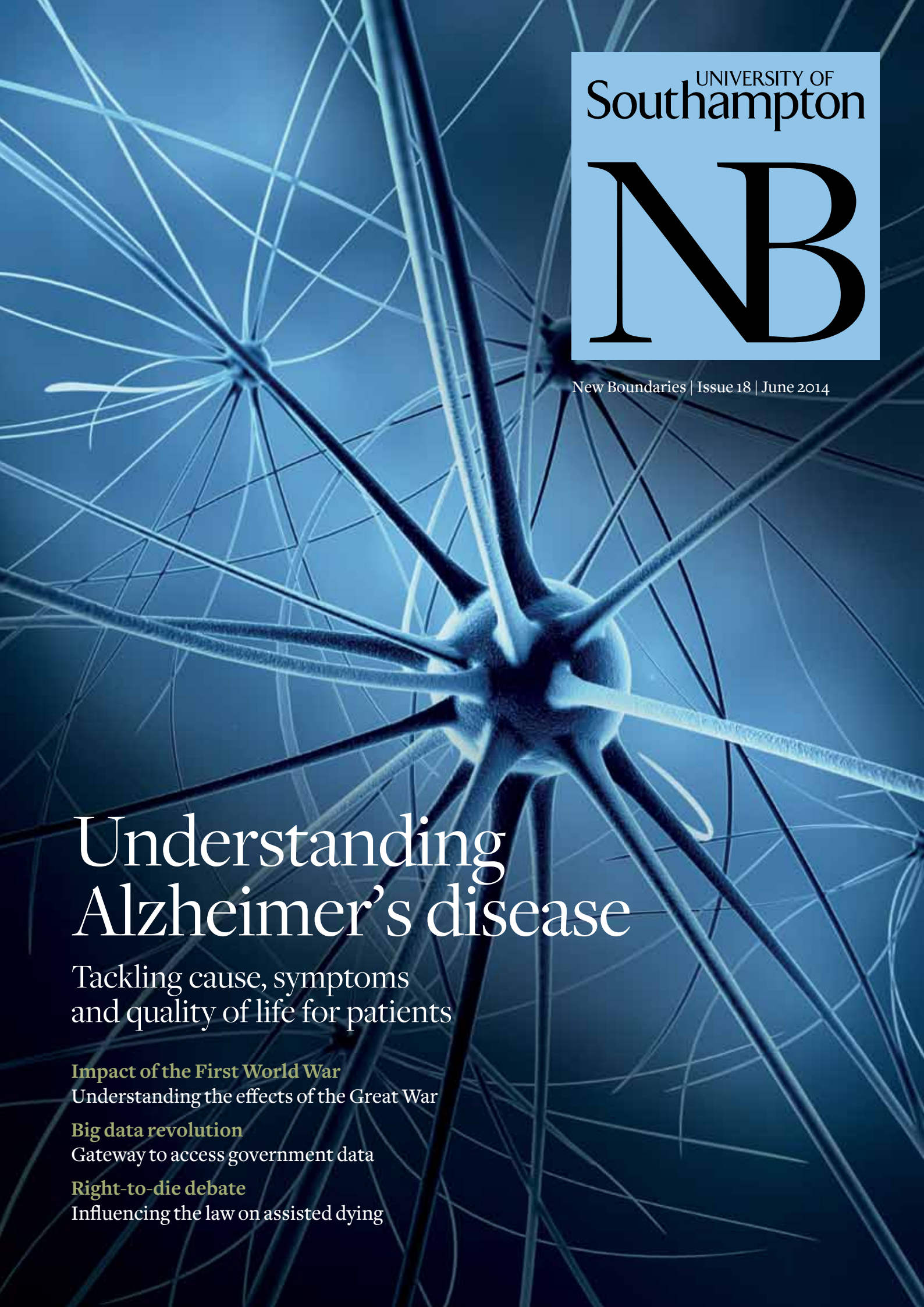

UNIVERSITY OF Southampton

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New Boundaries | Issue 18 | June 2014

Understanding Alzheimer's disease

Tackling cause, symptoms and quality of life for patients

Impact of the First World War
Understanding the effects of the Great War

Big data revolution
Gateway to access government data

Right-to-die debate
Influencing the law on assisted dying

In this issue

Welcome to *New Boundaries*, the University of Southampton's research magazine. In this issue, you will discover how our researchers are addressing some of the most challenging issues facing society today, from dementia in an ageing population to influencing the law on assisted dying.

Alzheimer's disease is the most common form of dementia, which is one of the most challenging health issues of our time. Research at Southampton is helping to tackle this issue by analysing the lifecourse of the illness to develop new and improved treatments. Discover more on page four.

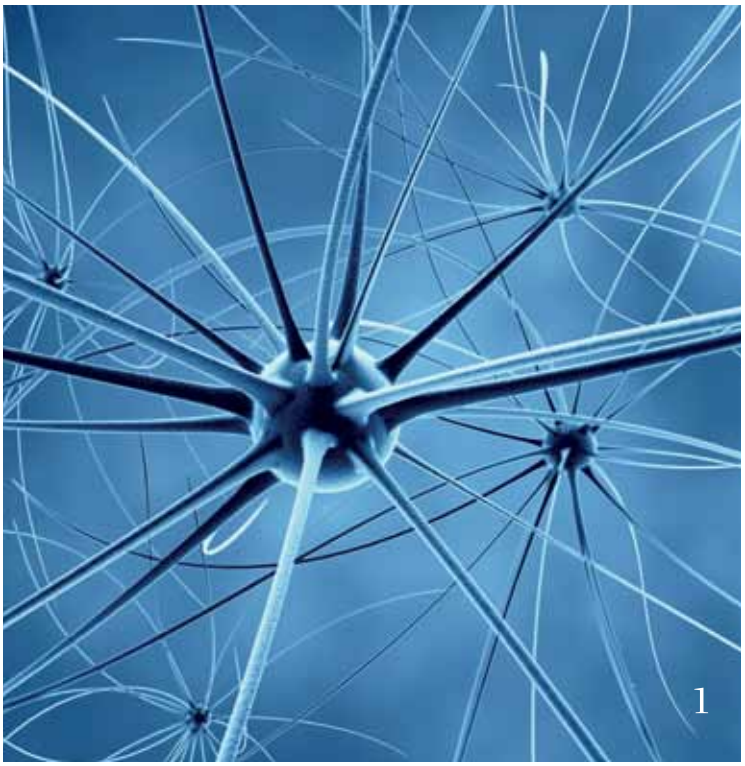
The First World War is arguably the first example of total war that the world has ever seen and in the centenary year of the beginning of this vast conflict, research at Southampton is looking at the impact it has had on the military, the public and our perception of war. Find out more on page 10.

On page 16 you can read how our statistics researchers collaborate with colleagues inside the University, in industry and across the world, and have built a global reputation for excellence over the last 10 years. In addition you can learn how Southampton is becoming a gateway for researchers across England to access government data.

Cardiovascular disease, often associated with high blood pressure, accounts for nearly a third of deaths globally. Discover, on page 22, how research carried out at Southampton suggests that light from the sun can reduce blood pressure and therefore could cut the risk of heart attack and stroke.

On page 26, join the discussion between Dr Penelope Gordon, Deputy Chief, Medical Academic and Research Affairs, at the Hamad Medical Corporation in Qatar, and Professor Hazel Biggs, Head of Southampton Law School around whether a person with a terminal illness should be allowed to seek assistance, and has the right to make the choice, to end their own life.

For more research stories and for our themed research publications, visit our website **www.southampton.ac.uk/research**



1 **Understanding Alzheimer's disease**
Tackling cause, symptoms and quality of life for patients.
Page 4

2 **Impact of the First World War**
Understanding the effects of the Great War.
Page 12

3 **Big data revolution**
Gateway to access government data.
Page 16

4 **Right-to-die debate**
Influencing the law on assisted dying.
Page 26

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We are keen to receive any feedback you have about *New Boundaries*. If you have any comments or suggestions, please send them to newboundaries@southampton.ac.uk

More highlights

Aerodynamics excellence
Forefront of aerodynamics and fluid mechanics research.
Page 14

Interactive technology for human performance
Combating inactivity and obesity.
Page 20

Sunlight reduces blood pressure
Novel treatments for cardiovascular disease.
Page 22

Understanding Alzheimer's disease

In 2013, there were an estimated 44.4 million people with dementia worldwide. According to Alzheimer's Disease International, this number will increase to an estimated 135.5 million by 2050. Research at Southampton is tackling dementia by analysing the lifecourse of the illness to develop new and improved treatments.

"We know that someone that is going to get Alzheimer's has a long window of time, as much as 10-15 years, of changes in their brain, before they have any symptoms such as memory loss. We hope to find out how the disease starts and clarify some of the drug targets, so that in time new treatments can be developed."

Dr Mariana Vargas Caballero,
Institute for Life Sciences

One in six people over 85 is at risk of getting Alzheimer's

Dementia is one of the biggest health challenges of our time; in the UK alone it affects around 800,000 people, but as well as taking a huge personal toll, it is estimated that the societal cost of dementia in the UK in 2012 was £23bn.

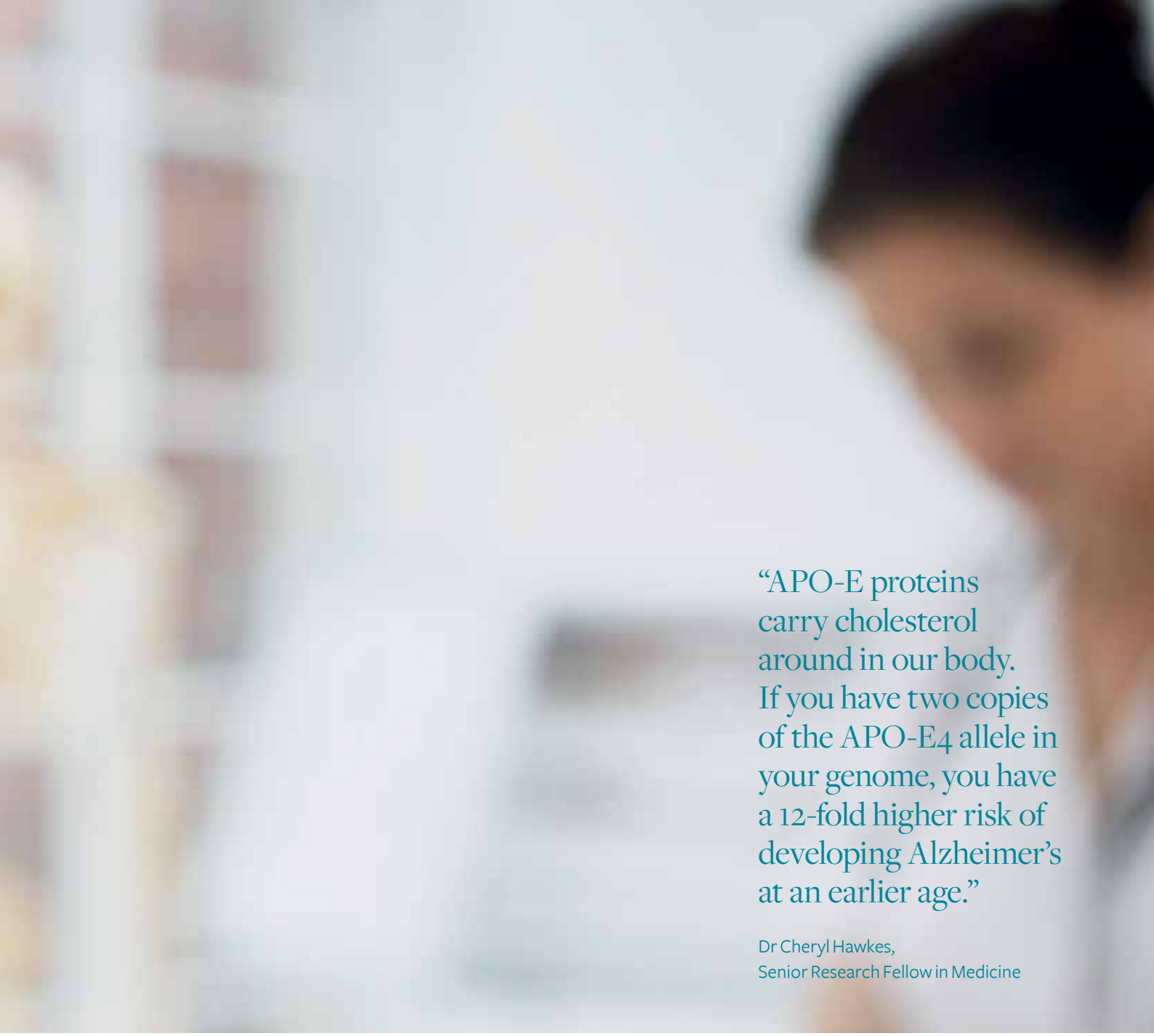
The term 'dementia' refers to a range of illnesses – of which Alzheimer's disease is the most common – that cause a gradual decline in brain function. "The biggest risk factor for developing Alzheimer's disease is age," says Dr Mariana Vargas Caballero from the Institute for Life Sciences, at the University. "And the risk of getting Alzheimer's for people over 85 is one in six," she adds.

Alzheimer's gene

Dr Cheryl Hawkes, Senior Research Fellow in Medicine at Southampton explains that in order to tackle Alzheimer's more needs to be done to identify people who might be at risk of developing the disease. Her research investigates apolipoprotein-E (APO-E), a class of proteins that appear consistently in genome-wide association studies of Alzheimer's. "APO-E carries cholesterol around in our body. If you have two copies of the APO-E4 allele in your genome, you have a 12-fold higher risk of developing Alzheimer's and at an earlier age," says Cheryl.

While Cheryl investigates how APO-E increases the risk of Alzheimer's disease, Mariana and her team investigate synaptic mechanisms in the brain, and look at how the building blocks of plaques and tangles, amyloid-beta and tau proteins, build up and affect neuronal connections leading to memory loss, one of the symptoms of Alzheimer's. "We know that someone who is going to get Alzheimer's has a long window of time, as much as 10-15 years, of changes in their brain, before they have any symptoms such as memory loss," she says. "We hope to find out how the disease starts and clarify some of the drug targets, so that in time new treatments can be developed," she adds.

Although a diagnosis of Alzheimer's disease can be devastating, people with the illness can be supported to manage their symptoms and live an active and enjoyable life for some time before the effects become severe.



"APO-E proteins carry cholesterol around in our body. If you have two copies of the APO-E4 allele in your genome, you have a 12-fold higher risk of developing Alzheimer's at an earlier age."

Dr Cheryl Hawkes,
Senior Research Fellow in Medicine

However, clinicians and carers have often noticed that when a person with Alzheimer's becomes ill with a secondary infection or disease their cognitive abilities go into a rapid decline, and symptoms such as depression and anxiety worsen.

Improving quality of life

Work by Hugh Perry, Professor of Experimental Neuropathology, and his colleagues at the University has generated new insights into the biological basis of the phenomenon, knowledge that could be used to modify the symptoms of Alzheimer's and make a real difference to the quality of life of people with the illness.

Inflammation is one aspect of the immune system that protects our body from infection and injury. It is activated by specialist immune cells, known as macrophages that are present in all the body's tissues. The macrophages act as a first line of defence by killing pathogens, such as viruses or bacteria, and promoting the repair of injured tissue.

The inflammation that plays a role in Alzheimer's disease is associated with the macrophages of the brain, known as microglia. Previous research has shown that people with Alzheimer's disease have more microglia in their brains than healthy people and that these cells are 'primed' or partially activated by the ongoing degeneration of neurons.

"When you get a disease or infection, you know about it because molecules released by immune cells communicate with the brain and you feel ill," says Hugh. "You might become feverish, want to stay in bed and sleep or lose your appetite, for example. Although unpleasant, these symptoms, known as 'sickness behaviours', are a beneficial outcome of the body's communication with the brain because they cause us to adopt behaviours that will help us fight off the illness."

This communication process involves the microglia, which in healthy brains are kept under tight control. However, in the brain of a person with Alzheimer's disease this communication process causes the primed microglia to become overactive and damage healthy brain cells, speeding up the progress of dementia. ▶

Alzheimer's disease involves the development of protein plaques and tangles in the brain structure, leading to death of brain cells

"Given our understanding of the mechanisms by which systemic inflammation communicates with the brain, we propose that comorbidities drive the progression of Alzheimer's disease. This could also be true for other neurodegenerative diseases."

Hugh Perry,
Professor of Experimental Neuropathology

Identifying molecular markers

Hugh and his team identified a number of molecular markers that are normally carefully balanced in immune cells, and observed their behaviour in microglia affected by neurodegeneration as well as microglia affected by neurodegeneration and inflammation. By doing so, they were able to understand the mechanism that caused the microglia to produce damaging inflammatory molecules.

"These signalling pathways to the brain are part of the complex mechanism of homeostasis, through which the body keeps itself in a state of equilibrium," comments Hugh. "It is only in relatively recent history that humans have lived long enough to develop degenerative brain diseases, so evolution hasn't caught up and found a way to protect us from this maladaptive response to the signalling process. Instead of being beneficial, in people with dementia the process has become damaging."

To build on the findings of preclinical experiments, Hugh teamed up with Clive Holmes, Professor of Biological Psychiatry at the University. Funded by the Alzheimer's Society, Clive and his research team recruited a cohort of about 300 people with Alzheimer's disease and monitored them over six months. The study looked at how their cognitive abilities changed as well as variations in their symptoms of sickness behaviour, such as depression, anxiety and apathy. This information was then related to whether they had had any infections during that six-month period.

The study found that people who had systemic inflammation – likely to be caused by secondary illnesses (comorbidities) common in older people – and an infection during the six-month period declined much more rapidly than those who didn't, showing a clear association between infection and the progression of Alzheimer's disease. It also showed that some sickness behaviours, such as apathy, depression and anxiety, were more frequent for people with infections and systemic inflammation.

Hugh says: "Given our understanding of the mechanisms by which systemic inflammation communicates with the brain, we propose that comorbidities drive the progression of Alzheimer's disease. This could also be true for other neurodegenerative diseases."

Broad applications

The University has been at the forefront of this area of research for many years, and while Alzheimer's disease has been the focus of recent studies, the work has implications for many fields of human neurodegenerative disease and has attracted wide interest. "The principles that underpin our findings are generic," says Hugh. "For example, there are researchers worldwide looking at the role of systemic inflammation in driving other diseases such as multiple sclerosis."

Related projects at Southampton are also ongoing. For example, Dr Jessica Teeling, Lecturer in Immunology, has teamed up with colleagues in ophthalmology to see if there is a link between inflammation and eye disease. Dr Tracy Newman, Lecturer in Clinical Neurosciences at Southampton, is working with colleagues at the University's Institute of Sound and Vibration Research to see whether systemic disease impacts on people with hearing problems.

"Achieving these kinds of innovations involves crossing boundaries and sharing ideas between basic scientists, clinicians, immunologists, psychologists, neurochemists and others."

From risk factors such as APO-E, investigating how amyloid-beta and tau proteins build-up affects memory loss, to understanding how other illnesses can cause deterioration in patients; Southampton researchers are tackling the lifecourse of Alzheimer's disease. "If we can start treating people early enough, and help people age in a healthier way, there is the potential to stem the growth of the disease," says Cheryl. "The aim is also to be able to identify a way in which amyloid-beta can be removed from the brain, so that the disease can be reversed."

For more information on research to tackle Alzheimer's disease at the University, visit **www.southampton.ac.uk/alzheimers**

Key facts

- By 2050 the number of people with dementia worldwide could increase to an estimated 135.5 million.
- In 2012 the estimated societal cost of dementia in the UK was £23bn.
- People who carry the APO-E4 gene have a 12-fold higher risk of developing Alzheimer's at an earlier age.
- For people over the age of 85, the risk of getting Alzheimer's is one in six.
- Research at Southampton is tackling dementia by analysing the lifecourse of the illness to develop new and improved treatments.

Impact of the First World War

The First World War is arguably described as the first total war that had an impact on everyone around the globe. In the War's centenary year researchers at Southampton are investigating its causes, and legacy from a military and civilian perspective.

Compared to conflicts after the Napoleonic Wars in the 19th century, the First World War lasted significantly longer and involved many more nations. "When we think of the conflicts from 1914-18, it is easy to focus on the fighting on the western front between Britain and Germany, but there was also fighting in the Middle East, south eastern and south western Africa," says Adrian Smith, Professor of Modern History at the University.

Complex causes

Adrian explains that the First World War is the first example of an industrial war and as industrialisation accelerated over the 19th century and into the 20th century, advanced industrial societies emerged, which used manufacturing to mobilise whole nations ready for war to an unprecedented degree. "The way that industry played such an important part in waging war is deep-rooted in the way it operated in an advanced capitalist society," he says.

Mark Cornwall, Professor of Modern European History at Southampton and Britain's leading authority on Austria-Hungary in the lead up to and during the First World War, explains that the causes of the First World War are complex.

He notes that the murders in Sarajevo on 28 June 1914 of Archduke Franz Ferdinand and his wife were notoriously the spark that ignited the Great War of 1914-1918. They were evidence of an unresolved 'Southern Slav problem' in the Habsburg Empire, and of serious social and ethnic tensions which the Empire's rulers seemed incapable of resolving.

"The regional context in which the murders occurred, especially in terms of Austria's relations with Serbia, remains controversial," he says. "I am exploring trends of loyalty and treason in the Habsburg Empire and how these produced the outbreak of war and the Empire's complete collapse in 1918."

"There has been a tendency in the last 20 years for historians to suggest that the Habsburg Empire was becoming more stable on the eve of the First World War, but my research suggests the opposite," says Mark. "By 1914, despite some domestic solutions, the imperial elite still faced major headaches because of continuing national and social tensions as the Empire modernised. This led them towards military solutions."

Cinema boom

It can also be suggested that the First World War was the catalyst for a cinema boom in the UK, which in turn meant that civilians, for the first time, were able to see and hear what the War on the western front was actually like for their soldiers.

"Cinema exhibitors showed recruitment drives, news reels and footage of soldiers marching off to war," says Dr Michael (Mike) Hammond, Senior Lecturer in English at the University. "This practical patriotism served two purposes, it allowed the general public to stay informed about the War, but it also allowed cinemas to incorporate themselves into the fabric of cities and the war effort," he adds.

In 1916, a film made by the War Office called *The Battle of the Somme* that was shot in the first week of the battle of the same name, was shown in cinemas as an hour feature. "This film can be seen as the most important film in British history, as it brought the middle class into the cinemas in numbers that had never been seen before," explains Mike.

Mike explains that the film showed the realities of war by showing the dead and wounded. "It was undiluted footage and provides us with no doubt that the War had an impact on the general population," he says. "But it also showed many regiments in such a way that many soldiers' faces' were on film. As a result, many people saw their sons, brothers or husbands, which was commented on in a number of local news reports at the time."

Roll of honour

Cinemas also participated in the war effort by showing a 'roll of honour'. The local community would send in pictures of soldiers that had enlisted, and these would be shown in a similar way to a roll call so that the public could see how many men were doing their duty from their area. "Towards the end of the war these rolls of honour had a different purpose – they showed the names of the soldiers that had died or were wounded in action," says Mike.

Civilians were expected to be patriotic as the nation was genuinely under threat, but in addition to this patriotism that was cultivated in part by the cinemas there was also the need for people not fighting to play their part and help industry provide the weapons and equipment.

Industrial legacy

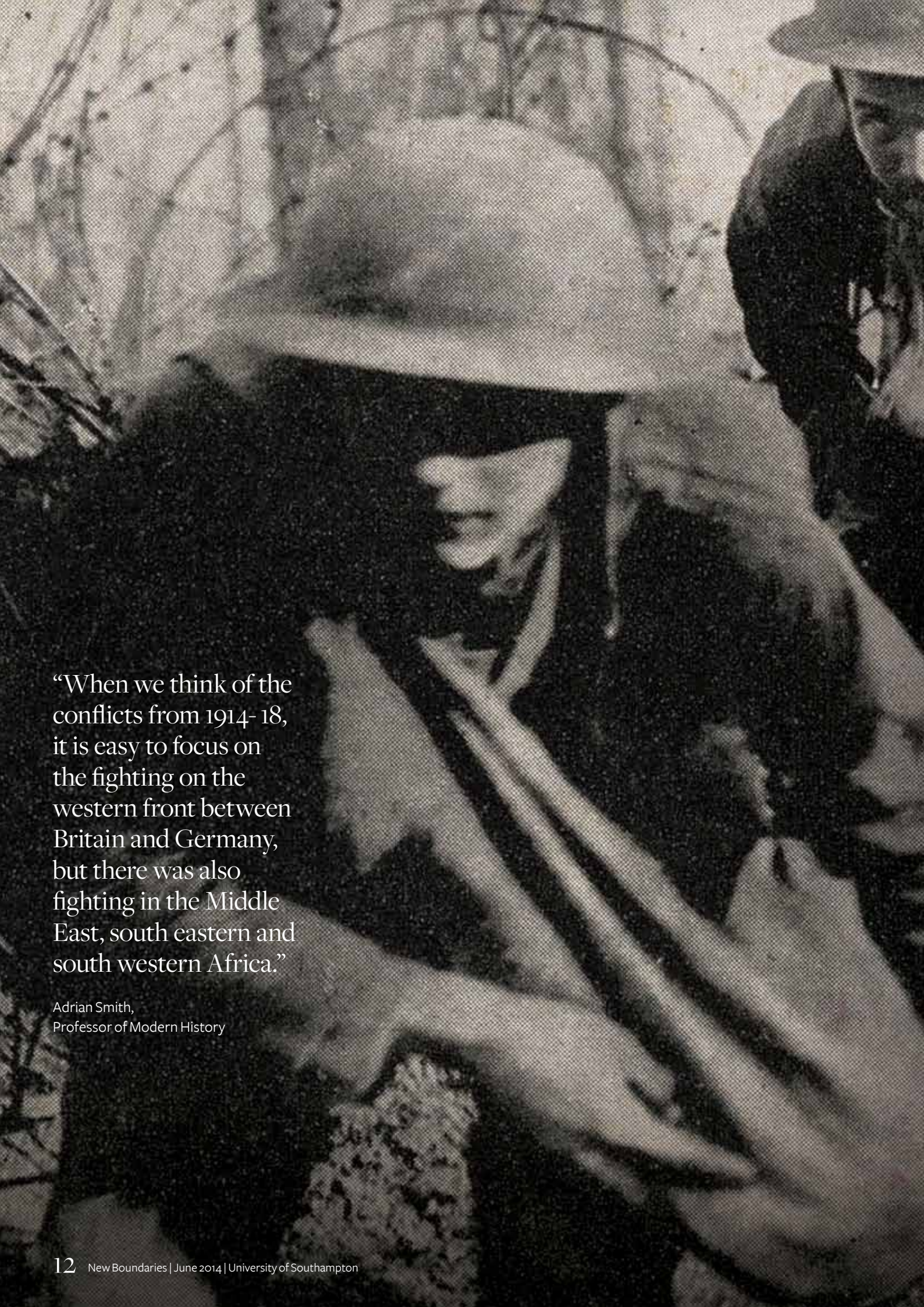
Adrian explains that there was a continuation of research and development and implementation of weapons of war and the adaptation of civilian technology – aviation being the most obvious example. And crucially because of the industrial nature of the war, not only was there technological advance, there was a huge increase in volume of production. "By 1918, the British were producing approximately 30,000 aircraft a year. This was easily done because even though the aircraft were sophisticated, you could easily break them down into small components that could be manufactured by non-skilled labour," he says.

Non-skilled labour was also used in the Second World War to produce military vehicles and weapons, and this could be seen as the legacy of the First World War in terms of how industry and civilians joined forces to help with the war effort. But by the end of the Second World War, technology had started to become too sophisticated for a non-skilled labour workforce. "You could build 1,500 Lancaster bombers with unskilled labour during the Second World War, but building a jet aircraft was a lot more challenging. The dawn of the jet age marks the end of the industrial war epoch," Adrian adds.

The role of the cinema during the war also informed the public about the conditions in the trenches and the issues that returning soldiers might encounter such as post-traumatic stress disorder (PTSD).

War aftermath

"PTSD has always been with us, but has only been understood as a disorder fairly recently. Soldiers in the First World War would have been diagnosed with shell shock if they were lucky; otherwise they would have been labeled as cowards or lacking in moral fibre," says Dr Lusia Stopa, Research Clinical Psychologist at the University. ▶



"When we think of the conflicts from 1914- 18, it is easy to focus on the fighting on the western front between Britain and Germany, but there was also fighting in the Middle East, south eastern and south western Africa."

Adrian Smith,
Professor of Modern History

Key facts

- The total number of military and civilian casualties in the First World War was over 37 million.
- Approximately 1,600,000 women joined the workforce between 1914 and 1918.
- 950,000 women were employed in the dangerous munitions factories.
- *The Battle of the Somme* film is the most important film in British history, as it brought the middle classes in the cinemas.

"It is likely that some soldiers who were shot for desertion were suffering from PTSD and were completely unable to face going back into combat."

Lusia explains that by the Second World War it was more likely to be described as combat neurosis or battle neurosis, but the stigma implicit in the idea that soldiers were weak or cowardly largely remained. A key aim of her research is to understand what keeps disorders such as PTSD going. "I investigate what blocks the natural process of recovery; if these factors are well understood then we can develop and improve treatments that will directly benefit patients," she says.

"The films and features in British cinemas demonstrated the futility of war," says Mike. He explains that in the 1920s war films highlighted how war impacted on soldiers physically and mentally. For example a British 1921 play, *A Bill of Divorcement*, written by Clemence Dane that was made into an American film in 1932 portrayed a family dealing with the aftermath of a soldier who was in a mental institution because of his experiences of war.

"By the 1930s films where the 'bad guy' had learned to kill during his time in the trenches were common. It is clear that films and plays of the period are critical of the war and show that the war had a major impact on people's lives," Mike explains.

"The major impact of the First World War is how we remember war in general," comments Mike. "It acted as a template to how the media interacts with a nation at war and the huge death tolls triggered how we show our respect for, and remember all the people that have lost their lives in conflicts over the last 100 years, across the whole world," he adds.

Mark comments: "The First World War completely transformed the European map through mass death, migration and a redrawing of state borders; in eastern Europe especially, we are still living with the consequences of this early 20th century revolution."

For more information on how our researchers are shedding light on the First World War, visit **www.southampton.ac.uk/greatwar_unknownwar**

"The major impact of the First World War is how we remember war in general. It acted as a template to how the media interacts with a nation at war and the huge death tolls triggered how we show our respect for, and remember all the people that have lost their lives in conflicts."

Dr Michael Hammond,
Senior Lecturer in English

Aerodynamics excellence

The University of Southampton is joining a new National Wind Tunnel Facility (NWTF) that will keep the UK at the forefront of aerodynamics and fluid mechanics research. *New Boundaries* talks to Professor Bharath Ganapathisubramani about Southampton's contribution to the NWTF and his aerodynamics research.

The aim of Bharath's research is to find ways to improve the efficiency of fluid flow systems that have an impact on fuel consumption and harmful emissions. "In order to reduce drag or improve mixing, we need to understand the turbulent flows relevant to many systems such as cars, aircraft etc," he says.

"We are currently doing a broad range of experiments in our facilities at Southampton including the RJ Mitchell Wind Tunnel to understand different types of turbulent flows. One example is the turbulence near a solid surface (called a boundary layer) where we use advanced optical diagnostic methods to understand the causes that may be responsible for drag. This would then inform us of ways to design new strategies to reduce drag."

Inspiration from nature

Bharath also investigates the aerodynamics of biological systems in order to develop micro air-vehicles. "I take inspiration from natural flyers – currently we are looking at the flexible wings such as those of bats," Bharath explains. "With flexible wings, bats can manoeuvre really well making them agile, so that they can change direction really quickly."

Micro-air vehicles are designed using traditional aerodynamic concepts that have been used to make larger aircraft, explains Bharath. "We are looking at the problem from a different angle. We are investigating the aerodynamics of alternative and new concepts in our wind tunnels in order to assess the feasibility of these new concepts for the next generation of micro-air vehicles. The bat-inspired flexible wing project is one such concept," he adds.

Bharath explains that the new NWTF consists of 17 different facilities spread across seven universities throughout the UK. "Three of these facilities are from Southampton: the Anechoic Wind Tunnel – the largest of its kind in the UK, the Towing Tank – the largest in the UK and comparable to other facilities in the world, and the R J Mitchell Wind Tunnel – the largest university-owned wind tunnel," he says.

The new Facility will support research addressing problems in many sectors, but with a primary focus on aerospace research, a key contributor to the UK's gross domestic product (GDP). The facilities will be available for use by researchers and industry and will be able to simulate a wide variety of environments to build understanding of both low and high-speed conditions.

New partnerships

Bharath explains that the three Southampton facilities will share in the £13.3m funding for the NWTF, with £10.7m coming from the Engineering and Physical Sciences Research Council (EPSRC) and £2.6m from the UK Aerodynamics Centre.

"These three facilities, together with the other 14 in the NWTF, form a complementary suite of facilities that can be used by researchers here at Southampton as well as researchers and industry from around the UK," says Bharath. "The new facility will definitely mean that there are more partner institutions to collaborate with on my research. Indeed, it has already resulted in new research collaborations across the country."

For more information on the wind tunnel facilities at Southampton, visit **www.southampton.ac.uk/windtunnels**

Population, education, tax, health and many other forms of government data will be available to researchers in England through the University of Southampton

Big data revolution

Statistics plays an important role in helping us understand our world and provides concrete data in order to inform policy. By providing a clearer picture of some of today's most complex problems, and providing access to government data to academics across the UK, the Southampton Statistical Sciences Research Institute (S3RI) is contributing to more effective solutions.

> "Over the past 10 years we have earned a global reputation for excellence in research into core statistical methodologies."
>
> Professor Steven Gilmour, Director of S3RI

S3RI is one of the largest groups of statisticians in the UK, bringing together researchers from mathematical sciences, social sciences, health sciences, geography, medicine and other disciplines. "Over the past 10 years we have earned a global reputation for excellence in research into core statistical methodologies," says Professor Steven Gilmour, Director of S3RI.

Tackling society's major issues

He explains that studies by S3RI researchers are helping to improve people's health and wellbeing, enabling industry to devise more accurate and efficient experiments and improving the quality of the information that underpins the planning of essential public services. "Our cutting-edge work is being taken up by clinicians, scientists, engineers and government bodies, as well as by people who need effective techniques to understand surveys and databases," he adds.

S3RI work spans five research themes: biostatistics, policy and evaluation, design and analysis of experiments, modelling and sampling, and survey methods. Our statisticians collaborate with researchers from the University and from other institutions worldwide, as well as sharing their expertise with partners from industry and the public sector, building productive relationships with organisations such as GlaxoSmithKline, the Met Office, the Office for National Statistics and the Environmental Protection Agency in the USA.

"S3RI is also involved in the whole life course of data," says Peter Smith, Professor of Social Statistics at the University. "We are international experts in the design of experiments and surveys used to collect data as well as in analysing complex data, and therefore have the methodological expertise across the board to do this." ▶

"Our vision is to see these data transformed into knowledge and evidence which can be used to inform public and economic policy – helping to tackle some of the major issues facing society, in an innovative and efficient way."

Peter Smith,
Professor of Social Statistics

State-of-the-art facilities

This world-leading expertise has led to the University leading a consortium of institutions that has been awarded £7.6m to help launch and run a project to give access to government data for academic research.

The Administrative Data Research Centre (ADRC) for England will enable information routinely collected by government departments and other agencies, such as tax, education and health data, to be shared with researchers. The centre, funded by the Economic and Social Research Council (ESRC), will be for approved academic projects and use anonymised data, accessed in a secure environment.

"Our vision is to see these data transformed into knowledge and evidence which can be used to inform public and economic policy – helping to tackle some of the major issues facing society, in an innovative and efficient way," says Peter who is the project lead.

"We will manage and maximise the use of new data linkages across government departments and sectors to give safe, secure and strictly managed access to anonymised data for research purposes," he adds.

Peter explains that holding this type of government data at an independent institution such as Southampton is the key to the project's success. "If the linked data were held by a government agency, for example Her Majesty's Revenue and Customs (HMRC) there may be concerns that the information would be used to investigate benefit fraud or other such issues. However, the linked data are only to be used in legitimate research, and having them stored in an independent place negates these issues," Peter says.

"As a founding partner of the Open Data Institute, the University is already at the forefront of innovation to help the public sector make more effective use of the information it holds. This project will extend and specialise our expertise in this field and provide a crucial facility for accredited academics conducting public policy related research," says Professor Don Nutbeam, Vice Chancellor of the University.

UK-wide network

The ADRC for England will be led by Southampton and run in collaboration with University College London, the London School of Hygiene and Tropical Medicine, the Institute for Fiscal Studies and the University of London's Institute of Education. It will be one of four such centres for England, Wales, Scotland and Northern Ireland, which with the newly formed Administrative Data Service (ADS) acting as a 'gatekeeper' to the research data, will form the Administrative Data Research Network (ADRN).

The four ADRCs and the ADS will benefit from a grants package totalling approximately £34m from the ESRC. This represents the first phase of £64m of ESRC funding of investment in big data, to support the development of a network of innovative centres to strengthen the UKs competitive advantage in this field.

Professor Paul Boyle, Chief Executive of the ESRC, says: "We are delighted to have played a leading role in the development of the national ADRN that will strengthen the UK's competitive advantage in big data. The core aim of the ADRN is to facilitate linkage of routinely collected administrative data, thereby stimulating opportunities for innovative research and policy-making. There will be benefits for researchers, government, local communities and the public – indeed; there is the potential for a revolution in our ability to answer a host of questions that were previously intractable."

Safeguarding data

The Southampton-based ADRC, hosted by S3RI, working with colleagues in Geography, Engineering and the Environment and the information and communications technology professional services department, iSolutions, will provide state-of-the-art secure facilities with access to high-performance computer systems, database management systems and advanced data analysis and statistical tools. This will enable administrative data sets linked across different services and government departments to be made them accessible for research.

"Initially researchers may have to come to Southampton to use the secure lab to access the data, and there will be controls regarding what data can be taken away from here. However, in the future it should be possible for researchers to access the data remotely," Peter says. "The idea is to set up a secure server that can have up to 100 concurrent uses, so we could have up to 100 projects being undertaken at the same time," he adds.

Looking to the future, the rise of big data will make it crucial to find robust ways of modelling variation within large and complex datasets to generate meaningful information. As hosts of the ADRC for England S3RI's focus will be on making sure that happens in the UK and internationally.

For more information about the work carried out at S3RI, visit **www.southampton.ac.uk/s3ri**

Key facts

- According to computer giant IBM, 2.5 exabytes – that's 2.5bn gigabytes – of data were generated every day in 2012.
- Europe's governments are sitting on data assets that could be worth €40bn a year.
- Southampton is leading a project to give access to government data for academic research.
- Big data is the term for a collection of data sets so large and complex that it becomes difficult to process using traditional data processing applications.

Photograph: Jen Waak

Interactive technology for human performance

Lifestyle conditions from obesity and heart disease, to stress, are costing billions every year, and worse, they are killing us in record numbers. Professor of Computer Science and Human Performance m.c. schraefel talks to *New Boundaries* about how interactive technology may help reverse this pattern.

Q *What is human-computer interaction?*

Human-computer interaction (HCI) is usually about how to engage with a computational device as little and as efficiently as possible to support a task we wish to do.

Q *What is your research in the Human Performance Design Laboratory (HPDLab) about?*

We are looking at the problem that while the brain is part of the body, culturally we treat the brain as if it's a separate organism. The consequence of this lack of movement (and associated illnesses like stress, lack of sleep, obesity, poor nutrition) is that the brain we so keenly privilege actually stops performing as well as it could.

Our work in the HPDLab focuses on the body as the space of interest, of interaction. Very few of us – not just computer scientists – have a very good understanding of how such a complex system works. So in effect we're developing a new discipline in the lab, Human Systems Interactions, where people develop expertise around the body as a complex system, and how to design interactive technologies to support this system better. For instance, I have proposed a model called the Inbodied Five (in5). in5 includes five interactions that are fundamental, which we do pretty much daily as humans. They are: move, eat, cogitate, engage, and sleep. How well we do them affects our quality of life.

Q *Can you explain more about in5?*

We can ask ourselves five questions: Our physiology is driven by movement, so am I moving enough? We need all the nutrients of whole food to function electro-chemically, so how am I eating? We need sleep for building memories, and replacing tissue, so am I getting enough sleep? Physical interaction with others has been shown to affect mortality, so do I socialise effectively? Our physical brains also grow stronger and even larger from different types of deliberate mental practice, so the last question is: am I regularly mentally challenging my brain in ways that let me build new knowledge? Given these concerns, our challenge is how to design technologies to help support these processes in line with people's values.

Our hypothesis is that technology is cheap and abundant relative to human expertise, so if we can design these processes well, we can create better environments for wellbeing just to happen, for everyone.

Q *What impact does your research have on society?*

If we coordinate our efforts, we will see the impact of our research on gross domestic product (GDP). For instance, right now we're running the goFIT challenge (www.gofit.southampton.ac.uk) at three universities (Southampton, Imperial College and London City) and one company (Baxendale), based on our software to help people track movement minutes over the course of a 12-week team challenge. If that helps staff and students develop a practice of more movement, which we know is related significantly to better health, reduced stress, better sleep, and thus more robust resistance to typical seasonal illnesses, it could lead to each participant taking, say, at least one less sick day per year. That's an immediate and measurable saving to an organisation; if you have 500 participants in an organisation that's equal to more than a year and a half for one full-time job. Imagine scaling up those kinds of effects across the country.

Q *What is your hope for Human System Interaction?*

That we can design systems that help us thrive. What if when we get up in the morning and look in the mirror, the mirror asks us: "how do you feel?" And because it's our system it has data about our bodies, our fridge, our eating, our schedule, it can help balance that information so that we can say: "I feel fantastic!" And if we don't feel great, it can help us work through what we might tweak to get from surviving to thriving – from helping us learn how to prepare better food to finding five minutes between meetings to walk up a few stairs as a restorative break. I like the mirror space as it seems a natural place to interact with ourselves – to reflect, as it were – on how we're doing.

These proposals aren't science fiction. We have the data and a lot of the technology to capture and integrate it. The human systems interaction part comes in to figure out how and when to bring the bits together to support us to achieve our potential as wonderful human beings.

Q *How important is interdisciplinary collaboration in your research?*

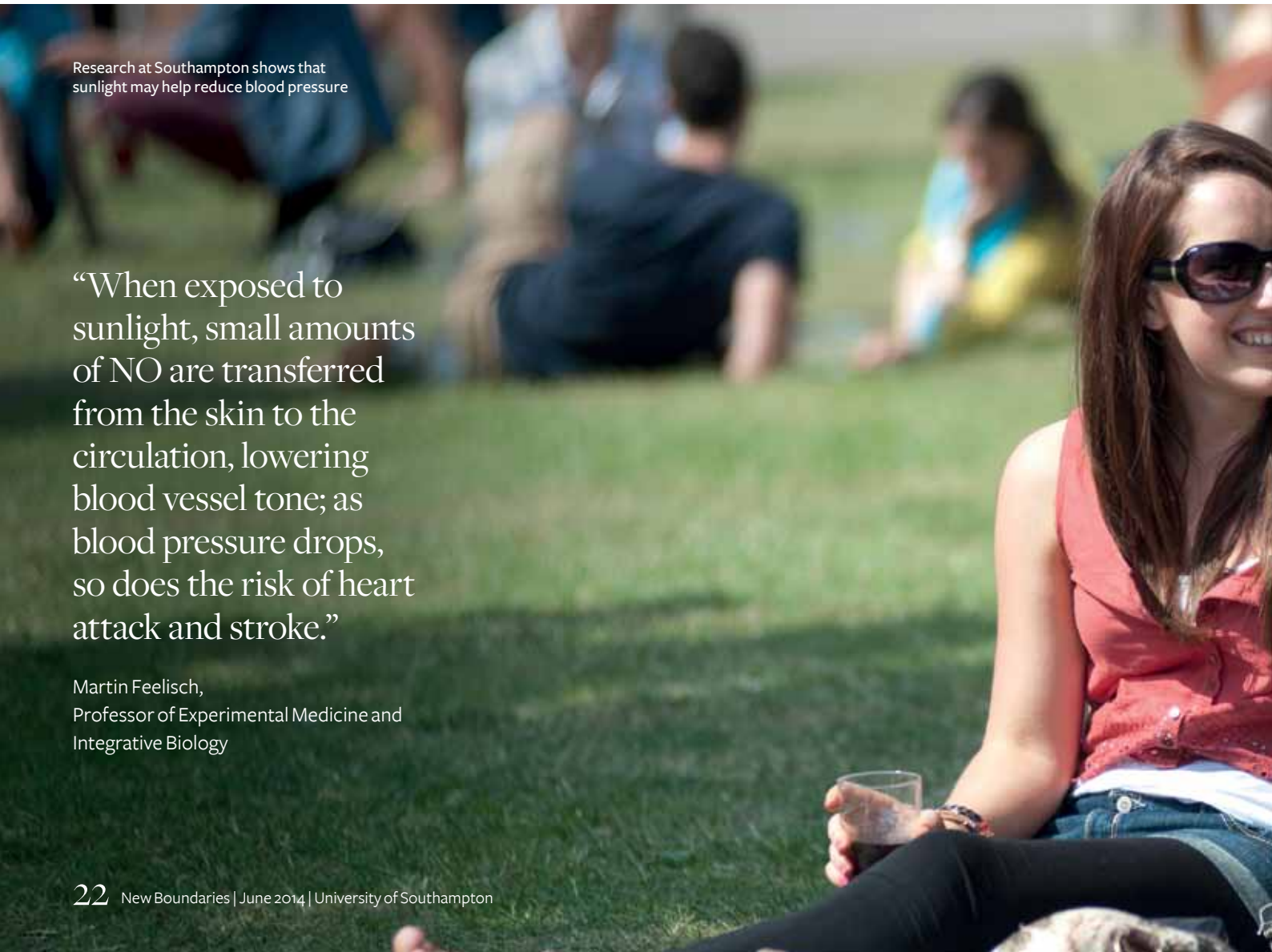
Our research by its nature is interdisciplinary and so it's really all about great people. We work with Professor Mark Hanson in Medicine at the University, who is concerned about lifestyle conditions and getting people as early as possible to build up lifetime practices for wellbeing. Professor Antony Kelly in Education at the University cares about improving performance in the classroom and leads international research on how to assess these kinds of parameters and understand how being a physical being affects learning.

Dr Stephen Rhys Thomas in Management understands that for this programme to have impact it has to be translated into business, and Professor Simon Liversedge in Psychology brings a profound understanding of cognitive performance with technology. Our postgraduate students need to learn those kinds of skills too along with computer science, physiology, neurology in order to be not just brilliant, but resilient researchers and contributors to our global society's future wellbeing.

For more information on m.c.'s work, follow her **@mcphoo** or visit **www.ecs.soton.ac.uk/mc**

Sunlight reduces blood pressure

Cardiovascular disease, often associated with high blood pressure, accounts for 30 per cent of deaths globally each year. Research carried out at Southampton shows that sunlight may help to reduce blood pressure and thus cut the risk of heart attack and stroke.



Research at Southampton shows that sunlight may help reduce blood pressure

"When exposed to sunlight, small amounts of NO are transferred from the skin to the circulation, lowering blood vessel tone; as blood pressure drops, so does the risk of heart attack and stroke."

Martin Feelisch,
Professor of Experimental Medicine and Integrative Biology

Lively debate

The debate over whether we should cover up when we are in the sun in order to prevent skin cancer or reap the potential benefits of sunlight by maximising our exposure to sunshine in a sensible fashion has been ongoing for decades. Now research carried out at Southampton and the University of Edinburgh, shows that sunlight is not only important to produce enough vitamin D, but also alters levels of the small messenger molecule, nitric oxide (NO) in the skin and blood, reducing blood pressure.

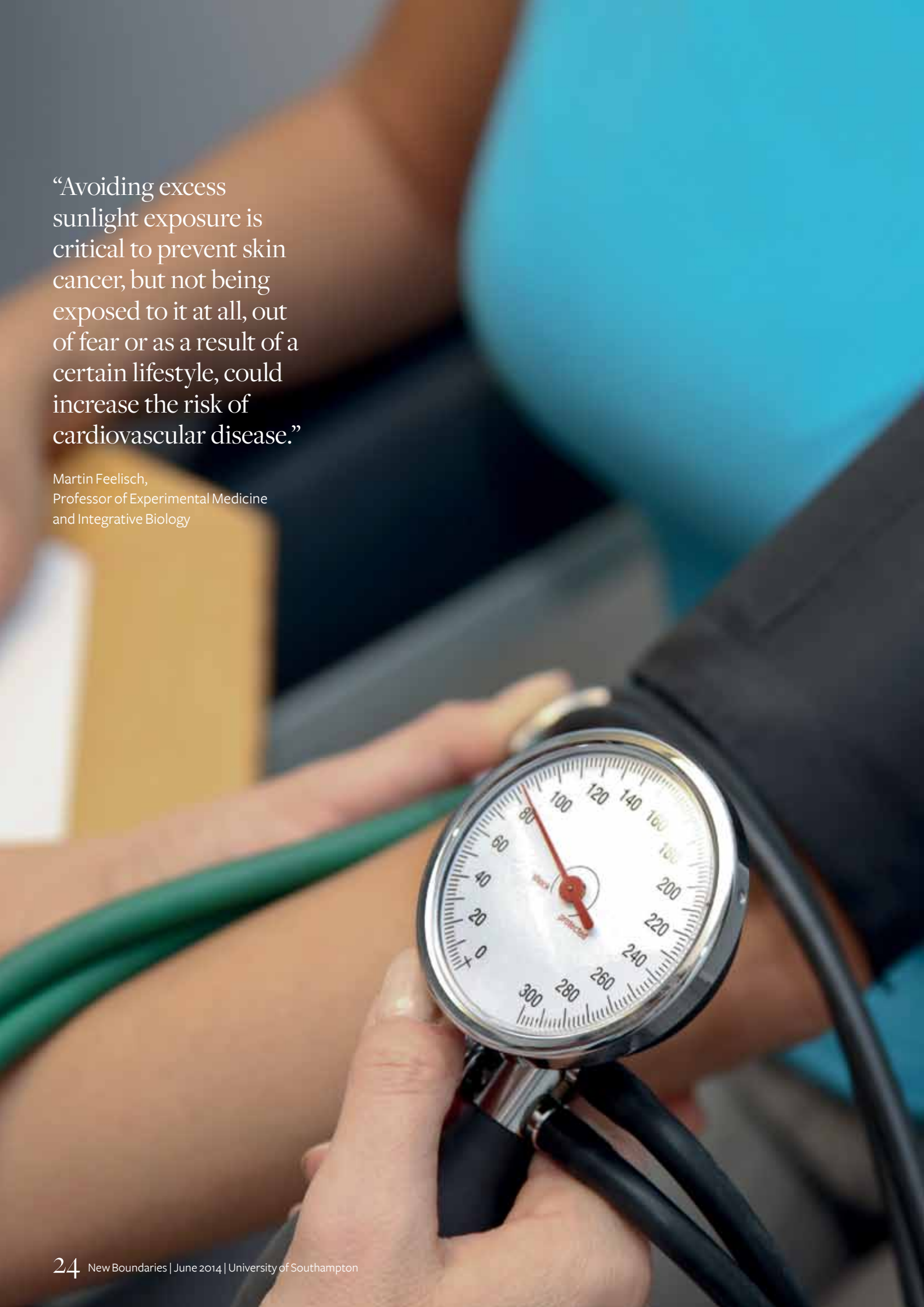
Martin Feelisch, Professor of Experimental Medicine and Integrative Biology at the University, comments: "NO along with its breakdown products, known to be abundant in skin, is involved in the regulation of blood pressure. When our body is exposed to sunlight, small amounts of NO are transferred from the skin to the circulation, lowering blood vessel tone; as blood pressure drops, so does the risk of heart attack and stroke."

Seasonal blood pressure

Hypertension, or high blood pressure, is a major risk factor to heart attack and stroke. It has been known for some time that there is a correlation between the distance people live from the equator and the changing of the seasons, and population blood pressure. This accounts for the north-south gradient of blood pressure around the globe and the fact that blood pressure is typically lower in summer than in winter. "It has not been clear what this relates to, but it was assumed to be linked to outdoor temperature," says Martin. "In our study we have taken great care to control temperature effects, allowing us to focus on studying the effect UV light has on blood pressure."

During the study, the skin of 24 healthy individuals was exposed to ultraviolet (UVA) light from tanning lamps for two sessions of 20 minutes each. In one session, the volunteers were exposed to both the UVA rays and the heat of the lamps. In another, the UV rays were blocked so that only the heat of the lamps affected the skin. "The majority of vitamin D in our body is produced in the skin with the help of UVB light; we wanted to minimise those effects and make sure our experiments were not influenced by classical vitamin D pathways. So we used UVA light – the part of UV light that is closest to the visible region of the electromagnetic spectrum," explains Martin.

The results of the study suggest that UVA exposure dilates blood vessels, acutely lowers blood pressure, and alters NO metabolite levels in the circulation, without changing vitamin D levels. ▶



"Avoiding excess sunlight exposure is critical to prevent skin cancer, but not being exposed to it at all, out of fear or as a result of a certain lifestyle, could increase the risk of cardiovascular disease."

Martin Feelisch,
Professor of Experimental Medicine
and Integrative Biology

"As well as determining blood pressure, we measured changes in blood flow; we wanted to see if those changes were due to traditional means of regulating blood flow or whether they were independent of it," Martin comments.

Blocking enzymes

"We found that if we block nitric oxide synthase, an enzyme that produces NO in the vasculature, UVA light still increases blood flow, which suggests this effect is triggered by something that is already present, and is activated by the presence of light to give off the NO and dilate the blood vessels," he adds.

Further experiments indicated that pre-formed stores of NO in the upper skin layers are involved in mediating these effects. Using fluorescence microscopy the team looked at cross-sections of human skin exposed to the same UVA light, but labelled with a florescent marker that lights up when it is exposed to nitric oxide. "This enabled us to produce an image of the florescence to see where in the skin the majority of this material is located. And it turned out that it is in the upper layer of the epidermis which happens to be the part that is exposed to UV light the most," explains Martin.

Martin admits that early observations on pollution of the atmosphere and formation of N-nitrosamines from our food suggested that NO and its breakdown products, including nitrate and nitrite, were harmful. Nitrite and nitrate in particular were suspected to lead to an increase in cancer risk if ingested. However, five decades later it appears that the same chemicals, continuously produced and widely distributed throughout our body, in fact contribute to a number of effects beneficial to human health.

High performance

Nitrate has recently attracted the attention of high-performance athletes. Beetroot juice is a natural food source rich in nitrate and believed to be healthy. "Sports scientists have demonstrated that if you drink half a litre of beetroot juice before exercising you don't perform better in terms of maximal power, but you can achieve the same power output by consuming less oxygen," says Martin. "This has sparked much interest, with the result that there are fewer and fewer athletes that do not use beetroot juice as part of their training regime."

In aggregate, what these studies show is that there is a storage supply of NO sitting in our skin that can be activated by light to release NO into the circulation to lower blood pressure.

Martin says: "Our results are significant to the ongoing debate about potential health benefits of sunlight and the role of vitamin D in this process; clearly, vitamin D is just one part of the story. It may be an opportune time to reassess the risks and benefits of sunlight for human health and to take a fresh look at current public health advice. Avoiding excess sunlight exposure is critical to prevent skin cancer, but not being exposed to it at all, out of fear or as a result of a certain lifestyle, might increase the risk of cardiovascular disease.

Benefit versus risk

He adds: "Perhaps with the exception of bone and muscle health, the effects of oral vitamin D supplementation have been disappointing. We believe that NO from the skin is an important, so far overlooked contributor to cardiovascular health. In future studies we intend to test whether the acute effects we have observed hold true in a more chronic setting and identify new nutritional strategies targeted at maximising the skin's ability to store NO and deliver it to the circulation more efficiently."

The question as to whether sunlight could be part of a treatment plan to lower blood pressure and prevent cardiovascular disease in the future is still unsure – it's early days. In countries blessed with considerably more sunshine than the UK, such as Australia, exposure to the sun is of great concern and there is soon to be a ban on solarium use. "However, we believe that applying sunblock at every occasion to protect against deleterious effects of sunlight may not be in our best interest either. If we are not careful recalibrating the public health message from time-to-time as new results emerge people may become even less inclined to go outdoors and expose themselves to sunlight in the future," warns Martin. "If sunlight avoidance turns out to be a new risk factor for cardiovascular disease we could see these numbers rising even further."

The need to work long hours indoors or to not expose oneself to the sun due to the risk of melanoma could become a risk to develop high blood pressure in itself. We know a lot about how diet and physical activity help with our fitness, but compliance is the problem, explains Martin. "Moreover, if you compare the number of deaths from melanoma to deaths from cardiovascular disease, you find that those for cardiovascular disease are much higher. So, if there is anything we can do to tap into a small percentage to reduce this, it will be worth doing."

For more information on Martin's research, visit **www.southampton.ac.uk/medicine/martinfeelisch**

Right-to-die debate

The public debate around whether a person with a terminal illness has the right to make the choice to end their own life is fraught with ethical issues; in the UK it is illegal to assist a person to end their own life.

Professor Hazel Biggs and colleagues at Southampton lead opinion and raise awareness of the assisted suicide debate

Dr Penelope Gordon, Deputy Chief, Medical Academic and Research Affairs, at the Hamad Medical Corporation in Qatar, asks Professor Hazel Biggs, Head of Southampton Law School what the University is doing to move the debate forward.

Dr Penelope Gordon (BM Medicine, 1977), Deputy Chief, Medical Academic and Research Affairs, Hamad Medical Corporation:

I currently work for the only government healthcare institution in Qatar, and my role is similar to a medical director. I oversee eight hospitals and work with diverse cultures to implement healthcare change.

My medical career for the most part has been involved in radiology for cancer care, and my last role was Director of Medical Education at Portsmouth Hospitals NHS Trust, where I was heavily involved in ethical issues when teaching young doctors.

Euthanasia, for me as a doctor, is wrong. If someone is terminally ill, a doctor should not be given the power to end that person's life. Doctors are there to promote life, and there are some very good pathways for palliative care available to healthcare professionals. Incidentally, as a result of good palliative care, the treatment a doctor gives could end up shortening that person's life, but will allow them to be comfortable at the end. I think a lot can be done to promote dignity in death and this is what we should be striving for.

On the other side of the debate, when an individual is mentally competent, but has a devastating illness, and feels that they want to end their own life, this is where it gets more complicated, especially if they are incapacitated and might need assistance.

There are also ethical concerns to take into account where family members are taking care of people with terminal illnesses. Individuals might feel coerced and feel like a burden on their families. From a legal perspective, it is difficult to say what is right, and I expect there is no easy answer. This is where the legal research that is going on at Southampton could be really useful in this debate, to clarify some of these difficult issues.

Professor Hazel Biggs, Head of the Southampton Law School:

Researchers in Southampton Law School's Centre for Health Ethics and Law (HEAL) are improving the way ethical issues in health policy are addressed in the UK and globally, and we are particularly influential in the assisted suicide debate.

There's always something in the press about this issue, whether it's a case in which someone is trying to promote a 'right to die', the Director of Public Prosecutions is issuing new guidance, or there are debates in parliament on proposed changes to the law. We engage with all aspects of the debate; the overarching aim of our work is to lead opinion and raise awareness.

My personal view is that if people are capable of making their own decisions and want to exercise their personal autonomy in that way, then the law should accommodate that. At the moment one of the issues is that as the advice and knowledge is not available to people, they are asking carers to help them, which can end up in botched suicide attempts.

It is not unlawful to commit suicide, but assisting someone to commit suicide carries a maximum prison sentence of 14 years. What we also see at the moment is a whole host of people traveling to jurisdictions where assisted suicide is lawful. However, anyone who helps someone travel to these places could also be prosecuted, but up until now no prosecutions have been made, even though we know that there are around 200 cases of this.

Guidelines issued to the Crown Prosecution Service by the Director of Public Prosecutions, effectively say that if someone is being assisted to die by a loved one or carer who is not acting in a professional capacity, they are less likely to be prosecuted than someone operating in a professional capacity. That means that doctors and nurses who would have the knowledge to assist someone in a safe way are more likely to be prosecuted.

It would be much more humane to formalise legal guidelines around this issue. One of the problems is that the law isn't brought in until the assisted suicide has taken place. If we formalised it, we could make sure that no one was being pressured into it, that it really was their considered wish and that they were competent to make that decision.

The sanctity of life is obviously a huge issue and for medical professionals the first imperative is to cure and sustain life. However, the reality is that in some situations this is not possible anymore. The law says that a doctor is entitled to do what is reasonable and proper in the circumstances where it is not possible to save a life. So for example it is lawful to provide high doses of pain killers even if you know that a side effect could be that the person stops breathing. Medicine is about caring, but it is not always about curing. It is about keeping people comfortable and making sure that their end of life happens in a way that they would want it to.

For more information on Hazel's work, visit **www.southampton.ac.uk/heal**

In brief

Silver shoppers

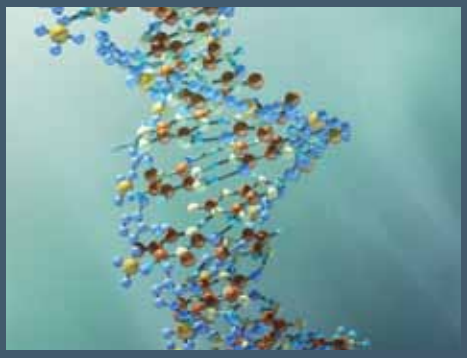
Research at the University's Winchester School of Art is investigating the challenges elderly consumers face in supermarket shopping and develops solutions to improve their experiences.

An ageing population is a global challenge. According to the Ageing Population Report 2011 from the Office for National Statistics, 23 per cent of the UK population will be over 65 years old by 2035, compared to 15 per cent in 1985.

Dr Yuanyuan Yin, Lecturer in Design Management, in collaboration with Tsinghua University in China, has identified challenges common to both UK and Chinese shoppers. "Participants from both countries commented that the supermarket shelves are too high, information on the labelling is too small and the aisles are too narrow," says Yuanyuan.

Yuanyuan and her team have developed seven new products which can help make shopping easier for elderly consumers, ranging from a foldable 'smart trolley' to a 'mini-market', which combines the benefits of online shopping with enabling elderly people to come into the store to socialise.

"Following our preliminary study, one to the UK's largest retailers, Sainsbury's, has applied some of our suggested methods to its daily working across its stores nationally. For example, we identified that consumers have problems with reading information such as the 'best before' date on packaging, so for the products Sainsbury's produces it has increased the size of this text," Yuanyuan explains.



Lego-like DNA

Scientists at Southampton have helped to develop artificial membrane pores, using Lego-like DNA building blocks, which could provide a simple and low cost tool for drug discovery and diagnostic devices.

Membrane pores are the gateways controlling the transport of essential molecules across the otherwise impermeable membranes that surround cells in living organisms.

Building synthetic pores that could be used for drug delivery out of proteins can be risky and time-consuming. A more straightforward approach is to use Lego-like DNA strands that easily fit together, which are chemically much simpler than proteins, are far easier and more predictable to work with.

Using this DNA-origami approach, the team built a tiny nanotube measuring around 10,000 times smaller than the width of a human hair. This formed the main part of their artificial nanopore. However, to insert the tube into a cell membrane, a key challenge had to be addressed: the water-soluble DNA-based structure will not embed itself into the greasy membrane, which is composed of lipids.

"To overcome this, we chemically attached two large anchors to the DNA tube, made of molecules which have a natural affinity for lipids. These porphyrins were then able to embed the tube into the membrane," says Dr Eugen Stulz, Senior Lecturer in bio-organic and materials chemistry at Southampton.

Safe nursing staff levels

Nursing academics from Southampton have been commissioned to conduct a government-backed review of the evidence on nurse staffing.

The University won an open tender from the National Institute of Health and Care Excellence (NICE) to support the development of guidelines on safe staffing as part of the UK government's response to the Francis report.

Led by Professor Peter Griffiths, Chair of Health Services Research with colleagues from the University's Centre for Innovation and Leadership in Health Sciences and Work Futures Research Centre, the team will analyse evidence about safe staffing levels on hospital wards.

Professor Griffiths will be joined by Jane Ball, Deputy Director of the National Nursing Research Unit. They worked together on the RN4CAST study which found that hospitals with better staffing had measurably fewer patient deaths.

"Getting NICE to come up with guidance on safe staffing is an important part of the government's response to the Francis Enquiries into failings at Mid-Staffordshire Hospital and other reports of staffing related care failures in NHS hospitals, says Peter. "We are very pleased that our research in this area has put us in a position to support NICE by undertaking evidence reviews."

Training the scientists of tomorrow

Postgraduate training at the University of Southampton in engineering and scientific fields, important to the UK's economy, has received a major funding boost through three new Centres for Doctoral Training (CDTs).

Southampton's new CDTs come on top of the 72 Centres unveiled by the EPSRC in November 2013, when three new CDTs in, Next Generation Computer Modelling, Theory and Modelling in Chemical Sciences, and New and Sustainable Photovoltaics, involving Southampton were announced.

Now, Southampton is leading the new CDT in Web Science Innovation, which will train 65 students to innovate in the shaping of Web growth, Web practices and Web policy. We have also established a groundbreaking CDT in Energy Storage and its Applications in collaboration with the University of Sheffield. Finally, Southampton is also involved in a new CDT in Oil and Gas Research, funded by the Natural Environment Research Council (NERC) and led by Heriot-Watt University.

Professor Judith Petts, Pro-Vice-Chancellor (Research and Enterprise) at Southampton, says: "We are delighted to be leading these new Centres for Doctoral Training. They cover areas of research that are vital to our country's future and we are very pleased to be so directly involved in providing the highly skilled scientists and engineers that are crucial to the UK economy."

In brief

Improving embryo implantation

Fertility experts at the universities of Southampton and Warwick have found new insights into why some fertilised eggs can embed in a uterus and why some do not.

One in six couples will experience some sort of infertility, which can be both frustrating and daunting, and many will turn to IVF. But the big problem with IVF is still the low chance of getting embryos to implant.

Led by Nick Macklon, Professor of Gynaecology and Obstetrics at Southampton and Professor Jan Brosens at Warwick, the research has shown that if the embryo quality is poor, the endometrium will subdue a large number of the genes involved in determining whether the embryo is accepted.

During the study, which also involved the University of Utrecht, the researchers took the fluid in which the embryos had been cultured and incubated it with endometrial stromal cells. They then measured the reaction of the genes in the endometrium.

"Our research has shown that one of the signals which the uterus can pick up on in determining the quality of the embryo is the amount of trypsin it gives off. The lack of trypsin signals appears to indicate to the endometrium that the embryo's quality is not very high and initiates a reduction in receptivity to implantation."

Changing season patterns

A study at Southampton suggests that on average the end of Autumn is taking place later in the year and Spring is starting slightly earlier.

A team led by Professor of Geography Peter Atkinson used data from over a 25-year period, from satellite imagery to examine changes in the growth of vegetation in the northern hemisphere.

The Southampton researchers, working with the Department of Remote Sensing at the Birla Institute of Technology in India, examined Global Inventory Modelling and Mapping Studies (GIMMS) satellite data. The imagery allowed them to look in detail, at the growth cycle of vegetation – identifying physical changes, such as leaf cover, colour and growth.

The team were able to examine the data in several different ways, looking at 'mosaic' vegetation (grassland, shrubland, forest and cropland); broad-leaved deciduous forest; needle-leaved evergreen forest; needle-leaved deciduous and evergreen forest; mixed broad-leaved and needle-leaved forest; and mixed-forest, shrubland and grassland. They interrogated data across all the groups, but recognised that forests provide the most reliable information, as they are less susceptible to year-on-year human intervention.

Professor Atkinson says: "There is much speculation about whether our seasons are changing and if so, whether this is linked to climate change. Our study is another significant piece in the puzzle which may ultimately answer this question."

Bespoke Arabic symbol dictionary

Researchers from Southampton are part of an international collaboration that will develop the world's first culturally specific Arabic symbol dictionary.

Language dictionaries supported by symbols and pictures are widely available in American and British English with many thousands of images representing vocabulary, but currently there is no freely available culturally specific Arabic symbol dictionary.

The Qatar National Research Fund has awarded a $891,000 grant to Dr Mike Wald and his Access Technologies team in the Web and Internet Science Research Group at the University; the Hamad Medical Corporation, in Qatar; and Mada – the Qatar Assistive Technology Centre, in Doha; to produce the dictionary.

"The ability to communicate is very important and requires skills that are not always available to everyone due to disability, lack of literacy and lack of language skills when travelling. A person visiting an Arabic-speaking nation without access to the language or knowledge of the alphabet may find it hard to communicate without help," says Mike.

The team will use crowdsourcing to identify appropriate imagery to build the dictionary of frequently-used words based on Modern Standard Arabic. "We are delighted to be part of this international team that will be pulling together resources from across the globe to develop a new Arabic symbol dictionary," Mike adds.

Combating poverty and poor health

A team of researchers led by Southampton has launched an online project to map detailed population information from countries around the world.

The global human population is growing by over 80 million a year, and is projected to reach the 10 billion mark within 50 years. The vast majority of this growth is expected to be concentrated in low income countries, and primarily in urban areas.

The WorldPop website (www.worldpop.org.uk), principally funded by the Bill and Melinda Gates Foundation, aims to provide open access to global demographic data which can be used to help tackle challenges such as, poverty, public health, sustainable urban development and food security.

The website currently provides freely-available data for Central and South America, Africa and Asia – providing maps of population numbers and age distributions, births, pregnancies, urban growth and rates of poverty.

Geographer at Southampton Dr Andy Tatem, who is leading the project, says: "Our maps and data are helping charities, policy-makers, governments and researchers to make decisions which affect the quality of people's lives. These could be as diverse as predicting the spread of infectious diseases, planning the development of transport systems or distributing vital aid to disaster zones."

For more information on these stories, visit **www.southampton.ac.uk/research**

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