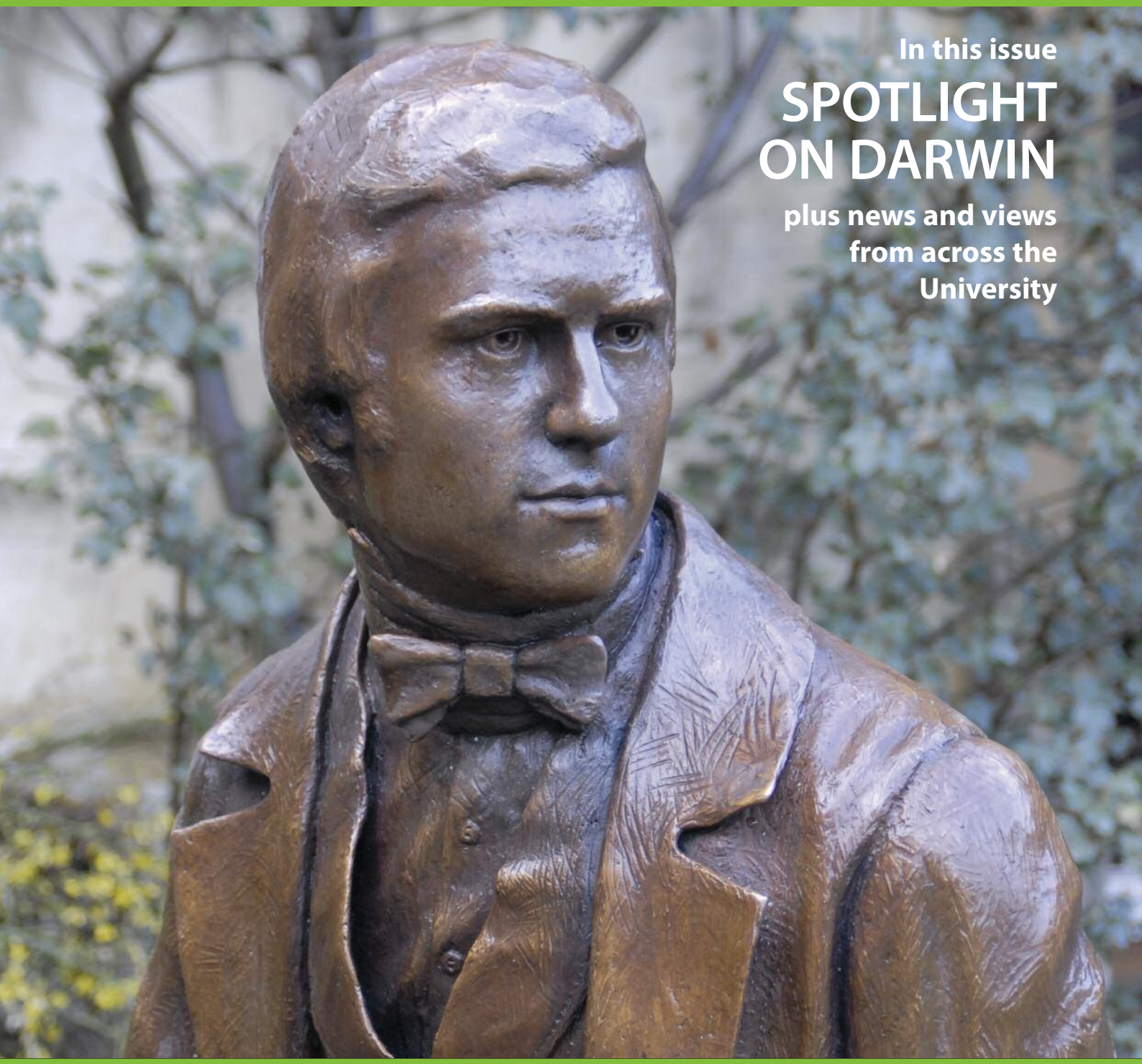
RESEARCH HORIZONS



In this issue

SPOTLIGHT ON DARWIN

plus news and views from across the University

UNIVERSITY OF CAMBRIDGE
800 YEARS
1209 ~ 2009

University of Cambridge research magazine
www.research-horizons.cam.ac.uk

Issue 9 | Summer 2009

Welcome to the summer issue of Research Horizons, in which we join the celebrations* of Charles Darwin's birth 200 years ago and the publication of his work *On the Origin of Species* 150 years ago.

Cambridge is home to a treasure-trove of Darwin's artefacts and documents. The world's largest collections of his plant, animal and geological specimens, his correspondence and manuscripts, notes and experiment books can be found in our libraries and museums. As a result, the University has become a focal point for research on the pioneering Victorian naturalist. His theories of evolution, natural selection and the origin of species lie at the heart of many research areas today – whether it's the pattern of butterfly wings, biological complexity, human origins, viral evolution or optimising engineering design. This issue brings you a flavour of this research at Cambridge: the remarkable stories surrounding Darwin's artefacts, and the new dimension Darwin's theories have brought to understanding the world we live in.

Research Horizons has its own new dimension this issue in the shape of knowledge transfer (KT). At the core of this catch-all term is the mutually beneficial exchange of knowledge between academia, business and the public sector. A great many examples of KT activities happen across the University and we'll be covering these in subsequent issues; we set the scene this time with an article that draws together the different forms KT can take, and how these are supported in Cambridge.

The life-sized bronze statue featured on our front cover was unveiled at Christ's College on the bicentenary of Darwin's birth by Chancellor of the University HRH Prince Philip, Duke of Edinburgh. Sculpted by Anthony Smith, who (like Darwin) was a student at Christ's, the statue captures Darwin, aged 22, in the final year of his undergraduate study in Cambridge, six months before embarking on the HMS *Beagle* voyage that set him on the path to the theory of evolution.

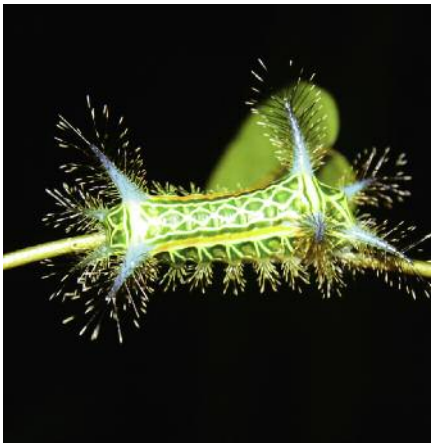
Louise Walsh

Dr Louise Walsh, Editor
research.horizons@rsd.cam.ac.uk

*See page 35 for the Darwin 2009 Festival and other Darwin-related events.

THE SYNDICS OF CAMBRIDGE UNIVERSITY LIBRARY

Mr Darwin's postbag



TROPICAL BIOLOGY ASSOCIATION

Cambridge Conservation Initiative

Contents

Cover photograph of Christ's College's bronze sculpture of Charles Darwin, created by Anthony Smith (Photographer: Anthony Smith).
Edited by Louise Walsh.
Designed by Cambridge Design Studio (www.cambridgedesignstudio.org).
Printed by Falcon Printing Services Ltd (www.falcon-printing.co.uk).

Supercharged rice: the answer to famine?

An ambitious project that aims to increase rice yields could provide the solution to future food shortages.

RAYMOND PANALIGAN/INTERNATIONAL RICE RESEARCH INSTITUTE

A worldwide consortium of experts that includes Dr Julian Hibberd in Cambridge University's Department of Plant Sciences has been brought together to re-engineer rice in efforts to avoid future shortages of a cereal consumed by about half of the world's population. This major scientific endeavour is under the leadership of the International Rice Research Institute in the Philippines, and is funded by an $11 million grant from the Bill & Melinda Gates Foundation.

'About a billion people worldwide currently live on less than a dollar a day, and 850 million live in hunger,' explained Dr Hibberd. 'By 2050, the demands of increasing population growth and urbanisation are predicted to result in mass malnutrition. One way to alleviate this problem is to develop higher-yielding rice.'

In an innovative approach, the C_4 Rice Consortium plans to reconfigure the photosynthetic pathway used by rice. Some plants are capable of converting the energy from sunlight into chemical energy more efficiently than others. This mechanism, known as C_4 photosynthesis because the carbon is fixed into four-carbon sugars rather than the usual three-carbon compound, can produce higher yields. The goal of the Consortium is to convert rice from a C_3 to a C_4 pathway.

Cambridge's contribution is to unpick and rebuild the C_4 apparatus at the molecular level. Dozens of genes are known to be involved, and alterations will be required in the biochemistry of photosynthesis, leaf anatomy and cell biology. The collective expertise of the Consortium will be required to construct and test the prototypes of a C_4 rice plant. If the basic science is successful, the first varieties will be available 10–15 years later.

'There is biological precedent for changing from a C_3 to a C_4 pathway in plants, since it's known to have evolved independently many times,' said Dr Hibberd. 'The challenge is how to repeat the process in rice in the necessary time frame to avoid potential food shortages in the future.'

For more information, please contact Dr Julian Hibberd (julian.hibberd@plantsci.cam.ac.uk). Dr Hibberd was recently identified by *Nature* magazine as one of five 'crop researchers who could change the world'.

Cambridge confirmed as global leader in health science

A partnership that includes the University and its three principal NHS Trust Partners has been named a top-flight Academic Health Science Centre.

The UK's Department of Health has designated Cambridge University Health Partners as one of five Academic Health Science Centres (AHSCs) from among the leading university medical centres in the country. AHSC status recognises partnerships between world-class universities and leading NHS organisations that have the potential to compete globally and to speed up the process of taking research breakthroughs into NHS patient care.

The organisations that make up Cambridge University Health Partners are the University of Cambridge, Cambridge University Hospitals NHS Foundation Trust, Cambridgeshire and Peterborough NHS Foundation Trust, and Papworth Hospital NHS Foundation Trust.

In forming a formal alliance, the four organisations will be brought closer together in pursuit of outstanding excellence in clinical care, clinical education and health research. The partnership will also work to accelerate innovation and generate wider economic and social benefits in the Greater Cambridge area as well as nationally.

Cambridge University Health Partners will be managed by a board that includes representatives of all four organisations; Professor Patrick Sissons, the Head of the School of Clinical Medicine and Regius Professor of Physic, will be Director of the AHSC. 'I am delighted that we have been judged worthy of this designation by a very distinguished panel of our international peers and by the Department of Health,' said Professor Sissons. 'This designation is an important recognition of the excellence of all four of our organisations and the great value we can bring collectively to research, education and patient care.'

Equipping nanoscientists of the future

Cambridge's new Doctoral Training Centre (DTC) in NanoScience will train a new generation of nanoscience entrepreneurs.

In a matter of months, the first cohort of 10 students will begin their four-year training in nanotechniques, innovation and business practice. In total, over 50 PhD students during the next five years will be trained in the skills and experience needed to become nanoscience entrepreneurs, thanks to a new Doctoral Training Centre in Cambridge funded by £6.8 million from the Engineering and Physical Sciences Research Council (EPSRC).

Directed by Professor Jeremy Baumberg with co-director Professor Mark Blamire, the DTC draws together a team from the Departments of Physics, Materials Science, Engineering and Chemistry. The training includes a first year of taught courses, rotating around the four departments, followed by an interdisciplinary PhD placement in one of the nanoscience research groups around the University. An important element of the programme is exposure to innovation and business courses through the University's Judge Business School.

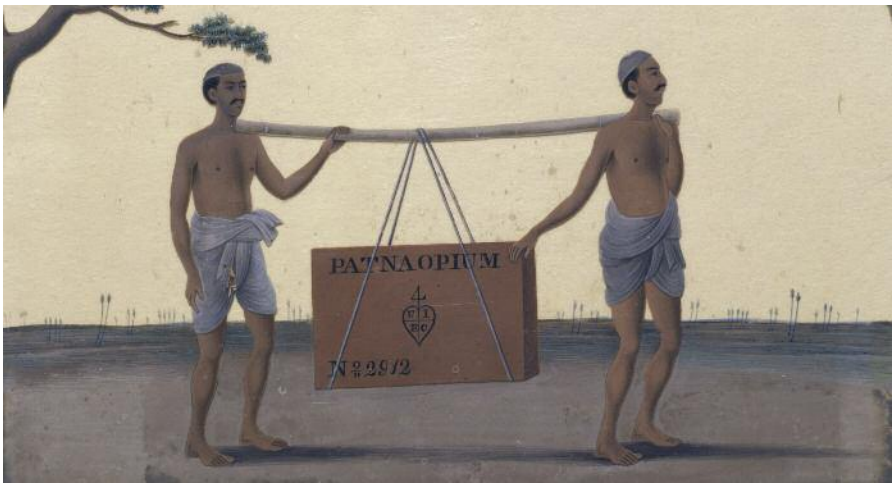
'This is a wonderful investment in young researchers, complementing the strong nano-fabrication infrastructure and world-class interdisciplinary groups across the University of Cambridge,' commented Professor Baumberg. 'The DTC will provide postgraduates with a broader experience than currently possible in either graduate research or technological innovation and will help them to forge lasting links with industry.'

The DTC is part of a £250 million initiative to create 44 training centres across the UK and train over 2000 PhD students. Minister of State for Science and Innovation, Lord Drayson, explained the importance of this move: 'Britain faces many challenges in the 21st century and needs scientists and engineers with the right skills to find answers to these challenges, build a strong economy and keep us globally competitive. EPSRC's Doctoral Training Centres will provide a new wave of engineers and scientists to do the job.'

For more information, please contact Professor Jeremy Baumberg (ajc267@cam.ac.uk) or visit http://np.phy.cam.ac.uk/NanoDTC1.htm

A history of drink and drugs

A large interdisciplinary network is aiming to shed light on the practices, rituals and attitudes surrounding intoxication.



©VICTORIA AND ALBERT MUSEUM, LONDON

Painting by Shiva Lal, commissioned by the East India Company in the 1850s, showing the transport of opium

Dr Phil Withington from the Faculty of History has been funded by the Economic and Social Research Council (ESRC) to explore the historical and cultural perspectives of intoxication and intoxicants. 'Intoxication is a subject that attracts significant contemporary public attention – whether it's debates over licensing and 'binge drinking', or the categorisation and policing of addictive substances,' said Dr Withington. 'Because the problem of intoxication is trans-historical and trans-cultural, we can arrive at a better appreciation of this preoccupation through historical and anthropological comparison.'

One strand of his research has been the formation of an interdisciplinary network to consider questions relating to the consumption of intoxicants of all kinds. Currently numbering over 50 individuals from 27 different institutions, the network includes Cambridge researchers Dr Victoria Harris, Dr Sarah Howard and Dr Craig Muldrew in the Faculty of History, and Dr Rebecca Flemming in the Faculty of Classics. Five members of the network, including Dr Withington, were recently asked to submit reports to a Parliamentary Health Committee considering the problem of alcohol.

Dr Withington convenes the network with Dr Angela McShane at the Victoria and Albert Museum (V&A). Network participants will share perspectives through a series of workshops at the V&A, a conference in Cambridge and an edited volume of essays.

'Intoxicants and intoxication is a topic that is proving increasingly important both as a subject in its own right and as a means of thinking about wider social identities, practices and processes in a range of historical and cultural contexts,' said Dr Withington. 'My own research, for instance, looks at the notion that the expansion in the market for intoxicants was a defining feature of early modernity. As such, intoxicants can be understood as one of the key drivers of social change in modern history.'

If you are interested in joining the Intoxicants and Intoxication in Historical and Cultural Perspective Network, please contact Dr Phil Withington (pjw1003@cam.ac.uk).

Innovator of the Year

Professor Stephen Jackson has been honoured for his innovative research on DNA repair.

The award, organised by the Biotechnology and Biological Sciences Research Council (BBSRC), honours the UK bioscientist who has been best at turning world-class research into a product, company, service or advice that has had an impact on our lives. Professor Jackson was named Innovator of the Year at the inaugural ceremony in March.

Professor Jackson's research into DNA damage and repair led to the formation of KuDOS Pharmaceuticals in 1997, following his discovery that it was possible, in principle, to develop drugs that specifically prevented certain DNA repair proteins from working in cancer cells, leaving normal cells unaffected. His work developing cancer therapies is now saving the lives of numerous patients.

'It's a tremendous honour to receive this prestigious award,' Professor Jackson commented. 'It really reflects that science, like that funded by BBSRC and Cancer Research UK in my group over the years, can yield both exciting science and commercial and social applications.' Professor Jackson is the Frederick James Quick Professor of Biology at the Wellcome Trust/Cancer Research UK Gurdon Institute.

Harnessing materials for energy

Cambridge has received £1.4 million funding to progress innovative energy solutions.

Research Councils UK (RCUK) has announced funding of £12 million to be shared among ten UK institutions to support collaborations between British universities and institutions in China, India and the USA. The £1.4 million Science Bridges Award to the University of Cambridge will help to take existing research through to prototype products in the field of energy-related materials.

Cambridge's team is led by Professor Colin Humphreys in the Department of Materials Science and Metallurgy, with Professor Tony Cheetham in the same department, Professor Sir Richard Friend in the Department of Physics, and Professor Ian White and Dr Vikram Deshpande in the Department of Engineering. It will build upon existing collaborations with the University of California at Santa Barbara (UCSB).

Five key themes are to be tackled with the principal aim of reducing the cost and increasing the efficiency of energy materials such as light-emitting diodes (LEDs) and solar cells.

Professor Humphreys' research on gallium nitride (GaN)-based LEDs recently reached a landmark with the development of a new technique to grow GaN on large silicon wafers, reducing the cost of the LED chip tenfold compared with previous approaches. The RCUK funding will continue this work, as well as build innovative multi-layer solar cells, and LEDs coated with novel phosphors to improve colour rendering for lighting in the home. Professor Cheetham, who leads the phosphor research, recently joined Cambridge from UCSB.

New approaches will be developed to make the harnessing of solar energy more viable. Cambridge-based researchers will focus on developing low-cost, moderate-efficiency, organic solar cells; whereas UCSB-based researchers will concentrate on developing more-efficient cells. Cambridge will also address low-cost manufacturing through the development of printing methods for organic film deposition, and will develop novel ultralight materials based on polymers, metals and composites for use in transportation.

'This exciting project using world-leading science from Cambridge and UCSB should result in new types of lighting, solar cells and materials for transport,' explained Professor Humphreys. 'This award will translate research into prototype devices that will save energy, reduce carbon emissions, and be not only cheaper but also better quality than existing devices.'

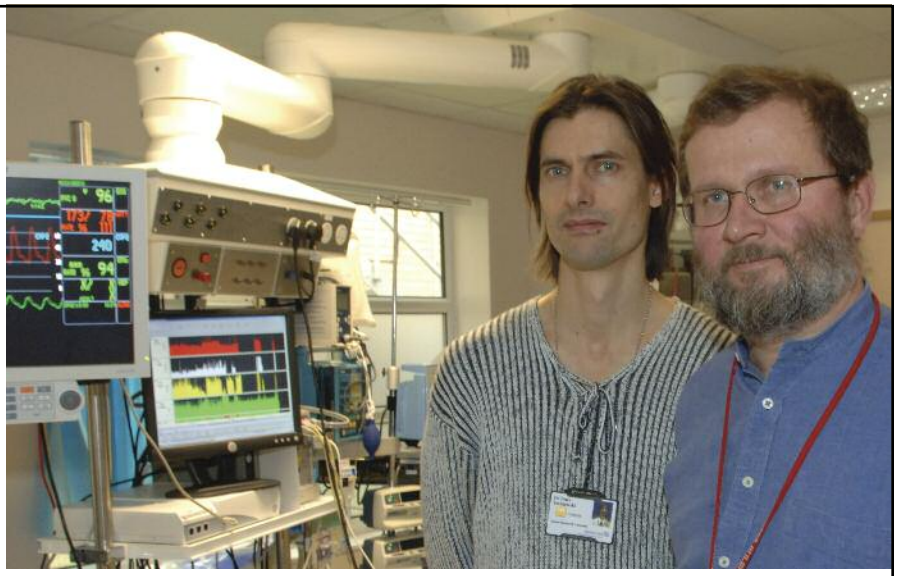
Lord Drayson, Minister of State for Science and Innovation, added: 'The RCUK Science Bridges Awards are an excellent example of how the UK is encouraging research which has both strong international collaborations and close links with business.'

For more information, please contact Professor Colin Humphreys (colin.humphreys@msm.cam.ac.uk).

cambridge enterprise
commercialising University science

A tool for monitoring neurological intensive care

Clinical researchers have developed software for interpreting the enormous quantities of data generated by bedside monitors.



Dr Peter Smielewski (left) and Dr Marek Czosnyka

Over the past decade, Dr Peter Smielewski and Dr Marek Czosnyka in the Neurosurgery Unit of the Department of Clinical Neurosciences have been developing software as an aid to monitoring patients in neurological intensive care. The intensive care multimodality monitoring system, or ICM+, has now been successfully licensed by Cambridge Enterprise Ltd as a research tool to medical researchers in over 30 centres worldwide.

The challenge addressed by ICM+ was to collate the huge array of complex, constantly changing data generated by bedside monitors, and to present them in a way that is quickly and easily comprehensible to medical staff.

At first, the software focused on data generated by monitoring patients with head injuries and hydrocephalus. But, the software is now increasingly being applied to conditions such as severe stroke, subarachnoid haemorrhage, cerebral infection and liver failure. 'Because the software has been licensed as a research tool, it provides a unified platform for collaborative studies with other medical centres, which feeds further development of the software,' explained Dr Smielewski.

The team also undertakes consultancy work through Cambridge Enterprise, to configure the software for specific needs and to provide advice to first-time users of the software. The majority of royalties received through the licence agreements are returned to the academics and the Department to provide much-needed funding for further research into finding solutions for helping patients in neurological intensive care.

For more information, please visit www.neurosurg.cam.ac.uk/icmplus/about.html or contact Cambridge Enterprise (Tel: +44 (0)1223 760339; email: enquiries@enterprise.cam.ac.uk; www.enterprise.cam.ac.uk).

Endless Forms

Science meets art at a ground-breaking exhibition revealing the interchange between Charles Darwin's revolutionary theories and art of the late 19th century.

'Endless Forms: Charles Darwin, natural science and the visual arts' presents a new perspective that explores both Darwin's interest in the visual arts and the vast range of artistic responses to his ideas. Developed by The Fitzwilliam Museum in association with the Yale Center for British Art, the exhibition is supported by the Wellcome Trust and the Philecology Foundation.

'Today, when science and art are generally considered as separate domains of intellectual and creative achievement, the notion that Darwin's ideas might have influenced the arts is perhaps surprising at first,' said Jane Munro, co-curator of Endless Forms and Senior Assistant Keeper of Paintings, Drawings and Prints at The Fitzwilliam. 'Yet the implications of his revolutionary ideas of evolution by natural selection had a profound effect on society at large, putting in question man's relationship to the natural world and challenging the understanding of what it meant to be human. As this exhibition sets out to show, artists were in no sense immune from this.'

NATIONAL GALLERY OF ART, WASHINGTON, DC; GIFT OF THE MORRIS AND GWENDOLYN CAFRITZ FOUNDATION

Martin Johnson Heade, Cattleya Orchid and Three Hummingbirds, 1871, oil on panel

Endless Forms draws together these wide-ranging artistic responses; from imaginings of prehistoric Earth, to troubled evocations of a life dominated by the 'struggle for existence'; from fantastic visions of life-forms in perpetual evolution, to images of colour and pattern in nature influenced by Darwin's own response to the beauties of the natural world.

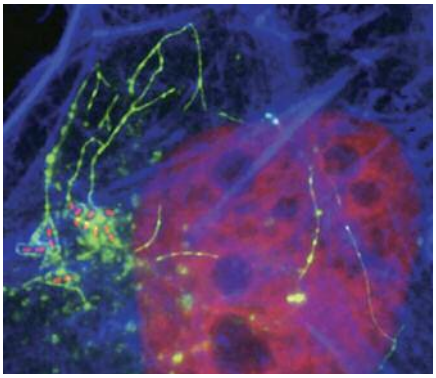
With nearly 200 exhibits from over 100 institutions worldwide – many on public display in the UK for the first time – the exhibition juxtaposes paintings, drawings, sculptures and early photographs with natural history specimens, maps of geological stratification, botanical teaching diagrams and vivid ornithological specimens, as well as rarely exhibited material from the Darwin Archive at Cambridge University Library.

Endless Forms will be on display at The Fitzwilliam Museum from 16 June to 4 October 2009 (www.darwinendlessforms.org).

Unravelling the secrets of *Salmonella* infection

Two new studies have uncovered important clues about how a prolific pathogen causes disease.

Salmonella bacteria are infamous intestinal pathogens that infect humans and animals, causing about 1.3 billion cases of human food-borne diarrhoea and systemic typhoid fever each year throughout the world. Following infection, the bacteria deliver a cocktail of virulence proteins that take control of the cell's cytoskeleton and networks of signalling pathways, growing inside infected cells in membrane-bound *Salmonella*-containing vacuoles (SCVs).



PROFESSOR VASSILIS KORONAKIS

***Salmonella* (red) in the process of establishing its vacuolar niche (green) in a human cell (cytoskeleton stained in blue)**

Understanding these events at a molecular level has been helped by findings published by Dr Daniel Humphreys and Dr Peter Hume in a team led by Professor Vassilis Koronakis in the Department of Pathology. The research, funded by the Wellcome Trust, has uncovered features of an unexpected pathway by which *Salmonella* manipulates the host cell to promote its own growth. *Salmonella* was engineered to deliver a mutant protein that stalled activity of the protein it binds to in the infected cell, thereby capturing it. Using protein biochemistry and fluorescence microscopy, it was shown that the *Salmonella* protein subverts the assembly of protein complexes required for membrane fusion and formation of intracellular organelles, ensuring a safe, rich, intracellular replicative niche for itself. Not only does this study suggest potential new targets to counteract disease but it also uncovers new aspects of mammalian cell biology.

Meanwhile, scientists at the Department of Veterinary Medicine have pioneered a technique to track the pattern and spread of bacterial infection within the body. The team led by Dr Andrew Grant, Dr Pietro Mastroeni and Professor Duncan Maskell developed molecular tags to mark populations of otherwise identical bacteria; in combination with multicolour fluorescence microscopy, these tagged bacteria could then be tracked during an infection. By constructing mathematical models, the team have managed to tease out the sequence of events, providing a more sophisticated picture of how an infectious disease is driven than previously possible. Thanks to recently awarded funding from the Medical Research Council (MRC), they are now ready to exploit these systems to understand the impact of key host and bacterial factors on the pathogenesis of *Salmonella* at the level of individual bacterial subpopulations. In the long term, this technique will provide a basis for targeting individual bacterial components *in vivo* with novel drugs and vaccines that are directed specifically to the sites of infection.

For more information, please contact Professor Vassilis Koronakis (vk103@cam.ac.uk) and Dr Andrew Grant (ajg60@cam.ac.uk).

Greek Grammar to fill the gap

A new Grammar will be the first comprehensive description of the medieval and early modern Greek language.

For the past five years, a team led by Professor David Holton in the Modern Greek Section of the Faculty of Modern and Medieval Languages has been gathering, analysing and organising linguistic data for a new Greek Grammar. Co-directed by Professor Geoff Horrocks (Faculty of Classics), the project is staffed by two full-time research associates, Dr Notis Toufexis and Ms Marjolijne Janssen, and two honorary consultants, Dr Io Manolessou and Dr Tina Lendari, and is funded by the Arts and Humanities Research Council (AHRC).

Greek is one of the world's oldest recorded languages, with a documented history spanning 34 centuries. Although scholars have analysed and described the Greek of the Classical, Hellenistic and Roman periods in detail, the linguistic situation is much less studied after the end of Antiquity. At around 1100 AD the beginnings of the modern vernacular first became evident, and over the next 600 years the language underwent significant changes, with the medieval vernacular gradually acquiring the morphological and syntactic features that are characteristic of Greek today.

Fortuitously, 1100–1700 is also a period in which texts in the vernacular are available in sufficient quantities for researchers to observe trends and identify the factors that influence variation. 'But, despite the increasing availability of this material, there has been no systematic and detailed account of the development of the Greek language during this crucial period,' said Professor Holton. 'The Grammar aims to fill a serious gap in the history of Greek. This standard reference work will underpin a growing interest in medieval and early modern Greek literature and its historical, social and cultural context.'

The Grammar spans a geographical area from southern Italy to the Black Sea, encompassing written texts of all kinds, and giving a full account of linguistic developments within this period. It is a high-tech project, using electronic databases and digitised corpora to store and sort a mass of information. Once completed, the Grammar will be published by Cambridge University Press.

TOPKAPI SARAY MUSEUM, ISTANBUL

Sources for the Grammar include texts like this manuscript, Serailiensis graecus 35 (folio no. 34, recto)

For more information, please contact Professor David Holton (dwh11@cam.ac.uk) or see www.mml.cam.ac.uk/greek/grammarofmedievalgreek

Solar-powered racing heats up

Construction of the latest solar-powered racing car from the Cambridge University Eco Racing (CUER) team is under starter's orders.

LOVEGROVE STUDIO

Cambridge University Eco Racing's new solar racing car

The car, code-named 'Bethany', will compete in the World Solar Challenge in Australia in October 2009. Designed by an independent student team, and sponsored by Cambridge Precision and Hewlett-Packard, the vehicle showcases cutting-edge environmentally friendly technology that is applicable to the next generation of electric vehicles.

By taking an uncompromising approach to efficiency and performance, CUER has developed a vehicle capable of cruising at 60 mph using the same power as a hairdryer. The car will weigh just 160 kg and sports 6 m^2 of the world's highest efficiency silicon solar cells. To achieve the car's extraordinary performance, CUER's engineering team has systematically reduced energy usage for each part of the car.

'At a time when the automotive industry is being forced to look at a low-carbon future,' said CUER's Team Manager, Anthony Law, 'our vehicle demonstrates the enormous potential of electric vehicle technologies.' The hope is that 'Bethany' will provide the UK's best-ever performance in the 3000 km endurance race across the Outback.

For more information, please visit www.cuer.co.uk

More stories published online…

Secret of night vision uncovered

Cambridge physicists have discovered that the ability of nocturnal animals to see in the dark lies in the unusual way that DNA is packaged in retinal photoreceptor cells.

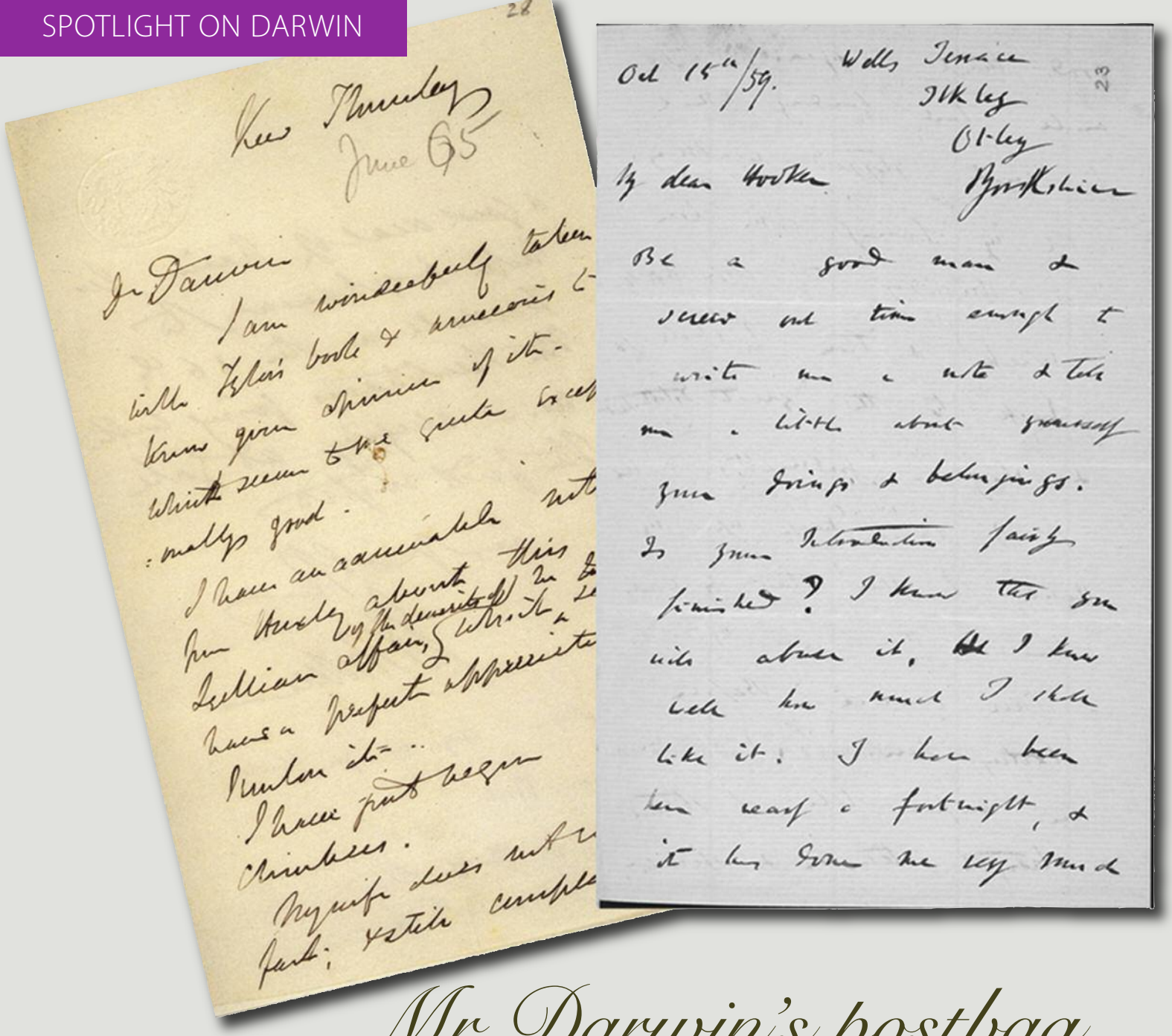
Endowment for Ancient Greek culture

An outstanding gift has endowed a new Professorship and will underpin research and teaching focused on the cultural achievements of the Ancient Greeks.

Bold leaders inspire faithful followers

New research from the Department of Zoology has shown that it's not just personality that counts in fish leadership, it's how other fish respond to it.

To view these stories and much more, please visit www.research-horizons.cam.ac.uk



Mr Darwin's postbag

Through the Darwin Correspondence Project, a rich collection of letters held at Cambridge University Library is both transforming our understanding of one of the greatest scientists of the 19th century and providing a panoramic vision of the era in which he lived.

Two centuries after his birth, Charles Darwin is probably one of the most famous scientists who ever lived, and certainly the most controversial. Yet, far from being the isolated genius of legend, Darwin was a prolific correspondent, who used letters very much as we use email. They were the lifeblood of his research. His correspondence provides us with a remarkable record of intellectual development, from his voyage around the world on HMS *Beagle*, to the decades formulating and honing his theories. They also provide a window onto his extraordinary global network of informants – the Victorian men and women who provided him with observations on the fauna, flora and peoples of the world: from gardeners, nurserymen, geologists and naturalists, to diplomats, army officers, novelists and suffragettes. They offer a remarkable picture of civil discussion and reasoned debate, from which we would do well to learn.

Today, the world's largest archive of Darwin's correspondence, together with his notes, manuscripts and annotated books and periodicals, is housed in Cambridge University Library. The richness of this resource has made the Library an international centre for studies of Darwin and 19th-century science. Scholars from all over the world regularly visit the manuscripts room and communicate with its expert staff. They also depend on the Library's collection of 19th-century books and scientific periodicals, unrivalled in its accessibility and extent.

These remarkable resources have led to an ambitious project, now in its 35th year and planned to continue until 2025: to publish a comprehensive chronological edition of all known letters, both to and from Charles Darwin, wherever they might be in the world.

Building and interpreting an archive

The bulk of the collection was given to the Library by the Darwin family and the Pilgrim Trust in 1942, and since then materials have continued to be added. Work on publication of the letters began in 1974, with a team led by an American scholar, Frederick Burkhardt, with the aid of Sydney Smith, a zoologist in the University of Cambridge. The first 10 years were occupied solely by searching worldwide for any letters the team could find and putting them into initial chronological order – less than half of the known letters have a date written on them.

A total of almost 15,000 letters exchanged by Darwin with nearly 2000 correspondents, spanning the period from 1821 until his death in 1882, have now been located, some in libraries and some in private collections. One letter even turned up on a recent broadcast of the BBC's Antiques Roadshow. About 8000 are in Cambridge, including important materials on deposit from the Down House Trust.

Each letter requires painstaking transcription, retaining all original spellings (and mis-spellings!), followed by annotation. Crucial bits of information are gradually fitted together, each informing and being informed by another. The result gives not just a new perspective on the 19th century, but fundamental insights into our own controversies about science and religion, the nature of evolution, and issues in ecological science. In this way, the meticulous research required to annotate the letters becomes the starting point for further understanding.

All the letters are being published in chronological order in the complete edition of the *Correspondence of Charles Darwin* by Cambridge University Press, of which the 17th of a planned total of 30 volumes will be published this summer. The letter transcripts and notes are also made freely available in a searchable online database five years after printed publication (www.darwinproject.ac.uk). As new letters come to light, or as new information on their contents or dating becomes available, the database is revised. The aim is to provide a unique, comprehensive and reliable source of information on his correspondence, as well as major topics in Darwin's life and work.

Funding – past and future

A project on this scale requires commitment from funding partners who understand the importance of supporting accessible, innovative research carried out to the highest standard over many years. Contributions from private donors have been essential for the research to progress, as well as long-term support provided by the Andrew W. Mellon Foundation, British Ecological Society, Isaac Newton Trust, John Templeton Foundation, National Endowment for the Humanities, and National Science Foundation. Funding is currently being sought for the next phase of work.

Professor Jim Secord and Dr Alison Pearn

For more information, please contact Professor Jim Secord, Director (jas1010@cam.ac.uk), and Dr Alison Pearn, Assistant Director (ab55@cam.ac.uk), of the Darwin Correspondence Project (www.darwinproject.ac.uk).

Darwin after *On the Origin of Species*

The Darwin Correspondence Project is entering a new phase: the letters to and from Darwin as he formulated his thoughts on the descent of man.

Publication of *On the Origin of Species* in 1859 is often presented as the climax of Darwin's career. In fact, it was only a beginning. Darwin knew that once he had gone public with his theory of evolution by natural selection, much more would be demanded of him. Twenty-three years of astonishing scientific productivity ensued, and in that time Darwin's correspondence grew phenomenally.

One of the topics barely touched on in *Origin* was the evolution of man. Darwin had always planned to include a chapter on humans, but left it out lest it led to unnecessary controversy. During the later years of the 1860s, accused of concealing his opinions, Darwin began to gear up for a full-scale assault on the citadel. Where did humans come from? Why are there different sexes? Why do races differ from one another? Are there characteristics – language, music, morals, rational thought – that decisively separate humans from the rest of the animal kingdom?

The Correspondence Project has now reached the moment when these fascinating questions come to the fore. Tackling human origins with the same tools that had proved so successful in understanding the rest of nature, Darwin extended his global network of correspondents, making enquiries among missionaries, soldiers, merchants, diplomats and travellers. The result, *The Descent of Man, and Selection in Relation to Sex,* appeared in two volumes in 1871, and a closely related work, *The Expression of the Emotions in Man and Animals*, was published in the following year.

In producing the volumes of letters dealing with *Descent* and *Expression*, the Project has plans for an extensive programme of supporting research, focused on the issues of race, gender and human nature. Work on this phase will be carried out through a new association between the Correspondence Project and the History of Science Department at Harvard University, where the work will be led by Professor Janet Browne, author of an award-winning two-volume biography of Darwin. This exciting transatlantic initiative aims to open up new perspectives on what is, by any standard, among the most significant episodes in modern history.

Darwin on locust dung

What would you do if someone sent you locust dung in a letter? For Charles Darwin, this became a welcome contribution to solving one of the many fascinating puzzles opened by the epoch-making *On the Origin of Species*. The little packet of dung, along with a host of other information, was sent to Down House by James Philip Mansel Weale, a naturalist and farmer in Cape Colony in southern Africa.

'When I rec^{d} the locust-dung I c^{d} not imagine what it was,' Darwin replied, '& I might have gone on guessing till doomsday.' Once he read Weale's letter, he knew what to do. Dissecting the dung under his microscope, Darwin found seeds of plant species that he subsequently germinated in his greenhouse at Down House. Samples were sent to his close friend, the botanist Joseph Hooker, who identified some of them as carrot-seed grass, a noxious weed that was adversely affecting the quality of the wool produced in the Cape. Because Darwin knew that locusts could be blown far out to sea, he recognised that the seeds in their dung could assist in the distribution of species, an important fact for a new edition of *Origin*.

On the wings of a butterfly

Since Darwin's time, Amazonian butterflies have fascinated evolutionary biologists as examples of evolution in action.

On reading Henry Walter Bates' 1862 account of his travels in the Amazon, Charles Darwin was captivated not only by Bates' description of the stunning diversity of butterfly species and wing patterns found in the Amazonian jungle, but also by the impressive mimicry between unrelated species. Darwin wrote: 'It is hardly an exaggeration to say, that whilst reading and reflecting on the various facts given in this Memoir, we feel to be as near witnesses, as we can ever hope to be, of the creation of a new species on this earth.'[1]

Bates hypothesised that mimicry evolved to confuse predators. Edible butterflies, for instance, copied the wing patterns of toxic species so that predators would avoid eating them. He also described what looked like evolution in action: he observed a continuum, from variable species, in which different wing patterns were found together in the same locality, through to related species with different wing patterns. Now, 150 years later, modern science has taken this to another level, with new research that aims to study the predictability of evolution by revealing the genetic basis of wing pattern mimicry.

The importance of pattern

We now recognise that not only do edible species mimic nasty ones (today called Batesian mimicry), but that several nasty species can also benefit from mimicking one another (Müllerian mimicry) – bees and wasps being a familiar example. Many of the Amazonian butterflies described by Bates are in fact Müllerian mimics, and the best-studied group are the genus *Heliconius*, the passion vine butterflies. Work by Dr Chris Jiggins' group in the Department of Zoology has focused on *Heliconius* butterflies as a case study in evolutionary biology.

By testing the role of *Heliconius* wing patterns in the wild, Dr Jiggins and others have confirmed Bates' hunch: changes in wing pattern play a big role in determining how successful the butterflies are in both mating and avoiding being eaten. Using flapping models with different patterns, the researchers have shown that the butterflies choose to mate with individuals that look the same as themselves; because of this, over time, different patterns are likely to split into new species. In addition, hybrids between populations with different patterns have intermediate patterns that are not recognised by predators as harmful and therefore suffer disproportionately from attacks, reinforcing the split into new species.

This dual role of wing patterns in signalling both to predators and to potential mates makes pattern a 'key trait' for speciation. As Bates suggested, shifts in wing patterns do indeed lead to the evolution of new species.

Selection signatures

One of the current hot topics in evolutionary biology is to what extent we can predict the genetic path of evolution. One particular *Heliconius* species (*Heliconius melpomene*) is an ideal system in which to address this question because it has many geographic populations with very different colour patterns.

***Heliconius*, or passion vine butterflies**

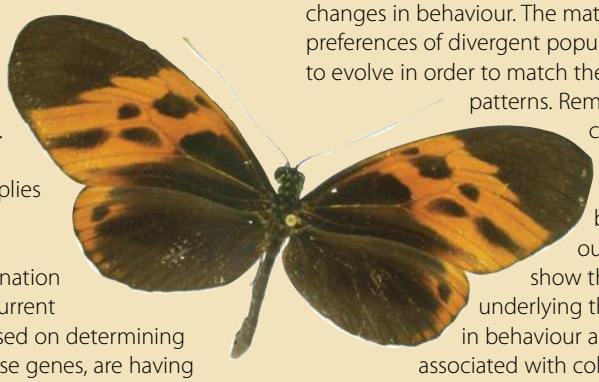
A major new project focusing on the genetic basis of wing patterns has commenced in the Jiggins lab with funding from the Biotechnology and Biological Sciences Research Council (BBSRC), Royal Society, Leverhulme Trust and Natural Environment Research Council (NERC).

Over the past decade, the researchers have been collecting different forms of *H. melpomene* from around South America, carrying out genetic crosses at a field station in Panama. These crosses have shown that dramatic differences in colour pattern are controlled by just a handful of genes and that these genes are clustered together on four out of the 21 *Heliconius* chromosomes. The genes act as wing pattern 'switches', turning on and off the presence of major pattern elements, such as a large red forewing band.

DR MATHIEU JORON

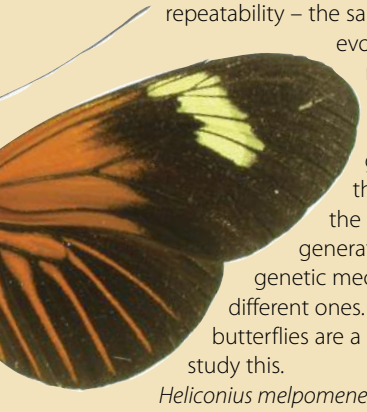
The challenge is to find out precisely what these genes are and how they work.

In collaboration with the Wellcome Trust Sanger Institute, regions of the butterfly genome are being sequenced to identify the specific nature of the pattern switches. The expectation was that the switches would correspond to well-known genes, perhaps controlling wing development or colour pigments. In fact, the two genomic regions studied so far each contains around 20 genes, none of which is known for its involvement in these processes. This is in itself exciting as it implies that novel mechanisms of pattern determination are operating; current research is focused on determining which, of all these genes, are having an effect in the butterfly.



Genetics of mimicry

What attracted Darwin and others to mimicry as a case study in evolution is its repeatability – the same patterns evolve in distantly related species. A key question for an evolutionary geneticist is therefore whether the patterns are generated by the same genetic mechanisms, or different ones. Again, *Heliconius* butterflies are a good system to study this.



Heliconius melpomene co-mimics another species, *Heliconius erato*, all over the neotropics – in any location you care to look you will find that the two species have evolved identical patterns. Recently, in collaboration with research groups in the USA, it has been shown that pattern switches in the two species are controlled by the same regions of DNA, such that genes at identical locations in the genome code for either a red forewing band or a yellow hindwing bar. This implies that evolution of the same mimicry patterns in the two species has been made easier by a shared genetic system. While predation against abnormal wing patterns drives the evolution of mimicry through Darwinian natural selection, a shared developmental system may bias the raw materials in favour of certain kinds of patterns.

Of course, the link between wing pattern adaptation and speciation requires changes in behaviour. The mating preferences of divergent populations need to evolve in order to match their wing patterns. Remarkably, crossing experiments currently being carried out in Panama show that the genes underlying these changes in behaviour are closely associated with colour pattern genes. It seems that there are 'hot spots' in the genome for evolutionary change, influencing traits as diverse as wing patterns and mating preference.

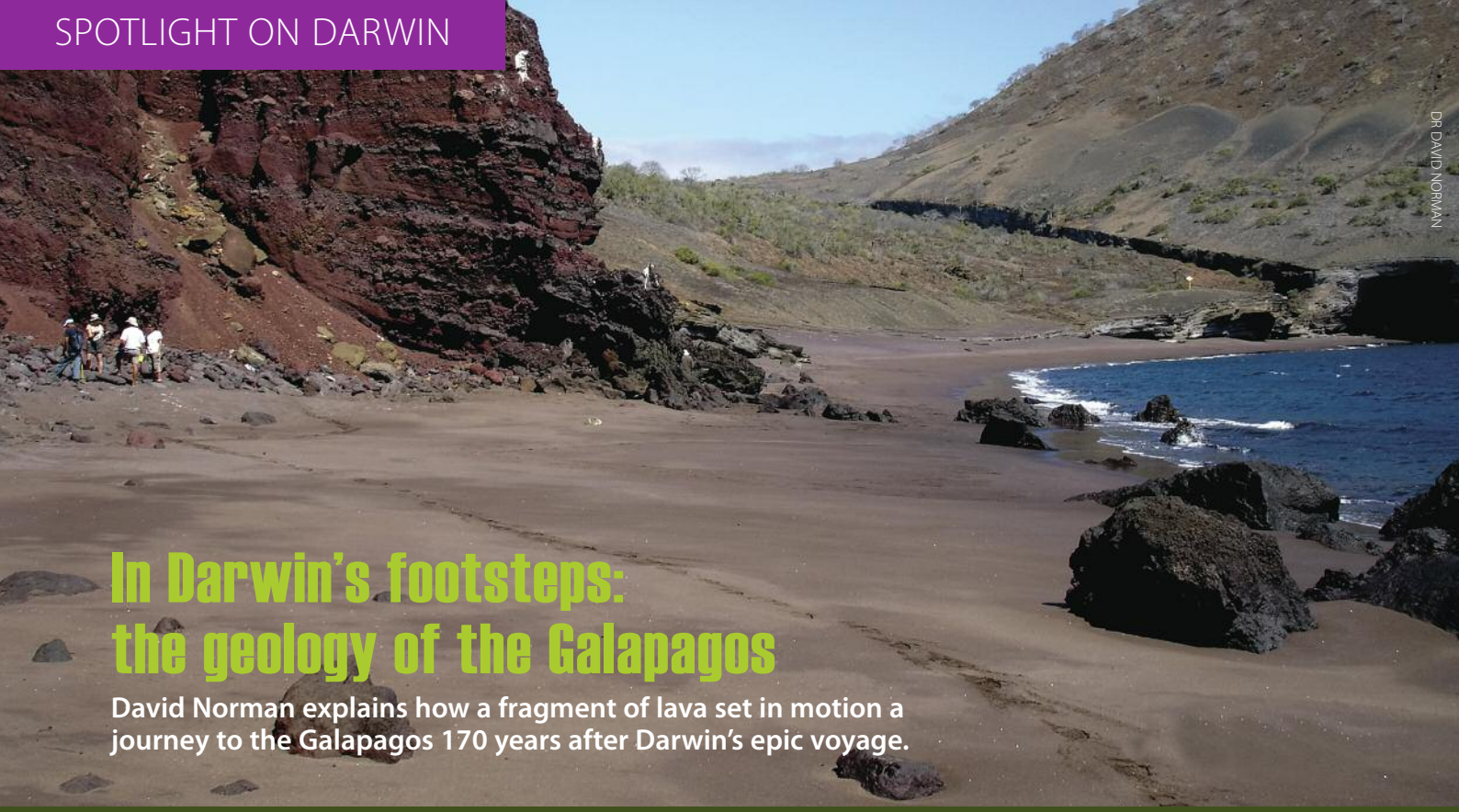
An enduring example

It is an exciting time to be studying butterfly mimicry. The combination of population genetic, developmental and behavioural approaches is starting to answer the issues Darwin and Bates themselves debated – questions that were posed at the very dawn of evolutionary biology. Throughout the intervening decades, *Heliconius* butterflies have persisted as an example of evolution in action. With the imminent sequencing of the *Heliconius melpomene* genome, they will no doubt continue to be so for some time yet. Charles Darwin would surely have approved.

[1][Darwin, C.R.] 1863. [Review of] Contributions to an insect fauna of the Amazon Valley. By Henry Walter Bates, Esq. *Transact. Linnean Soc.* Vol. XXIII. 1862, p. 495. *Natural History Review* 3, 219–224.

Dr Chris Jiggins

For more information, please contact the author Dr Chris Jiggins (c.jiggins@zoo.cam.ac.uk) at the Department of Zoology.



DR DAVID NORMAN

In Darwin's footsteps: the geology of the Galapagos

David Norman explains how a fragment of lava set in motion a journey to the Galapagos 170 years after Darwin's epic voyage.

Buccaneer Cove (with the flanks of Cerro Cowan in the background), Isla Santiago, Galapagos, where Darwin landed in 1835, as photographed by the Cambridge expedition retracing Darwin's footsteps

A dispute over the provenance of some of Charles Darwin's rock collection, now housed at Cambridge's Sedgwick Museum of Earth Sciences, led to an expedition to the Galapagos two years ago that in turn has resulted in an entirely new analysis of the geology of the Archipelago. The specimens are part of a collection of some 2500 rocks, minerals and fossils collected by Darwin on his 1831–1836 voyage aboard HMS *Beagle*.

Journey to the Galapagos

The germ of an idea to re-visit the Galapagos took hold when Dr Sandra Herbert, a visiting scholar from the University of Baltimore, noted a longstanding dispute concerning the provenance of lava rocks labelled by Darwin as 'trachyte' collected on James Island (now known as Isla Santiago). According to established understanding of the island's geology, the rocks could not have come from the island; by implication, either Darwin had mixed them up or the Sedgwick Museum had inadvertently mislabelled the specimens during curation. Perhaps by re-visiting the island, establishing Darwin's route and collection sites, the matter could be cleared up once and for all?

In 2007, an expedition led by Dr David Norman, from the Department of Earth Sciences and Director of the Sedgwick Museum, arrived at the Charles Darwin Research Station in the Galapagos Archipelago; members of the expedition included Dr Sally Gibson and Andrew Miles from Earth Sciences, Dr Herbert and Dr Dennis Geist (University of Idaho). This would be only the second time the geology of Isla Santiago had been investigated since the 26-year-old Charles Darwin set foot there in 1835.

With funding from the US National Science Foundation, Christ's College and Trinity College, the team integrated historical research with the collection of new rock samples from individual lava flows that have occurred at intervals across Isla Santiago. Fresh samples of rock were collected, with special permission from the Parque Nacional Galapagos, yielding an entirely new collection of volcanic rocks that reflect different phases of eruptive activity across the island.

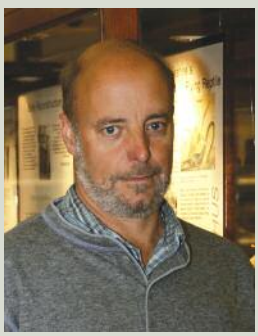
The geological history of the island itself is now the subject of further investigation in the laboratory using the new samples. It is already clear from this ongoing research that the island has an unusual history, with volcanic activity still evident in the recent historic past; this alone indicates that the hot mantle 'plume' that lies beneath the oceanic plate upon which the Galapagos sit has an unusual shape and dynamic relationship with the islands above.

And the piece of lava?

Almost as we have come to expect, Darwin's notes were correct (and the Museum curators had not slipped up either!). The rock type that Darwin identified as a 'trachyte' was found again (despite proving somewhat elusive) on the flanks of Cerro Pelado, a near-perfect small volcanic crater close to the summit of the island. And indeed all the major locations visited by Darwin yielded rock types that reflected his original collection held in Cambridge.

This information will also enrich the lines of investigation pursued by Dr Lyall Anderson, Isaac Newton Trust Research Fellow at the Department of Earth Sciences. Dr Anderson is taking a fresh look at the collection in the context of Darwin's early thoughts on geology, using Darwin's copious geological field notebooks housed at the University Library.

Clearly, as has proved so often to be the case, Charles Darwin chose to land on, and sample from, a particularly interesting place both scenically and biologically, …and geologically.



Dr David Norman

For more information, please contact the author Dr David Norman (dn102@cam.ac.uk). Dr Norman is Director of the Sedgwick Museum and a palaeontologist in the Department of Earth Sciences. 'Darwin the Geologist', a major exhibition at the Sedgwick Museum, opens on 7 July 2009 (www.sedgwickmuseum.org).

Collaboration between the University Herbarium and Microsoft Research Ltd will make a unique botanical collection available to a world-wide audience.

Displaying the foundations of evolutionary thinking

The Department of Plant Sciences at Cambridge houses over a million pressed, mounted and named plant specimens. Amassed over three centuries, the collection includes about 2700 plants collected by Charles Darwin on his HMS *Beagle* trip and the most comprehensive and up-to-date collection of British plants.

In offering a rare and unparalleled insight to the diversity of plants, the Herbarium has become increasingly precious given today's growing urgency to catalogue biodiversity. But, like many museum collections of this scale and fragility, its holdings are only available, in a controlled manner, to academic visitors to Cambridge. To increase its accessibility to a global audience, while preserving the integrity of this historical treasure, a project began three years ago to put specimens from the Herbarium on the web. With funding and technological support from Microsoft Research Ltd, Professor John Parker, Curator, and Gina Murrell, Assistant Curator, have been developing a coherent, logical and imaginative web portal to be made available for academic research and teaching, and for the enjoyment of everyone.

Henslow's vision and Darwin's gift

The Herbarium was the creation of John Stevens Henslow, Professor of Botany and founder of the Botanic Garden at Cambridge. Henslow's research on the nature of species was at its peak in the 1820s when Darwin attended his lectures and field trips, and it was Henslow who recommended Darwin for the *Beagle* voyage. When Darwin visited the Galapagos, he collected and dried all plants in flower, sending them back to Henslow to be mounted. Henslow had informed him that oceanic islands such as the Galapagos were rich in endemic species, a fact that helped crystallise Darwin's theory of the origin of species.

Henslow's Herbarium has increased in size enormously over the 200 years since then, particularly in 1866 when 55,000 specimens of the Lindley Herbarium were added; the Lindley collection provides a remarkable history of 19th-century plant-hunting explorations of North America and Australia. The plants of the whole world, and particularly of Great Britain and mainland Europe, have enriched the collection through gifts, exchanges, benefactions and purchases.

Promoting research

The major research project in the Herbarium is the preparation of the most definitive account of the British and Irish flora ever undertaken, based around this superb collection. Peter Sell has worked in the Herbarium for over 60 years and, in collaboration with Gina Murrell, has for 20 years been compiling the taxonomy, ecology and distribution of every species to create a botanical snapshot of the millennium. Volume 3 of this five-volume set has just been published by Cambridge University Press.

As well as a fundamental botanical research purpose, there is also an important historical perspective to the Herbarium. Darwin's plants give a fascinating glimpse into the origins of Darwin's thoughts, showing how Henslow gave Darwin concepts of populations, variation and the nature of species. Henslow intentionally organised his Herbarium collections to serve as an experimental tool for an inquiry into species and their limits. But whereas Henslow held a creationist's viewpoint, Darwin's own views changed as his theories of evolution by natural selection gradually took shape.

UNIVERSITY HERBARIUM, DEPARTMENT OF PLANT SCIENCES

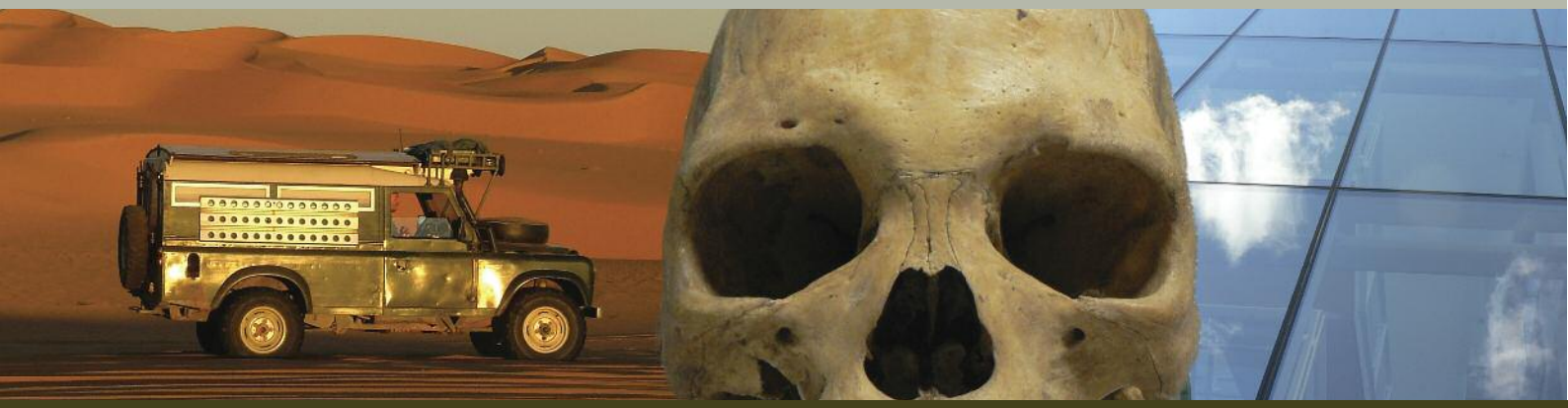
Four specimens of a grass (*Vulpia*), showing extreme size variation in a population at Bahia Blanca, Patagonia, collected by Darwin but mounted by Henslow in Cambridge while Darwin was still on the *Beagle*

An auspicious date

The aim of the five-year digitisation project is to place about 50,000 specimens on the web by 2011. The Henslow and Darwin collections are the priority, with a launch date of 24 November 2009, the 150th anniversary of the publication of Darwin's *On the Origin of Species*. Each Herbarium sheet is being digitally photographed, an appropriate database has been developed and data have been input, and a robust infrastructure to deliver fast, interactive responses in real-time to search queries is currently being built.

Professor John Parker

For more information, please contact the author Professor John Parker (jsp25@cam.ac.uk) at the University Herbarium, Department of Plant Sciences.



Leverhulme Centre for Human Evolutionary Studies

Cambridge anthropologists are increasingly looking at human evolution not just as a path through the remote past, but also as a way to explore humanity today.

Cambridge has a long tradition of research into human evolution. Alfred Haddon, the founder of the Faculty of Archaeology and Anthropology, was one of the first generation of Darwinists who explored the human world through the lens of evolution; Louis Leakey, who opened up the African search for human origins predicted by Charles Darwin, is one of the most notable of Cambridge anthropologists. In recent years, that tradition has been turned from the contributions of scattered individuals to a full institutional commitment. The Leverhulme Centre for Human Evolutionary Studies (LCHES) was founded in 2001 by Dr Marta Mirazón Lahr and Professor Robert Foley to be at the forefront of international research; it reflects both the growing power of evolutionary science and the endless fascination with the origins and nature of our own species.

Fossils, tools, apes and genes

When we think of human evolution and how it is researched, a number of images come to mind. One might be some African desert, yielding rare fossils of our ancestors. Another might be an archaeologist, digging up the earliest evidence for complex tools. In another direction lies the study of living apes, whose behaviour can provide clues about ancestral forms. More recently, the use of genetics has become more visible, with patterns of contemporary genetic diversity throwing light on evolutionary patterns in the past. Genes are now even being extracted from fossils, to add to the evidence. And, finally, we can even think of the ways in which anthropologists and psychologists, studying people today, can make inferences about evolutionary history and processes, and ultimately about human nature. LCHES was designed to bring all of these together.

Understanding humans is a question of evolution

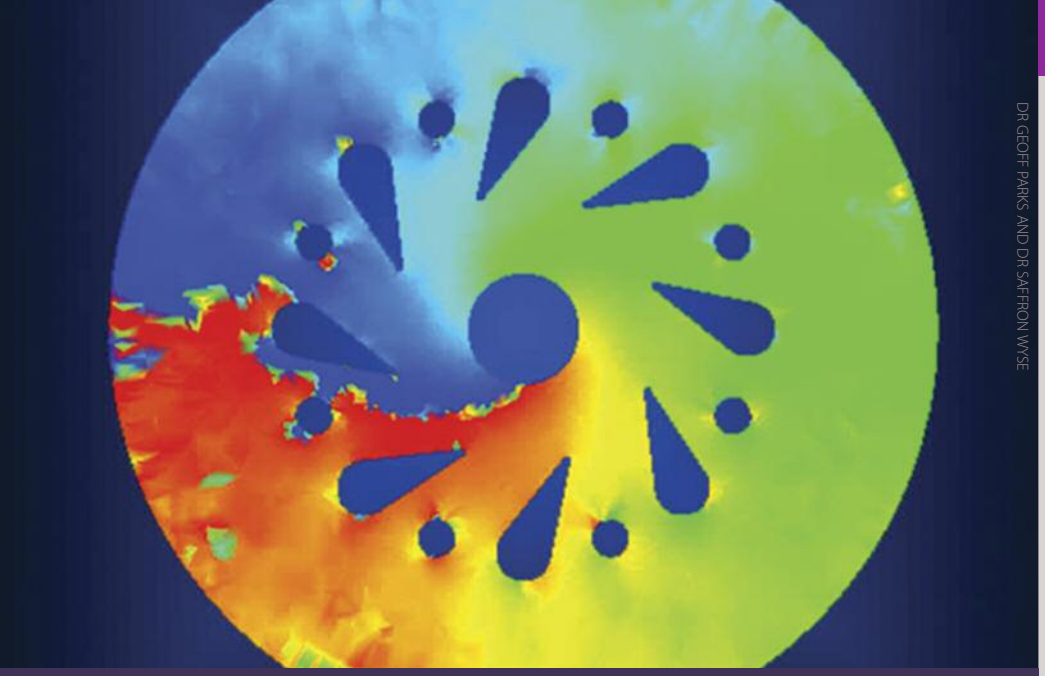
A multidisciplinary institution has to be more than the sum of its subjects. At the heart of LCHES is the simple idea that research should be question-driven. Different questions require different techniques and methods and, in particular, combinations of approaches. For example, we can ask where and when modern humans evolved, and evolutionary genetics can indicate Eastern Africa as the most probable location. But it is only by integrating these predictions with the exploration for fossils and archaeology in places such as northern Kenya that research can both give substance to the genetics and provide an understanding of *why* we evolved there.

The aim of the Centre is to act as the means by which researchers from a wide breadth of disciplines – anthropology, archaeology, linguistics, genetics, psychology, zoology and evolutionary aspects of geography – can formulate and develop joint research programmes. This has led, for instance, to an exploration in India, Papua New Guinea and the Solomon Islands of how genetic diversity can be shaped by language barriers and thus influence evolutionary history. Finding out how humans have come to vary so much in size has brought together anthropologists studying hunter-gatherers in the Philippines with evolutionary theoreticians who are unravelling the biology of size and demography. Geneticists are searching for the underlying genetics of size and shape, while anthropologists are searching the museums of the world for skeletons that can track this in the past. And understanding how humans became dependent upon culture has led to archaeologists working with living apes to see how they use and exploit technology.

Evolution naturally makes one think of the past, but that evolutionary past lives on in us today. Understanding how we survived in the past may be a step towards future survival.

Professor Robert Foley and Dr Marta Mirazón Lahr

For more information, please contact the authors Professor Robert Foley (r.foley@human-evol.cam.ac.uk) and Dr Marta Mirazón Lahr (m.mirazon-lahr@human-evol.cam.ac.uk) at the Leverhulme Centre for Human Evolutionary Studies (www.human-evol.cam.ac.uk). **External funding for the Centre has come from the Leverhulme Trust, the Wellcome Trust and Cambridge in America.**



DR GEOFF PARKS AND DR SAFFRON WYSE

Several performance measures must be considered when designing the combustor for an aeroengine

Design optimisation by evolution

By adopting the principles of natural selection, engineers are using survival of the fittest to breed better design solutions.

An important legacy of Charles Darwin's theories, unimaginable 150 years ago, has been the development of a thriving field of computational science based around the ideas of evolution by natural selection. Evolutionary computation, as it is known, encompasses a variety of methods, the most well known being evolution strategies, genetic algorithms and genetic programming. All seek to solve challenging optimisation problems (the problem of finding the *best* solution from all feasible solutions) in a vast range of application areas.

Although the methods differ in the detail of their implementation, they all follow the same basic blueprint: 'parents' are selected from a current population of available solutions, with better (fitter) solutions being selected more often; 'offspring' are bred by combining portions of the parents' 'chromosomes' (the set of parameters that define the solution); and finally, small random 'mutations' are made to the offspring's chromosomes, analogous to the copying errors that occur in real-world biological reproduction. The end result – the algorithm – can often succeed in solving problems where other methods fail.

Engineering design

The Computational Design Group, led by Dr Geoff Parks within the Cambridge Engineering Design Centre, aims to improve the design process and designed products by developing methods that effectively exploit the potential of computational optimisation to enhance the creativity and decision-making of engineering designers.

The optimisation of an engineering design is usually a multi-objective task: the designer wants to improve several objectives, or attributes, of the design simultaneously. Inevitably these objectives are often in conflict as it's frequently not possible to improve one objective for an optimised design without making another worse. Evolutionary computation methods can readily be adapted to tackle multi-objective problems. In so doing, they identify the trade-off surface – the set of solutions for which it is impossible to improve one objective without another deteriorating – allowing the designer to make a fully informed choice of final design.

There is widespread interest in applying these types of optimisation technique to real-world engineering design problems. Researchers in the Computational Design Group are using evolutionary computation to tackle a diverse range of design optimisation problems: from improving hybrid electric vehicle drive systems; to trading off reduction in pollutants and noise in aeroengines; to designing cheaper, more compact space satellites.

Selective breeding

Developing evolutionary algorithms that perform well on particular applications can pose challenges. It is not always straightforward to find a suitable way to encode designs 'genetically' such that when two good solutions are combined there is a reasonable chance that the characteristics that made them good are preserved in their offspring. Interesting research questions under investigation by the group also surround the issues of how parents are selected. In a virtual world, one can try schemes that would be physically or ethically impossible in the real one. The rules of the game can change too: for instance, the group has found that, in multi-objective optimisation problems, genetic diversity is often naturally maintained in the population as it spreads out across the trade-off surface and therefore highly selective breeding schemes in which only the best solutions are allowed to reproduce can be very effective.

By adapting the principles of Darwinian evolution, we can develop methods that enable engineers to design better submarine propulsion systems or nuclear reactor reload cores or… in fact, the potential applications are about as diverse as the natural world itself.

Dr Geoff Parks

For more information, please contact the author Dr Geoff Parks (gtp10@cam.ac.uk) in the Engineering Design Centre at the Department of Engineering. **Much of the group's research is supported by the Engineering and Physical Sciences Research Council (EPSRC).**

What Darwin didn't know: viruses and evolution

Once a retrovirus has infected a cell, its RNA genome is replicated into DNA (depicted here in red), which integrates into the genome of the infected cell

Scientists in the Department of Veterinary Medicine are studying viruses as pathogens in host populations, endeavouring to understand the implications of our shared evolutionary history.

When Charles Darwin's *On the Origin of Species* went to press in 1859, viruses had yet to be discovered – it would be another 40 years after publication before the 'concept of viruses' was proposed, and a century later before breakthroughs in viral research would provide a clear understanding of their genetic make-up, how they replicate and how they cause disease. Perhaps one of the most unexpected findings has been the discovery of the degree to which viruses have been an evolutionary force, as witnessed by the accumulating genetic and immunological evidence of the ancient battles between viruses and their hosts. Scientists in the Laboratory of Viral Zoonotics led by Professor Jonathan Heeney are asking key questions about the evolution of viral pathogens by studying the transmission of viruses from animals to humans.

Epizootics and zoonotics

Human epidemics caused by highly contagious acute infections such as influenza and severe acute respiratory syndrome (SARS) loom foremost in our minds when we think of the large-scale transmission of viruses that have the capacity to cause high morbidity and mortality. But some of the more insidious viral infections may have a much greater impact on global health because, in the early stages, they cause subclinical infections, with the disease developing slowly and sometimes going unnoticed for many years. Human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) are examples that have caused relatively silent epidemics, in some cases infecting hundreds of millions globally.

Epidemics are not confined to humans. Not only have we witnessed animal epidemics (epizootics) that all too recently have circulated through our domestic livestock (foot and mouth disease, classic swine fever and bluetongue), but animal viruses can also be transmitted to humans under a variety of conditions. A recent example of this type of zoonotic transfer is the bird-to-human transmission of the highly pathogenic avian flu virus, which raised global concern regarding a new human flu pandemic.

How do these viruses evolve to enable them to cross between species? What

complex series of events is required for the virus to infect humans and sustain infections at sufficient levels in a new species to become readily transmissible within a new population? Why are some individuals protected from developing full-blown disease despite being infected? These are the sorts of question that interest scientists in the Laboratory of Viral Zoonotics. This line of research involves the application of new molecular technologies to address aspects of zoonotic infections of importance to both veterinary and human health.

Fossils of ancient virological battles

Of particular interest to the team is a family of viruses known as the retroviruses, so named because of the 'reverse' way they reproduce themselves. Once a retrovirus has infected a cell, its RNA genome is replicated, or 'reverse transcribed', into DNA. This becomes integrated into the genome of the infected cell, so that it is copied every time the infected cell divides. Such integration explains why some viral infections such as HIV (the cause of AIDS) or human T-lymphotrophic virus (the cause of T-cell leukaemia or encephalopathies) are, in essence, persistent life-long infections. Sequencing of the human genome has revealed that retroviral integration has in fact been ongoing for millions of years. Human genomes, and those of other mammals, are littered with retrovirus-like elements as remnants of virus integration. Fortunately, most have become defective and are no longer replication competent, and are often considered by others as junk DNA. Professor Heeney considers them as 'viral fossils'.

Evolution of resistance

As a consequence of the thousands of years of battle between host and virus, our bodies have evolved many mechanisms to block or cripple those viruses that have the potential to threaten the survival of species. Understanding these processes and how hosts have evolved such viral defences may provide new insight into the co-evolution of species and viruses.

One area of research in Professor Heeney's lab is the study of the recent ancestor of HIV, the simian immunodeficiency virus (SIV). Of particular interest is the elucidation of how SIV evolved from being a virus of non-human primates to being a new pathogen of humans, and how previous animal hosts developed mechanisms of disease resistance. Humans show a spectrum of disease progression following HIV infection, with some individuals being highly susceptible to infection, while others have increased resistance. Research in Professor Heeney's lab is analysing how different natural African primate hosts have developed a relative resistance to AIDS-like diseases caused by these viruses. The data suggest that the animals have evolved mechanisms to control immune activation caused by new viral pathogens.

Another line of investigation is focused on how intrinsic host restriction factors (cell factors that can block or impair a stage of the viral life cycle) in a variety of non-human primates have influenced the evolution of different SIV viruses. At one stage in this evolutionary process, a subtype of SIV was transmitted from chimpanzees to humans, giving rise to the subtype of HIV-1 that has become the globally distributed human pathogen that causes AIDS. Understanding how pathogens have been kept under check in certain species, and how these species have undergone selection and developed resistance, will provide important insight into new treatments for other threatened species.

Understanding the good, the bad and the ugly

Linked to this area, a major effort in the lab is focused on identifying new types of virus that have adapted so well to their hosts that they have gone unnoticed under normal circumstances in healthy individuals. These viral infections may circulate within the human population without causing overt disease yet, subclinically, influence our daily health and wellbeing; moreover, if associated with other infections, such as those that cause hepatitis, these viruses may accelerate or alter the course of the disease. One project in the lab is investigating a highly contagious norovirus (a variant of the virus that causes winter vomiting disease in humans) that is completely asymptomatic in normal healthy mice but only rears its head and causes disease when the mouse genome loses particular genes responsible for natural antiviral responses. It is hoped that studies such as these will shed light on where disease outbreaks come from and how they persist.

Developing vaccines

The expectation is that lessons can be learned from understanding features of the long and intimate evolutionary history shared by mammals and retroviruses. Much of the knowledge of protective host responses to viral infection that is being uncovered in Professor Heeney's group is being translated into the development of vaccines to combat complex persistent RNA viral infections such as HIV and HCV. Working with teams in London and Lausanne, the first early clinical trials have recently been completed, and subsequent trials to optimise immunity and delivery are being planned. New vaccine candidates are also in development and the outcome of their use for the containment of rapidly evolving blood-borne pathogens such as HIV and HCV is being actively studied.

Cambridge Infectious Disease

Cambridge Infectious Disease (CID) is a Cambridge-wide initiative to bring together diverse groups studying aspects of infectious diseases, with the aim of coordinating the University's commitment to tackling global health challenges imposed by infectious diseases of animals and humans. Many internationally recognised research groups spread across departments and disciplines in Cambridge are working in this area. By building capacity in infectious disease research and teaching, and by attracting new research partnerships and funding, the goal of CID is to amplify Cambridge's impact on human and animal health worldwide.

In the spirit of commemorating Darwin, CID has this year chosen the theme 'Infectious Diseases and Evolution' for a meeting to be held on 22–23 October 2009; further details will be posted on the CID website.

For more information, please visit the CID website (www.infectiousdisease.cam.ac.uk)

Professor Jonathan Heeney

For more information, please contact Professor Jonathan Heeney (jlh66@cam.ac.uk) at the Department of Veterinary Medicine. **Professor Heeney's research is funded by the US National Institutes of Health and the Bill & Melinda Gates Foundation; a number of students and fellows in his laboratory are supported by the Wellcome Trust.**

PROFESSOR RAYMOND E. GOLDSTEIN

Stirring tails of evolution

***Volvox*: a multicellular alga with thousands of biflagellated cells on its surface; the smaller spheres are daughter colonies**

Researchers in Cambridge are studying how the generation of fluid flow by organisms may have played a role in the evolution of biological complexity.

One of the truly remarkable recent discoveries in biology is a connection between the swimming of microscopic green algae and the process that determines that your heart is on the left. The link is provided by cilia, the microscopic appendages whose beating propels algae through their fluid environment and which also set up circulating flows in a developing embryo that establish the left–right asymmetry. Cilia play an important role in many aspects of life, from the reproductive system, to the kidneys, eyes and the respiratory tract.

The ubiquity of cilia speaks to the importance of fluid mechanics in biology, but they may also have a role in one of the most fundamental issues in evolutionary biology: the origin of evolutionary transitions from single-cell organisms to multicellular ones.

A general (but by no means universal) rule of nature is that larger organisms are more complex, when measured by the number of distinct types of cell present. This undoubtedly reflects the fitness advantage conferred by a division of labour among specialised cells over a situation in which all cells are totipotent (able to do all the functions of life). The evolution of beating cilia (also termed flagella), for instance, increases fluid flow across the organism, improving the exchange of nutrients and waste products with the environment. Increasingly, these biological issues are also being seen as physical ones, involving many different disciplines – from fluid dynamics to mechanics and signal processing. Professor Raymond E. Goldstein's research group in the Department of Applied Mathematics and Theoretical Physics combines theoretical and experimental studies of biological complexity to investigate these kinds of issues in evolutionary biology.

The importance of being spherical

Volvox is something of a model organism in evolutionary biology. Only half a millimetre in diameter, it has thousands of biflagellated cells on the surface of an extracellular matrix, and daughter colonies that grow up inside. It is one of the evolutionarily advanced members of a lineage of species that starts at the most simple end of the spectrum, with the single-cell organism *Chlamydomonas*. The cells of the smaller species are all totipotent, whereas from *Volvox* onwards nature has decided to

specialise into two distinct cell types – flagellated somatic cells on the surface which perform photosynthesis and beat their flagella, and interior non-flagellated germ cells that are the sole reproductive cells.

Volvox's specialisation represents one of the most basic divisions of labour in biology and the question of why nature has chosen the size of *Volvox* as the scale for differentiation is a central one for research in this area. Because these organisms are spherical it is also easier to develop realistic mathematical theories. Examining these species as a function of their size, we recognise that their ability to take up nutrients by diffusion increases only with their radius; whereas, with all their metabolic tissue on the surface, their needs will grow with the surface area. Thus, beyond a critical radius, V*olvox* cannot live by diffusion alone. The research in Professor Goldstein's group has suggested that the fluid flows driven by flagella act to enhance nutrient uptake in a way that removes this bottleneck. The principle is akin to the chilling effect of wind on the skin, where airflow past the skin's surface enhances heat transport perpendicularly, from the body to air.

The connection to germ–soma differentiation comes from the 'flagellation constraint', the fact that the protein building blocks of flagella are also used in structures that pull chromosomes apart during cell division. For these organisms, nature does not allow 'multi-tasking' and flagellar beating ceases during cell division. Hence, sequestering the reproductive processes on the interior without compromising the external fluid flow may be nature's way of preserving the metabolic activity of the larger organisms.

Steering without a cox

If *Volvox* relies on fluid flow, a natural question is how the flagellar movements at the multicellular level are coordinated. Lacking any cytoplasmic connections between its thousands of surface somatic cells, *Volvox* functions 'like a ship with a thousand oarsmen and no cox'. It displays accurate phototaxis (swimming towards the light) as each cell is programmed to modulate the beating of its flagella in response to the signal received by its eye spot, a primitive photoreceptor. Because each colony spins about a fixed body axis as it swims, each of the thousands of eyespots is constantly receiving a signal modulated in time as they face towards and away from the light; the flagellar beating is correspondingly regulated up and down periodically. It turns out that many simple (and even advanced) organisms swim in spiralling paths that produce such periodic signals, and therefore a quantitative understanding of how accurate homing motion works under these constraints has broad implications.

An emerging hypothesis is that the spiralling motion actually enhances the phototactic fidelity. Because these multicellular organisms have no central nervous system, evolution has apparently endowed each somatic cell with just the right 'program' of response to light to enable directed motion. The response is a transient one in which cells on the dark side of the colony beat faster than those on the light side. This arrangement is possible only if the response time of the flagella is comparable to the rotational period, a kind of 'fine-tuning' that is well known in biology. Professor Goldstein's group has recently developed a novel apparatus to track the phototactic trajectories of organisms from *Chlamydomonas* to *Volvox* as they respond to changes in directional light signals and is using high-speed imaging to study the flagellar response under those same conditions.

Synchronised swimming

These questions have led the group back to the simplest of these organisms, *Chlamydomonas*, to understand how its two flagella synchronise. Using state-of-the-art high-speed imaging methods, postdoctoral researchers Dr Marco Polin and Dr Idan Tuval and PhD student Knut Drescher have discovered that the beating of the two flagella is actually quite complicated: the cell regulates the flagellar beating so that they switch back and forth between being so close in frequency as to become synchronised by the fluid flows they create, to being far enough apart that they beat approximately independently. Careful study of the statistics of these alternations has been used to determine the strength of the fluid dynamical coupling that drives synchronisation, providing the first quantitative test of emerging theories of this phenomenon.

Moreover, the alternation between synchrony and asynchrony leads to swimming trajectories that are combinations of straight paths and sharp turns, producing a 'random walk'. This kind of behaviour is well known in bacteria, which have very different kinds of flagella, but was not known for these organisms. The full implications are still to be worked out, but they probably represent a strategy for searching the space around them. Indeed, the transition from this erratic search mechanism at the scale of a single cell to the more stately cruising of a *Volvox* colony provides yet another example of the way in which size is related to complexity.

Understanding the origins of biological complexity is a goal that involves merging techniques and concepts from many different disciplines and, just as biology is increasingly incorporating maths, so too are mathematics and physics rising to the challenges presented by biology.

Professor Raymond E. Goldstein

For more information, please contact the author Professor Raymond E. Goldstein (reg53@cam.ac.uk) at the Department of Applied Mathematics and Theoretical Physics. **Professor Goldstein is the Schlumberger Professor of Complex Physical Systems and is funded by the Biotechnology and Biological Sciences Research Council (BBSRC), Engineering and Physical Sciences Research Council (EPSRC), Medical Research Council (MRC), Leverhulme Trust and European Commission Marie Curie Programme.** **Videos related to this article can be found at www.youtube.com/Goldsteinlab**

Miranda Gill traces shifting 19th-century perceptions of eccentricity, from its association with the intoxicating lure of modernity and fashion to the murky underworld of circus freaks and half-mad visionaries.

Rethinking eccentricity

Since the 18th century, English culture has been associated (both by the English themselves and by continental observers) with unusual tolerance towards unconventional and peculiar individuals. Even today, eccentricity is often seen as an obligatory component of the English national character. The eccentric is typically portrayed as a harmless and amiable figure, someone who provides others with a pleasant diversion from the tedium of everyday life.

But how historically representative are these received ideas of eccentricity? This question has formed the basis of my research and the subject of my recent book, which seeks to investigate more sceptically the cultural and ideological functions of eccentricity.

My research starts from two sets of assumptions: first, that eccentricity is neither timeless nor universal; second, that it is by no means always harmless and absurd. Eccentricity is, instead, a historically relative and context-dependent term, which must be situated within the broader histories of individualism and deviance. Eccentricity often elicited violent and conflicting responses, and was associated with potentially disturbing figures such as the insane, social marginals, human 'monsters' and the tempestuous Romantic genius. Beliefs about eccentricity varied widely across European national traditions, and were underpinned by complex assumptions about gender and class.

I chose 19th-century Paris as the focus of the study precisely because its culture was significantly different from English culture. The modern concept of eccentricity had crystallised in 18th-century England, a culture increasingly interested in poetic and psychological originality. Pre-Revolutionary French culture, by contrast, was markedly hostile to both originality and individual difference. It asserted that elegance was timeless, upheld rigid ideals of good taste and decorum, and stressed the need for social conformism. It was precisely the initial strength of French resistance to the values of eccentricity, I suggest, which make its reception after 1830 so revealing of tensions in French cultural identity.

Ambivalent emotions

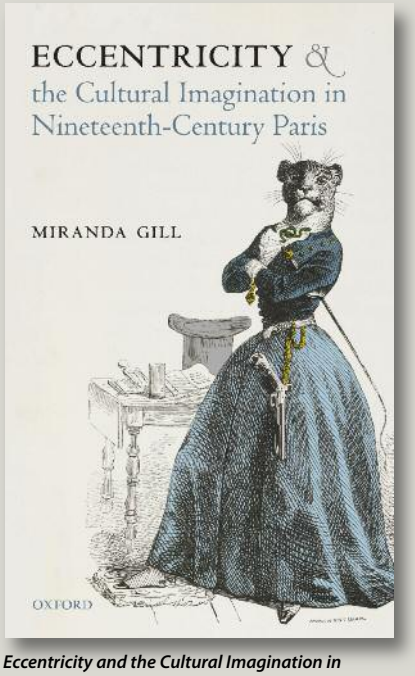
Breaking with convention aroused highly ambivalent responses in 19th-century Parisian readers, writers and spectators. Eccentricity was debated in a wide range of sources, including etiquette manuals, fashion magazines, newspapers, novels, plays, political pamphlets, and scientific and psychiatric treatises. On the one hand, the scandal of 'standing out' evoked the aspirations of the bourgeoisie, namely its dreams of freedom, creativity and individuality. On the other, it symbolised the deepest anxieties of this class, the threat of madness, monstrosity and sin. Eccentricity was therefore simultaneously desired *and* feared, incorporated into *and* rejected from bourgeois identity.

Why were the French so ambivalent towards eccentricity? The French Revolution in 1789 inaugurated a century of unprecedented social and political instability, generating a strong desire in the French elite to create social cohesion and order. An orderly society entailed the suppression of any challenges to social norms. At the same time, however, the influence of Romanticism led to an increasing desire for individual freedom and fulfilment, whilst the bourgeoisie had strong faith in social and intellectual progress. The latter tendencies inevitably led to many norms and traditions being called into question, and 19th-century Parisian culture was at the forefront of attempts to probe the fragile boundaries between conformism and eccentricity. Three cultural fields in which this is most evident are fashion, bohemia and science.

Followers of fashion

Eccentricity in Paris of the 1830s was linked to flamboyant new fashions and the seductions of commodity culture. The values of fashion, including novelty and bizarreness, were diametrically at odds with the traditional values of French politeness and etiquette. Eccentric styles epitomised the intoxicating dangers of modernity, and were championed by a range of unconventional figures, including male and female dandies and the aristocratic figure of the *lionne* or lioness. The *lionne* rejected the fragility and hysteria associated with respectable women, and engaged instead in energetic 'masculine'

Eccentricity in 19th-century France was often linked with flamboyant new fashions, as seen here for the central figure of the female 'lionne'; image from Edmond Texier's *Tableau de Paris*, 1852, Vol. 1 (8000.a.30)



***Eccentricity and the Cultural Imagination in Nineteenth-Century Paris* by Dr Miranda Gill is published by Oxford University Press**

pursuits such as horseriding and smoking. But increasingly, such eccentricity was linked to *demi-mondaines* and courtesans, who, it was feared, were corrupting the morality and health of the social elite.

Bohemian culture

After Napoleon III's coup d'état of 1851, the social position of the writer and artist became more problematic. Eccentricity was associated with the artists, social marginals and urban poor who inhabited 'the unknown Paris'. This murky underworld fascinated bourgeois observers as much as it horrified them. Writers and journalists documented their ambivalent responses to exhibitions of human freaks in the fairground and to the half-mad visionaries of bohemian street culture. They were uneasily aware that they too failed to conform to bourgeois norms and that some eccentrics might be unrecognised geniuses.

Scientific theory

The popularisation of medical theories of national decline after 1851 led to increasing moral panic. Eccentricity was interpreted as a symptom of insanity and concealed deformity, and eccentrics were often portrayed as a dangerous social menace which psychiatrists and legislators struggled to contain. Despite this, many writers, including Gérard de Nerval, Jules-Amédée Barbey d'Aurevilly, Charles Baudelaire and Jules Vallès, championed 'pathological' and 'monstrous' forms of eccentricity. Their writing constitutes an act of symbolic resistance to a culture which defined normality, virtue and health in increasingly restrictive and unimaginative terms.

A contemporary debate

In charting the history of eccentricity, one conclusion I arrived at was that beliefs about precisely how much individuals are permitted to diverge from social norms differ considerably between cultures in response to very specific socio-historical factors. Gender appears to be central to the imagination of deviance in this period since what was deeply eccentric for women was often considered quite normal for men, and vice versa. Ultimately, the experience of ambivalence is inseparable from European modernity: eccentricity represents one compelling set of values (novelty, freedom, individuality) which clashed significantly with other, equally compelling values (stability, order, community). In many ways, this type of clash is central to debates in contemporary moral and political philosophy about the plurality of values and goods.

The interdisciplinary focus of the project continues to develop, as it traces the migration of concepts and metaphors between literature, popular culture and science. Continuing to emphasise the ways in which social and psychological categories are implicitly shaped by values and norms, my research is now focusing on a cultural history of paranoia and suspicion in French modernity.

Dr Miranda Gill

For more information, please contact the author Dr Miranda Gill (mfg24@cam.ac.uk) at the Department of French, in the Faculty of Modern and Medieval Languages.

What is knowledge transfer?

As we launch a new section in Research Horizons to highlight examples of knowledge transfer at the University, we begin by asking: what is it and how does it happen?

Knowledge transfer (KT) is a term used to encompass a very broad range of activities to support mutually beneficial collaborations between universities, businesses and the public sector. It's all about the transfer of tangible and intellectual property, expertise, learning and skills between academia and the non-academic community. It's also well recognised by government and funders as an important return on the UK's investment in academic research, one that provides a significant driving force for enhancing economic growth and societal wellbeing. For academics, KT can be a way of gaining new perspectives on possible directions and approaches for research. This two-way exchange element of KT is at the heart of successful and sustainable collaboration.

Academics are often asked to consider the potential audiences, impact and applications for their work, and increasingly there are opportunities to apply for grants specifically with non-academic collaborative partners. In response, Research Councils UK (RCUK) has recently launched the RCUK Knowledge Transfer Portal as a single point of access for those interested in KT schemes and activities (www.rcuk.ac.uk/innovation/ktportal).

Making the most of research

Discussion around KT often focuses on the formation of spin-out business, or the licensing of intellectual property (IP), based on the outputs of university science and technology-related research. Although these are vitally important areas, KT actually encompasses a much broader range of activities and is not limited to the science and technology disciplines. In terms of activities, KT can be split into six types:

People: When students graduate and join the workforce, they bring with them new knowledge and are effectively helping to 'regenerate the gene pool' of industry. The temporary placement of students and graduates in companies or in the public or voluntary sectors can be a more directed way of exchanging knowledge on a shorter term basis. One of the longest standing schemes is Knowledge Transfer Partnerships (www.ktponline.org.uk), funded by the Technology Strategy Board and supported by most UK Research Councils.

Publication and events: Knowledge is transferred through publication of research outputs, and through events and networking. In Cambridge, events can vary from Horizon Seminars (which provide a first look at new findings and developments at the University and are organised by Research Services Division) to the Corporate Gateway (offering a bespoke programme of customised meetings with leading University researchers and new technology companies in Cambridge).

Collaborative research: This is a powerful means of creating opportunities for innovative knowledge exchange. In Cambridge, examples include the Cambridge Integrated Knowledge Centre (CIKC), which brings together University research, industry secondments, business acumen and manufacturing expertise to help those with exploitable concepts to achieve commercial success in photonics and electronics; and the Institute for Manufacturing (IfM), which creates new ideas and approaches to modern industrial practice – from understanding markets and technologies, through product and process design, to operations, distribution and related services. As a whole, the University typically engages in 650 research agreements, worth £22 million, with industry annually.

Consultancy: The provision of domain-specific expert advice and training to external clients by university staff can be a very effective KT mechanism – it can provide a platform for the exchange of both explicit and more tacit knowledge, and a window on areas of possible collaboration. Support for consultancy is one service offered by Cambridge Enterprise Ltd (www.enterprise.cam.ac.uk). The IfM also disseminates its research outputs through consultancy services provided by the University-owned company IfM Education and Consultancy Services Ltd. Together, Cambridge Enterprise and IfM provide consultancy support to more than 200 companies annually.

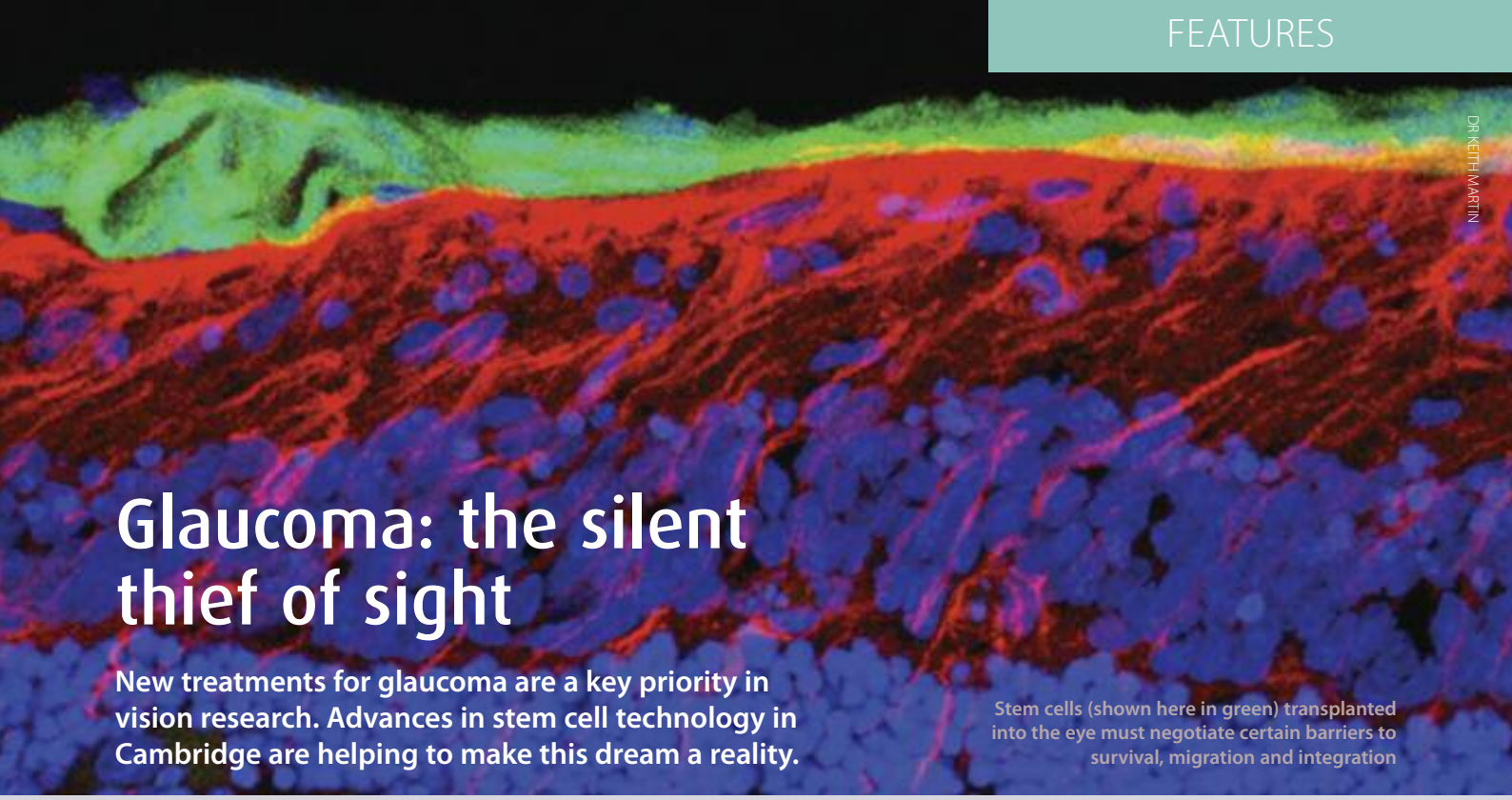
Licensing: Licensing the right to use specific research outputs (IP such as patentable ideas) is an important KT mechanism. Information on IP that is available for licensing is accessible through various websites, but successful licensing arrangements are long-term relationships often leading to research collaborations and individual contacts. Licensing is a key area of activity for Cambridge Enterprise, with about 50 new commercial agreements closed annually and a portfolio of over 450 active licence agreements.

New businesses: Bringing research outputs to market through the formation of a new business can be particularly appropriate when the application represents a 'disruption' to the current market or sector, or where there isn't any obvious external partner to whom the idea could be licensed. New businesses based on research outputs often build their business models around collaboration with larger, established firms to access expertise, equipment and routes to market. Cambridge has a well-developed ecosystem for supporting this, including student business-plan programmes, area angel networks and access to capital through Cambridge Enterprise Seed Funds (see: www.enterprisenetwork.group.cam.ac.uk).

KT is a contact sport

Three key factors seem to underpin successful KT. First, it's not a 'zero cost' activity; it takes effort and time to make it work. Second, it is a 'contact sport'; it works best when people meet to exchange ideas, sometimes serendipitiously, and spot new opportunities. Third, it needs practical, timely and active support at an institutional level – within companies and universities – encouraging a culture of open access and open innovation.

For more information, please contact the author Dr Tim Minshall (thwm100@eng.cam.ac.uk) at the Centre for Technology Management in the IfM (www.ifm.eng.cam.ac.uk). Dr Minshall has extensive experience of supporting industry–academic collaboration, technology transfer and open innovation.



DR KEITH MARTIN

Glaucoma: the silent thief of sight

New treatments for glaucoma are a key priority in vision research. Advances in stem cell technology in Cambridge are helping to make this dream a reality.

Stem cells (shown here in green) transplanted into the eye must negotiate certain barriers to survival, migration and integration

Glaucoma is the leading cause of irreversible blindness worldwide. Dubbed the 'silent thief' because of the insidious manner by which many patients have already suffered significant visual loss before they are diagnosed, glaucoma affects more than 60 million people, over 6 million of whom are blind in both eyes. Currently, the only treatment that can slow the progression of disease is to reduce the eye pressure medically or surgically. However, for some patients, visual deterioration continues unabated even with this intervention. Once vision is lost, it cannot be restored.

Glaucoma has been highlighted as a priority eye disease by the World Health Organization's global initiative to eliminate avoidable blindness by the year 2020. This recognises the urgent need to find new treatments that can prevent blindness in the most severely affected patients and to restore some useful vision to those blinded by the disease.

Towards stem cell therapy

The potential use of stem cell therapy in the treatment of glaucoma has aroused great interest, and Cambridge researchers are leading the way in this field. Glaucoma involves the progressive death of retinal ganglion cells (RGCs) – the eye cells that carry visual information from the eye to the brain via the optic nerve – and it's hoped that stem cells can be used to protect surviving RGCs and to replace those that are too damaged to function. This is the goal of Dr Keith Martin and colleagues at the Centre for Brain Repair, who have pioneered a new technique to study the barriers that reduce the survival, migration and integration of stem cells transplanted into the retina.

The model involves the use of a very specific set of tissue culture conditions that enable tissue from a rat's eye to be kept alive much longer in culture, remaining healthy, maintaining its layered architecture and retaining the ability to make new proteins. The tissue responds to stem cell transplantation in a similar way to that of the eyes of living animals, enabling the researchers to transplant stem cells onto living tissue in a controlled environment and to test treatments to improve integration of the transplanted cells.

To catch a thief

Replacing damaged RGCs will be a challenging procedure, involving the establishment of complex connections with the retina and brain, and requiring a much better understanding of the inhibitory environment of the mammalian retina. Not only will Dr Martin's research help to understand the barriers that prevent stem cell transplantation, but it will also help to catch the thief in action – by understanding the pathogenic sequence of eye pressure and neurodegenerative events as they occur.

Dr Keith Martin

Prestigious prize for replacing animal use

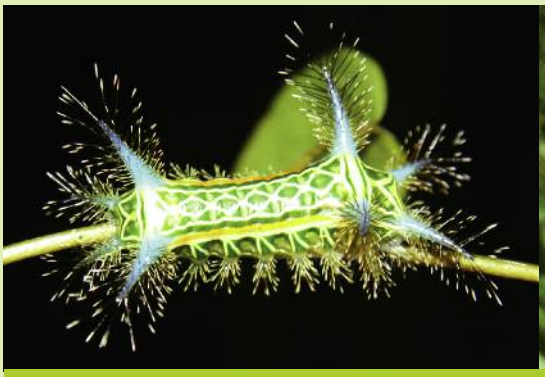
Dr Keith Martin and PhD student Thomas Johnson were recently awarded a major prize by the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) for the UK research that has done most over the preceding two years to replace, refine and reduce animal experiments. Until recently, injecting cells into the eyes of anaesthetised animals has been the only way to understand the barriers that prevent the integration of transplanted stem cells into the retina. The £10,000 GlaxoSmithKline (GSK)-sponsored prize recognises the fact that this new retinal culture system allows much of this work to be carried out without the need for animal procedures.

For more information about NC3Rs, please visit www.nc3rs.org.uk

For more information, please contact the author Dr Keith Martin (krgm2@cam.ac.uk) at the Centre for Brain Repair in the Department of Clinical Neurosciences. **This research was published recently in *Investigative Ophthalmology and Visual Science* and was funded by a GSK Clinical Fellowship to Dr Martin.**

Cambridge Conservation Initiative: transforming international biodiversity conservation

'Conserving global biodiversity presents us with a major challenge in the 21st century, requiring interdisciplinary collaboration across research, policy, practice and education. By creating CCI, the Cambridge conservation community has taken a unique step towards tackling this challenge in a most exciting and innovative way.'
Professor Alison Richard, Vice-Chancellor



The Cambridge Conservation Initiative (CCI) is a new and pioneering partnership formed by the University of Cambridge and leading conservation organisations. Its aim is to create an international centre of interdisciplinary collaboration and outreach that will transform conservation research, policy and practice for the benefit of biodiversity and humanity.

Scale of the challenge

Biological diversity – the myriad of genes, species and ecosystems – underpins the life-support systems for our planet and for the survival of life on earth. Clean air, pure water, foods, medicines and natural materials are all produced or maintained by the plants, animals and microbes that make up biodiversity and the 'ecosystem services' they provide.

However, an increasing body of research, including significant contributions from Cambridge, shows that humans are destroying species, habitats and ecosystems more rapidly and more extensively than ever before. Extinction rates of species are estimated to be more than 1000 times higher than would occur through natural evolution and, if climate change continues at current levels, a third of all living species are likely to be committed to extinction by 2050. In a global assessment of ecosystem services it was recently concluded that 60% are being seriously depleted or used unsustainably. It has become clear that such widespread impacts on biodiversity have profound negative implications for human welfare.

Set against this gloomy picture for global biodiversity is some more encouraging news. Our detailed knowledge of the status and distribution of species and ecosystems, and of the threats they face, is growing rapidly. An impressive range of government legislation and policy for biodiversity conservation and wider environmental management has appeared over the past 25 years, at local, national and international scales. Public understanding of nature, its beauty, value and rapid demise, has grown enormously. Such public interest and concern has resulted in an increasing number of organisations that carry out a wide range of practical conservation programmes. Yet, despite such progress, extinctions continue and habitat loss remains a major threat to life on earth and human wellbeing. If progress is to be sustained, there needs to be a new approach that will bridge the gulf between research, policy, practice and training in biodiversity conservation. This challenge is at the heart of CCI.

Pioneering change

CCI will carry out innovative research across disciplines and forge entrepreneurial collaborations that generate cross-cutting policy analysis and evidence-based practical advice, drawing on and integrating biological, social, economic and political science. Through its members (see panel), CCI will harness a unique and diverse international network across business, government and intergovernmental agencies, civil society and academia.

Research has already benefitted from the types of collaborations it is anticipated that CCI will foster on a larger scale. For example, Professor Bill Adams in the Department of Geography has been working with the International Union for Conservation of Nature (IUCN) and a wide international network on a project to develop the next generation of thinking about sustainable development, recently published by IUCN as a book entitled *Transition to Sustainability: Towards a Humane and Diverse World*. Professor Andrew Balmford and colleagues in the Department of Zoology have worked with RSPB to coordinate a major review of the economic consequences of losing what is left of wild nature; the conclusion – that converting remaining habitat patches typically results in a net economic loss to society as a whole – was presented by RSPB and BirdLife International at the World Summit on Sustainable Development as well as to the UK Prime Minister. Professor Bill Sutherland, also in Zoology, has been bringing together a diverse array of policy makers to identify new problems facing biodiversity and key unanswered questions; in parallel, he has been working with conservation practitioners across the world to document evidence-based solutions.

Although CCI is still in its infancy, some innovative integrated approaches have already been created. In a Shared Challenges Programme between CCI members, collaborative projects have started on, for example: assessing the value of biodiversity in climate change adaptation; identifying the impacts of biofuel production on biodiversity; using remote sensing to measure and evaluate biodiversity; and developing mechanisms for biodiversity offsetting (similar to carbon offsetting).

Thanks to the generous support of Arcadia, the charitable foundation of Lisbet Rausing and Peter Baldwin, CCI has just appointed its first Executive Director, Dr Mike Rands. The Executive Director's role is to accelerate activities, foster new collaborations and partnerships, and drive forward plans for a purpose-built environmentally sound centre for biodiversity. Created around a new University of Cambridge Institute for Biodiversity Conservation, the centre will also host founder partners and other organisations, providing a vibrant intellectual environment and organisational hub with operational economies of scale and shared facilities.

LEFT TO RIGHT: TROPICAL BIOLOGY ASSOCIATION (TBA); JAMIE GRUNDY/TBA); MNS/BIRDLIFE

Cambridge already has the largest cluster of conservation expertise in the world but the new centre will deliver a step change in our ability to attract researchers, engage with the policy sector and the business community, and deliver training and outreach. CCI's goal is to harness for biodiversity conservation Cambridge's exceptional power to shape thinking of mainstream decision makers and to exert decisive influence in the global arena.

Professor Bill Adams (back left), Professor Bill Sutherland (back right), Professor Andrew Balmford (left) and Dr Mike Rands

For more information, please contact the authors Dr Mike Rands (mr494@cam.ac.uk; CCI Executive Director, Judge Business School), Professor Bill Adams (wa12@cam.ac.uk; Department of Geography); Professor Andrew Balmford (apb12@cam.ac.uk; Department of Zoology) and Professor Bill Sutherland (w.sutherland@zoo.cam.ac.uk; Department of Zoology) or visit www.conservation.cam.ac.uk

Founder members of CCI

BirdLife International is a strategic global partnership of conservation organisations in over 100 countries, working to conserve birds, their habitats and global biodiversity, and to promote sustainability in the use of natural resources (www.birdlife.org).

British Trust for Ornithology is an independent scientific research trust, investigating the populations, movements and ecology of wild birds in the British Isles (www.bto.org).

Cambridge Conservation Forum is a network that links the diverse Cambridge-based community of conservation practitioners and researchers working at local, national and international levels (www.cambridgeconservationforum.org.uk).

Fauna & Flora International acts to conserve threatened species and ecosystems worldwide, delivering global and regional programmes of conservation and community projects (www.fauna-flora.org).

International Union for Conservation of Nature (IUCN) is the world's largest professional global conservation network, and supports scientific research, manages field projects and unites conservationists to develop and implement policy, laws and best practice (www.iucn.org).

RSPB is the largest wildlife conservation organisation in Europe, and works to secure the conservation of biodiversity – especially wild birds and their habitats – through research, education, habitat management and advocacy (www.rspb.org.uk).

TRAFFIC is a global wildlife trade monitoring network which works to ensure that trade in wild plants and animals is not a threat to the conservation of nature (www.traffic.org).

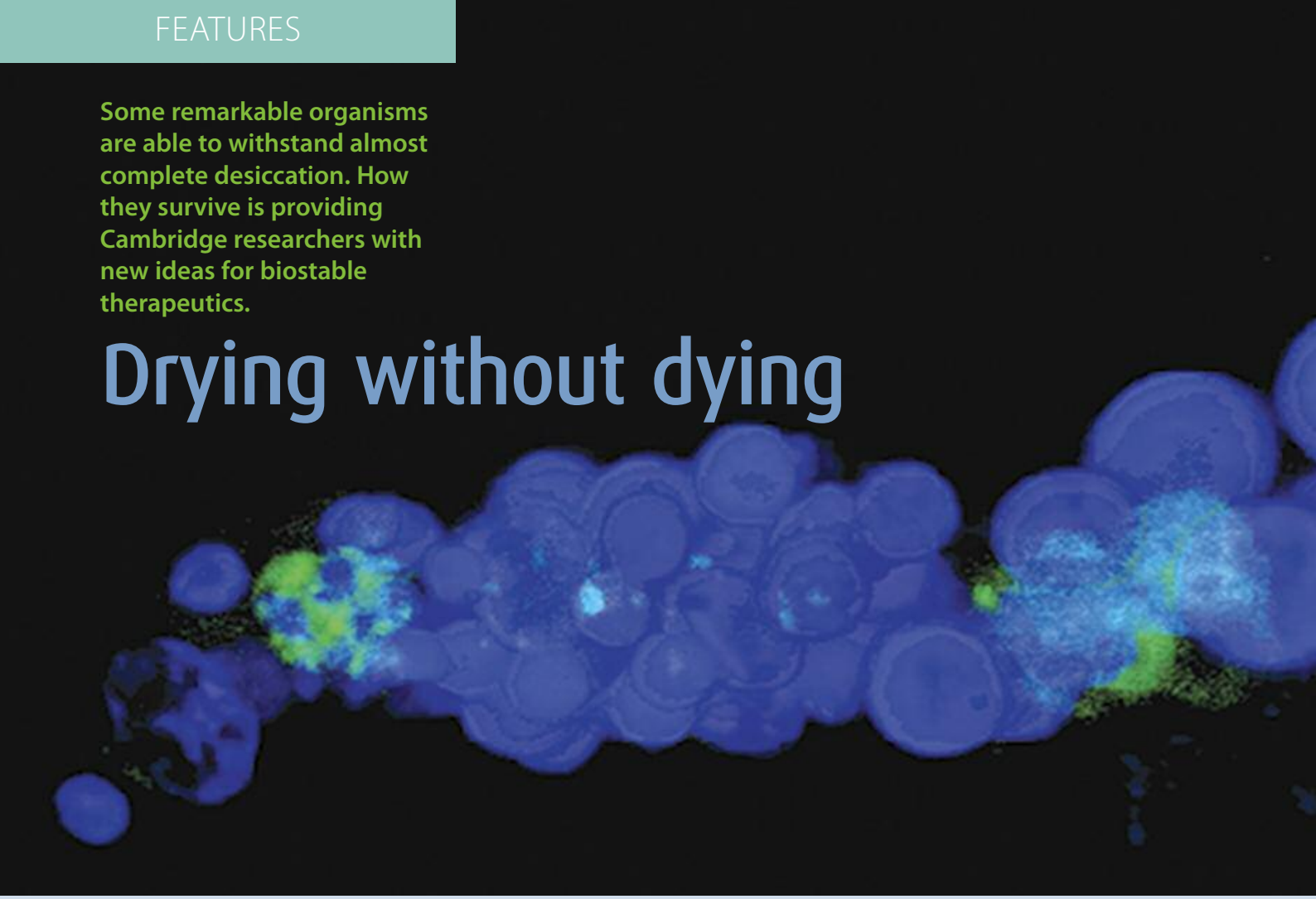
Tropical Biology Association works in partnership with African institutions to build expertise in biodiversity conservation and research (www.tropical-biology.org).

UNEP World Conservation Monitoring Centre is a branch of the United Nations that undertakes synthesis, analysis and dissemination of global biodiversity knowledge for conventions, countries, organisations and companies (www.unep-wcmc.org).

University of Cambridge core Departments involved in CCI are Zoology, Plant Sciences, Geography, Land Economy, Judge Business School and the Cambridge Programme for Sustainability Leadership (CPSL; formerly the Cambridge Programme for Industry).

Some remarkable organisms are able to withstand almost complete desiccation. How they survive is providing Cambridge researchers with new ideas for biostable therapeutics.

Drying without dying



Resurrection might seem an unpromising topic for scientific research, but there are well-characterised organisms, including some animals and plants, that are able to enter, and recover from, an apparently lifeless state. They can remain in suspended animation for long periods, perhaps for decades, but then resume their normal lives, apparently unaffected.

Life without water

Dr Alan Tunnacliffe, Reader in Biotechnology at the Department of Chemical Engineering and Biotechnology, and his research team are working on one means by which nature is able to cheat death. This is called anhydrobiosis, derived from the Greek for 'life without water', and occurs in organisms that are able to withstand almost complete desiccation.

The ability to survive extreme dehydration is remarkable for a living organism since it is widely accepted that life *is* water, and usually there is a limit beyond which further loss of water is fatal. Humans are typical in this respect, as water comprises approximately two-thirds of our body weight, and loss of just 15% of this is life threatening if not treated rapidly. Anhydrobiotic organisms, by contrast, are able to survive loss of most of their body water, which is reduced to 10% or less of body weight in the dried state. When dry, no signs of life can be detected: metabolism is completely shut down and only resumes when water is present once more.

When dry, anhydrobiotic creatures can tolerate an astonishing range of environmental stresses, including extremes of temperature and pressure: from –270˚C, which is close to absolute zero, to +150˚C, well above the boiling point of water; and from the vacuum of space to a thousand atmospheres in a pressure chamber. After this mistreatment, they can still be revived by rehydration without ill effect. It is perhaps not surprising that one proposal for how life originated on Earth is that anhydrobiotic organisms were carried through space from another planet.

Animal magic

One type of animal that can perform the anhydrobiosis trick is the bdelloid rotifer, a harmless, normally aquatic, creature that is less than a millimetre in size. Bdelloids are ubiquitous in freshwater environments throughout the world, particularly in temporary pools where the ability to survive desiccation offers a selective advantage. Dr Tunnacliffe's group is studying two different species of rotifer, one collected from a bird bath in his back garden, and the second from a billabong in Australia. They can be grown easily in the laboratory, feeding happily on bacteria or other small organic particles. They also reproduce asexually – no males have ever been found – so that large cultures can be derived from single individuals. This results in a population of genetically identical animals (a clone), and clones of many thousands of rotifers can be produced in the laboratory.

Other small animals are also able to undergo drying without dying, including some species of nematode worms, normally found in soil or on leaf litter, and thus frequently subjected to drought; these animals have also been adapted to life in the laboratory.

How do they do that?

The ready availability of large numbers of bdelloid rotifers and nematodes allows biochemical and genetic studies to be carried out that should eventually unravel the mystery of anhydrobiosis. Initial work has focused on simple sugars that are able to protect biological molecules against desiccation damage. Many of the plants that undergo anhydrobiosis, the aptly named resurrection plants, contain large quantities of sucrose – the same sugar used to sweeten tea or coffee. Researchers have discovered that another related sugar, trehalose, seems to be involved in protecting some animals and microorganisms from dehydration stress. Both sugars are thought to protect drying organisms by forming organic glasses inside cells and around sensitive molecules, trapping them in space and time.

DR CLAUDIA PINELLI

Water-loving (hydrophilic) proteins protect organisms such as this nematode during desiccation by stabilising proteins within their cells (nematode ovary shown: blue, location of DNA; green, location of hydrophilic protein)

Water-loving proteins

Other similar molecular magic tricks are sure to be discovered since bdelloid rotifers are now known from the group's research to be unable to produce trehalose. One class of molecules that offers an alternative to the 'sugar solution' to the anhydrobiosis problem is that of water-loving (hydrophilic) proteins. Recent research in the Tunnacliffe lab has discovered such proteins in bdelloid rotifers and indeed many other desiccation-tolerant organisms, including plants and microorganisms.

A major problem for proteins in a drying cell is loss of three-dimensional (3D) structure, resulting in the proteins clumping together to form aggregates, which can be toxic to the cell. Hydrophilic proteins are unusual in that they lack a defined 3D structure and seem able to protect other proteins around them, either in the test tube or a living cell, from aggregation. Further work has shown that hydrophilic proteins might also offer protection to cell membranes during desiccation, and help to prevent cells becoming leaky under stress.

Biostable medicines

An understanding of the drying-without-dying trick is not only of scientific interest but could also have important medical applications. For example, many drugs and vaccines are fragile molecules that lose their potency if not kept cool. This limits their effectiveness in many developing countries, where refrigeration is not always available. The difficulty in maintaining a 'cold chain' from point of manufacture of a medicine to its point of use has been highlighted by the World Health Organization as a major hurdle in bringing some treatments, regarded as routine in the developed world, to less-developed regions. A technology that allows medicines to be dried, conferring on them the remarkable biostability of anhydrobiosis, could be of enormous benefit, and this approach is already being used by some vaccine manufacturers.

Dr Tunnacliffe has recently received funding from the European Research Council (ERC) to take this idea a step further. Understanding how a rotifer or nematode survives drying should allow the application of what has been learned in these organisms to a mammalian cell. Such driable-but-viable cells could have applications in tissue engineering where new cell-based therapeutics are envisaged. At the moment, for example, producing an artificial pancreas capable of secreting insulin in response to high blood sugar levels as a treatment for diabetics requires the handling of fragile live cells. If these cells could be dried in a viable form, the accompanying biostability should make such artificial organs more like off-the-shelf medicines, easy to store and with a long shelf life; rehydration could be performed just prior to use. Although this scenario currently sounds like science fiction, the humble, harmless rotifer is teaching us that it might not be too far away.

Dr Alan Tunnacliffe

For more information, please contact the author Dr Alan Tunnacliffe (at10004@cam.ac.uk) at the Department of Chemical Engineering and Biotechnology.

Tracing popular beliefs from medieval to early modern times is highlighting the durability of debates about the dead.

From beyond the grave

DR CARL WATKINS/ALL SAINTS CHURCH, NORTH ST, YORK

'Death personified'; detail from a late-medieval window in All Saints Church, North St, York, depicting signs from the Book of Revelation of the end of the world

It has become something of a newspaper commonplace that men and women of the modern West share an unusual aversion to death. Where once it was subject to intimate ritual among neighbours, and kin gathered around the domestic deathbed, it is now hidden, hospitalised and a 'modern taboo'. Even less has been said about the dead themselves and their changing place in the imagination. Yet, as medieval historian Dr Carl Watkins is finding, an exploration of cultural change in attitudes to death over a long span provides a fascinating means of understanding how ordinary people relate to the dead and conceive of their fate.

Dr Watkins' research requires consideration of obvious otherworldly places – heaven, hell, the cleansing fires of purgatory, the idea of judgement at the end of time – but also the less travelled byways. How have people related to their ancestors? How have they imagined the ancient dead whose traces (from saints' bones to megalithic monuments) lie in their midst? Through tracing attitudes from the middle ages to the dawn of modernity, recorded in parish records and church archives, the research is showing that debates about the dead and patterns of thinking about their place have proved durable down the centuries.

Defining purgatory

One recurring theme is the fate of those deemed too sin-stained for immediate transit to heaven but not wicked enough for hell. The perennial problem posed by this spiritual 'middling sort' was solved by the medieval church when it gave purgatory sharp definition as the place where traces of sin might be cleansed in fire before the soul entered paradise.

Although, in the mid-16th century, Protestant reformers abolished purgatory as unscriptural, niggling questions remained about the fate of the majority. Could they really be consigned to hell's fires? Still queasy about this, some Victorian churchmen reinvented the concept: worried by a loving God who still sent some into eternal fires, they 'emptied' hell entirely by arguing that universal salvation was possible. This even led the former Prime Minister William Gladstone to fear an epidemic of social disorder if the deterrent of hell was, in effect, abolished.

But did the saved not become complacent about their blissful condition? From indications in the New Testament that the saved and damned might see each other's fate, an idea was spun out in lurid medieval visions in which the elect were briefly shown hell to redouble their own joys. Even as late as the 19th century, preachers were still drawing on the same idea, although modified for refined Victorian sensibilities: smoke from hell's fires would waft discreetly through heaven to remind its inhabitants of their blessed estate.

Back from the dead

Popular beliefs about ghosts are perhaps the most tenacious aspects of 'death culture'. Of course, deciphering these beliefs entails taking folklore seriously as a historical source. Folk stories were lovingly accumulated by collectors from the second half of the 17th century onwards, and the reactions of these learned observers can be as telling as the tales they set down. Although usually sceptical and detached, they sometimes slip in autobiographical comment on their own hopes and fears about death and the dead, and sometimes betray how stories in which they are immersed then infiltrated and shaped their own beliefs.

What this research is beginning to suggest is that many beliefs about the dead and debates about their fate were perennial ones, transcending some of the great cultural and religious changes wrought in the medieval and early modern worlds.

Dr Carl Watkins

For more information, please contact the author Dr Carl Watkins (csw14@cam.ac.uk) at the Faculty of History.

Tales of Vikings and Irish, clerics and kings

Máire Ní Mhaonaigh is unravelling legends within gems of literature surviving from medieval Ireland.

Nestling in the westernmost corner of Western Europe ('next stop America'), Ireland is often seen as part of a Celtic fringe. Yet, in medieval times, it formed a major intellectual hub, and the wealth of documents that have survived from the period in vellum manuscripts cast light not just on Ireland's own sophisticated civilisation but on developments in Europe as well.

Unlike clerical counterparts in other places, Irish monks wrote in Latin but also composed copiously in their own language from the 6th and 7th centuries AD onwards, making Old Irish the first vernacular to have achieved literary status. Among their various works are secular narratives dealing with themes as diverse as kingship and kinship, heroism and love. These serve as the most insightful of social commentary, illuminating how society functioned and depicting people's most pressing concerns.

Medieval spin doctors

Literature is not history, of course, and unravelling the layers of complex texts is often a forensic affair. With recent funding from the Alexander von Humboldt Foundation, Dr Máire Ní Mhaonaigh's research is concerned with disentangling earlier texts copied over centuries and surviving in manuscripts of the 12th century and later. The reproduction of texts provided ample opportunity for enterprising scribes – the spin doctors of their own time – to put their own subjective slant on events, producing skilful propaganda glorifying their own masters and putting their own issues centre stage. Discerning these biases enables us to evaluate their writing and use it to understand the machinations of life in the authors' own day.

Mythologising history

In the case of stories concerning real figures, historical sources can provide a measuring stick to determine the degree of mythologisation that has taken place. One particularly powerful ruler, Brian Boru, who died at a ripe old age in battle in 1014, emerges as a wily politician and skilful military campaigner from a reading of contemporary chronicles. Literary works in Irish and in Norse tell a different, much augmented tale, depicting him as conqueror of irrepressible Vikings, a veritable saviour of his own people. It was in his descendants' interest to peddle this positive image; having a glorious ancestor meant that they too might be deemed great. In the 12th century, Brian's great-grandson, Muirchertach, who proudly bore his forefather's name Ua Briain ('descendant of Brian') as a surname, commissioned a literary biography of his family hero. *Cogadh Gáedhel re Gallaibh* (The Viking–Irish War) served as a reminder to potential opponents of what Uí Briain (O'Briens) were made.

Church and 'State'

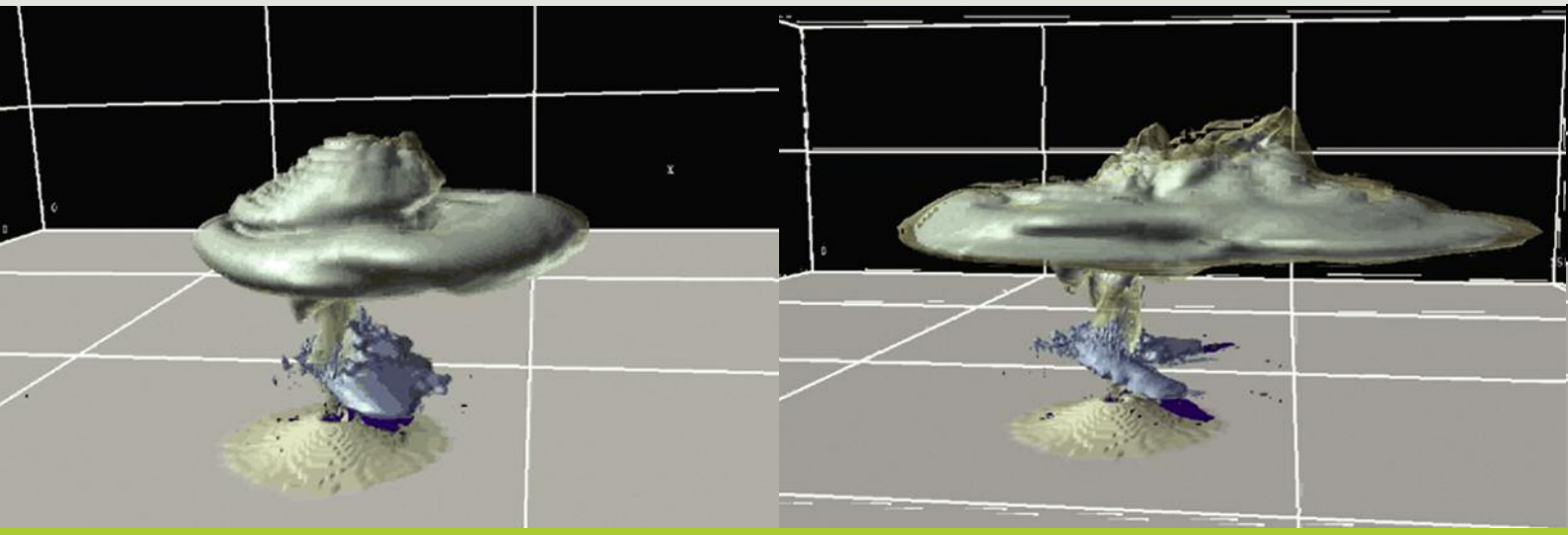
Muirchertach was a powerful patron of church reform and his clerical companions bolstered his political ambition by producing useful documents like *Cogadh* in return. Such constructive cooperation had for centuries ensured that various facets of the life of Ireland's ruling elite were recorded either as 'facts' or in literary form, providing an unrivalled picture of the upper echelons of a society which constituted part of the European norm.

This fruitful fusion was not to continue, and the large 12th-century codex, the *Book of Leinster*, in which the *Cogadh* is preserved, may have been one of the last such compilations to have been produced in an ecclesiastical embrace. Nonetheless, the 600 years or more of intense intellectual involvement between clerics and royalty in Ireland offers an unparalleled glimpse of this remarkable time.

Opening page of the text *Cogadh Gáedhel re Gallaibh* from the *Book of Leinster* (Trinity College Dublin, MS 1339, p. 309a)

Dr Máire Ní Mhaonaigh

For more information, please contact the author Dr Máire Ní Mhaonaigh (mnm21@cam.ac.uk) at the Department of Anglo-Saxon, Norse and Celtic.
Dr Ní Mhaonaigh's book *Brian Boru: Ireland's Greatest King*? was published by Tempus in 2007.



New understanding of the physics of clouds is helping to model both climate change and the impact of volcanic eruptions and wild fires.

Unclouding uncertainty in climate modelling

Our climate is the net result of many complex processes that transfer and redistribute the Sun's energy through the Earth's atmosphere, oceans, land and ecosystems. Because these processes are basically nonlinear, their interaction unavoidably leads to chaotic variability of climate and weather on various time scales, and we rely on climate models to achieve some sense of the dynamics of weather and to predict future climate. Currently, one of the greatest sources of uncertainty in climate modelling is posed by clouds, which are not resolved individually but instead are averaged. Professor Hans-F. Graf's group, based in the Department of Geography and part of the Centre for Atmospheric Science (see panel), is developing a new technique for global and regional climate modelling that moves beyond treating clouds as 'one-size-fits-all'.

Cloudy issues

Climate models consist of a set of coupled differential equations based on first principles of physics that are solved numerically by dividing the planet into a three-dimensional grid. Available computer power dictates that each grid is typically 100–300 km in size. Unfortunately, any processes that are smaller cannot be explicitly resolved and have to be 'parameterised' as an average. Among these are clouds: the standard approach has been to create an average cloud that has to mimic all the effects of the cloud spectrum of different-sized convective clouds. Of course, in nature, the cloud spectrum is highly variable depending on the actual weather situation and location, and clouds can range from a few hundred metres to a few kilometres in scale.

Clouds are extremely important for realistic model simulations since they are the ultimate drivers of the global atmospheric circulation. Water vapour carrying latent heat is transported upwards by convection or in large weather systems (fronts), where it cools and eventually forms clouds; precipitation as rain then releases the latent heat. This convection is strongest in the tropics, where the vapour-laden trade winds from both hemispheres converge, forming deep, rain-producing convective clouds. It is here that the atmosphere receives the energy that drives the whole global circulation.

Clouds are also highly relevant to changes in climate that result from human activities. Changes in land use affect reflectivity and evaporation from soil and vegetation, and hence the transfer of energy to the atmosphere; fossil fuel burning and industrial processes increase aerosols that reflect sunlight or absorb solar and terrestrial radiation. Both land use change and aerosols have an effect on cloudiness and precipitation at both the local and the micro scale.

Predator–prey

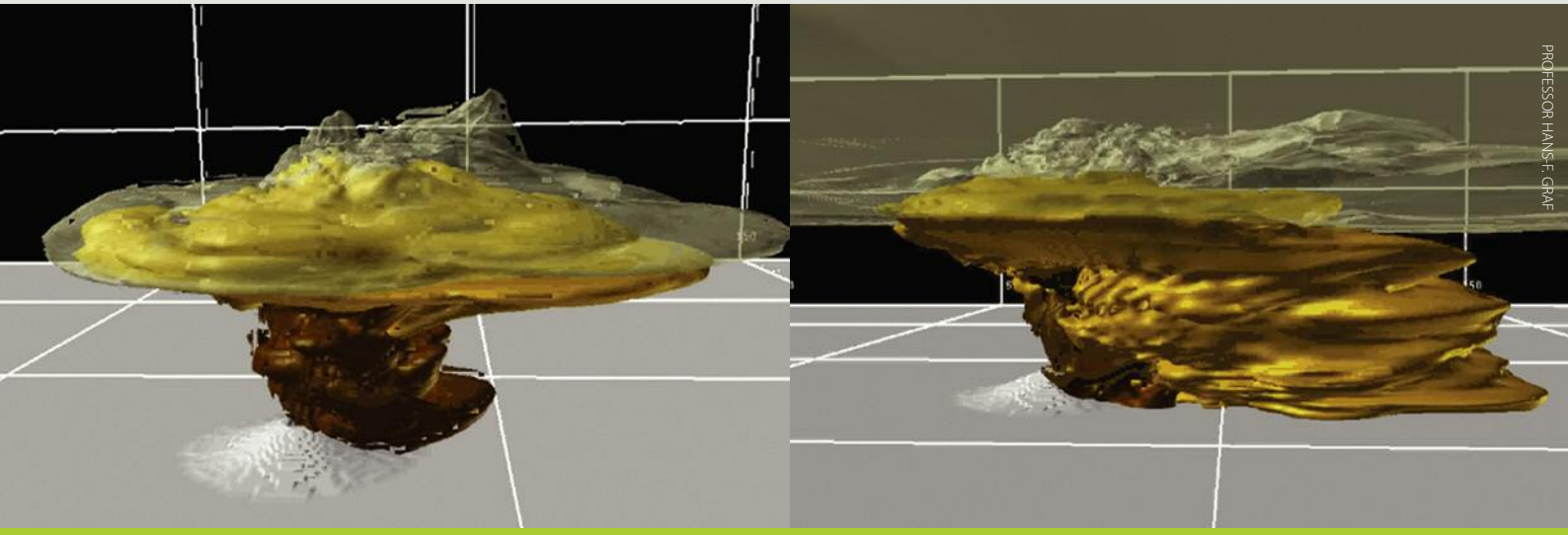
The innovative approach adopted by Professor Graf's group has been to simulate the behaviour and microphysics of convective clouds using a concept more familiar within population dynamics: they treat clouds as individuals that compete for food.

This technique allows the separation of individual clouds from a larger set of clouds that can potentially evolve under a given weather situation (that is, at a specific time and in a specific grid cell of the model). The system is based on the solution of a set of Lotka–Volterra-type differential equations, also known as predator–prey equations from their use for describing biological systems: the clouds (the 'predators') have a limited 'food' supply of convective available potential energy (the 'prey', this being the amount of energy available for convection), for which clouds of different characteristics (size, depth) are competing.

By capturing the variations of cloud spectra in a statistical sense, cloud microphysics can be treated explicitly and it is now possible to determine in-cloud vertical velocities, interactions with aerosols, convective transport, rainfall intensity and radiation effects.

Forest fires and volcanic ash

The team has been focusing on a variety of different types of cloud – most notably the effects of smoke on clouds and precipitation over Amazonia and Indonesia. Initially funded by the European Union, the project is now contributing to the Danum-OP3 consortium that spans eight UK institutions and is funded by the Natural Environment Research Council (NERC) to investigate the effects of the replacement of pristine rain forest by oil palm plantations in northern Borneo. Recently published data show how the smoke from the extreme peat fires that plagued Indonesia and surrounding countries for months during 1997–8 reduced the amounts of rainfall in the area. The reduced rainfall, in turn, increased the residence time of the smoke particles in the atmosphere, thus aggravating the situation.



PROFESSOR HANS-F. GRAF

ATHAM can be used to predict whether ice is formed within a volcanic plume; here, rainwater (dark blue), cloud water (light blue) and ice (grey) are modelled in the images to the left; and particles of ash (large, dark brown; coarse, light brown; fine, grey) are modelled in the images to the right

A second focus has been the development and application of the Active Tracer High-resolution Atmospheric Model (ATHAM). The development of this high-resolving model started immediately after the eruption of the Mount Pinatubo volcano on the Philippines in the early 1990s, when Professor Graf was at the Max Planck Institute for Meteorology in Hamburg. The model simulates convective plumes at resolutions down to a few tens of metres and was initially used to understand the dynamic, microphysical and chemical processes within volcanic eruption plumes. An important question was whether these vigorous convective systems could effectively transport magmatic halogen compounds into the stratosphere, where they could harm the ozone layer. The model has also been used successfully to simulate big fire storms induced by wild fires, and the results have proved that pollutants from these fires are introduced into the lower stratosphere.

Further applications of ATHAM are under current investigation by Dr Michael Herzog in Professor Graf's group, particularly in relation to aviation safety. Fine silicate ash from volcanic eruptions poses a severe risk for aeroplanes. Although ash clouds can be detected by satellite monitoring, they are often obscured by ice particles residing above the ash, and ATHAM can be used to predict whether ice is formed within a volcanic plume. Further plans with ATHAM are ongoing with support from a joint Chinese–German research project that will study the effects on weather and climate in Southeast Asia resulting from the dramatic changes of land use and ecology on the Tibetan plateau during the past 60 years.

'In many climate models... cloud feedbacks remain the largest source of uncertainty.'
Report by the Intergovernmental Panel on Climate Change, 2007

Professor Hans-F. Graf

For more information, please contact the author Professor Hans-F. Graf (hans.graf@geog.cam.ac.uk) at the Department of Geography.

Centre for Atmospheric Science

The Centre for Atmospheric Science is one of the premier groups in the UK for atmospheric studies. It encompasses research in three departments:

- **Department of Chemistry:** Numerical modelling of tropospheric and stratospheric chemistry/climate (Professor John Pyle), instruments and measurements (Professor Rod Jones), measurements of gas kinetics (Dr Tony Cox) and studies of atmospheric aerosols (Dr Markus Kalberer).
- **Department of Applied Mathematics and Theoretical Physics:** Investigation of fundamental aspects of atmospheric dynamics and physical processes (Professors Peter Haynes and Michael McIntyre).
- **Department of Geography:** Research on convection, modelling plumes and stratospheric dynamics (Professor Hans-F. Graf and Dr Michael Herzog).

The Centre is co-directed by Professor John Pyle and Professor Peter Haynes.

For more information, please contact Professor Peter Haynes (P.H.Haynes@damtp.cam.ac.uk) or visit www.atm.ch.cam.ac.uk

Cancer Research UK is the world's leading independent charity dedicated to cancer research, spending around £300 million a year on world-class research to beat cancer. In November 2008, the charity launched a five-year plan to focus research on core areas of science that will have the greatest impact on reducing cancer deaths, with an emphasis on cancers that have poor survival rates.

CANCER RESEARCH UK

Formed in 2002 by the amalgamation of the two largest UK cancer charities – the Cancer Research Campaign and the Imperial Cancer Research Fund – Cancer Research UK continues a century-long history of funding cancer research. Its annual research budget funds the work of over 4500 scientists, doctors and nurses across the UK, including research at a number of specialised institutes and centres. The most recent of the core-funded institutes, the **Cambridge Research Institute** (CRI; see panel), is a flagship research enterprise located on the Cambridge Biomedical Campus.

In 2007–8, Cancer Research UK spent just over £31.5 million on laboratory research and clinical trials in Cambridge; around £17.5 million of this annual research spend provided core funding for the CRI.

Funding by Cancer Research UK covers all aspects of cancer research, from understanding fundamental cancer cell biology to large epidemiology studies across entire populations of people, as well as training the next generation of research scientists. Some examples in Cambridge include:

- Several programme grants and a significant element of core funding to the **Wellcome Trust/Cancer Research UK Gurdon Institute**, where research is helping to uncover what goes wrong when a cell becomes cancerous, by investigating the processes that ensure that cells function correctly during normal development.
- Funding the two UK arms of the largest study of diet and health ever undertaken – the **European Prospective Investigation into Cancer and Nutrition (EPIC)** – a long-term study of more than half a million people in 10 European countries. The University of Cambridge manages the Norfolk arm of EPIC, which has recruited more than 30,000 people.
- Scientists at the **Strangeways Research Laboratory** and **Department of Oncology**, who are searching for genes that increase cancer risk and investigating how the effects of the genes combine with lifestyle factors to cause cancer.
- **Cancer Research UK PhD Training Programme in Medicinal Chemistry** (see panel), a collaborative initiative that brings together research groups with expertise in synthesis chemistry, pharmacology, biochemistry and cancer biology to train synthesis chemists to PhD level.

For more information, please visit www.cancerresearchuk.org

Linking the laboratory to the cancer clinic

The Cambridge Research Institute (CRI) is driving the development of new approaches for the early detection, prevention and treatment of cancer.

The CRI is the most recent of five comprehensive research institutes core funded by Cancer Research UK. Housed in the magnificent, custom-built, £50 million Li Ka Shing Centre, the Institute is located on the Cambridge Biomedical Campus. With more than 250 scientists in 19 research groups, it is one of the largest cancer research facilities in Europe.

Officially opened in early 2007, the Institute is already internationally acclaimed for the high calibre of its research. 'We've been able to hit the ground running,' said Director Professor Sir Bruce Ponder, 'and this is largely because the funding we receive from Cancer Research UK means that we can guarantee salary, staff, laboratory space and core facilities, so the individuals we recruit have minimal interruption to research as they set up their laboratories.'

Group leaders have been carefully chosen with complementary research interests in mind – roughly half are engaged in the study of fundamental aspects of cancer cell biology and half in technology-based or clinical-based research; over a third are clinically qualified. Many of the group leaders hold joint appointments with the Hospital, the University (seven within the Department of Oncology) or research institutes on the Cambridge Biomedical Campus. CRI's location on the Campus offers outstanding opportunities for such interaction because of its proximity to the Cambridge University Hospitals NHS Foundation Trust (Addenbrooke's), the University School of Clinical Medicine and its associated institutes, and the Medical Research Council (MRC) Laboratory of Molecular Biology and four MRC Units.

All of these interactions are crucial to the success of the Institute, as Professor Ponder (who is also Head of the Department of Oncology) explained: 'It's no good creating a freestanding institute that's got a 'moat' around it – we work hard to be fully connected with Cambridge's research environment and the Hospital, both to expand our intellectual base and to ensure that laboratory advances are translated into benefits to cancer patients as quickly as possible. The joint appointments really make these interactions work, and is another reason we've been able to get off the ground so quickly.'

KEITH HEPPELL

Recent research highlights include the discovery of precisely why some women develop resistance to the breast cancer drug tamoxifen. Dr Jason Carroll, who leads the Nuclear Receptor Transcription Laboratory, explained: 'We knew that women developed resistance to tamoxifen but previously our understanding of why this occurred could be compared with trying to fix a broken car without knowing how the engine worked. Now we understand how all the engine parts operate and we can try to think about ways to make repairs.'

Professor Kevin Brindle, who leads the Molecular Imaging Laboratory, has developed a way of scanning the body using magnetic resonance imaging to a level of precision that could be used to detect cancer earlier, as well as for the evaluation and design of novel cancer therapies. Dr David Tuveson has set up a facility in the clinic for treating patients with pancreatic cancer and a matching experimental system in the laboratory to test and refine potential new treatments.

To strengthen cancer research collaborations across Cambridge, a virtual community has arisen with the CRI as its nucleus. The Cambridge Cancer Centre (CCC) forges links between cancer researchers in the biological and physical sciences, clinicians and local biotech companies. 'CCC creates an environment in which basic research can have a practical application, collaborative projects can be developed, and new interdisciplinary work can be pump-primed,' said Professor Ponder, who chairs the CCC Steering Committee. 'We're now moving into a new phase with the CCC in which we're identifying collaborative research themes and developing the organisational structures that will help to drive them forward.'

What happens next at the CRI? Research at the Institute will bed down and integrated programmes will continue to develop. The top floor of the Institute is being kept in reserve. 'In a few years' time,' said Professor Ponder, 'the science at the Institute will have matured to the point where we will be able to make intelligent choices about what we need to add. My colleagues and I believe that we have something really special at the CRI, and I'm delighted to say that the funders and local community share our enthusiasm.'

SHAUN NEAVES

Professor Sir Bruce Ponder

For more information, please visit www.cambridgecancer.org.uk and www.cancer.cam.ac.uk

Training chemists to identify cancer targets

Rigorous interdisciplinarity lies at the heart of a graduate programme to train the next generation of synthetic chemists.

The Cancer Research UK PhD Training Programme in Medicinal Chemistry has been in operation in Cambridge since 2006. To date, 12 PhD students have embarked on training that exposes them to over 30 world-class research groups from 11 departments with facilities in synthesis chemistry, pharmacology, biochemistry and cancer biology. A further eight will join the Programme over the next two years.

In the first nine months of the Programme, first-year students are brought up to speed in cancer-focused research by a combination of PhD-level laboratory rotations, taught courses and hot topics. As they move into their second year, students settle into their chosen three-year PhD project with a primary chemistry supervisor and other supervisors from the biology sectors.

Dr Rebecca Myers, who coordinates the Programme from the Department of Chemistry, described how it broadens the mind: 'The new students are incredibly enthusiastic about the lab rotations and the challenges they present. They often arrive with well-defined ideas on what aspect of cancer-related medicinal chemistry they would ultimately like to research. Yet this typically transforms as the students come to see the breadth of cancer research ongoing in the University and how chemistry can interface with it.'

Programme Director Professor Shankar Balasubramanian (Herchel Smith Professor of Medicinal Chemistry in the School of Clinical Medicine and the Department of Chemistry) explained the importance of this interdisciplinary training: 'Through providing practical and intellectual experience of cancer biology to early career synthetic chemists, the Programme is putting in place the tools that will help them identify appropriate cancer targets for drugs of the future.'

Symposium day for the current students

For more information, please contact Dr Rebecca Myers (rmm32@cam.ac.uk) or visit www-medchem.ch.cam.ac.uk

Professor David MacKay

Internationally known for his work on information theory, machine learning and novel forms of communication, Professor David MacKay has devoted much of his time recently to public teaching about energy. His well-received book *Sustainable Energy – Without the Hot Air* was published in December 2008.


DR DAVID STERN

Whether he's developing a means of communicating in any language with any muscle, debunking energy myths by establishing how the numbers add up, or analysing the fractal Fibonacci spirals of a cauliflower and the internal workings of his Psion organiser, David MacKay, Professor of Natural Philosophy at the Department of Physics Cavendish Laboratory, has an extraordinary diversity of interests.

For the past decade, one of his principal research projects has been Dasher, a machine-learning system that allows individuals to write without a keyboard. The user creates sentences by navigating through letters in a continually unfurling alphabetical display, effectively navigating in the library that contains 'all conceivable books'. Navigation can be controlled by any muscular movement, even breathing or just gazing, while the software consults an archive of training text to predict what the user might write next. Dasher is available as open-source software free to anyone wishing to use it.

David MacKay's research group is also developing Opengazer, free software that can use the images from an ordinary webcam to estimate the direction of your gaze. Funding has recently been granted from the European Union as part of AEGIS, a worldwide consortium led by Sun Microsystems to build accessibility support into the next generation of rich internet applications and mobile devices. Combined with Dasher, the aim of Opengazer is literally to allow users to write with their eyes.

Sustainable Energy – Without the Hot Air, David MacKay's contribution to the energy debate, was driven, as he explained, 'by outrage at inaccurate statements made about sustainable energy, together with embarrassment that I didn't know the numbers myself.' The resulting book provides a straight-talking, honest look at the figures: Can we live on renewables? What are the reasonable options for producing energy? How can we make a *big* difference to reducing our demand? 'By helping people understand just how big the energy challenge is,' he explained, 'I hope to promote constructive conversations about energy, instead of the perpetual Punch and Judy show of anti-wind and anti-nuclear. We need a plan that adds up.'

What would others be surprised to learn about you?
I love and cherish my 15-year-old Psion 3A Personal Digital Assistant. I have at least five of the same model and when they break down I take them apart and carry out surgery to fix them. I've also twice played in the World Ultimate Frisbee Championships (we lost) and the temperature of my home is usually 13˚C in winter, although perhaps this isn't surprising about me, as turning down your central-heating thermostat is one of the best energy-saving things you can do.

Have you ever had a Eureka moment?
My Eureka moment was realising that you could take an existing data compression idea called arithmetic coding, turn it on its head by visualising it on a computer screen, and achieve the goal of helping someone to communicate using a single muscle.

What's the best piece of advice you've ever been given?
'Friends come and go, enemies only accumulate.' I'm not sure how good I've been at following this advice but I'm hoping that I'm improving with age.

What motivates you to go to work each day?
My main motivation is to understand things. The reason I love this job is I'm free to work on anything I want to. I can choose fun things, often serendipitously. Dasher resulted from a random conversation on a bus with a colleague who was mocking the size of the keyboard on my Psion; we brainstormed on how we could come up with a communication solution that doesn't assume writing is about pushing buttons or using a pen. By the end of the bus journey, we'd named Dasher (for its effortless speed) and I'd started writing the first prototype.

What is your favourite research tool?
It has to be Google. For all my recent work on energy I've learned so much useful and authoritative stuff in a fast and efficient way using this search engine.

What will the future look like in 2050?
One possible future is that we'll have lots of green, energy-efficient systems. But another possible future is a world of energy wars over the diminishing fossil fuel resources. Realistically, I don't think we can rely on inventions still to come; the responsible thing is to imagine that today's technology is what we've got to work with. If we go for strong energy efficiency measures and a really big building programme of green energy systems then it will be possible to carry on a lifestyle similar to today's. It's possible but it's not going to be easy.

FORTHCOMING EVENTS: SAVE THE DATES!

5–10 July 2009

The Darwin 2009 Festival
Cambridge

The Darwin 2009 Festival is an anthology of the science, society, literature, history, philosophy, theology, art and music arising from the writings, life and times of Charles Darwin. Speakers include Richard Dawkins, Steve Jones, Ruth Padel, Ian McEwan and Dame Gillian Beer. As part of the wider Festival, Cambridge's museums, galleries and other venues will be running programmes of music, drama, film and tours, which will explore the past, present and future of the natural world in the light of evolutionary understanding. Please visit www.darwin2009.cam.ac.uk for full details of events and to book tickets.

Other Darwin-related exhibitions in Cambridge this year include:

Beetles, Finches and Barnacles
University Museum of Zoology
A permanent exhibition on how Darwin's experiences in zoology shaped his ideas on evolution and natural selection, using many of the specimens he collected throughout his life, especially during the *Beagle* voyage.
www.zoo.cam.ac.uk/museum

Carnivores: plants that bite back and other Darwin discoveries
Cambridge University Botanic Garden
A permanent display exploring the diversity of trap mechanisms, from the springs of the Venus Fly Trap to the sticky glue of the Sundews, and examining some of Darwin's breakthrough experiments.
www.botanic.cam.ac.uk

Endless Forms: Charles Darwin, natural science and the visual arts
The Fitzwilliam Museum, 16 June–4 October 2009
A major exhibition exploring the influence of Darwin's discoveries on 19th-century artists and their work, featuring nearly 200 exhibits from over 100 institutions worldwide.
www.darwinendlessforms.org

Darwin the Geologist
Sedgwick Museum, from 7 July 2009
A permanent exhibition telling the story of the rock specimens that Darwin collected on the *Beagle* voyage and how he analysed and used them in his early scientific work as a geologist.
www.sedgwickmuseum.org/exhibits/darwin.html

A Voyage Round the World: Charles Darwin and the *Beagle* collections in the University of Cambridge
Cambridge University Library, 7 July–23 December 2009
An exploration of the *Beagle* voyage as a pivotal experience in Darwin's life, using Darwin's manuscripts and specimens from the University's collections.
www.lib.cam.ac.uk

1 October 2009

Horizon Seminar 'Energy & Environment'
Centre for Mathematical Sciences, Cambridge

There is an imperative need for a shift in society's approach to climate change and energy if the risk of serious social, environmental or economic harm is to be limited. This Horizon Seminar will highlight the need for the key infrastructure components of energy, water, waste and mobility to work together, as well as the importance of moving from short-term decision making to long-term sustainable growth. Horizon Seminars are organised by Research Services Division. Please visit www.rsd.cam.ac.uk/events/horizon/ or email horizon@rsd.cam.ac.uk for further information.

Your way into Cambridge

Research Horizons is produced by the University of Cambridge Research Services Division, 16 Mill Lane, Cambridge, CB2 1SB.

If you would like information on research funding or working with the University, please contact:
Research Services Division
Tel: +44 (0)1223 333543; Email: rsd.enquiries@rsd.cam.ac.uk
www.rsd.cam.ac.uk

If you would like information on commercialisation of University intellectual property, please contact:
Cambridge Enterprise Limited
Tel: +44 (0)1223 760339; Email: enquiries@enterprise.cam.ac.uk
www.enterprise.cam.ac.uk

If you have an enquiry relating to the magazine, please contact:
Dr Louise Walsh, Research Horizons Editor
Tel: +44 (0)1223 765443; Email: research.horizons@rsd.cam.ac.uk
www.research-horizons.cam.ac.uk

If you have a more general media enquiry, please contact:
The Office of Communications
Tel: +44 (0)1223 332300; Email: communications@admin.cam.ac.uk
www.cam.ac.uk

Are there areas of research that you would like to see covered in Research Horizons? We welcome suggestions, feedback and comments: please send ideas to the Editor at research.horizons@rsd.cam.ac.uk