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re: search

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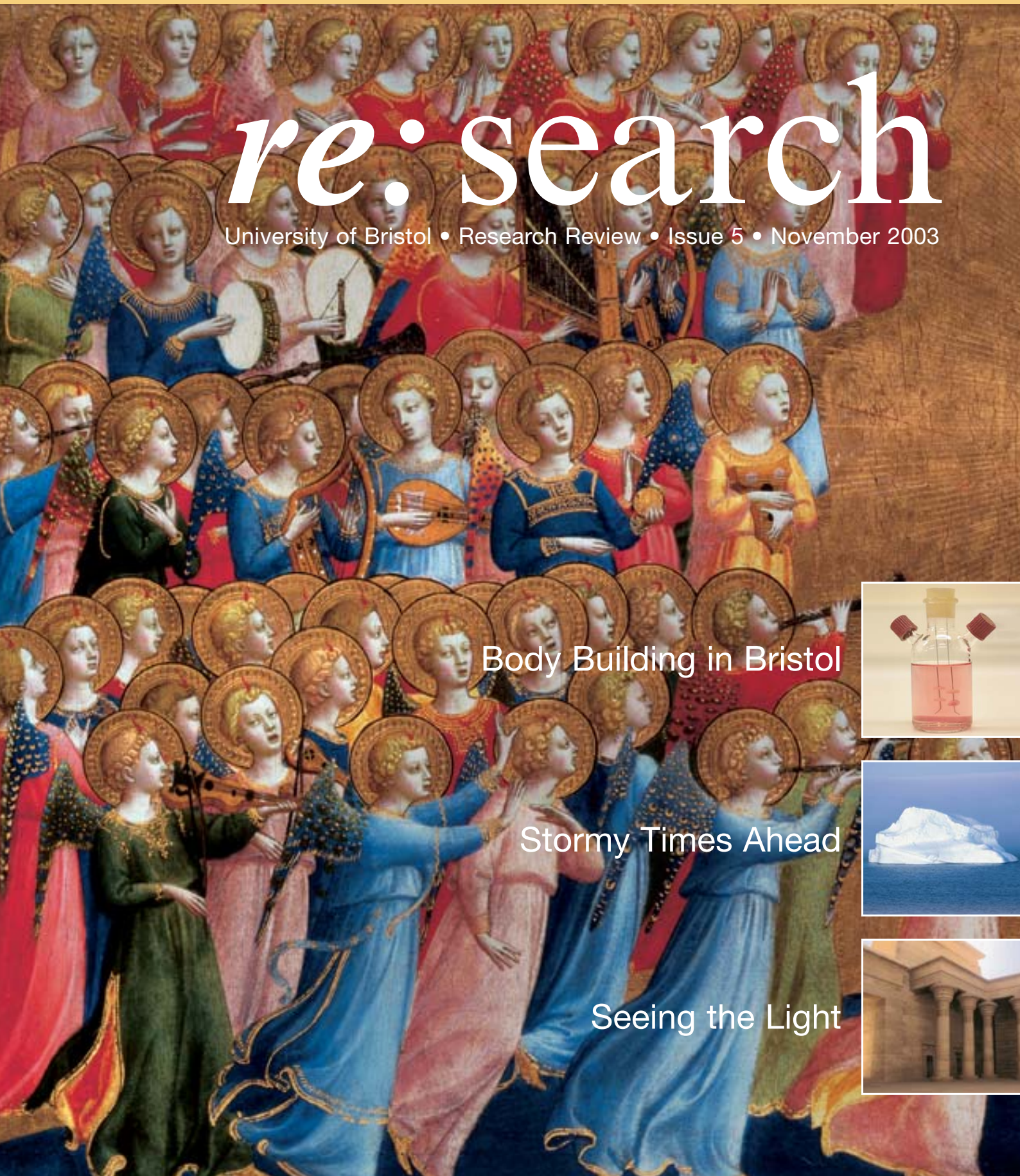

Body Building in Bristol

Stormy Times Ahead

Seeing the Light

re: search

Research and Enterprise

With increasing competition for funds and divergent demands from the various funders of research and other university activities, universities throughout the UK are facing a time of challenge and change. In response to these challenges, the University of Bristol has clearly stated its vision for research in its Research Strategy, outlined in the last issue of re:search. An exciting aspect of this vision is the formal recognition that, whilst fundamental research remains the corner stone of the research base, the University will also develop a portfolio of activities deriving from and supporting its fundamental research.

In practical terms this means that enterprise, in the broadest interpretation, will be integrated into our core activities of teaching and discovery so that knowledge exploitation, technology transfer and enterprise are embedded in all University activities. This joint agenda of research and enterprise will be managed strategically by the University Research Committee, whose membership includes recently appointed Faculty Research Directors. It will be fully supported by the division of Research and Enterprise Development.

This approach will enhance our fundamental research base and is also a vital component in ensuring that the University of Bristol is a key player in the knowledge-driven economy, producing tangible benefits from its research for both the University and the community at large.

Dr Siân Thomas
Director of Research and Enterprise Development

Front and back cover image:
Fra Angelico's 'Christ Glorified in the Court of Heaven'.

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pre: view

Body Building in Bristol

As the population ages, the concept of 'regenerative' medicine is becoming recognised as an important new approach to solving many of our long-term healthcare needs. ***Anthony Hollander***, Professor of Rheumatology and Tissue Engineering in the Division of Medicine, describes some of the advances being made towards this brave new world.

Bristol has a long tradition of engineering. Brunel led the way in the 19th century with his construction of such wonders as the Great Western Railway, the Clifton Suspension Bridge and the SS *Great Britain*. In the 20th century the aerospace industry literally took off in Bristol, with the design and construction of Concorde as its flagship. At the start of the 21st century we have a new engineering goal: the construction of tissues and organs. It is part of a new programme of regenerative medicine that will ultimately revolutionise healthcare.

The aim of regenerative medicine is to restore normal function to organs and tissues that do not function properly as a result of disease, traumatic injury or birth defects. This can be achieved using a range of therapeutic approaches that primarily include stem cells, tissue engineering and gene therapy.

Our rapidly expanding knowledge of the cellular basis of disease, and the genes that might make individuals particularly susceptible, will give us ample opportunity to reverse the processes of tissue destruction. Since the world's ageing population will increasingly present healthcare organisations with an unprecedented demand for solutions to the failure of tissues and organs late in life, the time is now right for regenerative medicine to be developed and exploited clinically and commercially.

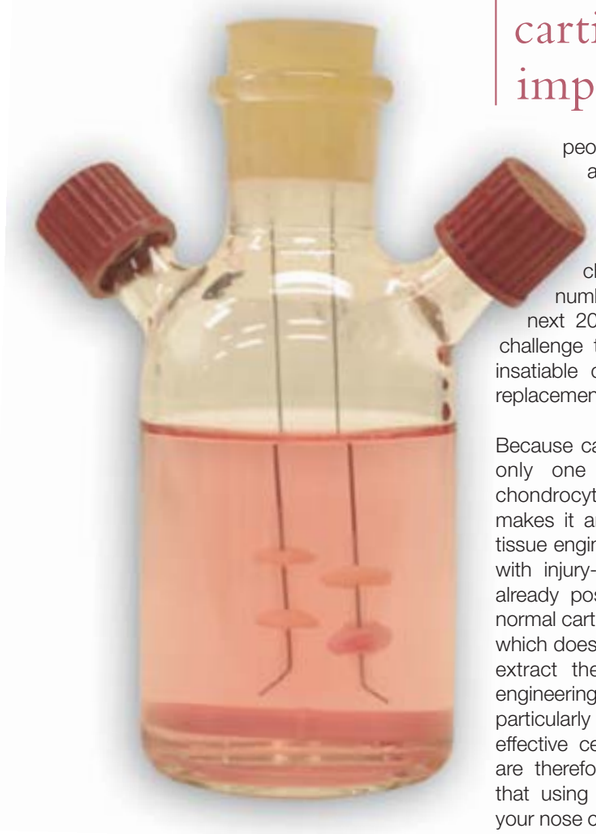
> The ageing population will present healthcare organisations with unprecedented demands

In the three- to five-day-old embryo, a small group of about 30 cells 'differentiate' into the hundreds of highly specialised cells needed to make up an adult organism. However, a small number of undifferentiated 'stem cells' persist in some tissue, such as bone marrow. The human body has over 200 different kinds of these specialised cells that help maintain the function of the particular tissue or organ in which they are found, but in order for the body to function normally, these cells must be continuously replaced when they die. Stem cells, on the other hand, have the unique property of almost indefinite self-renewal. They are the Peter Pan of the cellular world, although they can be persuaded to 'grow up' if they are exposed to the right biological signals.

As we get older mature cells become less good at doing their job and are often rather poor at generating tissue. We can get around this problem by obtaining stem cells and giving them the right signals to grow into the particular kind of mature cell that we need.

To grow and use an engineered tissue you need to start with the best available cells, put them onto a scaffold material that will help to guide their growth, → and then find a way of implanting the constructed tissue into the body. Mature cells taken from a tissue biopsy must be increased to a much larger number, seeded onto a scaffold material and grown in a bioreactor that provides gentle movement as the new tissue forms. This movement is essential to ensure that nourishment reaches the very centre of the growing tissue.

Gene therapy is the introduction of new genes into the body in place of faulty ones and is likely to be of most benefit for patients with inherited disorders resulting from a single gene. However, we can also put new genes into cells that are going to be used for tissue engineering. By using a genetic switching mechanism it is possible to turn on the gene while the tissue is growing in the laboratory and then switch it off before the engineered product is implanted into the body.



A simple bioreactor containing early-stage tissue-engineered cartilage

Osteoarthritis provides an excellent example of why regenerative medicine must become an essential therapeutic tool and how stem cells, tissue engineering and gene therapy will be used together. Osteoarthritis is predominantly an ageing disease. It develops when cartilage, the shock-absorbing protective tissue found wherever bone meets bone, becomes damaged and erodes away, and the underlying bone becomes thicker. By the time you are 65 there is a 50 per cent chance that you will have damage associated with osteoarthritis. This translates into almost eight million people in the UK with osteoarthritic joints, a million of which are severe enough to require specialist health care. Demographic changes suggest that these numbers will double over the next 20 years, presenting a huge challenge to the NHS in meeting an insatiable demand for hip and knee replacements.

> By the time you are 65 there is a 50 per cent chance you will have damage associated with osteoarthritis

Because cartilage is unusual in having only one single cell type – the chondrocyte – its relative simplicity makes it an ideal target for repair by tissue engineering. For younger people with injury-induced osteoarthritis it is already possible to take a biopsy of normal cartilage from a part of the knee which does not carry much weight and extract the chondrocytes for tissue engineering. In Bristol however, we are particularly interested in finding more effective cells for cartilage repair. We are therefore exploring the possibility that using cells from the cartilage in your nose could be an improved way to grow tissue that will be implanted into your knee.

But for older people with osteoarthritis the mature chondrocytes often do not function well enough for tissue engineering. For these patients, taking adult stem cells and turning them into fresh, young chondrocytes may be the best answer. Consequently, we are developing new ways of extracting the rare stem cells found in bone marrow and turning them into mature cells. We may need to use specifically designed drugs or introduce new genes to influence the way in which the stem cells grow in the laboratory.

> Tissue cells grown from the cartilage in your nose could be implanted into your knee

Stem cells, gene therapy and tissue engineering, the three mainstays of regenerative medicine, will offer us the opportunity to help patients with all sorts of chronic disease that we once thought untreatable. Diabetes, multiple-sclerosis and kidney disease are all potential targets. Our challenge now is to persuade industry and government to invest fully in this exciting area of research and to inform the public about our ideas so that they are not fearful of this brave new world, but embrace it with open arms. ■

www.bris.ac.uk/Depts/DivMed

This work was supported by grants from the Arthritis Research Campaign (ARC), the European Union and the Biotechnology and Biological Sciences Research Council. Professor Hollander's Chair of Rheumatology and Tissue Engineering is funded by an endowment from ARC.

Stormy Times Ahead?

Dr ***Jonathan Bamber***, senior lecturer in the School for Geographical Sciences, is the lead investigator on a multi-institute project aimed at investigating how changes to the ice cover in the Arctic may affect the future climate of north-west Europe. Could it be the storehouse for major climate changes over the next century?

We are eternally fascinated by the weather – it is an essential topic of conversation. Huge sums of money are invested in trying to predict what it is going to do tomorrow, the day after or even a week into the future. But what about next year, the next decade or even the next century? What does the climate hold in store for us over these timescales? These are the sorts of questions that the project will try to tackle.

seven degrees centigrade in just a few decades. Such a large and rapid shift would have devastating socio-economic consequences if it happened today, but during the relatively warm inter-glacial period that we are now in (known as the Holocene and covering the last 12,000 years) there is no evidence for such dramatic climate shifts. Does this mean that the Holocene is more stable than the glacial period that preceded it, or is the

called the thermohaline circulation. The thermohaline circulation of the North Atlantic (of which the Gulf Stream is a part) keeps the UK several degrees warmer than it would otherwise be at these latitudes. But as this warm water mixes with cold water coming from the Arctic Ocean, it cools and becomes so dense that it sinks. Over time this dense water warms up and returns to the surface. The sinking regions and the return of water to the surface

> Large and rapid climate shifts would have devastating socio-economic consequences

Funded by the Natural Environment Research Council under a scheme called RAPID, the multi-institute project aims to investigate potential triggers for abrupt climate change. These abrupt changes have been known to occur in the past, particularly during the last glacial period between about 120,000 and 12,000 years Before Present (BP). The changes then were as much as

global warming that we apparently see today pushing the climate system towards an unstable threshold? This is one of the key questions that the project seeks to address.

The density of sea water is controlled by its temperature (thermo) and its salinity (haline), thus the circulation of water driven by density differences is

eventually form an enormous closed loop, termed the 'global thermohaline conveyor belt'. It is widely believed that this thermohaline circulation of the oceans played a key role in the rapid changes that occurred during the last glacial period. During this time the ice sheet covering North America (called the Laurentide) would, from time to time, spew out huge armadas of ➜

➜ icebergs into the North Atlantic, freshening the surface waters which eventually shut down the thermohaline circulation and triggered a major climate shift.

Today there is no Laurentide ice sheet, but there are other sources of freshwater, namely the Greenland ice sheet and Arctic sea ice. In the past few decades both of these ice masses have been observed to be shrinking and, if

Some surprising results have already been obtained. In 2002, Bamber and a team of NASA scientists carried out an airborne survey of several glaciers and ice caps in the Svalbard Archipelago in the high Arctic (Spitsbergen lies in this group of islands). They measured changes in the surface elevation of the ice masses over a six-year interval, with centimetre accuracy. To their surprise they found that although most of the glaciers were shrinking as expected,

> Although most of the glaciers were shrinking, the largest ice cap in the area was growing

the predictions of global warming over the next century are accurate, this mass loss looks set to greatly accelerate. The Arctic is particularly sensitive to global warming because of a strong positive feedback between snow cover and temperature – as snow and ice disappear more solar radiation is absorbed by the much darker land and sea surface underneath, further enhancing the warming effect, which results in the disappearance of more snow. Thus most climate models predict that global warming will be substantially amplified in the Arctic. The key question Bamber and his team aim to address is: will the increase in freshwater from the Arctic be sufficient to reduce or shutdown the thermohaline circulation and, paradoxically, cause a cooling in northern Europe?

the largest ice cap in the area (the size of Devon) was growing. It turns out that the most likely explanation for this puzzling result is a rise in snowfall caused by an increase in areas of open water, due to the retreat of sea ice that normally covers the ocean, even in late summer. Arctic sea ice is predicted to retreat even more over the next few decades and it seems likely, therefore, to result in a more vigorous hydrological cycle. In other words, more rain! How far beyond the Arctic the effects of the increase in precipitation will be felt is currently being investigated using sophisticated computer-based climate models.

Bamber has teamed up with experts from several institutes including the Southampton Oceanography Centre, the Met Office Hadley Centre for Climate Prediction and Research, and the Department of Meteorology at the University of Reading. Together they will pool their expertise in observing and modelling how the oceans, atmosphere and cryosphere (glaciers, ice sheets and sea ice) interact in order to produce a suite of sophisticated computer models designed to reproduce present-day and future climates. The models exist in part, but need to be able to 'talk' to and interact

with each other so that feedbacks between the different components of the climate system (as illustrated by the results obtained from Svalbard) are captured. The models also need to be fully validated against present-day observations to ensure that they realistically reproduce past climate trends.

When this validation phase is complete the team will use the models in two ways: first to help understand the underlying processes controlling the stability of the climate system and second to see how close to the edge we really are. Although it is beyond the team's remit or capability to offer solutions, forewarned is at least forearmed! ■

www.ggy.bris.ac.uk

Could increased melting of the Greenland ice sheet affect the Gulf Stream and result in a regional cooling in north-west Europe?

Both images: Bamber

Sea ice in the Arctic is disappearing so fast that the Arctic Ocean could be completely ice free in summer within a hundred years

Photograph of the Pylon of Kalabsha temple as it appears today

Computer generated simulation of the Pylon of Kalabsha as it would have appeared more than 2,000 years ago

How can we tell how things would have looked to people in the past? It was this simple question that led *Kate Devlin*, *Veronica Sundstedt* and *Alan Chalmers* from the University's Computer Science Department to become involved in realistic graphics and archaeology.

Seeing the Light

Computer-generated images are becoming a popular way of presenting archaeological information. To date, however, the emphasis has been on using these images for display purposes, with interpretation and research taking second place to the demand for a visually stunning presentation. In realistic computer graphics, the main goal is the creation of images that are perceptually equivalent to a real scene. So for computer graphics to benefit the archaeological community they must offer the archaeologist the chance to extend or enhance their analysis of a site or artefact. Furthermore, the accuracy of the images produced should be quantifiable – the archaeologist must be confident that what they see in the generated image is comparable to what would have been seen originally.

Initial work in this area began in 1994 and in 2001 Dr Alan Chalmers and Duncan Brown (Southampton City Heritage Services) won Bristol University's first Business Plan Competition with 'ArchLight', a system for producing highly realistic, computer-generated environments. Since then the research of the computer graphics group has focused on one area of realistic simulations that is often neglected: original lighting. Light cannot be captured in the archaeological record and consequently its importance is not always considered in interpretations of past environments. The ways in which we view, perceive and understand objects is governed by our current lighting methods – steady, bright electric light or large windows – but in order to understand how an environment and its contents were viewed in the past we must consider how they were illuminated.

> The archaeologist must be confident that what they see in the generated image is comparable to what would have been seen originally

Standard three-dimensional modelling software tends to base the lighting conditions on daylight, fluorescent light or filament bulbs, and not the lamp and candlelight used in past. Realistic lighting simulation must address both the physical interaction of light in a scene (how light is distributed) and the spectral profile of the light source (the colour of the light). With control over this, an accurately lit representation of an environment can be achieved and the virtual version of an original site or artefact can be manipulated without having to physically touch or harm the real version.

Once an archaeological site or artefact has been modelled in a three-dimensional modelling package it must be rendered. That is, the colours, textures, light and shading are computed thus producing the final images from the three-dimensional geometry. In order to obtain an approximation of the original lighting in an archaeological representation, two factors must be addressed in the rendering process. First, the spectral composition of the light – the colour of the light given off by the burning fuel – must match that of the fuel type that would have been used in a specific archaeological instance. Second, the distribution of this light – the path it takes around a scene and ➜ the reflections and inter-reflections that occur – must mimic the behaviour of light in the real world.

The only trace of light in the archaeological record is the methods used to provide it, be they hearths, candles, lamps or windows. In pre-industrial societies, daylight was the regulating factor of the working hours. If we compare that to conditions today, sunlight is far less relevant to how we work. The evidence from architecture tells us the most about lighting – a lack of glass and a need for security often meant smaller windows, therefore dimmer interiors. Going further back in time, the unyielding darkness of a deep cave would require some form of artificial light for navigation purposes alone. It seems plausible that objects and environments were affected by the limitations of lighting, and this influence may have extended into their design. By recreating the means of illumination for a given environment and simulating it accurately, the archaeologist may (literally) find new ways of viewing things.

> The only trace of light in the archaeological record is the methods used to provide it – hearths, candles, lamps or windows

The initial step in recreating the light source involves experimental archaeology. In consultation with the Department of Archaeology, various types of light sources were physically recreated. These included tallow candles and reeds, an animal fat lamp, beeswax candles and olive oil lamps. Each of these fuels produces a different colour when burnt. To obtain this unique spectral profile for each fuel, detailed data were gathered using a spectroradiometer, a device that measures the absolute value of the spectral characteristics without making physical contact with the flame. The values obtained from the original light sources can then be used as lighting values for a computer-generated model, so that a scene can be rendered under its appropriate lighting conditions.

One of the most recent projects undertaken was Veronica Sundstedt's MSc dissertation on the ancient Egyptian temple of Kalabsha. In 1963 the temple, which dates back to 30 BC, was moved to a new site in order to save it from the rising waters of Lake Nasser. Working closely with Egyptologists it has been possible to use computer graphics and information from the archaeological record to recreate the temple, place it back to its original location and orientation, and illuminate it as it may have appeared some 2,000 years ago. An animation was created showing how sunlight would have affected the perception of the temple over a ten-hour period in January 30 BC. A comparison of this animation and the video footage taken at the site in January 2003 enables the Egyptologists to compare just how the new location and orientation of the temple, in addition to the damage, has altered its appearance. The interior of the temple was also modelled in detail. This allows the Egyptologists to see how the hieroglyphics would have been perceived in the past – not as they are seen today, unpainted (the paint having long since faded) and under modern lighting – but brightly painted under the illumination of sesame oil lamps.

Overall, this research into colour and light has shown how easy it is for our own preconceptions to intrude into the ways we view archaeological objects or sites, but a definitive explanation should never be expected in archaeology. Visualising a past environment is fraught with difficulties from the outset, so a means of validating computer-generated representations provides an exciting opportunity to explore and test new ideas, with computer graphics becoming as beneficial to the archaeologist as they are to the public. ■

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This research was published in UNESCO's 'World Heritage in the Digital Age' 30th Anniversary Digital Congress. www.cs.bris.ac.uk/Research/Graphics/index.html

Computer generated hieroglyphics lit by electric light

Computer generated hieroglyphics lit by sesame oil lamp

Computer generated hieroglyphics with restored colours

Fra Angelico's 'Christ Glorified in the Court of Heaven'. © The National Gallery, London

Middle Aged Heaven

I do not imagine that many of us spend much time thinking about what heaven might look like, even supposing we believed such a place to exist at all. But whether it exists or not, Dr ***Ad Putter***, Director of the Centre for Medieval Studies in the English Department, spends his time researching it.

If you ever wish to find out more about heaven – would like to know, say, what colour of shoes is in fashion there, whether people there have bodies, and if so, what they do (and don't do) with these bodies – I can recommend to you the literature and art of the Middle Ages. In this period, the reality of heaven was never in serious doubt. Medieval representations of the cosmos duly map heaven beyond the spheres of the planets and the fixed stars. In numerous medieval maps of the world, the earthly paradise is given an exact location (in the Far East).

Do celestial beings have bodies or not?

Alexander the Great was famously believed to have knocked on the very gates of paradise, and to have been refused entry by an angel who curtly reminded him he was only a mortal. Medieval minds turned readily to the Otherworld, because it mattered more than life itself that people got to heaven or at least to purgatory. Not surprisingly, then, the precise conditions of life after death were the focus of intense speculation and sometimes controversy. One such controversy raged over the question I raised earlier: do celestial beings have bodies or not? On the authority of St Paul, who had spoken unambiguously of 'celestial bodies' (I Corinthians, xv), the view that we would be pure spirits in heaven was eventually declared anathema, though it would have simplified the work of medieval theologians if things had gone the other way. Bodies bring with them all manner of complications: eventually their age had to be decided on (all early thirties – the perfect age), and likewise their sex (we shall be male or female as we are now, though sex in the other sense will interest us no more) and their physical condition perfected, regardless of any disfigurement of our terrestrial body.

In its scrupulous attention to detail, and the coherence of the logic that determines each detail, heaven is one of the most impressive medieval 'cathedrals of the mind'. And as with real cathedrals, the architecture of this mental construct changed with the passing of time. Corresponding roughly with the transition from Romanesque to Gothic is the change from visions of heaven as a garden (which is what the word 'paradise' originally meant) to visions of heaven as a walled city. Both ideas have precedents in the Bible – the garden in Genesis and the Song of Songs, the city in the Book of ➜ Revelation – but the resurgence of cities in the 12th century helped reinvigorate the concept of heaven as a large city.

The subject of medieval heaven is a vast one, and serious study of it calls for expertise in a wide range of disciplines, including history and art history, letters, music and theology and others. This is why the Centre for Medieval Studies at Bristol University, which brings together medievalists from all relevant disciplines across the Arts Faculty, has joined forces with leading scholars from other universities to explore heaven as it was envisaged by medieval people in art and literature, and in popular and academic thought.

What machinery was used to hoist angels up and down?

The Centre has organised a two-year research programme, generously sponsored by the Read-Tuckwell Foundation and the University's Institute for Advanced Studies. The programme includes several public lectures, delivered by distinguished guest speakers from other universities, and culminates in an international and interdisciplinary conference. The topics of the speakers give some indication of the fascinating issues surrounding medieval heaven.

How was heaven portrayed on stage in medieval mystery plays – what machinery was used to hoist angels up and down, for example? To what extent is it defensible or heretical for a woman mystic to say that she has seen God face to face in this life when that is supposed to happen in the life hereafter? How can writers do justice to the notion that heaven is complete when their literary resources are inevitably incomplete? And finally, how could such theological speculations produce the finest poetry of the period, in Dante's *Divina Commedia*?

If you would like to know the answer to some of these questions, why not register for the conference or attend the public lecture 'After Life Now: Dante, Resurrection, and the Politics of Charity' by Dr Robin Kirkpatrick on Wednesday, 3 March 2004 at 2.15 pm? It will take place in the English Department, 3-5 Woodland Road, Bristol. ■

www.bristol.ac.uk/Depts/Medieval

Envisaging Heaven in the Middle Ages

16-18 July 2004
Clifton Hill House, Bristol

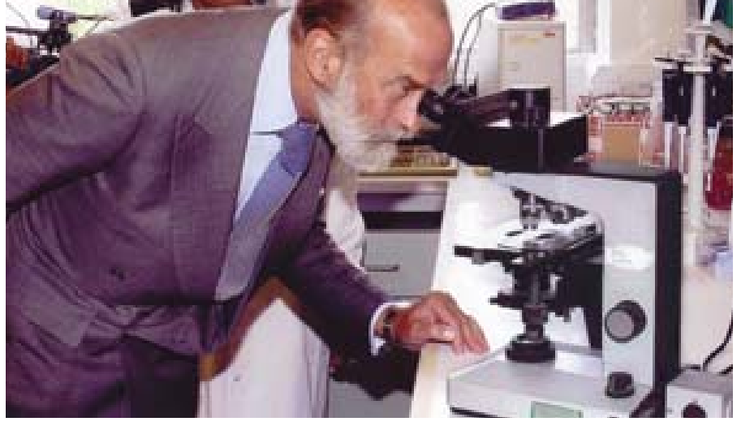
Keynote addresses:

Bernard McGinn
(Professor of Divinity, University of Chicago)

Pamela Sheingorn
(Professor of History of Art, New York University)

Barbara Newman
(Professor of English and Theology, Northwestern University)

The conference is devoted to issues concerning the representation and functions of heaven in medieval art, literature, and popular and academic thought. If you would like to offer a paper or require any further information, please contact: *a.d.putter@bristol.ac.uk, or see the website.*



Prince Michael of Kent opened the new Wolfson Laboratories in the Division of Ophthalmology

Remodelling the Eye

Behind every successful medical innovation lies years and years of research, usually done in universities. Professor ***Andrew Dick***, Head of the University's Division of Ophthalmology, reveals some of the exciting research that may result in new treatments for eye disease.

Improvement in future health care relies heavily on translating advances made in the research laboratory into real treatment in the clinic. So above the waiting rooms at Bristol's Eye Hospital, a purpose-built modern speciality hospital, sit the laboratories of one of the leading eye research centres in the country – Bristol University's Division of Ophthalmology. Additional research laboratories, housed in the Medical School, were opened in July by Prince Michael of Kent, patron of the National Eye Research Centre.

The Bristol Eye Bank, part of the University's Division of Ophthalmology but funded by the Department of Health, issued its first corneas in March 1986 and is now the country's largest eye bank. In the UK last year almost 2,300 people had their sight restored through a cornea transplant – two-thirds of which were supplied by the Bristol Eye Hospital. Its Director, Professor John Armitage, was instrumental in establishing this facility. Pertinent to its success was the fact that it was the first eye bank in the UK to use a new method of storage for corneas – organ culture.

When one thinks of organ and tissue storage for transplantation, there is an assumption that they are frozen. In the case of corneas, however, laboratory and clinical studies have demonstrated that the action of freezing can cause significant damage. The one alternative – refrigerated storage – allows corneas to be kept for a few days, but Armitage's innovative work introduced methods of storing corneas in a nutrient medium at close to normal body temperature, extending their storage time to a month. This not only greatly reduced wastage of valuable corneas, but helped to transform routine corneal transplantation in the UK from an emergency out-of-hours procedure to a scheduled operation that could be planned well in advance, to the benefit of both patients and hospitals. Importantly, doctors also have more time to find the most suitable patient for each cornea, which results in better grafts.

Innovative research extended the storage time of corneas to a month

Nevertheless, cryopreservation (freezing) of the cornea offers the only truly long-term method of storage for corneas, and Armitage's group is currently investigating the feasibility of ice-free cryopreservation by vitrification. When a liquid vitrifies (turns to a 'glass' without any ice forming), it does not undergo a phase change – such as when water turns into ice – but it acquires the physical properties of a solid owing to an enormous increase in viscosity during cooling. As a result, the mechanisms of injury associated with the formation of ice are avoided. But to attain this state requires exposure of cells and tissues to very high concentrations of solutes so work is ongoing to discover what solutions are most suitable.

But having retrieved a cornea and successfully restored the sight of your patient is by no means the end of the story. While most corneal grafts last for many years, 25% survive less than five years, resulting in the need for a second corneal transplant, which is likely to survive an even shorter time.

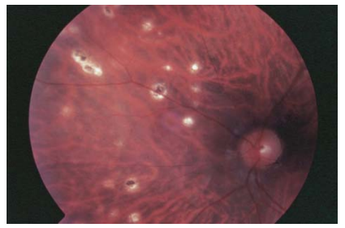
One of the main causes of corneal graft failure, as with other transplants, is rejection of the foreign tissue by the immune system. To understand why this happens, a very large multi-centre study of corneal transplants – over 1,000 grafts – is in progress under → Armitage's supervision. Ultimately it is hoped that it will provide answers to questions such as whether tissue matching is required, the need for immune suppression, and whether it is possible to predict which patients are more likely to reject their transplants.

Another area of research is Professor Dick's programme that looks at how cells in the retina control inflammatory responses. There is a disease in humans called 'uveitis' (pronounced UV-itis), which is an autoimmune disease similar to arthritis or multiple sclerosis. Inflammation is caused by the body attacking tissue when the autoimmune response is turned on. In uveitis it attacks the retina, resulting in a 25% chance of losing your sight.

A 70% response rate in patients not responding to conventional drugs

It is well known that in rheumatoid arthritis a small protein called 'tumour necrosis factor' (TNF) is released by cells, causing the violent inflammatory response. Using animal models, Dick's team showed that TNF is also a promoter of inflammatory responses in the eye. In collaboration with colleagues in Oxford who designed what is called a 'fusion' protein which binds to the TNF and neutralises it, the team in Bristol then established its effectiveness in experimental models. They have now just finished their first highly successful clinical trial, testing it in patients with uveitis. The outcome was a 70% response rate in patients who were not responding to conventional drugs. As a result the team is negotiating with biotech companies to develop a drug to inhibit uveitis.

Another aspect of this research is looking at the way the retina itself controls inflammatory responses by the cells inside it. Macrophages are specialised cells of the immune system, designed to facilitate immune responses to prevent excess tissue damage and then mop up the rubbish.



Retina showing lesions as a result of inflammation and uveitis

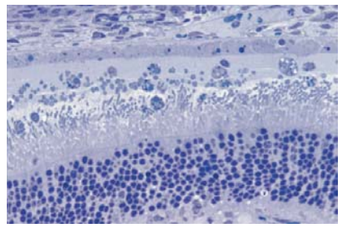
Collaborative work with industry, DNAX Inc in USA, is investigating mechanisms to generate compounds and drugs to facilitate repair of the retina, so that it may be possible to return inflamed tissue to its original state by controlling the macrophage function.

Finally, and perhaps most excitingly, the most recent development in 'remodelling' is with neural progenitor cells, or stem cells. In the brain these progenitor cells can be 'switched on' to generate a range of cell types required to repair damage to the brain. But although the retina consists of neural (nerve) tissue that is similar to the brain, it has always been understood that it does not contain progenitor cells that would help remodel the system. Dick, however, found this difficult to accept and in a paper published in September's issue of the *British Journal of Ophthalmology* he and his team report the very first evidence of progenitor cells in the retina. This is an extremely important landmark that might ultimately lead to a whole new area of treatment for retinal disease.

The very first evidence of stem cells in the retina

Already they have a research programme that has been able to grow progenitor cells from biopsies of human retina, and are looking at what conditions are required to turn them into nerve cells, supporting cells of the retina, or photo receptor cells. If they can understand that, then they are well on the way to controlling eye disease by helping the injured retina to restore itself. ■

www.bris.ac.uk/Depts/Ophthalmology



Detail of retina with uveitis

re: Bristol Neuroscience

Bristol Neuroscience is a new University venture which aims to increase awareness and communication between neuroscientists, particularly those based at University and hospital sites, which are spread around the city.

In September, more than 100 people gathered for Bristol Neuroscience's first symposium which included talks on basic scientific research – the cutting edge of molecular and cellular biology – as well as the realities of the clinic – diagnosis of stroke, its treatment, and the huge impact stroke has on both the individual and the whole of society. Bridging the two were representatives from the pharmaceutical industry discussing the question of how drug companies can turn scientific research into drugs to be used in the clinic.

The symposium revealed that a large gap exists between the questions being addressed in the lab and the problems faced by clinicians when treating patients who have suffered a stroke. Although research has made great progress, yielding drugs that appear to have huge potential, these drugs have consistently faltered during clinical trials.

Optimism was high, however, that ways would be found to overcome this gap. In order to do so, it is essential that research scientists and clinicians work together more closely. Bristol Neuroscience will facilitate this, greatly improving communication between the lab bench and the hospital bedside. ■

www.bristol.ac.uk/neuroscience

re: Hidden Suicide Rates

The conventional method for measuring suicide trends involves combining data from male and female suicides, across all age-ranges. But Professor David Gunnell and Nicos Middleton, in the Department of Social Medicine, suggest that suicide assessment which focuses on the age of the individual, or 'potential years of life lost' (PYLL), provides a different perspective of suicide trends. PYLL assumes that an individual will live to 65, so if they commit suicide at 20 they have lost 45 years of potential life.

Gunnell and Middleton's research shows that although age-standardised suicide rates fell by 18% between 1981 and 1998, the PYLL increased by 5% due to an increase in suicides in young men.

The masking of the PYLL occurs because the standardised suicide rate is created by pooling different age-specific and sex-specific rates into a single figure, thereby ignoring the differing trends within specific population groups. Their findings suggest that nations with similar patterns of suicide to those seen in England and Wales, such as Australia and the USA, might also have reductions in overall suicide rates, yet deteriorating rates in young people. Such deteriorations are especially important if they signify a decline in young people's mental health. ■

www.epi.bris.ac.uk

Desert Island Dreaming

Imagine being on a desert island – or anywhere else in the world for that matter – and instantaneously being able to call up a piece of film and watch it on a portable device that provided images of unparalleled quality. Turning this into reality is the dream behind 3C Research, a University-based company.

The city of Bristol has long been renowned for its activities in TV production and high-tech electronics. In 3C Research, world-class expertise developed at the University will join forces with a range of industrial partners, including Granada, Toshiba and Qinetiq, to look into the technological future. Recently awarded £7.6m by the Department of Trade and Industry to progress its adventurous research programme, 3C Research will bring together a dynamic mix of academic research excellence, production creativity, and technological know-how. With the industrial partner support, funding available for the programme is over £11m in the first three years.

Increasingly people are looking to be liberated from sitting at a desk in order to access information, but this requires significant advances in equipment portability and access to interactive information, as well as the applications that support them. The dramatic advances in multimedia services and the new, user-friendly devices needed to deliver the dream will build upon five projects that arose out of research originally done in the University's Electrical and Electronic Engineering and Computer Science departments.

Motion Ripper

Generating realistic animation is an expensive and highly skilled process. Motion Ripper aims to provide animators in the broadcast and games industries with a suite of tools that will enable them to produce complex, realistic animation quickly and easily.

Access to Granada's online video database will provide the project with an extensive range of motions to sample. Ultimately, using the software being developed, animators will be able to extract (rip) motion data from the reference video which can then be used in a computer graphics scene to drive character motion. Unique versions of these motion 'signatures' will then be automatically generated, allowing the animators to extend clips or create complex effects. For example, the motion signature of a bird flying can be translated to create a plane that flaps its wings.

As well as developing the software necessary to enable these effects, an online database of motion signatures will be produced by Matrix Data who bring a high level 'semantic' approach to metadata cataloguing and classification. Metadata is the descriptive information about the data and the semantic approach uses a global classification system that can be processed by anyone in any way. The final outcome of the Motion Ripper project will be online databases that can be rapidly searched for audio clips and images to enhance the entertainment industry.

ICBR – Intelligent Content-Based Retrieval

If a producer does not have the funding or time to go to South Africa and film ➜ a lion chasing zebras, how can he find such a clip amongst all the film footage available? Television and film producers have a real need to be able to organise, store and retrieve vast amounts of media images. Furthermore, their requirements are growing as more and more media becomes available. The ICBR project proposes to solve the problem by combining a large-scale multimedia server and database with intelligent shot-recognition and retrieval software.

> The motion signature of a bird flying can be translated to create a plane that flaps its wings

When completed, the ICBR demonstrator will include a set of software tools for the automatic recognition of images and audio, and for the shot selection and editing of television programmes. The system will select video and audio material according to pre-set criteria, which will include image-similarity measures and object recognition. The selected media will then be presented in an ordered way ready for incorporation into an editing system in order to construct new sequences or complete programmes.

RoD – Rendering on Demand

The computer graphics industry, and in particular those involved with films, games and virtual reality, continues to demand more and more realistic computer-generated images. Despite the ready availability of modern, high-performance graphics, the complexity of the content being modelled and the high fidelity required of the images means that rendering such images (a technique for producing images from their three-dimensional geometry) is simply not possible in a realistic time-frame on a single computer.

RoD aims to provide a high-performance, high-fidelity rendering system that will be accessible from many locations. This will enable users to submit their content to the system and see the desired images rendered in a reasonable, and ultimately real-time, time-frame. RoD will achieve this goal of 'realism in real-time' by combining parallel processing – a number of computers working in tandem – with visual perception techniques. These utilise the fact that the human eye fails to notice certain aspects of an image. ➜

Since the human eye fails to detect certain aspects of an image, significant time can be saved by not reproducing those parts we will not notice

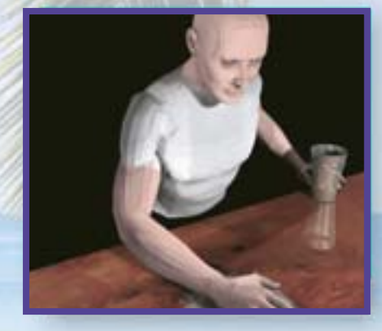
→ By exploiting our understanding of the human visual system, significant time can be saved by simply not rendering those parts we will not notice.

OSIRIS – Open Infotainment Services In Radio Interconnected Systems

With the Government aiming to extend the information age to everyone, a key requirement will be fast, flexible and reliable broadband access if the opportunities and benefits of a knowledge-based economy are to become inclusive, and the promise of 'access to the internet for everyone who wants it by 2005' is to be realised. Wireless technology is widely regarded as a means of enabling this revolution, however significant research and development is still necessary before wireless can offer 'wired quality' at a realistic price for the mass market. OSIRIS aims to address this need with the development of novel technologies that will provide an adaptable and resilient radio infrastructure. This will give everyone, everywhere, at any time, seamless access to top-quality broadband internet facilities via hand-held devices that tap into a network of public hotspots.

ROAM4G – Robust and Scaleable Multimedia Content Delivery over Optimsed 4G Communication Networks

Future wireless networks will also support high-speed communications in dense urban and other environments. However, the delivery of video to a wireless device in a mobile environment remains a challenging problem. ROAM4G will provide a robust and scaleable coding solution for high quality multimedia streaming and conversational/interactive services. Application areas for this include video-enhanced services for mobile devices such as mobile phones, video conferencing, home networks for broadcast



distribution, image and video database retrieval systems such as OSIRIS.

The three Cs in 3C Research stand for communications, computing and content. When combined in the exciting ways envisaged by 3C Research, these words will impact on the economy and people's lives in ways hitherto un-imagined – even on a desert island. ■

www.3cresearch.co.uk

re: Swinging in many tongues

At The BA Festival of Science in Salford this year, Dr Sotaro Kita of the Department of Experimental Psychology asked a group of English, Japanese and Turkish speakers to watch a cartoon featuring Sylvester the cat and his elusive prey, Tweetie Pie. He then asked them to describe particular scenes and observed any gestures they made while speaking.

Kita found that the speakers of the three different languages used different gestures to depict the same event, and that these gestures appeared to reflect the way in which the structure of their languages expressed that event. For example, the participants described a scene in which Sylvester swings across a street on a rope to catch Tweetie. The English speakers predominantly used arc gestures to depict the swing motion, while the Japanese and Turkish speakers tended to use straight gestures.

Kita suggests that this is because Japanese and Turkish have no verb that corresponds to the English intransitive verb 'to swing', so they use the straight gesture because they cannot easily express the concept of movement with an arc. English speakers, on the other hand, used the arc gesture because the language can readily express the change of location and the arc-shaped trajectory.

Kita concluded that at the moment of speaking language influences spatial thinking, such that English speakers tend to think about manner and trajectory simultaneously while Japanese and Turkish speakers may think about them separately. ■

http://psychology.psy.bris.ac.uk

Recreating a Lost World

The cataloguing of 57,000 files from the Chinese Maritime Customs Service sounds a dry and dusty business, but Dr ***Robert Bickers*** in the Department of Historical Studies believes they will transform our understanding of Chinese history during the late 19th and early 20th centuries.

The Chinese Maritime Customs Service (CMCS) was an international bureaucracy under the control of successive Chinese central governments, from its founding in 1853 until its abolition by the communists in 1949. It was the only agency which functioned without interruption for this whole period. Established by foreigners during the Taiping Rebellion to collect taxes on maritime trade when the Chinese were unable to do so, its functions quickly expanded. It became responsible for domestic customs administration, postal administration, harbour and waterway management, weather reporting, and anti-smuggling operations. It mapped, lit and policed the China coast and the Yangzi river, and was involved in loan negotiations, currency reform, and financial and economic management. As a result, the CMCS archives now constitute one of the richest repositories for the study of the history of China during the late Qing and the Republic. Most of this material has never been published.

The CMCS has long been associated with the role of Britain in China in the late 19th century. Its senior staff were predominantly British and Sir Robert Hart, the second Inspector General, guided its development for almost 50 years from 1863 to 1908. Essentially established by Britons who were trained in the Consular Service, they brought British Civil Service expertise to the CMCS but had to marry this with Chinese administrative practices. With an overwhelming number of Chinese staff, and having to report to Chinese superiors, this middle layer of foreigners introduced western-style practises to the Chinese State, and the service became something of a hybrid. It was always a Chinese agency but was effectively 'outsourced' to foreigners. With trade the focus of the relationship between China and other foreign powers, having foreigners running the CMCS enabled the State to develop knowledge about international law, how international treaties were negotiated, and how to 'do' diplomacy – things that China was not experienced at and, as a result, was suffering from politically.

One clear example of the way in which this material will help the rewriting of modern Chinese history is the fact that it includes quarterly returns from each of the dozens of customs stations around the country, regarding the export and import of arms and ammunition, and other materials of war. Militarism and warlord violence was the characteristic feature of China in the 1920s and 30s, but scholars have lacked detailed evidence of the arms trade which underpinned the violence. These quarterly returns reveal information such as which ministry gave permission to which military commander to import, say, 10,000 rifles and 5,000 uniforms through this port, and from that foreign client. These shipments can now be tracked across the provinces to see where they end up and this information then cross-referenced with battle X when General Y took control of Z. So from these highly detailed, if rather dry data, a new picture of the shifting politics and power in regional China can be established. →

A new picture of the shifting politics and power in regional China can be established from these highly detailed, if rather dry, data

British and Chinese office staff in Nanjing in the 1930s

➜ But as well as providing historians with information about the politics of China during this period, there are fascinating questions to be asked about the men and their families – from light housekeeper to Inspector General. How did they learn the language; did they learn to adapt; and where did their loyalties lie? A Briton based in a port in the 1920s – was he a servant of the British Empire or the Chinese state? While a strong sense of a highly developed service culture emerges from these documents, there are interesting tensions between absolute loyalty to the CMCS – and men had to be loyal otherwise they did not get the plumb postings and instead rotted in obscure places – and national loyalties.

Germans and the lighthouse keepers were largely replaced by Scandinavians. Visitors' books for these lighthouses prove very entertaining. Two gentlemen seeking shelter from a storm while on a hunting trip in the 1880s remark how 'this was the cleanest lighthouse they have ever seen'. These little details provide an insight into how these men were making their own accommodations with China and Chinese society, whether it was lighthouse keepers finding some comfort for themselves – the offspring of their marriages or other arrangements would be shipped to an orphanage for Eurasian children in Shanghai – or more senior men negotiating their way with Chinese colleagues.

> The offspring of their marriages or other arrangements would be shipped to an orphanage for Eurasian children in Shanghai

And there was a fixed class divide. Although 'outdoor' staff – often people with no education – could work their way up through the outdoor hierarchy, they rarely crossed the divide to become 'indoor' staff.

These histories are not just about the British, however. Prior to the First World War, the CMCS preferred Germans as lighthouse keepers, because they kept the gardens tidy. But in 1917 the British persuaded the Chinese to expel all

Bickers and his colleagues, including four archivists at the Second Historical Archives of China in Nanjing, have been working on cataloguing the CMCS files for three years now. Originally catalogued on paper in an illegible handwritten Chinese translation, the archive is now being transferred from the original manuscripts in their original language – eighty per cent are in English – onto CDs. The project has been so successful and revealed so much fascinating material that Bickers and his collaborator – Hans van de Ven at Cambridge University – have just been awarded £300,000 from the Arts and Humanities Research Board to continue the work for a further three years.

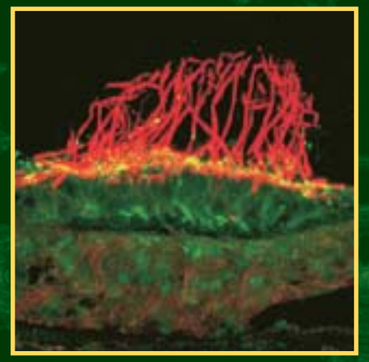
A post-doctoral assistant, Dr Yuehtsen Chung, will take the lead on collecting materials for the UK team and her own projects. Based in Nanjing for the first year, she will then complete the work in Bristol. As well as cataloguing the data, the archivists in China will construct databases on personnel, economic, financial and ecological history, and produce documentary collections on various topics relating to the history of the Customs Service and its significance in modern Chinese history. To assist others use the material, the team also aims to produce four guidebooks of annotated source materials, on the following themes: an institutional history of CMCS, department by department; the history of a typical customs station; the CMCS in international relations; and the socio-cultural world of the CMCS.

The catalogue will be published on a CD-ROM, and a selection of documents will also be published on microfilm, making them accessible to a wide range of researchers. ■

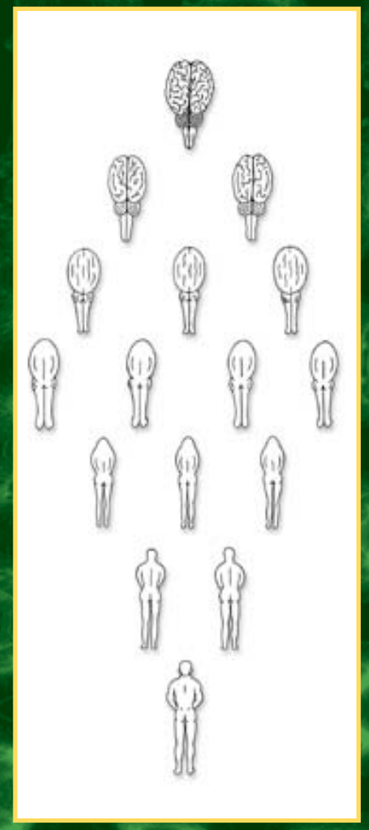
www.bris.ac.uk/Depts/History

Robert Bicker's book
Empire Made Me:
An Englishman Adrift in Shanghai
was published in September
2003 by Penguin Books.

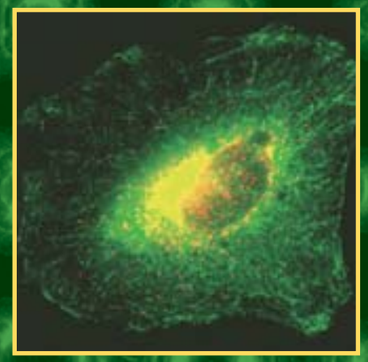
Winners of the Graduate School of Medical and Veterinary Sciences postgraduate art competition



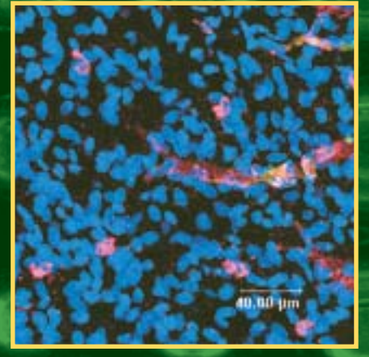
'Sensory hair cells of the vestibular apparatus' by Lisa Grant



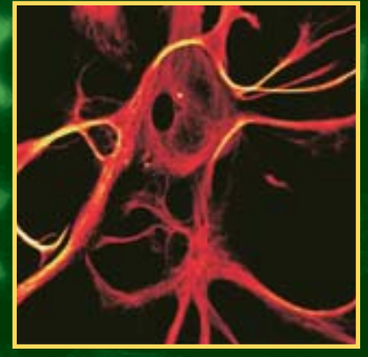
'Metamorphosis' by Abi Woollard



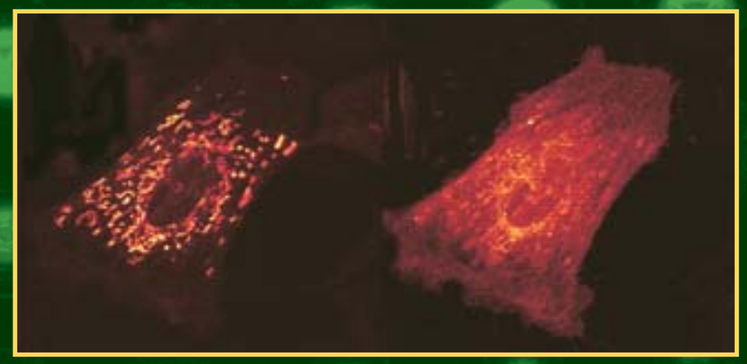
'The possibilities of immunostaining' by Krysten Palmer



'Angiogenesis 3' by Wenying Wang



'Astrocytes in culture' by Sarah Harris



'Mitochondria in myocytes' by Dirki Balaska

'Artistically modified immunostained cells' by Krysten Palmer

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