University of Bristol

re:search

University of Bristol • Research Review • Issue 22 • Winter 2009

Seeing is believing

The lifetime effects of stress

Understanding climate change

re: search editorial

How well do we understand climate change?

By the time this issue of *re:*search is in your hands, crucial decisions will have been taken at the United Nations Climate Change Conference in Copenhagen, based, we hope, on the most up-to-date information available. Such is the world's anticipation of what must be achieved there that, as *re:*search goes to print, a glance at the official website shows there are precisely two days, 20 hours, 29 minutes and 21 seconds to go. Once the conference starts, leaders of the world's 195 countries – backed by a 20,000-strong army of officials, advisers and experts – will attempt to thrash out a new international deal to tackle climate change. Whatever is agreed at Copenhagen will come into force on 1 January 2013 and supersede the 1997 Kyoto protocol.

But the battle for hearts and minds has never been harder to win. A poll published in *The Times* last month found widespread scepticism about climate change among the general public, with just one in four people seeing it as the world's most serious problem and only two in five accepting as scientific fact that global warming is largely man-made.

But is this really surprising? The article on page 16 reports six climate change-related papers involving researchers from the University that were published in prestigious journals during the month leading up to Copenhagen. From just this small selection it is evident there is much that people working at the coal face of climate change still do not understand. There is disagreement about how to interpret data and in particular there is clear evidence that the models used to predict what might happen to the climate in the future are only as good as the data that go into them.

However, I was struck when writing press releases about these papers how honest the researchers were prepared to be. They included in their quotes and papers phrases such as 'how difficult it is to accurately quantify such data', 'there are serious deficiencies in our understanding' and 'this led us to review what was missing from the model', despite colleagues from some other press offices suggesting that these kinds of comment only feed the 'climate change deniers'. Yes, taken out of context such comments might provide fodder for the sceptics, but the role of researchers and their press officers is to report the facts – and the fact is there is still much that we don't understand. We shouldn't be afraid of saying that.

Cherry Lewis
Editor

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Articles about research at Bristol University are welcome. Please contact the editor.

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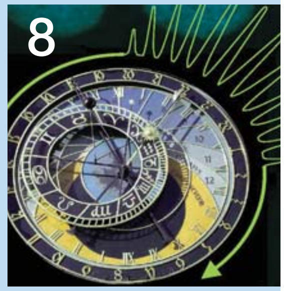


pre: view

Good vibrations

Energy harvesting – using vibrations from the environment to produce electricity – has been around for over a decade, but Dr Stephen Burrow and his team in the Department of Aerospace Engineering hope that within five years it could be powering devices such as heart monitors and mobile phones.

Vibrations caused by machines such as helicopters and trains could be used to produce power

Currently the team is exploring how vibrations caused by machines such as helicopters and trains could be used to produce power, but vibrations from household appliances and the movement of the human body could also be harnessed for this purpose.

"Vibration energy-harvesting devices use a spring with a mass on the end," explains Burrow. "The mass and spring exploit a phenomenon called resonance – the production of a large vibration in one object as a direct result of a relatively small vibration in another object – to amplify small vibrations, enabling useful energy to be extracted. Even just a few milliwatts can power small electronic devices like a heart rate monitor or an engine temperature sensor, but it can also be used to recharge power-hungry devices like MP3 players or mobile phones."

Existing devices can only exploit vibrations that have a narrow range of frequencies, so if the vibrations don't occur at the right frequency, very little power can be produced. This is a big problem in applications like transport or human movement where the frequency of vibrations changes all the time.

The Bristol team is therefore developing a new device where the mass and spring resonate over a much wider range of frequencies. This would enable a much wider range of vibrations to be exploited and so increase the overall contribution that energy harvesting could make to energy supplies. The team believes it can achieve this by exploiting the properties of non-linear springs which allow the energy harvester to respond to a wider range of vibration frequencies.

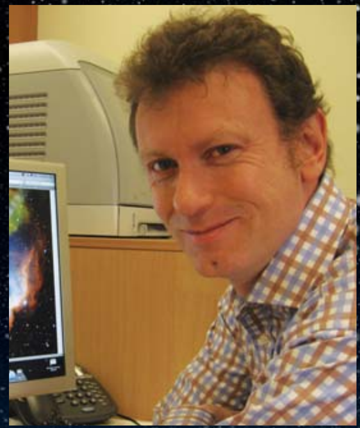
Energy harvesters generate low-level power on a similar scale to batteries but without the need for battery replacement or disposal of potentially dangerous and polluting chemicals. They are also suited to applications where hard-wiring would be impracticable, vulnerable to damage, or difficult to access for maintenance purposes.

"There's a huge amount of free, clean energy out there in the form of vibrations that just can't be tapped at the moment," says Burrow. "Wider-frequency energy harvesters could make a valuable contribution to meeting our energy needs more efficiently and sustainably." ■

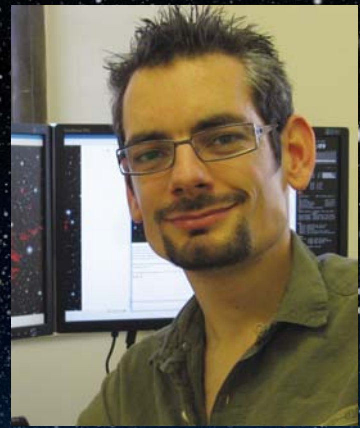
www.bristol.ac.uk/aerospace

This research is funded by the Engineering and Physical Sciences Research Council (EPSRC).

Whenever you look up at the stars you are looking back in time, as light from even our closest neighbour, Alpha Centauri, started its journey to Earth more than four years ago. It is a phenomenon that astrophysicists Professor Malcolm Bremer and Dr Ben Maughan from the Department of Physics grapple with daily in their research into deepest space.



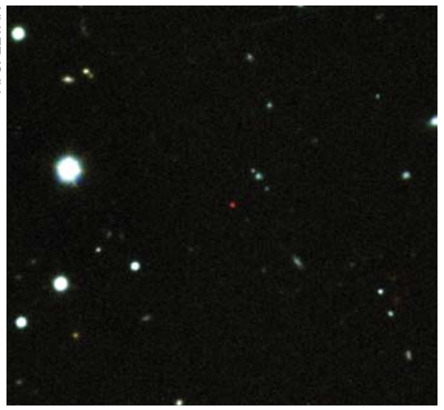
Professor Malcolm Bremer



Dr Ben Maughan

Seeing is believing

As telescopes become ever more powerful, we are able to observe objects closer and closer to the Big Bang. It is believed that the first stars formed when the Universe was very young – between 200 and 400 million years old – and the nearest we have got to seeing them is 630 million years from the Big Bang, when the Universe was less than five percent of its current age. The not so elegantly named 'GRB 090423' was discovered there, making it the most distant object yet seen in the Universe.



A. J. LEVAN

This image shows the afterglow of GRB 090423 (the red source in the centre) and was created from images taken at Gemini-South and the Very Large Telescope.

"GRB 090423 is an example of a gamma ray burst, the brightest and most violent explosions in the Universe," explains Bremer, who was involved in the observations. "The explosion, which only lasted a matter of seconds, is thought to have accompanied the catastrophic death of a very massive star. It would have been triggered by the centre of the star collapsing to form a black hole."

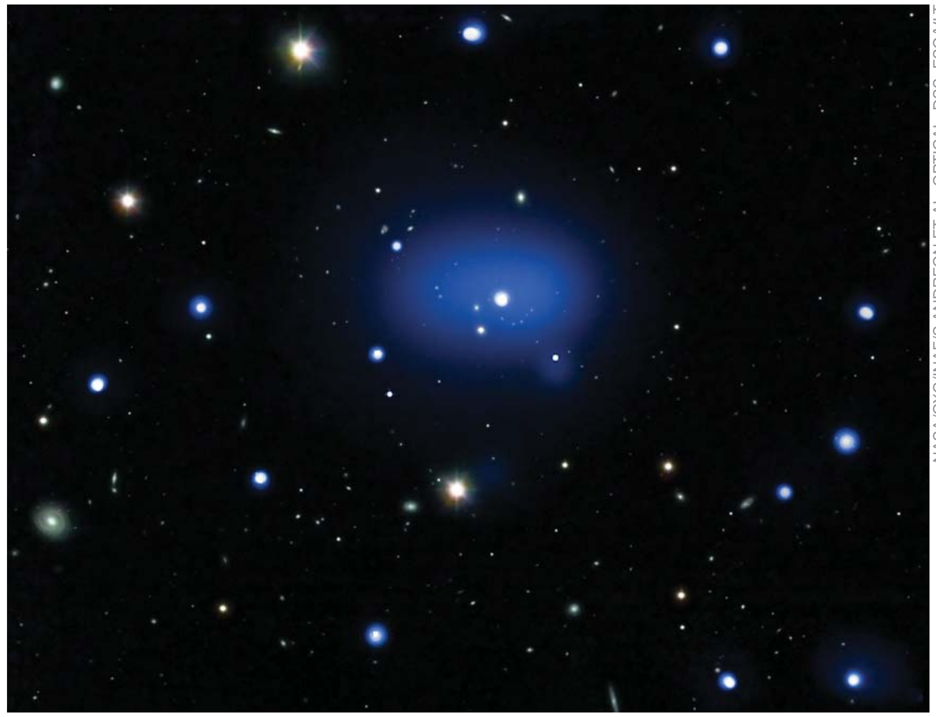
GRB 090423 is the most distant object yet seen in the Universe

GRB 090423 was discovered in April 2009 by a robotic spacecraft called *Swift* that was launched into orbit in 2004. The discovery of such a distant gamma-ray burst confirms that massive stellar births – and deaths – occurred in the very early Universe. Gamma-ray bursts release a tremendous amount of energy in a very short time, but despite GRB 090423's brief appearance, light from the explosion still managed to get here even though it took more than 13 billion years. However, as Maughan points out, while light years are a convenient shorthand to describe the vast distances to these objects, telling us how long their light has been travelling to reach us, the Universe has been expanding during that whole period, so the Earth and these objects are now even further apart than they were when the light we see was first emitted.

Closer to home is the galaxy cluster JKCS041. Because matter is not evenly distributed across the Universe, stars form into galaxies and galaxies cluster into groups, which may consist of hundreds or even thousands of galaxies, held together by a gravitational field. "You can imagine them being a bit like a swarm of bees buzzing around but not flying apart because they're held together by gravity," says Maughan. Galaxy clusters are the largest gravitationally bound objects in the Universe and at a distance of 10.2 billion light years, JKCS041 – the most distant galaxy cluster yet discovered – beats the previous record holder by about a billion light years. It sits on the cusp of the distance limit expected for a galaxy cluster, as physicists believe gravity could not have worked fast enough for them to cluster together much earlier.

JKCS041 was originally detected in 2006 in a survey using the UK's Infrared Telescope, but it was only identified as a galaxy cluster when data from this and other telescopes were combined with data from NASA's Chandra X-ray Observatory. Galaxy clusters are composed of approximately 85% dark matter, 12% gas and 3% star material. The gas is very hot and, according to the laws of physics, it should evaporate unless there is a strong gravitational field holding it in place, in the same way that the Earth's mass provides the gravitational field that holds our atmosphere in place. The fact that the intergalactic gas does not boil off into space is evidence that there is a massive amount of unseen material – dark matter – providing the gravitational field.

The hot gas emits strong X-rays and detection of these would confirm whether JKCS041 was an established galaxy cluster or one caught in the act of forming. Maughan analysed the data and verified that the extended X-ray emission seen by Chandra meant that hot gas did indeed exist between the galaxies, as expected for a true galaxy cluster. Further study of JKCS041's characteristics – its composition, mass and temperature – will reveal valuable information about how the Universe took shape.



NASA/CXC/INAF/S.ANDREON ET AL. OPTICAL: DSS; ESO/VLT

X-rays from Chandra are displayed as the diffuse blue region, while the individual galaxies in the cluster are seen in white, embedded in the X-ray emission.

Galaxy clusters are the largest gravitationally bound objects in the Universe

Maughan was also involved in tracking down a gigantic, previously unknown, assembly of galaxies, located almost seven billion light years away. The discovery, made possible by combining two of the most powerful ground-based telescopes in the world, provides insight into the 'cosmic web' and how it formed.

The most widely accepted cosmological theories predict that galactic matter clumps together on a scale even larger than galaxy clusters. In this 'cosmic web', galaxies embedded in filaments of light stretching between inky voids form a gigantic wispy structure. "These filaments are millions of light years long," explains Maughan, "creating enormous networks with massive galaxy clusters forming at the busiest intersections. Lurking like giant spiders, these clusters grow ever larger by greedily consuming the material that is funnelled on to them via the filaments."

Astronomers have struggled to determine how these structures come into existence, for although massive filamentary structures have been often observed at relatively small distances from us, solid proof of their existence in the more distant Universe has been lacking. Now, however, Maughan and the team have come a step closer to finding the evidence they need. Following the discovery of a filamentary large structure around a distant cluster of galaxies, they used two major ground-based telescopes to study this structure in greater detail. By measuring the distance from Earth to over 150 galaxies within it they obtained a three-dimensional view of the structure in which they identified several clumps of galaxies surrounding the main cluster. Some of the clumps are already feeling the fatal gravitational pull of the main cluster and will eventually fall into it. The filamentary structure is located about 6.7 billion light-years away from us and probably extends beyond the 60-million-light-year field of view probed by the team. It is the first time that such a rich and prominent structure has been observed in the distant Universe. Future observations have already been planned to obtain a definite measure of its size. ■

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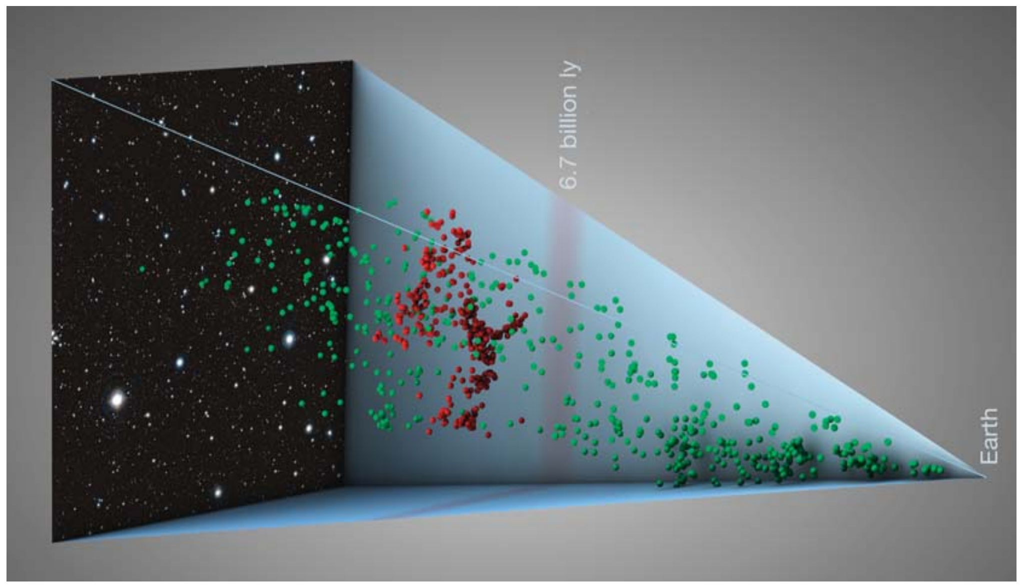


ESO/L. CALÇADA/SUBARU/NATIONAL ASTRONOMICAL OBSERVATORY OF JAPAN/M. TANAKA

This 3D illustration shows the position of the galaxies and reveals the extent of this gigantic structure. The galaxies located in the newly discovered structure are shown in red. Galaxies that are either in front or behind the structure are shown in green.

BOOKS, BOOKS, BOOKS

"To sit alone in the lamplight with a book spread out before you and hold intimate converse with men of unseen generations – such is a pleasure beyond compare."

Kenko Yoshida

"Never judge a book by its movie."

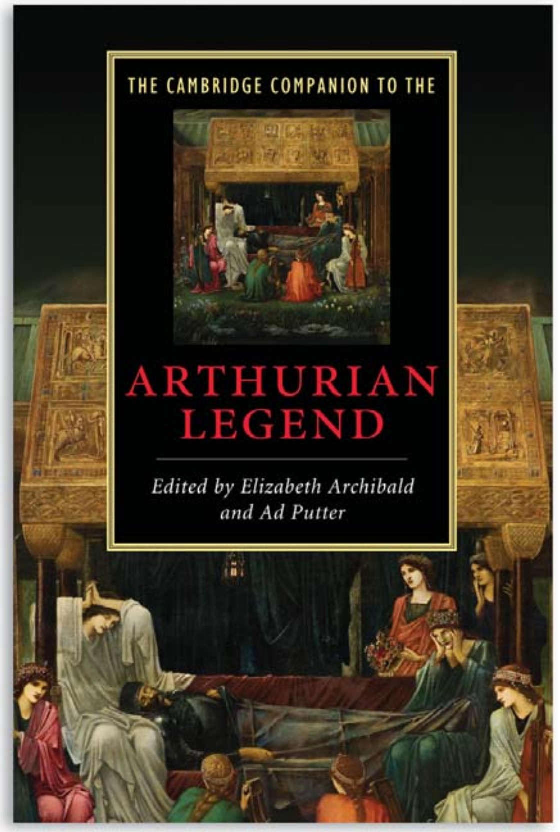
J.W. Eagan

"I find television to be very educating. Every time somebody turns on the set, I go in the other room and read a book."

Groucho Marx

"A book is like a garden carried in the pocket."

Chinese Proverb



The Cambridge Companion to the Arthurian Legend

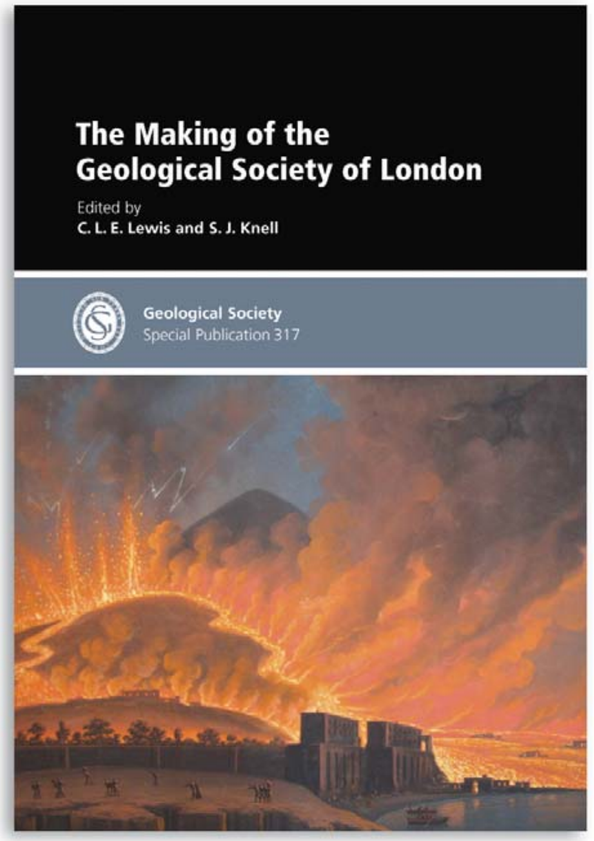
Edited by Professors Elizabeth Archibald and Ad Putter, Department of English

The Arthurian legend has inspired European writers and artists for almost fifteen hundred years. From shadowy beginnings in early medieval chronicles and poems, it has developed through medieval romance to modern films and TV series. What can account for the evergreen popularity of the 'Once and Future King'? There is no simple answer, but the *Companion* outlines the evolution of the legend from the earliest documentary sources to *Spamalot* and analyses how some of the major motifs of the legend have been passed down in both medieval and modern texts.

"The international team of contributors includes a strong Bristol presence," explain the editors. Indeed it does. Professor Ronald Hutton, Department of History, opens with a lucid account of the earliest Welsh and Latin sources and the thorny question of Arthur's historicity, then Ad Putter describes the 12th century when King Arthur acquired both an official biographer and a champion poet, who pioneered a new genre of Arthurian romance, introducing both Lancelot and the Grail. Emeritus Professor John Burrow covers the 14th century when Arthurian writing in English first flourished, and Elizabeth Archibald discusses some playful, ironic and openly critical treatments of the legend, showing that the makers of *Monty Python and the Holy Grail* are heirs to a long tradition. The final chapter, 'Arthurian Geography', is by Drs Robert Rouse and Cory Rushton, who both did their PhDs in the English Department at the University. They focus on the many places in Britain that have been associated with the legendary king over the centuries.

With a map of Arthur's Britain, a chronology of key texts and a guide to further reading, this volume will itself contribute to the continuing fascination with the King and his many legends. ■

Cambridge University Press, 2009



The Making of the Geological Society of London

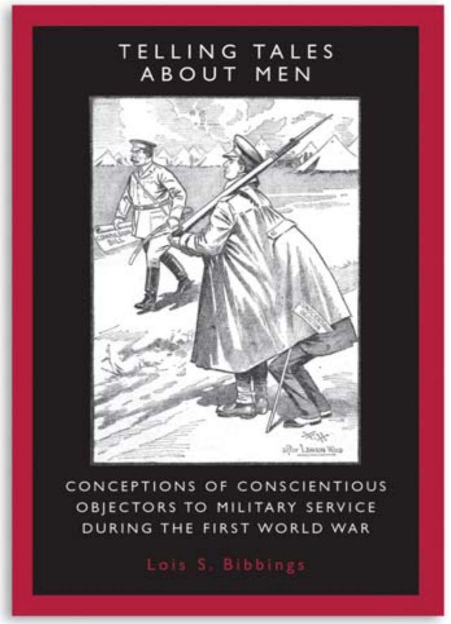
Edited by Dr Cherry Lewis, University of Bristol, and Professor Simon Knell, University of Leicester.

Founded in 1807, the Geological Society of London is the oldest geological society in the world. In celebration of its 200-year history, this book commemorates the lives of the Society's 13 founder members and sets geology in its national and European context at the turn of the 19th century. In Britain, isolated from the Continent for many years by continuing wars, geology was just emerging as a subject in its own right from three closely related disciplines – chemistry, mineralogy and medicine – disciplines that reflect the principal professions and interests of the founders.

The editors were particularly keen that this volume would first look in depth at the founders and the contributions each man made to the Society, and then examine the context of the Society's birth and the various developments that caused it to come into being. They hope to draw readers away from the conventional narrative about how the Society was inaugurated and challenge some of the myths that have grown up over the past 200 years. "As a consequence," says Lewis, "we could not help feeling somewhat conscious of the responsibility imposed on us from the future – were we creating our own myths to be challenged in a hundred years' time?"

The tremendous energy and co-operation of these 13 men, about whom little was previously known, quickly mobilised like-minded men around the country and fuelled the nation's passion for geology, which reached its peak in the 1830s; an enthusiasm that soon spread to the new countries of America and Australia. Two previously unpublished works from this period, essential to understanding the founding of the Society, are reproduced in this volume for the first time. The book closes with a review of the Society's 2007 bicentenary celebrations. ■

Geological Society Special Publication, 2009



Telling Tales About Men

By Lois Bibbings, School of Law

This book provides an intriguing account of how conscientious objectors, who opposed war on religious, moral and political grounds, were perceived during the First World War. Historically, conscientious objectors were imprisoned or otherwise penalised when their beliefs led to conflict with the government. Unsurprisingly, they were often deemed to be cowards, traitors, despicable criminals and degenerates. However, at the same time these men were sometimes considered to be heroes and patriots – upstanding and intensely moral folk.

Exploring the relationship between men, war, culture, patriotism and individual conscience, Bibbings draws on a range of materials and disciplines to produce this socio-cultural study. Sources include diaries, government papers, legal records, newspapers, magazines and novels, while the book is informed by writings from literary and gender studies, criminology, sociology, law and history. "We all know stories about the Great War," says Bibbings, "but these tend to focus on soldiers and warfare. What I wanted to do in this book was to explore the ways in which tales could be told about the men who refused to fight."

"The narratives about 'conchies' presented within these pages challenge established understanding about these men and makes a valuable contribution to existing literature about those who say no to war," commented the military historian, researcher and broadcaster, Julian Putkowski. "This is an original, culturally nuanced and engaging book which marries the personal with the political." ■

Manchester University Press, 2009

‘Realism’,‘perfectionism’ and the European Court of Human Rights

Professor Luzius Wildhaber, left, talks to Professor Steven Greer.

Earlier this year the University was delighted to host Professor Luzius Wildhaber, former President of the European Court of Human Rights. During his visit, Wildhaber spent time laying the foundations for a research project in collaboration with Steven Greer, Professor of Human Rights in the School of Law.

Research collaboration between judges, academic lawyers and social scientists is uncommon, even when the judge himself is also a distinguished academic. But it can lead to some illuminating insights. Greer first met Wildhaber on a visit to Strasbourg, the home of the European Court of Human Rights, in January 2004 when completing research for his book, *The European Convention on Human Rights: Achievements, Problems and Prospects*, that was subsequently shortlisted for the Hart Socio-Legal Book Prize 2008. This work builds on an argument made by Wildhaber and others that the central function of the European Court of Human Rights should not be the delivery of ‘individual justice’ – thereby addressing alleged breaches of the European Convention on Human Rights primarily for the benefit of individual applicants – but instead it should concentrate much more on the delivery of ‘constitutional justice’.

The main reason for this is that the European Court of Human Rights only has the capacity to adjudicate about five per cent of the 50,000 or so individual applications it currently receives per year. A key question, therefore, is how this five per cent should be selected.

The European Court of Human Rights only has the capacity to adjudicate about five per cent of the 50,000 or so applications it receives per year

The constitutional justice model argues that the current admissibility criteria are too wedded to individual justice and should be replaced by a ‘seriousness’ test which would mean two things: first, that only the most serious of the alleged Convention violations would be chosen for judgment, and second, that these should be settled not just for the benefit of individual applicants, but also in the interests of the many actual and/or potential victims whose interests the applicants could be said to represent.

However, although this ‘constitution-alisation thesis’ is increasingly the hub around which the debate about the future of the Convention system now revolves, it is not uncontroversial. Its key implication – that only applications alleging serious Convention violations should proceed to judgment – was, for example, vigorously opposed by Amnesty International and 113 other NGOs in 2004 in the closing stages of an official review of the Convention system. The review was prompted by the urgent need to find a solution to the Court’s burgeoning case-load and took over three years to conduct. But, in the event, it failed to deal with the problem effectively.

Less than a year after the reform package had been approved, and before it had been put into operation, the Council of Europe itself acknowledged that it would not improve things sufficiently and that further reform was therefore required. The crisis deepened in December 2006 when implementation was blocked by the Russian parliament. As a result, a pared-down version was introduced in the summer of 2009 for all of the Council of Europe’s 47 member states except Russia. This leaves complaints of Convention violation against Russia – the state with some of the gravest human rights problems in Europe – still governed by the discredited pre-reform procedures and the Court still drowning in a flood of individual applications.

The collaborative research upon which Greer and Wildhaber have embarked is linked to the constitutionalisation thesis but seeks to approach it from a fresh perspective. In his inaugural lecture as Professor of Human Rights in March 2008 – subsequently delivered in different forms in Malaysia, Australia and Croatia – Greer argued that human rights can be approached in five different ways. We can be indifferent to, or we can ignore them (‘indifference’). We can be hostile towards them and reject them in their entirety (‘hostility’). We can be ambivalent or sceptical about them, or accept them subject to significant reservations (‘scepticism’). We can endorse them realistically, acknowledging both their strengths and limitations, (‘realism’), or we can endorse them excessively by expecting more of them than they are capable of achieving (‘perfectionism’).

Greer argues that ‘scepticism’, ‘realism’ and ‘perfectionism’ now dominate global debates, including those about the role and future of the European Court of Human Rights, and that ‘realism’ is the most convincing and viable of all. He claims that at the core of the Court’s problems lies a “debilitating lack of realism about what its priorities should be in post-Cold War Europe. For example, in spite of the fact that the case-overload crisis has visibly been gathering momentum for nearly 20 years, the official response has been characterised by inertia, excessive bureaucratisation, chronic indecisiveness, institutional incoherence and minimalism. There has also been a profound reluctance to consider thoroughly what the function of the Court should be in an international environment that is radically different from the one in the 1950s into which it emerged”.

‘Constitutional justice’ is the only realistic model for case selection

Wildhaber adds: “Almost from the moment of my arrival in Bristol, Steven and I began discussing a number of possible avenues for research collaboration. But the one I liked best was the challenge presented by seeking to explore the implications of his ‘scepticism-realism-perfectionism’ model for the European Court of Human Rights. Of course, unsurprisingly, neither of us finds much trace of scepticism there! But we each agree that ‘individual justice’ has now been thoroughly discredited as a model for case selection. It simply expects more than can possibly be delivered. This leaves ‘constitutional justice’ as the only realistic alternative both for admissibility and for adjudication.”

Greer and Wildhaber hope their collaborative project will contribute to the, as-yet unresolved, debate about the case-overload crisis. They also want it to stimulate discussion about how appropriate criteria for ‘realistic judgments’ can be identified, and what difference the application of those criteria might make. ■

www.bristol.ac.uk/law

Professor Stafford Lightman

Professor Stafford Lightman and his team in the Laboratories for Integrative Neuroscience and Endocrinology are interested in how stress impacts upon human health throughout the lifespan – just how does it affect your body and the way it responds to disease?

The lifetime effects of stress

Stress-related disease is a rapidly increasing feature of our society, but the mechanisms through which stress causes disease are poorly understood. It is an area of research that fascinates Stafford Lightman, who has been working on finding answers to some of these questions for many years. Recently he has been able to demonstrate that events that happen to you around the time of your birth, or even before you are born, can have epigenetic effects on your later life. What that means is that while such events do not actually affect the genes themselves they can affect the way your genes function. So if you had a very stressful childhood, this can have long-lasting influences throughout the whole of your life.

Lightman has looked at these effects in rodents and has seen that if rats are stressed early on in their lives, this can change the way they produce their stress hormones throughout the rest of their lives. For example, if a mother rat neglects her pups, when those pups become adults and are examined to see how they respond to stress they have a much stronger response than pups that had caring mothers. In adult rats the levels of the stress hormone corticosterone in those stressed as pups goes much higher during a stressful event and lasts much longer than in rats that were well looked after as pups.

In humans the situation is much the same. If adult stress is superimposed on a stressful childhood, that combination not only means that are you more susceptible to stress in later life, but also that when you encounter a stressful situation your stress hormones – called cortisol in humans – dramatically increase. If these hormone levels are raised chronically for a long period of time, they can cause problems with the whole range of biochemical processes that occur within us and we become more susceptible to diseases such as depression, diabetes and hypertension, and also to memory loss. High levels of cortisol cause shrinkage of the hippocampus which can lead to poor memory function.

If stress hormone levels are raised for long periods we become more susceptible to diseases such as depression, diabetes and hypertension

Having established that stress hormones can have such effects, Lightman naturally asked the question – how does it happen? What he found was extremely interesting. It seems that cortisol is secreted in a circadian rhythm, which means that it has a peak level early in the morning and then decreases throughout the rest of the day. In humans, this peak occurs just before we wake up; cortisol is thus labelled as an 'anticipatory hormone' because it goes up in anticipation of what our body will need during the day. Since cortisol and corticosterone act on the liver to release glucose, this morning peak ensures that we have enough sugar in our blood to provide sufficient energy for us to function properly during the day. One fascinating outcome from Lightman's studies is the fact that the circadian rhythm of cortisol and corticosterone is made up of multiple pulses that occur roughly every hour, so in fact hormone levels are going up and down all the time, especially in the morning in humans when cortisol levels are really high and the pulses are very big.

The relevance of these pulses is that they allow the body's tissues to respond not just to the level of the hormones, but also to the frequency with which the hormone pulses occur. In fact, it is the basis of a digital signalling system. In arthritis, for example, the frequency of these pulses is doubled, allowing our natural hormones to moderate the disease process. Also, in patients with obstructive sleep apnea – an unpleasant condition in which people stop breathing for periods of a few seconds several times every night whilst they are asleep – the size of each individual cortisol pulse is markedly increased. This may well be one of the reasons why these patients develop high blood pressure, heart disease, diabetes and other stress-related disorders. Indeed, it is clear that in different physiological or pathological conditions not only do levels of hormones change but the frequency and pattern of their pulses change as well.

The circadian rhythm of cortisol and corticosterone is made up of multiple pulses that occur roughly every hour

The next step for Lightman and his team was to look at the molecular biology of these pulses to try to understand what was going on at the cellular level. What they revealed is that every single pulse of corticosterone in rats is associated with a pulse of corticosterone receptors charging into the nucleus of the cell, binding on to DNA and making messenger RNA. Almost all cells in the body have these receptors which can be thought of as the 'lock' in a cell that is activated by the hormonal 'key' of corticosterone. The messenger RNA that is made in response to these pulses is the signal for the production of new proteins by the cell and thus is vital for normal cellular function.

The other important discovery was that different tissues in the body experience these pulses in different ways. The liver, for example, is extremely sensitive to pulses and so immediately responds to every individual pulse. Some parts of the brain, however, need two or three pulses before a response is generated. This is useful, as in a stressful situation you need your blood sugar levels to rise very quickly, while the brain may need more time for preparation before it wakes up.

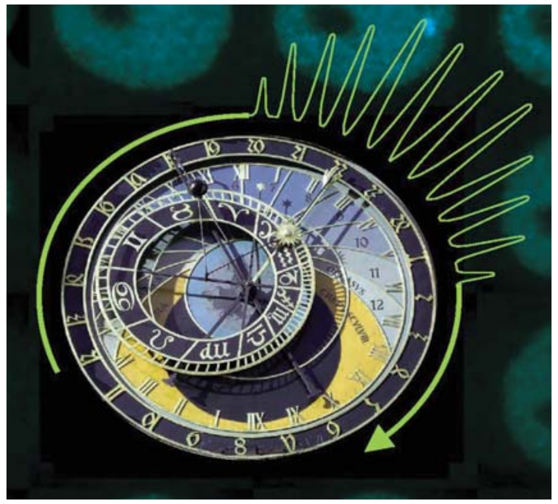
This research area is still in its infancy and its implications are not yet fully understood. However, what Lightman's group does know is that these fluctuations or oscillations of hormones, which are going on all the time, allow us to have a system that reacts extremely fast in stressful situations. When confronted with a lion, for example, you want to have a really massive hormone response so that your brain focuses on how to escape and your blood sugar goes up so you have the energy to run away very fast.

But what does all this mean in today's society where we are not often confronted by lions? "Now that we understand how these stress mechanisms work," says Lightman, "we can begin to work out why some people appear to be at greater risk than others of getting diseases that are associated with stress. Furthermore, we will be much better positioned to design therapeutic ways of dealing with it. In the longer term we hope to be able to identify people who have had a particularly stressful childhood, for example, and provide them with advice that will protect them from developing the diseases to which they will be susceptible."

In the future, Lightman hopes to better understand what is called the epigenome – the way that past experiences have modified our cells, making us more vulnerable to certain diseases. "We will be able to look at people who, perhaps because of their childhood experiences, have had a change in their epigenome, which means that their genes respond more readily to stress, thereby putting them at more risk of getting certain diseases. Whether or not it's a good or a bad thing, of course, one can argue about, but I think it will happen in the not-too-distant future. So personalised medicine won't only be related to the genes you have – your genome – it will also be related to your epigenome."

The Dorothy Hodgkin Building where Professor Stafford Lightman and his team are based.

We hope to be able to identify people who have had a particularly stressful childhood and provide them with advice that will protect them from developing the diseases to which they may be susceptible



Despite these fascinating results, there is still a great deal of work to be done investigating whether or not stress is a risk factor for all kinds of diseases. While we know, for instance, that there is a good correlation between being depressed and having a heart attack, we don't know what mediates that. "Is it because the individual has a cortisol abnormality?" asks Lightman. "We know that people who are depressed have abnormal cortisol secretion. Is that the link?" Clearly the answer to these questions with regard to specific individuals would be extremely valuable.

To help further this work, Lightman and his team were thrilled to discover recently they had won a grant of £1.7 million from the Wellcome Trust. They will use these funds to look at how different patterns of stress hormones can affect genes in the brain and the liver, as well as how these patterns affect memory and the development of diseases such as diabetes. Undoubtedly they will have more answers in a few years' time. ■

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Professor Varinder Aggarwal

BUILDING BLOCKS OF THE FUTURE

Professor Varinder Aggarwal is no ordinary builder. He and his team in the School of Chemistry have just discovered a new technique that could hasten the development of new drugs for today's incurable diseases – by building complex organic molecules.

Complex organic molecules are finding increasing applications in virtually all aspects of our lives, from the pill we take for heart disease and the insecticide used in the production of the food we eat, to the flat screens of mobile phones. However, the science of creating complex organic molecules, known as organic synthesis, is exacting. It requires years of training to master the principles and then, rather like building an enormous cathedral, many years to assemble the building blocks into the required molecule. So why is organic synthesis so hard?

Organic synthesis involves the piecing together of smaller organic building blocks until the target molecule is created, but this process is not as simple as putting one row of bricks on top of another. In organic synthesis the two ends of the building blocks first have to be activated in some way to make them attracted to each other so they can bond together. Once bonded, this new molecule is used in another reaction with a different building block, a process which is repeated again and again until the target molecule is formed.

However, as the molecule increases in size and complexity it becomes more and more difficult to activate only the site you want, without other sites being activated as well. As a result, unwanted compounds are formed in addition to the desired molecule. So the molecule has to be extracted from the mixture before the next step of activation and attachment of another building block can occur.

The breakthrough Aggarwal and his team of molecular chemists have made is that they have found a way of activating particular building blocks with complete selectivity for a particular site. More importantly, the product formed is

As the starting molecule passes down the assembly line, building blocks are added sequentially with extraordinary precision

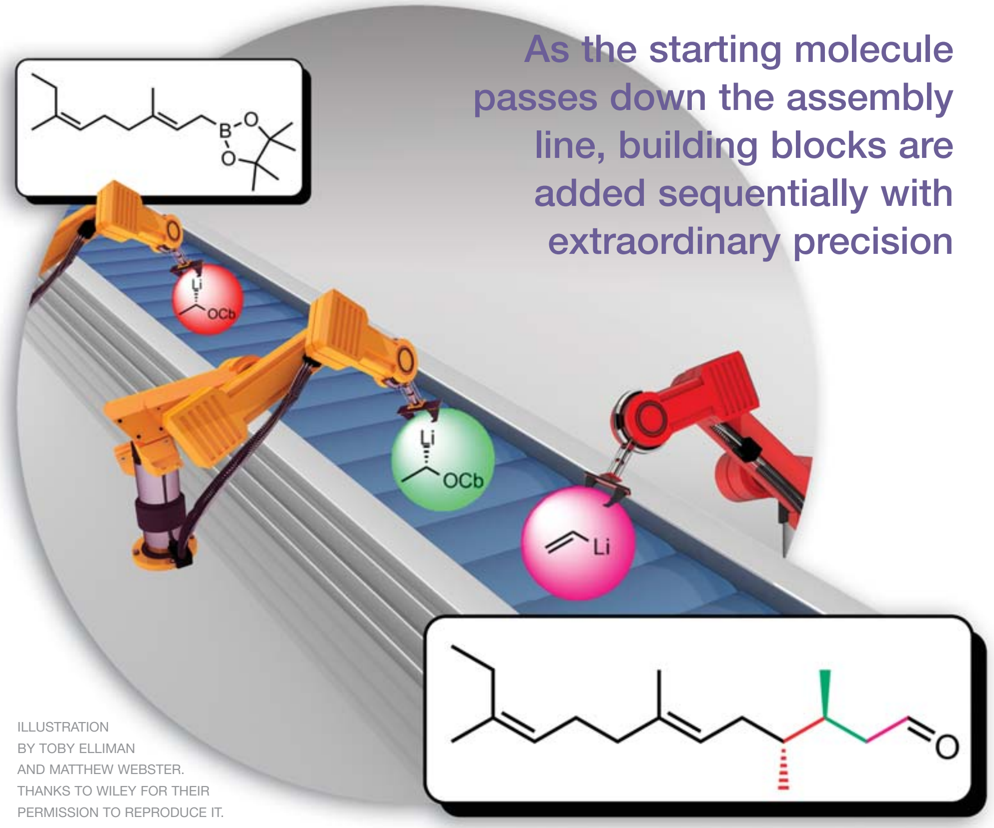

ILLUSTRATION BY TOBY ELLIMAN AND MATTHEW WEBSTER. THANKS TO WILEY FOR THEIR PERMISSION TO REPRODUCE IT.

ready-primed for reaction with the next building block without the need for further activation. This avoids the arduous task of selectively activating an increasingly complex molecule at a specific site; it is already done through some clever chemical gymnastics.

They have also shown that complex molecules can be created by repeated addition of these building blocks in a process analogous to a molecular assembly line. As the starting molecule passes down the assembly line, building blocks are added sequentially with extraordinary precision so that at the end of the process a complex molecule is created with specific shape and functionality.

It is hoped that the molecular assembly-line process can ultimately be automated so that complex organic molecules with specific architectures and functions can be created simply by pressing a few buttons.

These exciting new developments are enabling a technology with a potentially huge impact. Furthermore, they open up the scientific discipline of organic synthesis from the limited confines of the expert to a much broader pool of scientists. Physicists, molecular biologists and all the disciplines in between will no longer be limited in their scientific quest by molecules they can buy off the shelf – they will be limited only by their imaginations. ■

www.chm.bris.ac.uk

Professor Dek Woolfson

Engineering the chemistry of biology

Professor Dek Woolfson is based in the School of Chemistry and holds a joint appointment with the Department of Biochemistry, because his research is done at the interface between chemistry and biology. "We often think of biology as something magical," he says "but in many ways it's really applied chemistry." His current research is moving into the exciting and potentially controversial field of synthetic biology.

Individually, the words 'synthetic' and 'biology' seem to contradict each other: isn't biology – life and living organisms – just the opposite of synthetic? Apparently not, for today synthetic biology is a rapidly advancing new field of science. The phrase refers to the design and fabrication of biological components and systems that do not already exist in the natural world, as well as to the redesign and fabrication of existing biological systems. Woolfson is largely interested in understanding how molecules are built and assembled in biology and then applying this to build new molecules with desired functions.

"Synthetic biology is about improving our ability to engineer biology," says Woolfson, "and to engineer biology you have to understand the underlying chemistry. I don't think that this takes the wonder out of biology, it just gives us a handle and the tools to get in there and try to understand some of its processes."

Synthetic biology is about improving our ability to engineer biology, and to engineer biology you have to understand the underlying chemistry

Indeed, the first thing Woolfson does when setting out to engineer biology is to sit at a computer to look at the structure and chemistry of natural molecules, particularly proteins. He then asks the question, "What are the important bits of the chemistry that lead to the wonderful 3D structures proteins make and the functions they perform?" It is only when the chemistry has been understood that he ventures into the lab. There he attempts to string together amino-acid building blocks to make synthetic versions of proteins. In his own words: "We look at natural molecules and ask, 'How does nature do this?' And then we take those key features and build them into synthetic molecules to mimic the natural ones."

Specifically, Woolfson is trying to capture features of the materials that hold cells together and which provide the environment to turn collections of cells into tissues such as skin, liver and networks of nerves. This 'glue' is called the extracellular matrix (ECM). However, the ECM is made up of large, complicated molecules with lots of different chemistries, so Woolfson began to investigate whether it would be possible to build something similar to ECM, but out of much simpler and more chemically accessible materials. That was 10 years ago. Today he has developed nano-sized proteins that have been designed to 'self assemble' into long, spaghetti-like strings, which then become entangled to form a gel. In biology, proteins often self-assemble because one side hates water and the other side likes it, so they naturally stick together in a configuration whereby the water-hating side is protected and hidden by the water-loving side. Woolfson uses this principle to create his molecules and instruct their assembly.

The result is a hydrogel (a gel in which the liquid constituent is water) made up of these tiny, spaghetti-like strings of proteins which acts as a scaffold to support cell growth in much the same way as the ECM does. Furthermore, when people in Woolfson's group looked at the hydrogel using an electron microscope they saw that the gel had pore sizes of about 200 nanometres, which is approximately the size of pores in the ECM. These nano-scale holes allow nano-scale objects like proteins and nutrients to pass in and out and move around in the gel.

Woolfson summarises: "So the first point is that using these protein strings we've made a hydrogel in which we can cluster molecules and cells together. Secondly, it's percolated; it's got holes in it so proteins can pass in and out. And thirdly, we can manipulate it. Because of the simplicity of our system it's very easy – in principle – to add a smidgeon of something else that carries a signal that says, for example, 'turn this cell from a stem cell into something that makes cartilage'. So by using chemistry and self-assembly to build these things, we can add ingredients that make it useful."

One area the group is particularly interested in is growing nerves. At the moment, if someone has had an operation or injury that results in severed nerves, a nerve is taken from the outside of the foot, where it won't be greatly missed, and used to replace the damaged one. However, while the potential to grow such important biological components is enormous, the reality is still some way off.

One reason this particular method has such potential is that growing biological components in this way will mean they are biocompatible. So, in principle, once the job of growing new nerve tissue or cartilage has been done, the hydrogel will be broken down by the body, absorbed and disposed of. "When you're doing this kind of tissue engineering, what you want is to provide a cosy environment in which the cells you introduce can grow to become new tissue, but then you want everything else you put in there to get that going to disappear. You want the body to take over properly and behave as if the new tissue had always been there," explains Woolfson.

You want the body to take over and behave as if the new tissue had always been there

A bundle of five protein helices. It is structures like this that stack end-to-end to make strings of spaghetti-like protein.

The second advantage of this system is that protein strings don't necessarily have to be synthesised in the lab – bacteria can be used to produce them. That might sound extraordinary, but the best way of producing protein material is in big fermenters using bacteria. The bacteria are given the gene for a required protein and can be encouraged to just keep on producing it. Furthermore, in this system you know exactly what's in there, so there are no hidden surprises. In the case of Woolfson's hydrogels, they are 99.5% water and 0.5% of other things that can be added very precisely in order to alter functionality. "In a nutshell," concludes Woolfson, "there is almost no limit to what you can use it for." ■

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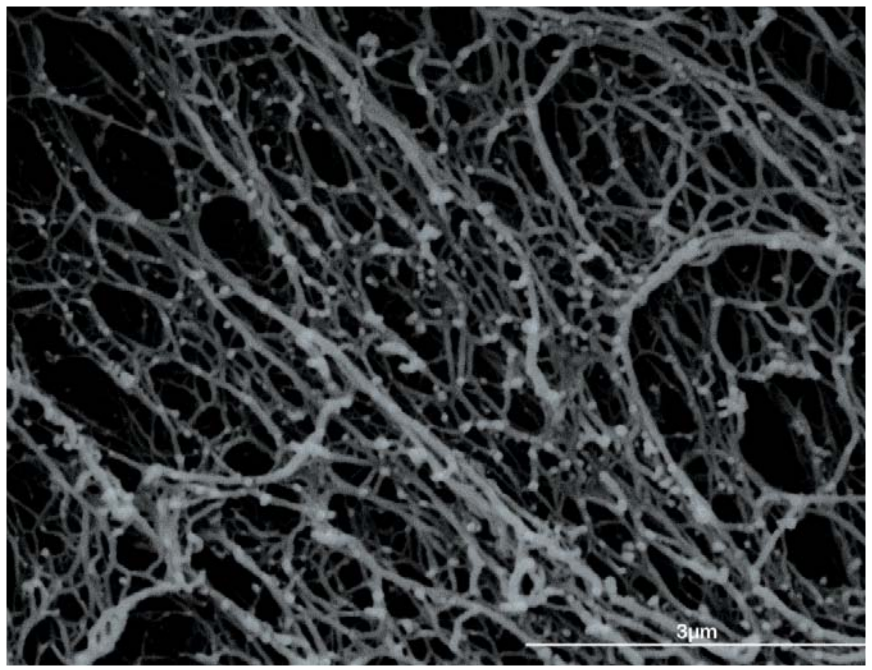
This research was funded by the BBSRC and involved a collaboration with Unilever.



These proteins form gels of interconnected fibres that support cell growth.

Common as dirt – is our most precious bank about to go bust?

Matt Fortnam in the Department of Earth Sciences talks to Professor Vala Ragnarsdottir, co-ordinator of the European SoilCritZone project, about the importance of soil, and draws comparisons between the global financial crash and the impending global soil crisis.

Fertile soil can be regarded as capital. Not the capital familiar to economists and stockbrokers, but something much more important. If soil is capital, then the trees, crops and wildlife that come from this soil are the profits which society depends upon for food and wealth – for its very existence. To yield higher profits, we need to protect and build our capital.

In the past 30 years, industrial agriculture has increased demand on the Earth's soil to such an extent that its capacity for renewal is being exceeded by one hundred times or more. In other words, we are consuming capital as if it were income. And, as any banker will tell you, confusing capital with income is a recipe for bankruptcy.

Since the end of World War II, the industrialisation of agriculture, or the 'Green Revolution', has generously plied the soils with readily available chemical fertilisers to replace the nutrients withdrawn by crops. Farms have seen the arrival of gigantic machinery to plough, spread and harvest ever-larger fields at higher and higher speeds. Insects are no longer a problem, defeated as they are by huge quantities of pesticides. Thanks to these technological advances, farmers have continued to supply enough food to feed the world's growing population. The cost of a basket of food has also fallen by half over the past 30 years, according to the United Nations Food and Agriculture Organization.

The demand placed on soil will become greater as the global population grows towards 10 billion by 2050

These advances, however, come at a price. Although not as publicly visible as the recent losses in the banking sector, the loss of productive soil is staggering. Soil degradation is harming the productivity of 40% of the world's agricultural land, and up to 70% in some regions, according to the International Food Policy Research Institute. Furthermore, the demand placed on soil capital will become greater as the global population grows towards 10 billion by 2050. The ability of soils with diminishing fertility to feed the world will be increasingly called into question.

Despite the achievements of the 'Green Revolution', advances in food production are masking the true debt that has accrued due to loss of the soil's capital. Just as consumers in the US and Britain were able to live beyond their means by borrowing money to buy houses and fund their lifestyles, we have been able to live beyond the means of the soil by borrowing fertility with synthetic nutrients to increase the productivity of fields.

Echoing the trouble faced by banks in managing their debts, soils are failing to cope with the shortfalls. If farmers continue to pursue current industrial agricultural practices, then soil, the life-sustaining bank, could go bust. And no amount of quantitative easing – or in this case chemical inputs and mechanisation – will revive it. To create capital, academics and policymakers must listen to and learn from farmers taking a different approach to producing food. The boom years for food production can no longer be taken for granted. Agriculture must adapt or else lose its most precious bank.

Top: Matt Fortnam. Above: Professor Vala Ragnarsdottir.

Local, traditional knowledge of how to support healthy soils offers alternatives to industrial agriculture. Organic, biodynamic and permaculture farming practices build the natural fertility of soil by using this knowledge and our understanding of how soils function naturally. Some farmers in Kenya, for example, have returned to the techniques of their ancestors with impressive results. Although these practices are spreading globally and there is growing evidence that they could feed the world, they often fall under the radar of politicians.

Local, traditional knowledge of how to support healthy soils offers alternatives to industrial agriculture

Over the past two years, SoilCritZone, a European Commission (EC) research project co-ordinated by the University of Bristol, brought together a network of over one hundred European, American, Chinese and African soil scientists to debate how to build on the work of their predecessors. "The focus for us in the foreseeable future is understanding how to restore soil and working out how to protect the vital functions that the soil provides society," says Ragnarsdottir, who co-ordinated the project but is now a Visiting Fellow from the University of Iceland.

CHERRY LEWIS

The project's report, released in September 2009, recommends that future research should integrate knowledge from all relevant disciplines to understand the 'critical zone' – a region extending from the very tops of trees, down through the soil, to the groundwater below. This is necessary because there is a need to better understand natural soil systems throughout their lifecycle, since they provide valuable lessons on how to create sustainable agricultural soil systems.

To understand the life cycle of soils, scientists need to model all the processes within and influencing the critical zone. Building such models is currently difficult since data from the various soil disciplines are recorded at different sites with different techniques. To remedy this, the report proposes the establishment of a network of soil observatories across Europe.

"We need data to be recorded at a number of soil observatories by scientists from all relevant disciplines," explains Ragnarsdottir. "By understanding how all the aspects of the critical zone interact, including the rocks, the animals and the weathering processes, we will begin to understand how to prevent the loss of the vital services provided by the soil in the future."

The models would use data from the observatories to inform policymakers and land resource managers of areas at particular risk of soil degradation in Europe. The EC will consider the recommendations of the project as part of its 'roadmap' for research in Framework Programme 7, which bundles together the European Union's (EU) research initiatives. The development of the proposed EU Soils Framework Directive, which aims to protect soils across Europe, will also draw upon the advice given by the SoilCritZone network.

The time has come for the different soil disciplines to work towards a common endeavour to restore soils to their former glory. All of their expertise will be required to understand the critical zone as a complete system. The proposed soil observatories may not make the knowledge of soils complete, but they will certainly reinforce the foundations for the successors of today's soil scientists to build on. ■

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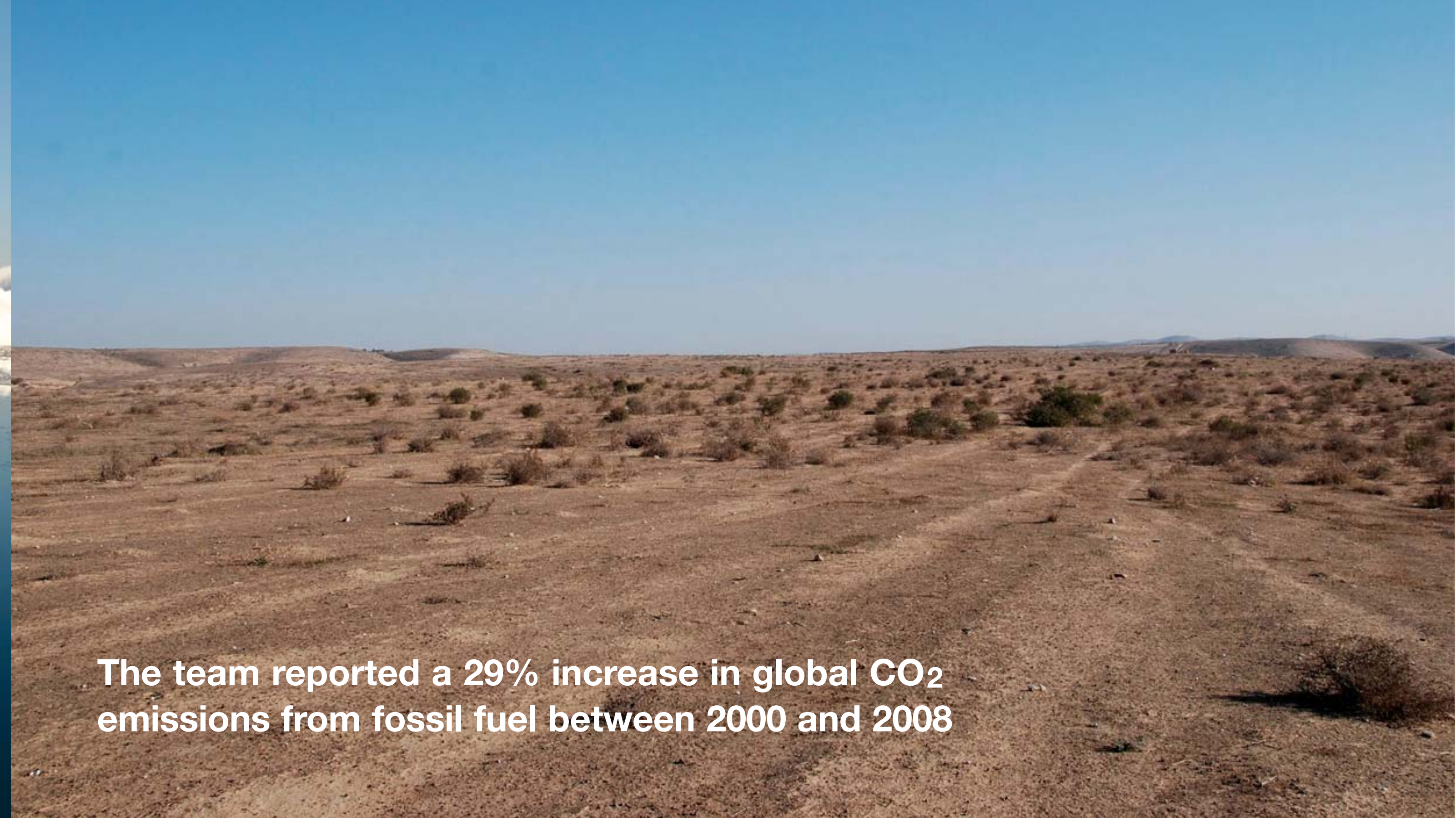
INFORMING COPENHAGEN



The team reported a 29% increase in global CO_2 emissions from fossil fuel between 2000 and 2008

The University has several groups that are among the leaders in the field of climate change research. In the run-up to the Climate Change Conference in Copenhagen, a flurry of articles was published in prestigious journals, six of which included researchers from these groups.

A study in *Science* (12 November) reported that satellite observations and a state-of-the art regional atmospheric model independently confirmed that the Greenland ice sheet is losing mass at an accelerating rate. This loss is equally distributed between increased iceberg production, driven by acceleration of Greenland's fast-flowing outlet glaciers, and increased meltwater production on the surface of the ice sheet. Since 2000, the Greenland ice sheet has lost about 1,500 Gt (1 Gt is the mass of 1 cubic kilometre of water), representing a global sea-level rise of five millimeters. Estimates suggest the ice sheet contains enough water to cause a global sea-level rise of seven metres.

The Greenland ice sheet contains enough water to cause a global sea-level rise of seven metres

Jonathan Bamber, an author on the paper, said: "It is clear from these results that mass loss from Greenland has been accelerating since the late 1990s and the underlying causes suggest this trend is likely to continue in the near future. We have produced agreement between two totally independent estimates, giving us a lot of confidence in the numbers and our inferences about the processes."

To help preserve the Greenland ice sheet, Pete Irvine and colleagues suggested in *Environmental Research Letters* (15 December) that light-reflecting geoengineering may be a way of cooling the Earth's climate. They used a model to predict what might happen if incoming solar radiation were reduced in a future where CO_2 is four times higher than pre-industrial levels, either by creating a 'sunshade' or by injecting sulphate aerosols into the stratosphere. Their results showed that if only a small fraction, 4.2%, of the sunlight that reaches Earth were deflected, the average temperature could be returned to pre-industrial levels and prevent the Greenland ice sheet from melting. However, although such schemes could cool the Earth's climate, they would also make it drier and change weather patterns. Reflecting only 2.5% of solar radiation, on the other hand, could reduce these undesired changes and still help prevent collapse of the Greenland ice sheet.

Reporting in *Nature* (19 November), a study re-evaluating records of 340,000-year-old East Antarctic ice cores showed that during brief periods between ice ages, temperatures were up to 6°C warmer than at present. Julia Tindall and others explained that until now, temperatures during warm periods between ice ages – known as interglacials – were thought to be slightly warmer than those of the present day. However, when they analysed Antarctic ice cores they were surprised to find peaks of relatively high temperatures. They concluded that previous temperature estimates from interglacial climates are likely to be too low and that the interglacial temperature of the level suggested by their research 'indicates there are serious deficiencies in our understanding of warmer than present day climates'. Tindall commented: "It is quite difficult to reconstruct temperatures from long ago. Although it is generally accepted that the climate was warmer during the last warm period, about 125,000 years ago, our results suggests it was much warmer than previously thought."

Dan Lunt and colleagues publishing in *Nature Geoscience* (6 December) also used data from the past to help understand the future. He and his colleagues compared temperature reconstructions of the Earth's environment three million years ago – when global temperatures and carbon dioxide concentrations were relatively high – to results from a global climate model used by bodies such as the Intergovernmental Panel on Climate Change. The temperature reconstructions were derived using data from three-million-year-old sediments from the ocean floor.

Lunt said: "We found that given the concentrations of carbon dioxide prevailing three million years ago, the model predicted a significantly smaller temperature increase than that indicated by the reconstructions. This led us to review what was missing from the model." The team found that the increased temperatures indicated by the reconstructions could be explained if factors that vary over long timescales, such as changes in land-ice and vegetation, are included in the model. This is primarily because such changes lead to more sunlight being absorbed, which in turn increases warming. Including these long-term processes in the model resulted in an increased temperature response of the Earth to carbon dioxide, indicating that the Earth's temperature is more sensitive to carbon dioxide than previously recognised.

The two other papers disagreed on the planet's ability to absorb carbon dioxide emissions. Wolfgang Knorr, publishing in *Geophysical Research Letters* (9 November), found that the amount of CO_2 absorbed by the oceans and terrestrial ecosystems – the planet's natural carbon sinks – has stayed approximately constant since 1850, despite emissions of CO_2 having risen from 2 billion tons a year in 1850 to 35 billion tons a year now. This suggests that the Earth's ability to absorb CO_2 is keeping pace with the rate at which we emit it into the atmosphere.

The results run contrary to a significant body of recent research which expects that the capacity of terrestrial ecosystems and the oceans to absorb CO_2 should start to diminish as CO_2 emissions increase, letting greenhouse gas levels skyrocket.

"Our conflicting results demonstrate what doing cutting-edge science is really like"

Indeed, according to research published in *Nature Geoscience* (17 November) just a few days later, emissions of carbon dioxide continue to outstrip the ability of the world's natural sinks to absorb carbon.

The *Nature Geoscience* team estimated that over the past 50 years, the amount remaining in the atmosphere 'had likely increased' from 40 to 45 per cent, suggesting a decrease in the efficiency of the natural sinks. Knorr's study, on the other hand, also found no increase in the airborne fraction during the past 50 years and that if anything the trend was negative at -0.2 ± 1.7% per decade, which is essentially zero. He therefore concludes that the capacity of terrestrial ecosystems and the oceans to absorb CO_2 has not diminished. The strength of his study, argues Knorr, is that it rests solely on measurements and statistical data, including historical records extracted from Antarctic ice cores – although we have already seen these are difficult to interpret – and does not rely on computations with complex climate models.

Both carbon sink studies were based on atmospheric composition data and statistical data on energy use and land use change, but differ in the way they calculate the trend, how they treat uncertainties in atmospheric concentrations and how they account for confounding climatic variability. Knorr explained: "Our apparently conflicting results demonstrate what doing cutting-edge science is really like and just how difficult it is to accurately quantify such data." Jo House, an author on the *Nature Geoscience* paper, concurred: "It is difficult to accurately estimate sources and sinks of CO_2, particularly in emissions from land use change where data on the area and nature of deforestation is poor, and in modelled estimates of the land sink which are strongly affected by inter-annual climate variability. While the science has advanced rapidly, there are still gaps in our understanding." ■

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