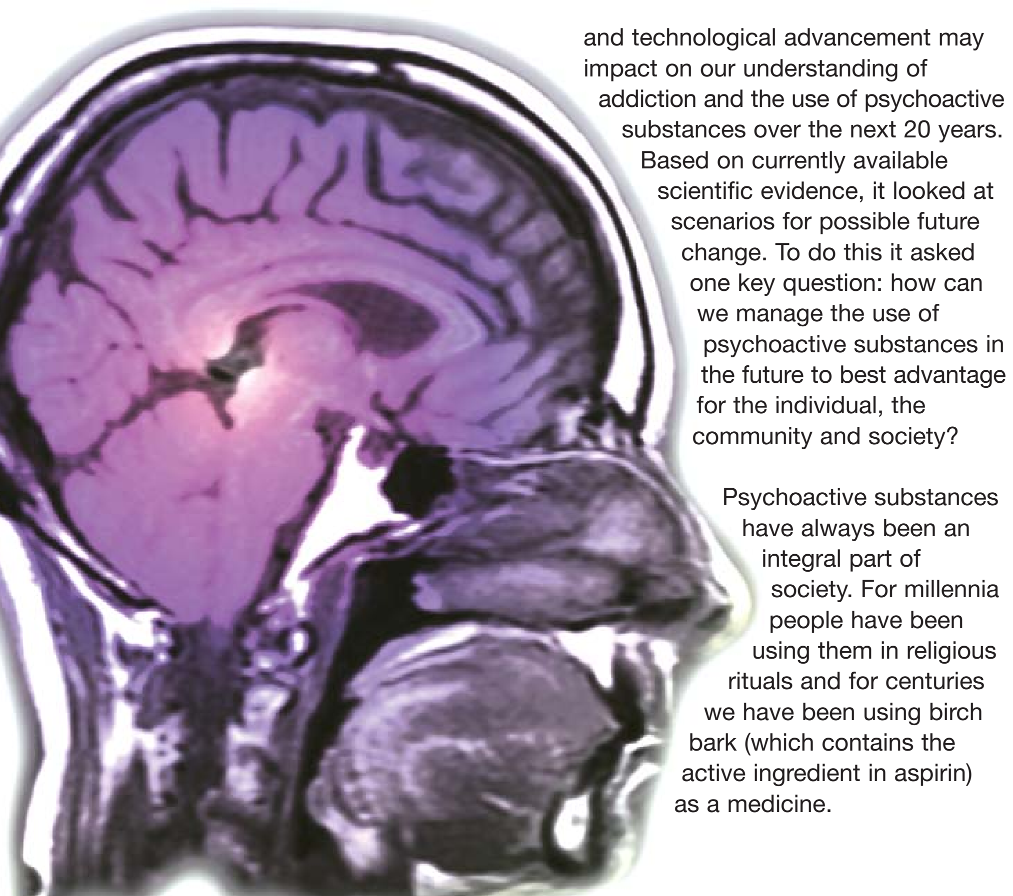


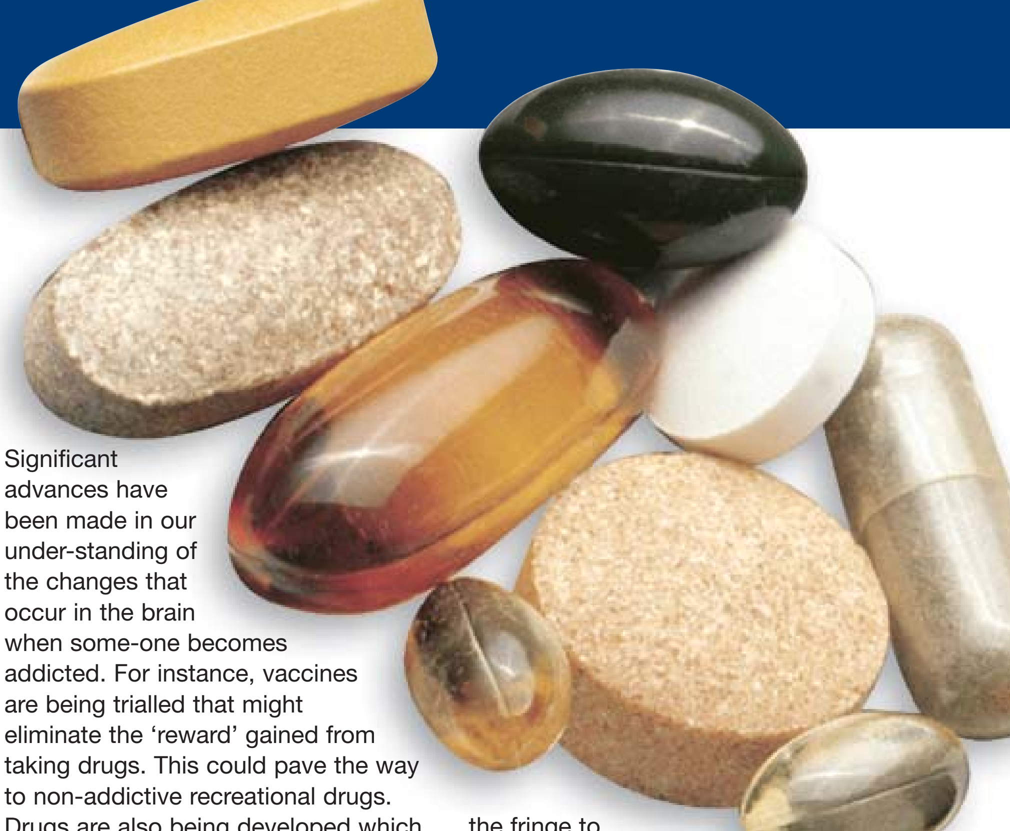
Psychoactive substances have always been an integral part of society. For millennia people have been using them in religious rituals and for centuries we have been using birch bark (which contains the active ingredient in aspirin) as a medicine.

A quick look down the aisles of a supermarket confirms how embedded in our culture and expectations these developments have become. But over the past ten years there have been significant advances which have moved us to a new under-standing of how our brains work, and how chemicals affect the brain's performance and our behaviour.

These advances are likely to be applied in three key areas to provide a better understanding of:

- mental health and the development of new treatments for it
- the effects of recreational drugs on different people and how to treat addiction
- cognition enhancers – substances that can enhance the performance of our brain in specific ways

A psychoactive substance is any substance that affects brain function through its chemical neurotrans-mitters. The term includes recreational, psychiatric, cognitive-enhancing and mood-altering drugs such as antidepressants.



The future for mental health

There is a large unmet need for medicines for mental health which is set to increase as the population ages. Treatments for mental health are therefore likely to develop in a wide range of areas, with new therapies emerging for diseases such as Alzheimer's, Parkinson's and schizophrenia, as well as stress, depression and anxiety. But given the difficulty of developing drugs that act on the brain's communications systems, other avenues are being pursued such as the use of stem cells to enhance parts of the brain that are underdeveloped or damaged, and the direct electrical stimulation of certain regions of the brain – already an effective treatment for Parkinson's disease – and which Professor Nutt and others at Bristol will soon be trialling for severe depression.

The current total economic and social costs of substance abuse in the UK are in the order of £13 billion a year

Depression is a growing problem for society. A number of treatments work by raising the levels of serotonin in the patient's brain and it now appears that serotonin may protect the brain by allowing it to repair itself through growing more nerve cell connections or even new brain cells – neurogenesis. This may open the way for new forms of drugs to treat moods. Behavioural and cognitive therapies are also increasing in importance with the growing recognition that we need to treat the individual's psychology and not just their physiology. In the future, we may see a growing use of mental exercises and this is likely to affect our education programme. There may be games for children that develop their brains to have greater capacity in later life.

Future treatments for addiction

It is undisputed that substance misuse can lead to significant harm to individuals, families and communities. It is estimated that the current total economic and social costs in the UK are in the order of £13 billion a year. The largest part of this relates to the estimated social costs associated with the victims of crime. The potential harm to health is also significant, with around 350,000 problem drug users in the UK.

Significant advances have been made in our under-standing of the changes that occur in the brain when some-one becomes addicted. For instance, vaccines are being trialled that might eliminate the 'reward' gained from taking drugs. This could pave the way to non-addictive recreational drugs. Drugs are also being developed which help people to forget experiences, so it might become possible to 'forget' an addiction. But this highlights the social issues of such advances, such as the importance of holding on to some memories so we do not make the same mistake twice. David Nutt has been involved in developing a drug that can block the memory-impairing actions of alcohol, while other scientists believe that they could produce a substance with similar effects to alcohol but with fewer harmful effects.

Future use of cognition enhancers

There is likely to be a blurring between drugs taken by someone who is ill and those that require 'mental cosmetics'. New psychoactive substances are being developed which improve performance of the healthy brain and it is likely they may be used more widely by healthy people to optimise their mental performance.

Modafinil, for example, makes the user think through issues more carefully before making decisions, while Ritalin is being used by a small number of students in an attempt to improve exam results and by business people to improve their performance in the boardroom. In a world that is increasingly stressful and competitive, the individual's use of such substances may move from the fringe to the norm, with cognition enhancers being used as routinely as coffee is today. But given that we do not allow sports people to take performance-enhancing drugs, is it fair to allow others to take cognition enhancers before an exam?

What strategic choices do we face?

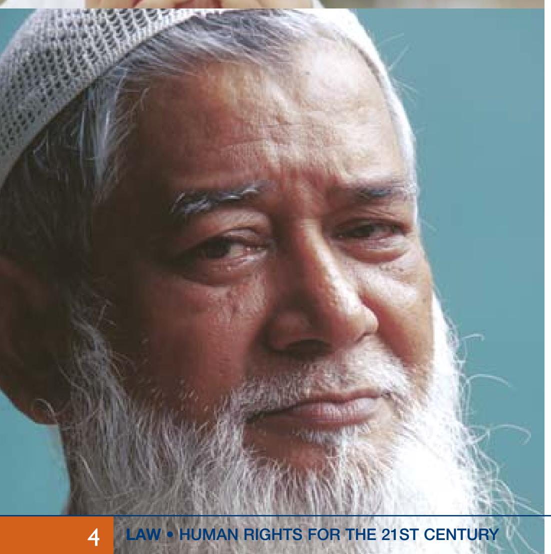
Though the effects of these changes are uncertain and some may be far in the future, we need to take action now if we are to manage the risks. We are faced with a number of difficult and sensitive choices but there are no simple decisions as each option includes advantages and disadvantages. In some areas it is not an either/or, it is more a question of finding the right balance between competing goals. The 'horizon scanning' approach taken by this report articulates Foresight's objective of providing Government and others with challenging visions of possible futures. It does not offer predictions, but it does raise issues and possibilities that policy makers and others might wish to consider. ■

We gratefully acknowledge access to the Office of Science and Technology's Foresight Report, Drug Futures 2025, *July 2005, on which much of this article is based.*

www.bristol.ac.uk/neuroscience

Human rights for the 21st century

Almost 60 years have elapsed since the Universal Declaration of Human Rights was adopted by the United Nations. Today it still remains a powerful instrument which continues to exert an enormous effect on people's lives all over the world. In the University's School of Law, human rights is a major research theme with individuals, such as Professors ***Malcolm Evans*** (left) and ***Steven Greer*** (right), advising governments at the highest level about their policies.



The Universal Declaration of Human Rights was adopted by the United Nations General Assembly 10 on December 1948, without a dissenting vote. It was drafted in the aftermath of the Holocaust, the Nuremberg war crimes trials, the Bataan Death March, the atomic bomb, and various other horrors of war. It was the first multinational declaration mentioning human rights by name, and the human rights movement has largely adopted it as a charter.

Over 95 per cent of applications are currently turned away at the door

Subsequently, the European Convention on Human Rights (ECHR), an international treaty that sets out fundamental rights for the benefit of persons within the European region, entered into force in 1953, inaugurating the first regional human rights system. People claiming to be the victim of a violation of these rights by a State Party may apply to the European Court of Human Rights (ECtHR) in Strasbourg, for redress. In 1998 the ECtHR became the first permanent human rights court in the world.

Human rights in Europe

Some 800 million people from 46 countries now fall under the jurisdiction of the ECtHR. With only one judge per member state the Court's adjudicative capacity is limited to about 700-800 cases a year. With individual applications currently running at 40,000 a year, a figure expected to rise to at least 80,000 by 2010, over 95 per cent of applications are currently turned away at the door without judgment on their merits and fewer still receive a judgment in their favour. Concerns have been expressed that the system will not live out the decade, let alone another half-century. Steven Greer, Professor of Human Rights in the University's School of Law, has been reviewing the achievements, problems and prospects of the ECtHR in a book soon to be published by Cambridge University Press, entitled *The European Convention on Human Rights: Achievements, Problems and Prospects*.

That the Court exists to enable individuals in member states to bring governments before an international court for violations of their basic human rights was not, in fact, one of the objectives which those who designed and drafted the ECHR wanted, or indeed expected, to achieve. The ECtHR was primarily intended to contribute to the prevention of another war between ➜

➜ western European states and the 'right of individual petition' only become mandatory in 1998.

Today, Greer believes, the Court's only viable role is the much more subtle one of promoting constitutional convergence in member states, and bridging greater Europe with the Europe of the EU, by providing a common 'abstract constitutional identity' for the entire continent. Cases should be selected for adjudication by the ECtHR largely on the basis of their constitutional significance and adjudicated in a much more constitutionally rigorous manner, with judgements binding on national constitutional and legal systems. Its resources need to be much more strategically targeted on those member states with the most serious structural compliance problems.

The vision of the ECtHR acting as a pan-European court of final appeal fearlessly remedying each and every individual human rights violation wherever it occurs throughout the continent is, sadly, not one it can ever hope to fulfil for sheer logistical and structural reasons.

Human rights in Africa and prevention of torture

On 14 February 2002 a momentous step forward was taken in the prevention of torture in Africa with the adoption of 'Guidelines and Measures for the Prohibition and Prevention of Torture, Cruel, Inhuman and Degrading Treatment and Punishment in Africa'. The workshop was held on Robben Island because of its historic associations. It was where Nelson Mandela was held during the apartheid years and became internationally known for its institutional brutality – thus the guidelines became known as the 'Robben Island Guidelines'.

Chairing the 26 participants involved in drafting the guidelines was Malcolm Evans, OBE, Professor of Public International Law and faculty dean. He has subsequently been involved in devising and drafting the 'Action Plan for the Implementation Guidelines'

People in the faculty are directly engaged with policy makers

and earlier this year the African Commission on human rights held its first meeting outside Africa. This was held here in Bristol and organised by Dr Rachel Murray, also at the University and also active in African Human Rights.

Importantly, Evans points out, work in this area is not just an academic pursuit. It is directly involved with international organisations; looking at the work of international bodies within other countries; going to countries to talk about the implementation of concrete recommendations and there directly engaging with policy makers, Foreign Office staff, non-governmental organisations (NGOs), and African organisations trying to oversee projects concerned with the roll-out of the guidelines in local police forces. It therefore has a direct bearing upon prevention of torture and the protection of individuals.

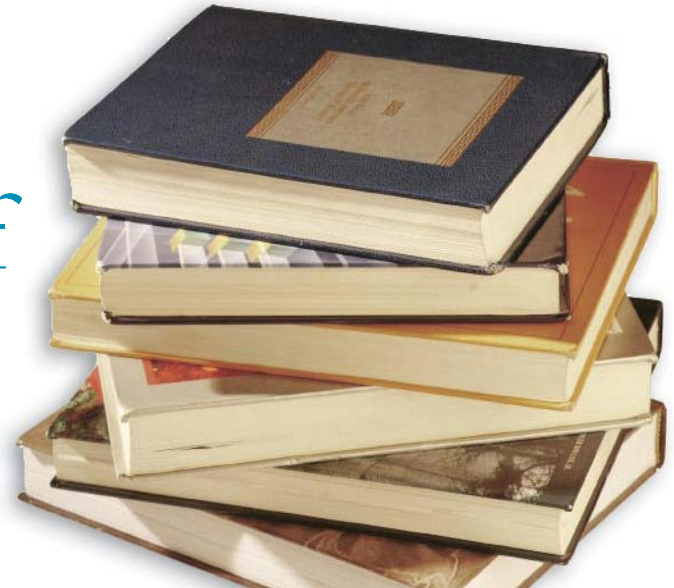
Human rights and religious freedom

Another practical area in which Evans and the School of Law are heavily engaged is the interface between religion and human rights, a subject of particular topicality at the moment. As a member of the organisation of security and co-operation in Europe's panel of expert advisers on freedom of religion matters, Evans receives frequent requests for help in practical situations. He may be asked for comment or advice on, drafts of legislation – for example, are they compatible with human rights standards? – or he may have to travel to discuss with people concerned in countries where there are problems whether it necessary to change laws, legislative structures, or procedures. Recently Dr Julian Rivers, Senior Lecturer in Law, attended a seminar in Strasbourg relating to the issue of religious symbols in general, and headscarves in particular, and Evans has attended all the round table discussions on human rights matters between the European Union and Iran.

These are the kind of issues where people in the faculty are directly engaged with policy makers in developing and influencing approaches. And it is why the work on human rights has become an important research theme within the University. ■

www.law.bristol.ac.uk

The long chain of reception



The word 'reception' has a special sense in the humanities. It is to do with our relationship with the past, its literature and culture. It is the way that works from the past have been interpreted or 'received' by those who came later – as well as the process of dialogue between the work and the present interpreter who is inevitably influenced by previous interpretations and prevailing theories. Professor *Charles Martindale*, Director of the Bristol Institute for Research in the Humanities and Arts, is probably the world's leading authority on theories of reception and the classics.

Take Shakespeare's *A Midsummer Night's Dream*. Since we know that Shakespeare read Ovid's *Metamorphoses* and that this had an influence on his play, we could say that *Dream* is a 'reception' of Ovid. But rather than just being inertly influenced by a text from the past, Shakespeare's role is as an active interpreter of Ovid's poem – he engages with it, interprets it, understands it in a certain way, and then incorporates that understanding into his own play. As a result, we may have our views of both Ovid and of ones, so there is a continuous chain stretching down from the original work to the current interpretation, which will be affected in various ways by that pre-existing chain. Sometimes you react, sometimes you say, "No, I don't agree with that way of reading Ovid". But even when you do that, you are still in the chain, you are not reacting only to the work itself.

This way of looking at the interpretation of works of the past is particularly associated with German hermeneutics and a philosopher called Hans-Georg Gadamer. The other view, that we about the 'original' meaning. Look at translation, for example. Translation puts the original work into *our* language with *our* concepts, *our* presuppositions, *our* prejudices and *our* instincts. So whichever way you look at it, there is always an act of mediation involved.

In collaboration with Professor David Hopkins from the English Department, Martindale is about to embark on a major work of reception – the *Oxford History of Classical Reception in English Literature*. To be published by Oxford University Press, this enormous project will take ten years to

It doesn't make any sense to talk about 'original' meaning

Shakespeare modified by our joint reception of the two different texts – the *Metamorphoses* of Ovid on the one hand and Shakespeare's *Dream* on the other.

So behind any interpretation of Ovid today lies a 'chain' of receptions. Right from Ovid's earliest readers people have been reacting, interpreting, responding, and producing new works based on Ovid. These affect later can know the past 'as it really was', is often called the 'positivist' view. But Gadamer argued, and Martindale agrees with him, that such positivism is a delusion – any interpretation is always a mediation between the work and the receiver.

If you look at the history of interpretations, what you find is that there are hundreds of different interpretations, so it doesn't make any sense to talk complete and involve more than 100 contributors to the five volume series. Martindale and Hopkins will be general editors of the whole enterprise, as well as editing the volume for 1660-1780. They will receive essays from the contributors and, through the editing process, make their own contribution to the long chain and its continued reception by the next generation. ■

www.bristol.ac.uk/arts/birtha

Designing your future

The Centre for Communications Research (CCR) is an internationally recognised interdisciplinary research centre. Established in 1987 by its Director, Professor *Joe McGeehan* CBE, the CCR's template for structure and operation across departmental and faculty boundaries has now been adopted around the world by many other leading research institutions.

Last year Joe McGeehan was voted sixth in the world in a list of top 10 technologists, compiled for the leading online IT magazine *silicon.com* – the voice of California's Silicon Valley. Bill Gates was second to Linus Torvalds – he designed the Linux operating system – at number one. One of the panelists said of McGeehan: "Working five to 10 years ahead of the industry, McGeehan is noted for advancements on mobile radio and speeding up the underlying transport layer for wireless networks to provide high-quality audio, video and data services. His work is really going to change how people look at mobility [in communications]."

It all started back in 1980 when McGeehan was a young academic working in the field of wireless communication. He was approached by the head of Securicor who asked him to design a new portable mobile radio for the drivers of his delivery fleet. Furthermore, the radio had to be highly competitive with other products then available. McGeehan's design was subsequently manufactured for Securicor by the Finnish firm Mobira-Oy (now Nokia) and this radio became the basis for Nokia's first mobile phone. Since then, McGeehan has pioneered many of the technologies adopted by industry for subsequent generations of mobile phones, as well as other areas of wireless communication.

Over the coming decade, evolution of the wireless internet will impact on society in ways we can hardly imagine. It will facilitate 'anytime, anywhere, anyhow, anything' communications. Imagine going online via your mobile phone as you eat your breakfast in the morning. You remain connected as you make your way to work, by car, public transport or on foot, and you are still online when you reach your desk. This requires high-performance, pervasive network coverage which, in turn, requires detailed network planning. This is especially the case in built-up areas, where the urban landscape creates significant challenges for the network planner.

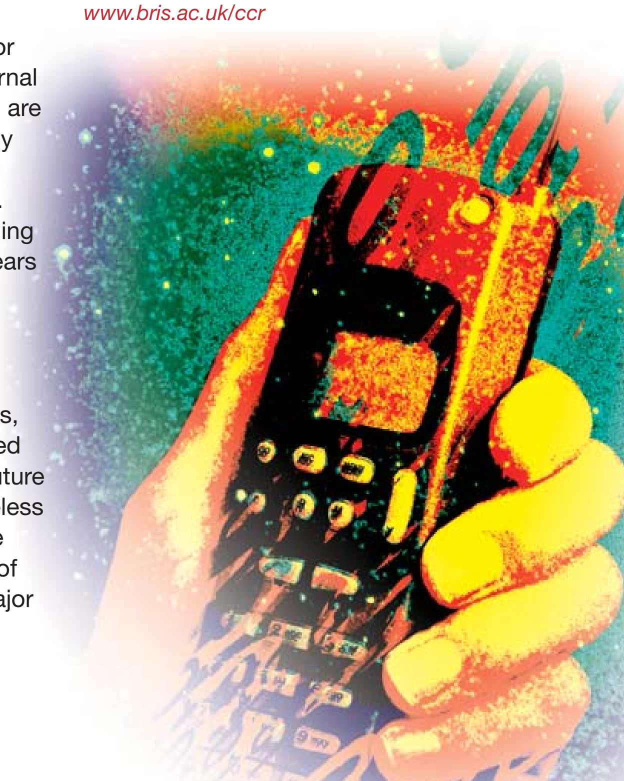
It will facilitate 'anytime, anywhere, anyhow, anything' communications

One vital approach to network planning is 'ray tracing'. By building detailed models of the landscape, ray tracing can provide comprehensive predictions of how wireless and mobile networks will perform in the field. This information is valid for single or multiple base stations, and for internal or external networks. Such models are highly complex and computationally intensive, even for moderately complex geographic environments. However, the CCR is currently leading the world in this field through its years of research into ray-tracing tools.

As a means of enhancing the efficiency of wireless links, the use of multi-element antenna arrays, or 'smart antennas', is now regarded as a key enabling technology for future wireless networks. The CCR's Wireless Group has conducted performance analysis and hardware verification of smart antennas and has been a major contributor to the adoption of this technology in numerous wireless access networks across the globe.

Often thought of as the brains behind the revolution in wireless communications, McGeehan is unusual in that he effortlessly straddles the public and private sectors. As well as being Professor of Communications Engineering and Director of the CCR at the University, he is Managing Director for Toshiba Research Europe Ltd's Telecommunications Research Laboratory. Toshiba is a vast multi-national corporation able to invest anywhere in the world. It is therefore a tribute to the region's telecoms and academic communities, and to Joe McGeehan's spirit and determination, that they chose to base their European telecommunications research centre here in Bristol. ■

www.bris.ac.uk/ccr



Exchanging keys in the Canaries

Cherry Lewis explores the unfamiliar world of quantum computation:

"When I went to see ***John Rarity***, Professor of Optical Communication Systems in the Department of Electrical and Electronic Engineering, his computer displayed a picture of a sun-set taken from one island, looking across to another, and an inset showing a map of the Canary Islands. What had all this to do with quantum computation, I wondered?"

Rarity's computer, and many others like it, represent the culmination of years of technological advancement that began with the ideas of Charles Babbage (1791-1871), early pioneer of the computer. Surprisingly, however, although computers have become more compact and considerably faster in performing their task, they are fundamentally no different from their ancestors because the task remains the same: to manipulate and interpret an encoding of binary bits into a useful computational result.

A 'bit' is a fundamental unit of information, classically represented as 0 or 1 in your computer. A file stored on your hard drive, for example, is described by a string of zeros and ones. But whereas your computer obeys the well-understood laws of classical physics, a quantum computer adheres to the laws of quantum mechanics, which differ radically from the laws of classical physics. In a quantum computer the fundamental unit of information is called a 'quantum bit' or *qubit*.

A qubit can exist not only in a state corresponding to the logical state 0 or 1 as in a classical bit, but also in states corresponding to a blend or *superposition* of these classical states. In other words, a qubit can exist as a zero, a one, or simultaneously as both 0 and 1. At Bristol, Rarity's group uses single photons (particles of light) as qubits – other groups use single electrons or single atoms. Interactions between those single quantum particles can be used to construct the fundamental 'gates' needed to build a quantum computer. Each gate operation 'entangles' two particles (qubits) and by repeating this operation one can build a multi-particle entangled state. Entanglement is a state of two or more quantum particles like photons, in which many of their physical properties are strongly correlated.

The entangled particles share information in a form which cannot be accessed in any experiment performed on either of the particles alone. This happens no matter how far apart the particles may be at the time. As the number of qubits increases, the number of superpositions increases dramatically, providing a vast number of testable solutions. Using suitable gate arrangements (ie a quantum computer), the correct solutions can then be extracted from the tests.

Richard Feynman was among the first to show how a quantum system could be used to do computations and eventually it was realised that a quantum computer would have capabilities far beyond those of any traditional computer. In particular, it could be used to factorise huge numbers extremely rapidly. It could do in seconds what it would take a classical computer many years to complete. With this breakthrough, quantum computing became transformed from an academic curiosity into something of world interest. But why? Other than mathematicians, who would be interested in very big numbers? And what has all this got to do with a map of the Canaries? ➜

Other than mathematicians, who would be interested in very big numbers?

Digital mock-up of the University's new Nanoscience Centre, due to be completed 2006.

➜ "What we were trying to achieve on the Canaries was prove that you can exchange keys over 150 kilometres, which will be a world record," Rarity explained. "The previous world record, held by our group, stands at 23 kilometres in free space (as opposed to down a fibre). We were doing a feasibility study trying to prove that in principle a ground to satellite key exchange is possible. We were doing it in the Canaries because Tenerife is home to the European Space Agency's Optical Ground Station where they do space-to-ground optical communications experiments."

"Exchange keys?" I ask. "What kind of keys?" "If a financial institution, for example, wants to send a secret to someone else, they could lock the secret in a 'box' before sending it". replied Rarity. "If the person receiving the box has the right key he can open it and read the secret. With digital communications the key is a string of 'bits' with which the secret is encoded and an identical bit-string (key) is needed to decode the message. To distribute keys we could send couriers on motorbikes with discs of information (keys) in briefcases handcuffed to their wrists. However, this method requires that we trust the courier. In our work we distribute the keys securely, using quantum means. We do this by using a very simple quantum computer which generates the same random bit-string in two places at once. Which brings us back to entanglement."

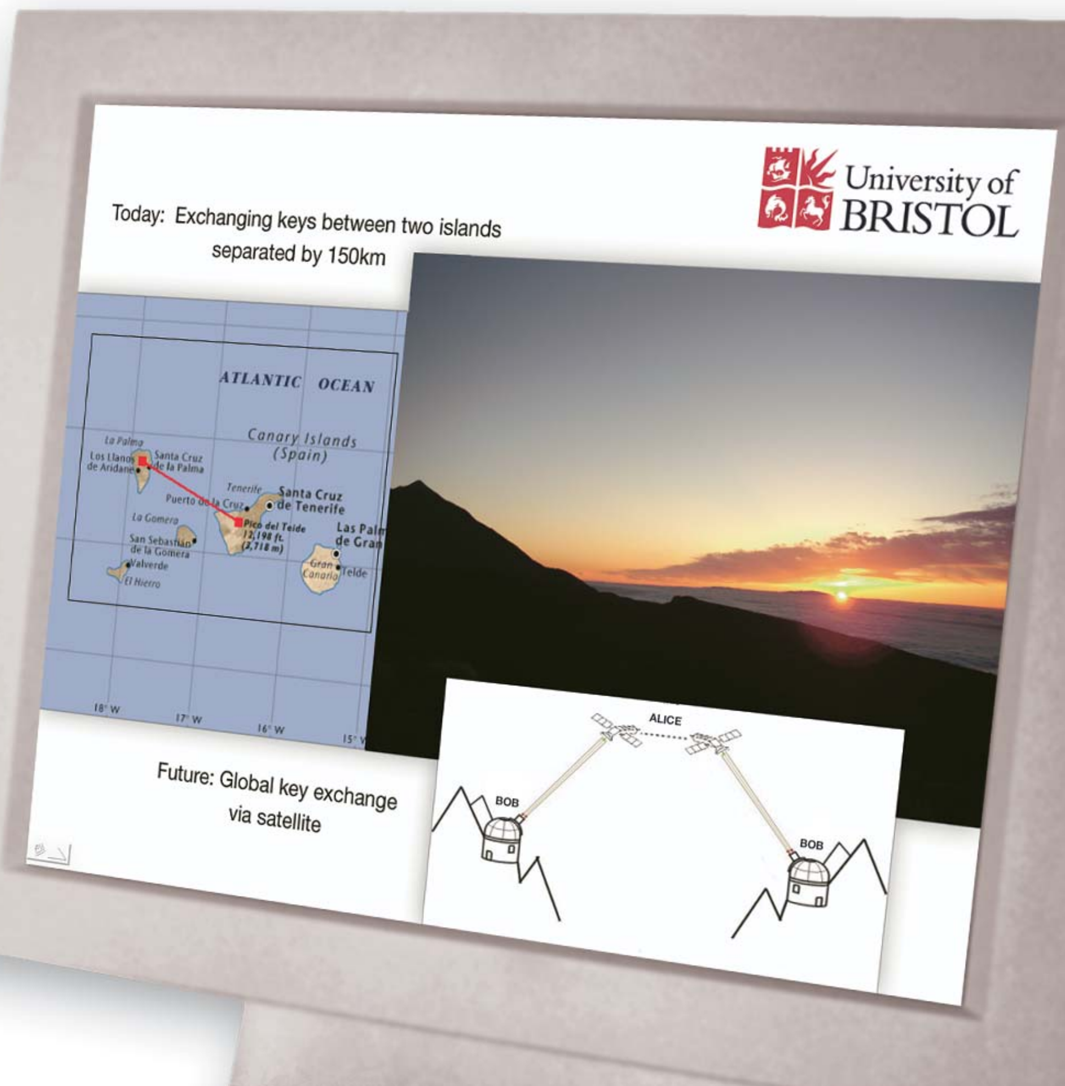
Entanglement is crucial for long-distance quantum key distribution, which uses entangled pairs of photons to encode the qubits. It relies on the fact that the information defining the key only 'comes into being' after measurements performed by 'Alice', the sender, and 'Bob', the receiver. The photons are distributed so that Alice and Bob each end up with one photon from each entangled pair and consequently each has a copy of the key. In Rarity's experiment in the Canaries, Alice and Bob are in fact two observatories located on two different islands, separated by 150 kilometres. The success of this experiment will demonstrate that key exchange to a satellite could be possible in future – their ultimate objective being to create a global key distribution system.

Of course, Rarity cannot send a whole message yet. All he is trying to do at this stage is establish an identical bit-string between the sender and the receiver over a relatively long distance. But the long-term implications for this technology are enormous.

Other work at Bristol is focused on low-cost, secure, key-exchange systems built from off-the-shelf components for consumer applications. For example, it could protect every transaction made at an ATM, and be a candidate to replace chip and pin – which is one of the reasons why the University is heavily investing in quantum information and nanoscience.

A brand-new Nanoscience and Quantum Information Centre is due to open in spring 2007. The basement will house 12 exceptionally 'low-noise' laboratories – acoustically, vibrationally, electrically and electro-magnetically – and will probably be the quietest experimental space in the world. The architectural design of the building also incorporates features and spaces to stimulate interdisciplinary interactions and innovation, from which new research directions will emerge. A number of senior appointments have recently been made in the areas of bionano-technology, nanobiophysics, chemistry and biochemistry and many world leaders in those fields are already queuing up to spend time in this novel, exciting space that will be buzzing with excitement about the unknown and unexpected. ■

www.bris.ac.uk/eeng/research/oph



The exabyte challenge

Our approach to dealing with data has essentially remained unchanged for the past 25 centuries: we categorise it, divide it into small chunks, then build indexes and catalogues so we can find what we want. But with terabytes of data becoming available every second, this is no longer a viable strategy. *Peter Flach*, Professor of Artificial Intelligence in the Department of Computer Science, argues that to combat this growing problem the 21st century needs highly innovative techniques for data awareness.

One exabyte (10^{18} bytes) is a rough – and probably conservative – estimate of the size of everything ever written, composed, filmed, painted, or in any other way 'recorded' by humans. By 2010, virtually all of this vast amount of data will be on line – and most of us will be able to access it from our homes, our mobiles, and other kinds of wearable devices. This constitutes a major change to our lives that is already raising new issues about how to collect and process the data and how to use it in research, as well as how it will impact on society.

Take photos from a digital camera, for example. There are billions of digital cameras around the world these days. Each high-resolution photo is a couple of megabytes and most people have hundreds, if not thousands, sitting on their computer – the digital equivalent of shoeboxes full of paper prints. If you don't annotate and categorise them immediately, it will never happen and you are unlikely to ever look at those pictures again. But what if the computer could find a particular photo for you, without you having to categorise them? Will computers ever adequately respond to queries such as 'find me that picture of Lisa and me on Christmas eve'?

The emergence of the World Wide Web in the past decade demonstrates an alternative to the divide-and-conquer approach of categorisation and indexing. For example, Google's search engine leaves the data in one enormous 'heap' and provides query-driven dynamic views on the data. But this syntax-based approach is already showing its limits, particularly when it comes to integrating data from diverse sources and formats (images, sound, text), incorporating semantics of the data and dealing with complex, interlinked data. Flach believes that this new complexity requires a new way of thinking and a new way of dealing with the data. Computing devices with 'data awareness' are needed – devices that make sense of the exabytes of data at our fingertips.

Will computers ever adequately respond to queries such as 'find that picture of Lisa and me on Christmas eve'?

While semantics, data fusion and complex data have all been studied widely in computer science and related disciplines, the exabyte challenge is about taking these techniques to the next level, in order to stop us from 'drowning in data while starving for knowledge'. A key factor here is interdisciplinarity. A deep understanding of the nature of scientific data and the scientific aims of the investigation, in particular, are crucial – hence the need to combine research and resources in a University-wide research theme. Today, most universities are highly fragmented environments that fail to exploit the considerable synergy that could result from combining diverse research areas. The Exabyte Informatics research theme, which includes research groups from each of the University's six faculties, provides a unique opportunity to truly exploit this synergy. ➜

➜ Flach and his group have already been thinking about creating a scientist's desktop – an environment something like Microsoft Office, but for scientists (and without the patronising paper clip!). Given a free hand, what would he want it to be like? Well, it could be something that proactively searches on the web for things a particular type of scientist might be interested in. It would effectively look over your shoulder while you are working and build up an idea of your profile – what kind of scientist you are, what kind of information you are seeking – and try to pre-empt your requirements. A simple example would be downloading an academic paper, and the computer could then start searching for all the papers referenced in it. You might not ever look at them, or even download them onto your computer – you just need to know that they are out there and available.

But such data mining brings its own problems. While the introduction of the web has encouraged scientists towards more openness and sharing, in fields such as bioinformatics their data may be their scientific capital – not everyone is willing to share. And that raises new issues of how you might be able to link these databases together and still maintain the benefits of that, while preserving the privacy of the database. These are complicated issues that would require input from the University's Centre for Information Technology and Law. And then there is the impact on society and education. How do we make use of all these data in teaching? The web itself does not determine how we are going to use it. It is just a piece of technology, like a blackboard or an overhead projector, and how we use it determines how useful it is. But it is the educationalists who must ask what they are trying to achieve with the web and to understand what can and cannot be done. It is not the job of the computer scientist to tell them how it should be used.

Initially the way this revolution will actually happen is from the bottom up via a number of pilot projects that will start increasing the awareness of people of what the issues are. There is a need for a co-ordinated effort – people talking to each other and determining the best way to achieve these things. Flach thinks that although things have moved at an incredible rate since the '90s, we are still in a transitional period of innovation. But we cannot sustain this rate of change. In 50 to 100 years' time the situation will be much more stable because the technologies will have proved themselves. Getting there, by making optimal use of the enormous potential of computing technology, will be as challenging as it will be rewarding. ■

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Information object	How many bytes?
A binary decision	1 bit
A single text character	1 byte
A typewritten page	2 kilobytes (KB)
The complete works of Shakespeare	5 megabytes (MB)
A library floor of academic journals	100 gigabytes (GB)
The print collections of the US Library of Congress	10 terabytes (TB)
All printed material in the world	200 petabytes (PB)
All words ever spoken by human beings	5 exabytes (EB)

The building blocks of life

The vast majority of life processes result from the binding of a protein molecule to another molecule. Understanding these interactions is the key to life itself. Professor *Leo Brady* runs the Biomolecular Structures Group in the Department of Biochemistry where they determine the structures of such molecules, which provide invaluable insights for the treatment of diseases.

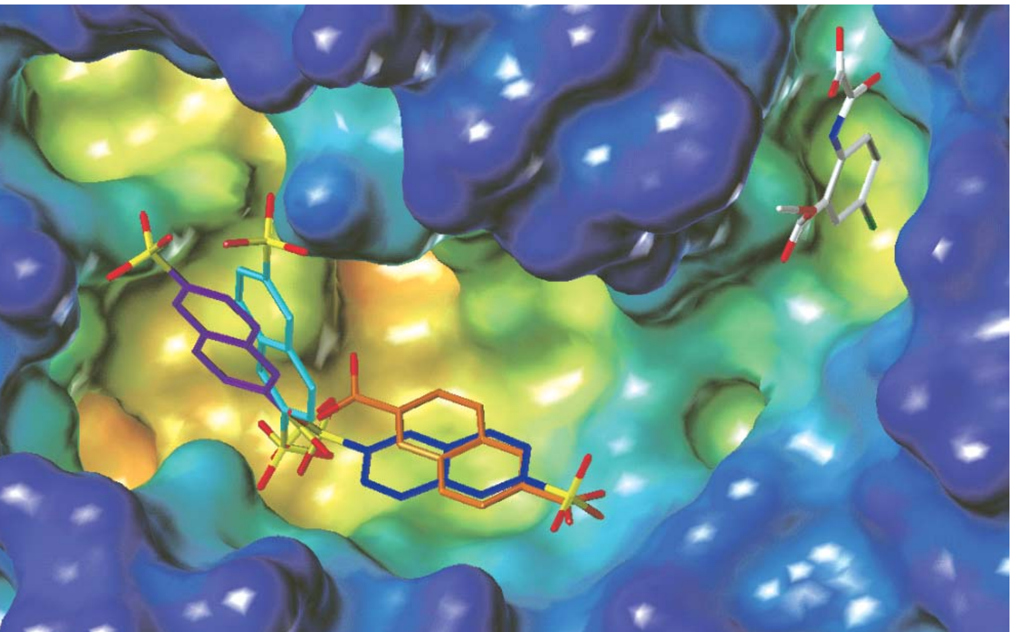
The modern field of structural biology originated in the 1940s with Linus Pauling (1901-1994), the only person ever to receive two unshared Nobel Prizes – for Chemistry in 1954 and for Peace in 1962. Often considered the 'founding father' of molecular biology, Pauling pioneered the structure-based approach to the study of biological systems that has formed the basis for most subsequent advances in understanding the molecular mechanisms of biological systems.

> It is only in the past decade that this rather academic pursuit has reached a level of understanding that can be exploited

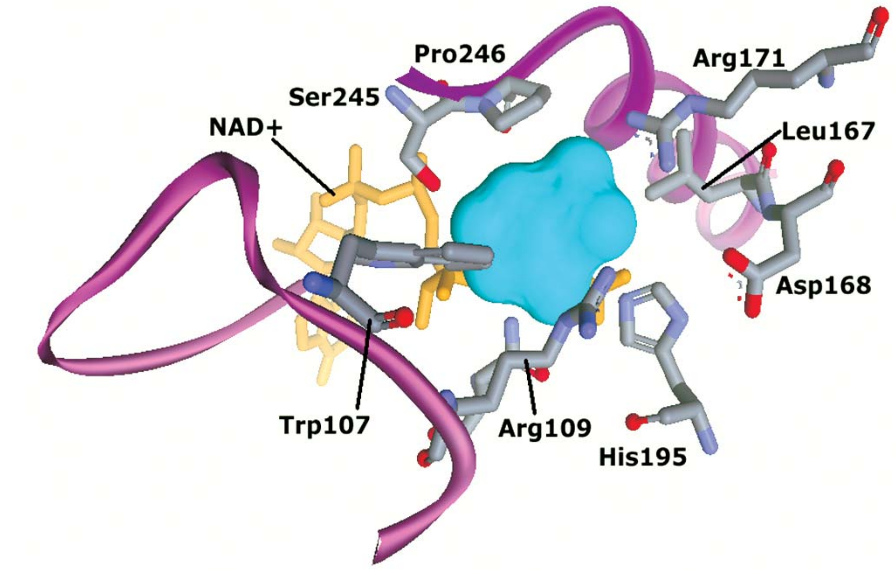
The basic premise underlying structural biology is that all life processes can be described by a variety of molecular processes. Therefore, in order to understand either a disease or normal functions of the body, it is necessary to first break down those functions into the actions of individual protein molecules, and then to determine the 'shape' of each of these proteins.

Proteins are the principal constituents of all cells. They serve as enzymes, structural elements, hormones, etc, and are involved in oxygen transport, muscle contraction, electron transport and various other activities throughout the body. Twenty different amino acids are commonly found in proteins and each protein has a unique, genetically defined sequence of amino acids which determines that protein's specific shape and function. But because a protein molecule is quite large, about 90 per cent of its function is defined by its shape, so understanding function means having a clear picture of the protein's shape. Through the study of protein structure, primarily using protein X-ray crystallography to determine its three-dimensional shape, Brady's group aims to probe crucial biomolecular interactions, central to a variety of diseases, with a view to using this information to accelerate the development of new drugs.

In normal biological function a protein will bind to another molecule, designed to fit into a specific location on the → protein's surface, rather like a key fitting into a lock. If the second, much smaller, molecule (the key) is the right shape to fit into the location (the lock), they will lock together and that will lead to a chemical change – a signal. That passes information on to the next molecule, and the next one, and so on until eventually your arm moves, for example. But what if you have a headache and wanted to stop the pain? In this instance the two molecules lock together but this leads to a pain signal which sends you off to the medicine cabinet for some aspirin. Since drugs are simply small molecules, they also bind to, or interact with, the larger proteins. In this case the aspirin molecule blocks the location filled by the 'pain' molecule so it cannot fit back in and cause further pain – headache goes away.



A series of designed, potential anti-malarial drugs shown bound within their target cavities on the surface of a malaria parasite protein.



A potential anti-malarial drug, shown in blue, nestled in to a cavity on the surface of a malaria parasite protein.

Until recently, when a new drug was needed to combat a particular disease, drug companies took a rather hit-and-miss approach to identifying which of the many millions of chemical combinations available might be appropriate as a drug. Put simply, they would culture the pathogen, grow it and then throw each chemical in, one at a time, and see which one killed it. Nowadays things are more sophisticated. Take Alzheimer's Disease that Brady's group work on – in collaboration with David Dawbarn's group in the Henry Wellcome Laboratories for Integrative Neuroscience and Endocrinology. The first question they ask is "What parts of the body go wrong in Alzheimer's Disease?" They then focus on the molecules that govern those functions. But before they can understand what is going wrong with those molecules they first need to understand what their normal state is – their normal shape.

> The first question they ask is 'What parts of the body go wrong?'

Once the structure has been determined, they identify which parts of its shape are important to its action. These locations then become the target (the lock) for suitable drugs. Using a computer they computationally 'test' which of the millions of drugs available might fit the target. The computer ranks them by how well they fit and identifies the ones most likely to work. These can then be chemically tested to reduce the numbers even further. At that point a pharmaceutical company may step in and, based on the information provided by such groups, 'design' a drug that will either keep the molecule in its normal state, or replicate the function that is failing. It is obviously a much more complex process than it sounds, but Brady believes the corner has been turned in the past ten years and that all new drugs developed in five or ten years' time will have some element of this design process.

Another disease members of Brady's group study is malaria. Malaria is caused by a tiny parasite that infects humans bitten by a mosquito carrying the parasite. In this instance they examine the components that make up the normal life-cycle of the parasite. But because this parasite only infects humans, it makes it complicated to develop drugs because they cannot be tested on animals. There are equivalent parasites that infect rats, for example, but while they are very similar to the one that infects humans, they are not quite the same. Thus there is always the dilemma that the drug might work very well against the parasite in rats but not in humans. So when the drug company trials them in humans, it may not have quite the right effect and might need to be modified in some way.

Something similar happened to Brady's group a few years ago when a new type of drug it had designed and developed in collaboration with GlaxoSmithKlein had to be shelved. But fortunately another compound picked up in their studies turned out to act against a completely different target to the one they were targeting, and has proved extremely effective in killing the parasite. This compound is now entering clinical trials as a new anti-malarial drug. Developing a new drug takes a very long time, 15 years on average, and is extremely expensive – one drug can cost billions of dollars to develop – but it is good to know there is still room for an element of serendipity now and then. ■

www.bris.ac.uk/biochemistry


Delivering public services

Governments around the world are searching for policies to boost the efficiency of the public sector. Professor *Simon Burgess* (Director) and *Carol Propper*, Professor of the Economics of Public Policy, illustrate how the University's Centre for Market and Public Organisation (CMPO) contributes to that endeavour.

The CMPO combines expertise in economics, geography and law. Its objective is to study the intersection between the public and private sectors of the economy, and in particular to understand the right way to organise and deliver public services. Much of its work seeks to answer key social science questions using large data sets to test predictions from theoretical models of behaviour. Examples of such questions are:

- What is the impact of school choice on pupil segregation?
- Does competition in healthcare lead to poorer outcomes?
- Do people have the potential for choice in the NHS?
- Are schools in the UK more ethnically segregated than our communities?
- Does performance pay increase public sector productivity?

As well as using traditional survey data, members of the Centre are exploiting large-scale data sets, some of which are collected for administrative purposes rather than for research. These include:

- the National Pupil Database, which contains information on all children in English state schools and includes information on their scores in national tests, where they live, and the resources of the household they live in;
- data collected by the NHS on every hospital admission in England and Wales.

Centre members also make extensive use of the Bristol-based 'Children of the 90s' study (or Avon Longitudinal Study of Parents and Children – ALSPAC).

The CMPO's aims are to produce scientific advances and to contribute 'hard' data to the public debate on social issues, and thereby inform policy-making.

Does competition in healthcare lead to poorer outcomes?

The introduction of competition and markets into public services has been a recurrent theme in recent reforms initiated by governments. However, whilst the rhetoric has been strong, evidence of the effectiveness of such reforms is somewhat weaker. Competition between suppliers of healthcare in the UK was introduced in 1991 on the basis of relatively little evidence about the impact of such competition on either costs or quality. Prior to that, publicly funded, hospital-based healthcare in the UK was supplied by hospitals that received funding directly from central Government, based on their local populations. In 1991 the Conservative administration introduced competition on the supply side of the healthcare market by creating a set of buyers, funded by central government, who were free to purchase healthcare ➜

➜ for their populations from both public and private sector suppliers.

Public sector suppliers were therefore set to compete both with each other and the private sector, for contracts from these centrally funded public buyers. Such competition was actively promoted up to the mid-1990s, and then somewhat downplayed. In 1997 the incoming Labour administration formally introduced policy change, stressing the role of co-operation over competition, though the separation between buyer and seller of healthcare remained – and remains currently.

Inevitably, some sellers of healthcare are located in markets which are inherently more competitive than others, due to them having a sufficient numbers of suppliers to be competitive. Thus the identification of the impact of competition is difficult, as location is intertwined with competitiveness. Nevertheless, it was possible for researchers at the CMPO to identify the impact of competition by comparing the difference in quality between those hospitals for which competition was possible and those for which it was not, between years when competition was actively promoted and those when it was not. 'Quality' was measured in terms of death rates from emergency admissions due to heart attack, within 30 days of admission to hospital.

The results showed that hospitals located in more competitive areas had higher death rates during the first part of the 1990s, but that those rates declined somewhat from 1996 onwards. The startling conclusion was that the cumulative impact of competition on death rates was estimated to more or less negate the fall in death rates due to technological innovation, experienced by the whole sector during the 'competitive' period.

Incentives in the public sector: evidence from a government agency

The Government in Britain employs a lot of people – about 3.5 million. The productivity of these workers is therefore a major issue for the economy. Performance-related pay is one way of focusing attention on the Government's priorities, as well as raising effort, but there is a lack of evidence about the impact of performance pay in the public sector. To this end, pilot incentive schemes were introduced in a few government agencies following a report for the Public Services Productivity Panel in 2000. Researchers in the CMPO are working on a quantitative evaluation of these schemes in Jobcentre Plus, Customs and Excise, and the Child Support Agency. Some of this research is still on going, but results from the first of these make interesting reading.

> Hospitals located in more competitive areas had higher death rates during the first part of the 1990s

Jobcentre Plus is one of the main government agencies dealing with the public; its role is to place the unemployed in jobs and administer benefits. The incentive scheme in Jobcentre Plus was based on teams, rather than individuals, and focused on five different targets that were measured with varying degrees of precision. Data from the agency's performance management system and personnel records, plus data on each Jobcentre Office's local labour market were used to allow analysis of three issues, the two main ones being:

- whether performance pay matters to public service workers;
- what the team-based incentive scheme implies.

The results show that the use of performance pay did have a significant effect on the prime target – job placements – but that this response differed between offices and districts. A substantial positive effect was found in small teams, but a negative response in large teams. One of the central concerns was the potential for a 'free ride', where some team members work less hard because the rewards for effort are spread throughout the team, although this can be counter-acted by informal peer pressure from fellow workers.

There are some obvious conclusions: team size needs to be small and preferably not dispersed over many sites, and the connection between effort and output needs to be as clear and as well measured as possible to avoid free-riding. The CMPO's results indicate that the use of incentive pay as a way of inducing greater output would be much more cost-effective than a general pay rise, given the right team size. ■

The CMPO is jointly funded by the Economic and Social Research Council and the Leverhulme Trust.

www.bristol.ac.uk/Depts/CMPO

A burning issue

In 1980 scientists discovered that the amount of carbon emitted into the atmosphere from the burning of biomass – rainforests, stubble fields and any other vegetation – was about the same as the amount of carbon emitted by burning fossil fuels. But until recently the emissions from burning biomass have not been included in models that analyse the impact of climate change. Dr ***Kirsten Thonicke*** in the School of Geographical Sciences is exploring this issue.

The world's climate varies naturally through time. Historical records show that the Thames froze over most years in the 16th and 17th centuries, while geological records suggest that there have been times when the Earth was ice-free. One factor controlling this natural variation in climate is the amount of greenhouse gases, like carbon dioxide and methane, in the atmosphere. But the climate is a highly complicated system, which means that computer models used to simulate it will always be a simplification of the 'real' world. The most sophisticated climate models available are built on our understanding of the physics controlling the circulation of the atmosphere and ocean, and how plants respond to these conditions.

These models are used to simulate future climate scenarios but they can also shed light on the past if information about prevailing climatic conditions is available. If the model simulates known conditions accurately, we can feel more confident that the model is producing robust predictions. Thonicke's recent work has focused on understanding the vegetation conditions that existed about 21,000 years ago when the ice covering the globe was at its maximum – the Last Glacial Maximum (LGM).

Using information from ice cores and from charcoal found in sediments or peat that resulted from the burning of biomass, reconstructions have shown that during the LGM temperatures were cooler, conditions were quite dry, and atmospheric carbon dioxide concentrations were lower than today. With a large ice sheet in the Northern Hemisphere, sea levels dropped and more land was exposed to become colonised by plants. This led to the development of different atmospheric circulation and climate patterns which forced a southward shift in vegetation zones, such as the boreal forest. However, lower carbon dioxide levels resulted in less woody vegetation ➜

> The climate is a highly complicated system. Computer models used to simulate it will always be a simplification of the 'real' world

➜ because it was harder for plants to photosynthesise. Consequently grasses expanded, increasing the frequency of fires. Overall, global emissions from burning biomass were slightly reduced because the increase in emissions in the tropics was more than compensated for by a decrease in the Northern Hemisphere, but the full implications of Thonicke's findings are still unknown and need further investigation. Once she has all the data they will be fed into climate simulation models to help refine predictions for future climate change.

BRIDGE – The Bristol Research Initiative for the Dynamic Global Environment – will use the improved understanding of these complex interactions provided by Thonicke and other members of the team to help predict future changes more accurately, and to assess their impact on all aspects of human society. BRIDGE will then make this information available to the Intergovernmental Panel on Climate Change, which ultimately feeds into governments' policy considerations. ■

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