UNIVERSITY OF Southampton

# NB

New Boundaries | Issue 20 | July 2015

# Antimicrobial arms race

## Tackling superbugs without drugs

**Predicting future warming from our past**
Measuring $CO_2$ levels of ancient oceans

**Compassionate duke**
Insights into the leadership of the Duke of Wellington

**Lighting up the world**
Celebrating the International Year of Light

# 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 antibiotic-resistant bacteria and climate change to bullying in schools.

The over-use of antibiotics and other antimicrobial drugs is a major problem spanning healthcare, farming and food production. Find out how a multidisciplinary team of our researchers are coming together to address the issue of resistant superbugs, from designing new methods of rapid diagnosis and innovative ways of cleaning instruments, to studying bacterial biofilms, human behaviour and new livestock practices. See page four for more.

Our researchers are harnessing the body's immune system to tackle blood cancers such as leukaemia and lymphoma. On page 14, find out how our scientists have developed a new drug that could prevent these cancers developing resistance to immunotherapy.

This year marks the 200th anniversary of the Battle of Waterloo. On page 20, discover how the Wellington Papers – a unique resource held by the University – sheds light on the leadership of the Duke of Wellington.

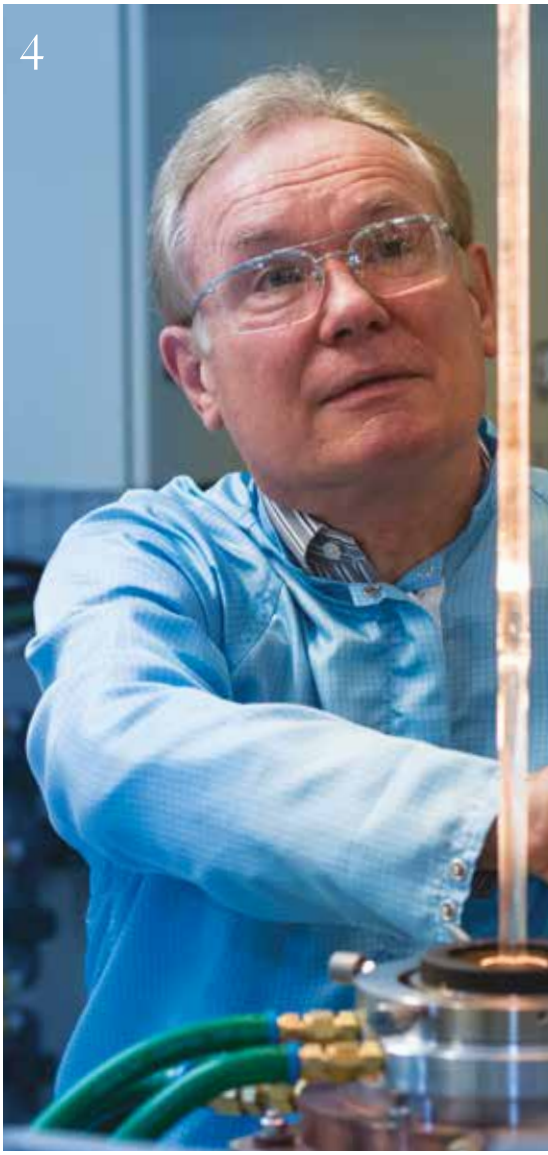
Nearly half of school children are affected by bullying at some point during their school life, often with long-lasting consequences. On page 22, find out how our researchers are helping to tackle this issue in primary schools.

Photonics is an enabling technology that has an impact on our everyday lives, from navigating airlines to powering the internet. To celebrate the International Year of Light, we talk to the Director of the University's Optoelectronic Research Centre, Professor Sir David Payne and Technical Consultant and Director of SPI Lasers, Dr Steve Norman to find out the impact the University and wider industry in Southampton has had on photonics worldwide. See page 26.

**Please send us your feedback**

You can view past issues of *New Boundaries* online at **www.southampton.ac.uk/research**

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


# Antimicrobial arms race

Antibiotic resistance has been identified by the World Health Organization as one of the most pressing challenges to global health today. *New Boundaries* finds out how Southampton researchers from across the disciplines are coming together to find a solution.

"The twin potential catastrophes of antimicrobial resistance – to healthcare and food production – are global, and so are the causes. Here at Southampton, we are working to rapidly translate the knowledge and discoveries from our research into products and policies that will benefit patients in the next five years."

Tim Leighton,
Professor of Ultrasonics and Underwater Acoustics

"Microbes are often found in communities called biofilms: dynamic environments that are very resistant to mechanical or chemical attack. In clinical settings they have been found to be around 1,000 times more resistant to antibiotics than free-living bacteria."

Dr Sandra Wilks,
Senior Research Fellow

Around the world, antimicrobial drugs – medicines designed to kill microbes such as bacteria, fungi and viruses – are being overused and this is accelerating the occurrence of resistant microorganisms. "We will never win this arms race against natural selection: when antimicrobials are applied, microbes of all types have proved very adept at developing resistant strains from the survivors," says Tim Leighton, Professor of Ultrasonics and Underwater Acoustics. Tim is Chair of the University's Network for AntiMicrobial Resistance and Infection Prevention (NAMRIP), which brings together engineers, physical scientists, life scientists, clinicians, social scientists, business and law to tackle antimicrobial resistance. This year NAMRIP received the UK's largest award, of around £870,000, in the Engineering and Physical Sciences Research Council's (EPSRC) Network for Antimicrobial Action 'Bridging the Gap' call. The Medical Research Council (MRC) has also announced further funding.

"By relying on medicines such as antibiotics, we are paving the way for routine operations and even childbirth to become significantly more hazardous," says Tim.

The overuse of antimicrobials does not only affect healthcare settings. Antibiotics are used widely in farming and fisheries, so reductions in the effectiveness of such drugs also has implications for global food production. The world's warming climate will exacerbate this problem: as flooding becomes more common, there will be more opportunities for infections to spread.

"There have been calls recently for drug companies to produce more antibiotics; this is missing the big picture by a long way," says Tim. "To mitigate against potential catastrophes in healthcare and food production, measures over and above the development of new antibiotics must be undertaken. This is what our multidisciplinary research here at Southampton is focusing on."

### Preventing infection

Preventing people from being exposed to microbes would minimise antimicrobial use. To address this, Southampton researchers are developing new microbe-resistant materials for instruments, dressings and catheters, devising new minimally invasive procedures, improving decontamination and waste disposal and revolutionising cleaning.

In a collaboration between the Institute of Sound and Vibration Research and Chemistry, Tim and his colleague Dr Peter Birkin have invented and patented a revolutionary new cleaning system, StarStream technology, which uses sound and tiny bubbles to dramatically improve the cleaning power of cold water. It is particularly effective on porous, or rough-coated materials and in hard-to-reach crevices that are difficult for conventional cleaning technologies.

Dr Sandra Wilks examining a crystalline biofilm on a urinary catheter

"We know that you should wash your hands for about 20 seconds in warm soapy water, but even in Britain the average is only around six seconds in cold water," says Tim. "We can't change people's behaviour – so what StarStream does is make cold water clean as effectively as warm soapy water." Commercial prototypes are now being developed in partnership with manufacturing company Ultrawave Ltd for industrial applications such as factory processing lines. There have been small-scale trials to to test the safety of using StarStream on hands, and further testing is planned to look at its effectiveness for this application and to extend this to look at its use in wound care.

"Colonisation of chronic wounds such as leg ulcers can impair healing, and significant healthcare resources are spent trying to reduce the bacterial burden. An easy-to-use technology that could safely and effectively clean wounds in any setting would be a major step forward," says Dr David Voegeli, Associate Professor of Nursing.

On a more fundamental level, to prevent infection we need to improve our understanding of the microbes themselves. "Microbes are often found in communities called biofilms: dynamic environments that are very resistant to mechanical or chemical attack. In clinical settings they have been found to be up to 1,000 times more resistant to antibiotics than free-living bacteria," says Dr Sandra Wilks, Senior Research Fellow in Biological Sciences.

Sandra is working with Professor Mandy Fader's Continence Technology team in Health Sciences to study urinary tract infections (UTIs) that are caused by biofilms on catheters. UTI is the second highest cause of healthcare-associated infection and having an indwelling catheter, for example after an operation, increases the risk of UTI by around five per cent for each day the catheter is in place.

A major challenge that has hampered the study of biofilms up until now is that when bacteria are stressed they go into a static state. This means they won't grow in a culture medium – the traditional way of detecting their presence. "This can lead to incorrect assumptions that an antibiotic is working when it isn't," says Sandra. "We are developing molecular probes and viability assays that can be applied directly to biofilms on solid samples, for example a catheter. Coupled with our specialised microscopy system, this enables us to analyse the biofilms in situ, without the need to remove the bacteria or use culture media." This research is bringing us closer to understanding the biofilm itself, which is key to finding alternative ways to tackle it.

### Preventing resistant strains

Another way to prevent infection is removing the environments that encourage resistant strains to develop. "This might be the body of the patient or farm animal, with simple measures such as ensuring the full prescription is taken rather than stopping

"This is an exciting development because it will be a mass-producible, cheap diagnostic test that can be used worldwide and requires no power source."

Professor Rob Eason,
Associate Dean for Research for the
Faculty of Physical Sciences and Engineering

Researchers overseeing the production of laser-written paper-based diagnostic strips

early when symptoms disappear," says Tim. "However, it goes much further, for example into the invention of sensors to detect infection early and identify the specific microbe present, so that narrow-spectrum antimicrobials can be used in place of broad-spectrum ones."

Our researchers are developing a mass-producible paper-based diagnostics platform that can rapidly test for the presence of pathogens. These test strips will be cheap, disposable, easily transported and won't require any pumps or batteries: the paper provides the wicking to transport the fluid through the test device. The aim is to develop these test strips to provide multiplexed tests – detecting more than one microbe, or pathogen, at the same time – as well as concentration-specific tests that tell the patient if they have a certain pathogen in their sample, and at what concentration or level of harm.

The test readout will be visual and easy to interpret, similar to a pregnancy test, so that the result will be available within minutes. There will also be the option to provide a coded or secure readout for diseases that have ethical implications.

"This is an exciting development because it will be a mass-producible, cheap diagnostic test that can be used worldwide and requires no power source," says Professor Rob Eason, Associate Dean for Research for the Faculty of Physical Sciences and Engineering at the University. "As well as in the more usual hospital environment, the tests can also be carried out in the comfort of the patient's own home and can be delivered by post, or, at the other extreme, rural environments in developing countries where access to medical care can be far from routine, and the test strips can be delivered in bulk via an airdrop for example."

Through our research, we are improving understanding of how society, climate, land and water resources interact to alter the risk of microbes moving from one host to another. "We must remember that a resistant strain in a UK hospital might have emerged because of livestock practices half way across the world, where increased flooding, culturally embedded practices, conflict, the movement of money and populations, and the accepted patterns of behaviour, create an environment very different to our own," says Tim, adding that conversely, resistant strains in these far-off countries might have their roots in the use of antibiotics in intensive cattle or fish farming in the UK.

Both farmers and healthcare professionals make decisions that can influence infection prevention, so understanding the human factors that affect the use of antibiotics in both agricultural and healthcare settings is an area we are focusing on here at Southampton.

### Ethical issues

As well as the health impacts of antimicrobial use, there are also ethical issues to consider, and our researchers are working with policy makers and practitioners to ensure that the different ways of preventing the overuse of antimicrobial medicines are done in a way that is ethically and legally justifiable.

"Whether it is questions about changing people's behaviour, allocating antibiotics as a scarce resource or whether we should be able to put someone with a non-treatable, antibiotic-resistant disease into isolation to protect the public, they all raise ethical and legal issues about what would be the most legitimate ways in which we should tackle the problem of preserving antibiotic effectiveness," explains Dr AM Viens, Associate Professor in Law and Co-Director of the University's Centre for Health, Ethics and Law.

For example, a major challenge is getting people to accept restrictions on access to medical treatment for the benefit of someone else – someone in society, or perhaps a future person who has not been born yet – just so we can preserve antibiotic effectiveness for them. Whether we can morally and legally say that a danger to a present patient should be increased even to a small degree to benefit a future patient is just one of the issues our researchers are addressing.

"The twin potential catastrophes of antimicrobial resistance – to healthcare and food production – are global, and so are the causes," says Tim. "Here at Southampton, we are working to rapidly translate the knowledge and discoveries from our research into products and policies that will benefit patients in the next five years."

For more information, visit **www.southampton.ac.uk/namrip**

# Sustainable tea

Climate change is likely to have a marked effect on global agriculture. Southampton researchers are working in Assam, India, to investigate the effects of climate factors on the production of one of the most important beverage crops in the world.

Tea pluckers at Borbam Tea Estate, South Bank Region, Assam

Much of northeast India is perfectly suited to tea crop cultivation. The climate is hot, with humid summers, severe monsoons, mild winters, and high soil fertility. Assam is the single largest tea-growing region in the world, manufacturing high-end graded black tea, which contributes to around 12 per cent of world tea production.

Lecturer in Geographical Information Systems, Dr Ellie Biggs, alongside her international team, is exploring the impact of climate change on tea production and the role of tea in sustaining livelihoods in Assam. "Tea crops in Assam are potentially under threat from changing climatic conditions, ranging from the annual flooding of the Brahmaputra River to seasonal droughts, to the increase in annual minimum temperatures and fluctuations in the timing and amount of rainfall," she explains.

Tea's optimal growing range is 13 to 30 degrees and requires a plentiful water supply. The pre-monsoon rain is traditionally very important for tea growth as this helps the first buds come through, which form the premium stock. "In the summer period, 35 degrees is being exceeded more regularly and the farmers, both smallholders and plantation managers, have noticed this. Through our research we are aiming to help them adapt to these changes so they can manage their land in a climate-smart way."

Funded by the UK-India Education and Research Initiative (UKIERI-DST), this research investigates livelihoods, climate change and agricultural practice to better understand the value of tea within the landscape and identify 'safe spaces' for tea plantations in Assam. Ellie's team is looking at the whole landscape in terms of sustainability: both the physical and social aspects.

## Physical effects

The research team is investigating a range of physical climate variables over a 10-year period: from 2004 to 2014. "Although in climate science 10 years is not enough to look at trends in the climate, this is as far back as the records go for yield data that are available to us, and from this data we can help the tea producers build up a longer-term picture,"

says Ellie. "As an example, we will be looking at whether exceeding certain temperature thresholds has an impact on yield, and whether there is a cumulative effect: for example, if these thresholds are exceeded in January, February and March, whether this has an effect on the tea yield in April."

The temperature and precipitation records come from the Indian Meteorological Department, which has gridded data across India so that, for example, the temperature at each tea garden is interpolated from the nearest measurement. In conjunction with yield data from each of the tea gardens, they will build up a picture of the effects of the local temperature and precipitation on tea production. This data will be run through two statistical models – one looking at monthly associations and the other looking at the seasons as a whole, year on year.

Preliminary analysis has been run for the North Bank tea growing region of Assam. Here the team have acquired monthly tea yield data from eight tea gardens. Findings for this region indicate that temperature is generally associated with an increase in tea productivity, except in September and November, and extreme precipitation has a positive association with tea yield for July and September.

"This particular tea growing region of Assam is situated within a rain shadow area of the state and as such we would expect that precipitation would have a potentially greater influence on tea productivity than temperature. Our preliminary results confirm that precipitation may be the predominant driving factor, with continuous periods of no rainfall highly associated with reduced tea yield," says Ellie.

These initial findings were presented at the World Water Congress in Edinburgh (25 to 29 May) by Ellie alongside her co-investigator from India, Dr Niladri Gupta and the project researcher Sukanya Saikia.

The Tea Research Association (TRA) in India provides advice for larger tea growers, helping them to respond to short-term changes in the weather. "We hope that our research will complement their advisory services through enhanced decision

"In the summer period, 35 degrees is being exceeded more regularly and the farmers, both smallholders and plantation managers, have noticed this. Through our research we are aiming to help them adapt to these changes so they can manage their land in a climate-smart way."

Dr Ellie Biggs,
Lecturer in Geographical Information Systems

support tools. We will be developing an easy web-based interface so they can query the data that we analyse to provide more climate-smart advice regarding how certain gardens can prepare for potential climate impacts year on year," says Ellie.

This will act as a two-fold decision support tool, providing more detailed climate information to the TRA to help them advise tea plantation owners, while also providing a 'pop-up' solution – via the open-access web tool – to smaller tea growers who have limited access to the main advisory service provided by the TRA.

### Social factors

The second part of the project involves quantifying the value of the tea-growing land to the people: from owners of the large commercial tea plantations, to the smaller scale smallholders and the tea workers themselves.

"Historically, tea is everything for livelihoods in this region," says Ellie. "There is a hierarchy in involvement, from plantation owners who supply the household name tea brands to the tea workers who don't get paid much at all." The team has carried out workshop sessions for plantation owners and smallholders to find out about their land management practices, for example how often they apply fertiliser and how they manage water resources. "Through this information we will be able to see how tea growers in different areas are managing their land at present and how closely they adhere to the advice given by the TRA," says Ellie.

As the global temperature warms, changes to tea-growing practices will have a knock-on effect on the livelihoods of the people who pick the tea. To address this, the team also carried out focus group discussions with the tea plantation workers to find out which livelihood factors are most important to them. The tea workers live on the estates and some are able to grow their own food crops in the wide drainages and valley fills within

'Cold weather practice' (one method of maintaining the tea plants during the winter season) at Gatoonga Tea Estate, Jorhat

the plantation. Traditionally, the women pluck the tea leaves, while the men prune and maintain the tea plantation. "Most tea workers are illiterate so we carried out focus groups whereby we formulated a group consensus on livelihood issues amongst workers. We split workers into single-sex groups per garden so that everyone would speak freely, as we have found from previous focus groups that in mixed groups the women's views tend to be overlooked."

### Giving back to the community

Following the workshops, the team gave presentations about their research to participants. "Increasing awareness of the research we are undertaking is essential for widening the interest in Assam's tea future. Not only will we disseminate research findings to the academic community, we will also produce policy briefs for tea stakeholders," says Ellie. "We will be providing training for the tea managers to use the web-based system we develop and we will be running community fairs where we will have visual displays of what we have found so that the tea workers who provided the information can see what the research is doing in practice."

The research findings are also feeding into the work of the UK-based organisation 'Tea 2030', which aims to support a more sustainable value chain for tea so that consumers can be confident they are purchasing tea from a sustainable and ethical source. Ellie will be co-running a climate change session at the forthcoming Ethical Tea Partnership annual event which engages members of the Tea 2030 consortium.

"Our research into understanding the tea landscapes of Assam contributes valuable information to the producers of the tea, as well as important information to promote more sustainable long-term practice and climate compatible solutions for tea production," Ellie explains.

To find out more, visit **www.teaclimate.com** and **www.southampton.ac.uk/ellie-biggs**

# Tackling resistance to cancer drugs

## Southampton scientists have developed a new drug with the potential to reverse resistance to immunotherapy, a growing problem in cancer treatment.

In recent years, targeted drugs made from engineered immune proteins – called monoclonal antibodies – have revolutionised treatment for cancers such as leukaemia and lymphoma. They work by sticking to specific proteins on the surface of cancer cells and flagging them up to be killed by the immune system. However, cancers can develop resistance to monoclonal antibodies, resulting in the treatments failing to have an effect in some patients.

Mark Cragg, Professor of Experimental Cancer Research at the University, says: "With more and more monoclonal antibody treatments being developed, there is an urgent need to understand how tumours become resistant to them and develop ways to overcome this. Not only does the new drug, called BI-1206, appear to be able to reverse resistance to a range of monoclonal antibodies, it is also effective at directly killing cancer cells itself."

BI-1206 showed remarkable success in laboratory tests for overcoming cancer's resistance to monoclonal antibodies like rituximab, which are currently used to treat some types of lymphoma and leukaemia. "We believe this is the first drug to reverse a cancer's resistance to monoclonal antibodies," says Mark. "The drug works in three ways: first it stops the rituximab from being swallowed up by the cancer cell, second it helps to target the cancer cell and third it helps the immune cells that destroy cancer cells to become more activated by binding to a molecule called FcγRIIB."

The study was a collaboration with Swedish pharmaceutical company BioInvent International AB and represents a six-year endeavour into improving antibody therapeutics for blood cancers. "It came about from a scientific meeting at Keystone in Canada in 2009," explains Mark. "We were working on antibodies to the same receptor in preclinical models in the lab and Dr Bjorn Frendéus, the Chief Scientific Officer at BioInvent, had just raised some unique antibodies to the human receptor, so we came together to develop and characterise them. We made the observation that the cancer cells swallow up the rituximab and that this happens because of the expression of the receptor (FcγRIIB) that is targeted by the new monoclonal antibody."

The researchers, who were funded by Leukaemia & Lymphoma Research and Cancer Research UK, found that it is possible to overcome cancer's resistance to many other antibody drugs by preventing the cancer cells from 'hiding' from immune cells. Mark's team at Southampton, along with BioInvent researchers, is now working on how to exploit this.

"We are always looking for new ways to understand and overcome resistance and to make new and better treatments," says Mark. "For example, we want to understand why some cancers express more FcγRIIB than others, whether this resistance mechanism is important for other therapeutic antibodies and what other mechanisms of resistance are at play."

"The University of Southampton is a great place to do this type of research because we have an excellent pipeline and ethos for translation: taking the original basic science and observations into pre-clinical work and then into clinical trials," he adds.

The new drug will be tested in patients with chronic lymphocytic leukaemia and non-Hodgkin's lymphoma in an early stage clinical trial later this year. The trial will test the drug's safety in humans and if it has any anti-cancer effects when combined with rituximab.

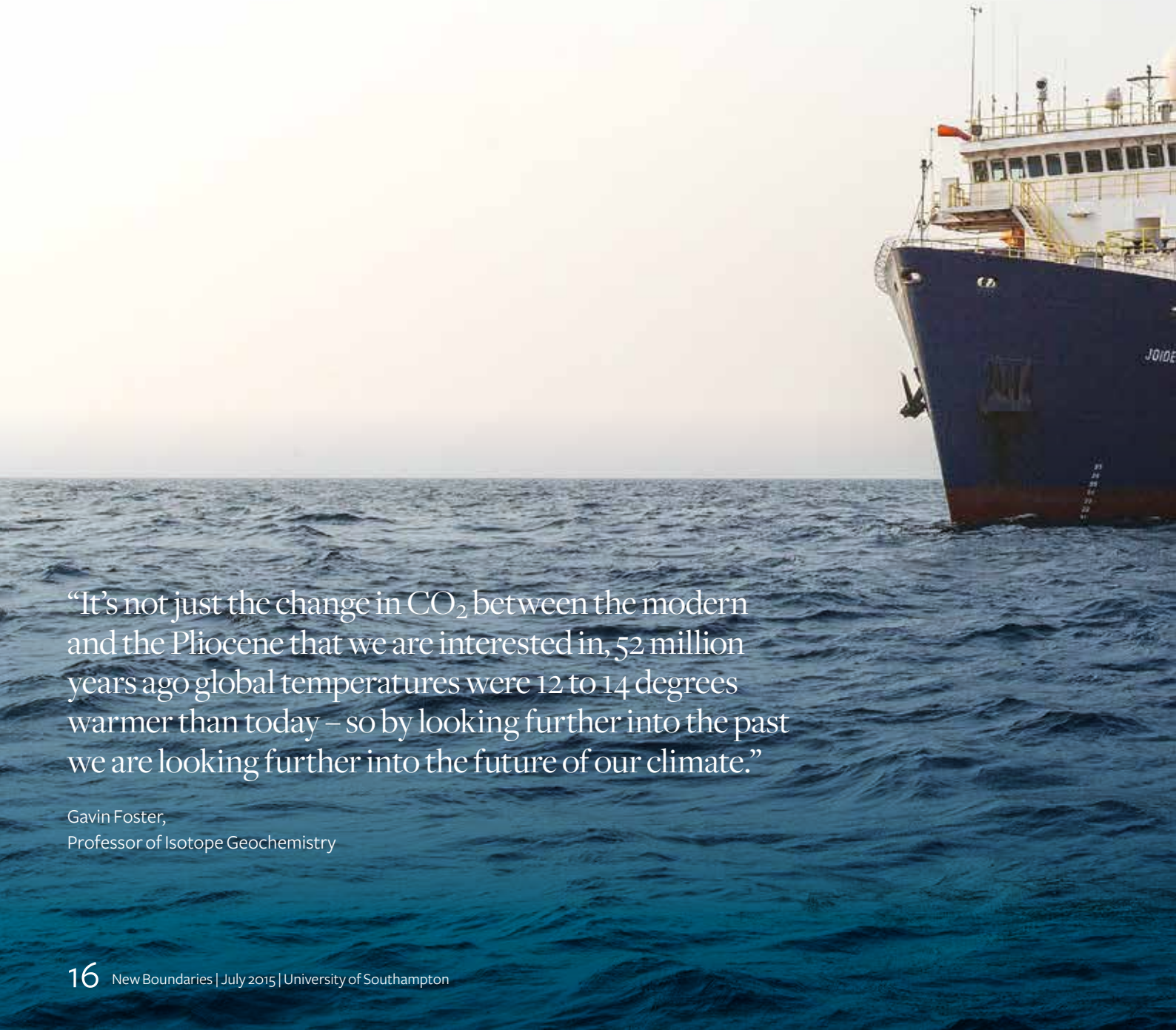
**Building on success**

Building on its cancer immunology research expertise and recent successes in immunotherapy trials, the University of Southampton has launched a major fundraising campaign to raise £25m to open the UK's first dedicated Centre for Cancer Immunology at Southampton General Hospital in 2017. The Centre will be the first of its kind in the UK and will bring together world-leading specialists in a unique state-of-the art centre. The aim of the new Centre is to accelerate research progress, conduct more clinical trials and save more lives from cancer.

For more information about the University's groundbreaking cancer research and the state-of-the-art Centre for Cancer Immunology due to open in in 2017, visit **www.southampton.ac.uk/youreit**

# Predicting future warming from our past

Southampton-led research on prehistoric levels of carbon dioxide in the oceans gives an insight into the Earth's future warming. *New Boundaries* finds out more.



"It's not just the change in $CO_2$ between the modern and the Pliocene that we are interested in, 52 million years ago global temperatures were 12 to 14 degrees warmer than today – so by looking further into the past we are looking further into the future of our climate."

Gavin Foster,
Professor of Isotope Geochemistry

The *Joides Resolution*: a drill ship of the Integrated Ocean Drilling Program. Image courtesy of William Crawford, IODP/TAMU

A multinational research team, led by scientists at the University of Southampton, has developed a new record of the carbon dioxide ($CO_2$) content of the Earth's atmosphere during the Pliocene – between 2.3 and 3.3 million years ago.

During the Pliocene, the Earth was around 2°C warmer than it is today and atmospheric $CO_2$ levels were around 350 to 400 parts per million (ppm), similar to the levels reached in recent years. By studying the relationship between $CO_2$ levels and climate change during a warmer period in Earth's history, the scientists have been able to estimate how the climate will respond to increasing levels of $CO_2$ in the future, a parameter known as 'climate sensitivity'. The findings, which have been published in *Nature*, also show how climate sensitivity can vary over the long term.

"Today the Earth is still adjusting to the recent rapid rise of $CO_2$ caused by human activities, whereas the longer-term Pliocene records document the full response of $CO_2$-related warming," says Gavin Foster, Professor of Isotope Geochemistry at the University, who co-led the study.

**Innovative method**

The international team, which also included academics from the Autonomous University of Barcelona and the Australian National University in Canberra, studied the composition of shells of ancient marine organisms that inhabited the surface waters of the ocean millions of years ago to measure its carbon content.

The established way of studying the atmosphere's prehistoric composition is to analyse ice cores taken from Antarctica. "These ice cores give us the well-documented


"Here at the University of Southampton we have the largest boron isotope group in the UK – we are one of the few labs in the world that can do this type of analysis."

Gavin Foster,
Professor of Isotope Geochemistry

climate cycles every 100,000 years: warm 'interglacials', where $CO_2$ levels are high, followed by cold 'glacials', where $CO_2$ levels are low," explains Gavin. "However, the ice cores only go back around 800,000 years and none of the interglacials during this period have been as warm as our climate today." So in order to get an insight from the past about our current climate, a different approach was needed.

Gavin and his team developed a new way of measuring the $CO_2$ content of ancient oceans: by analysing the ratio of two isotopes of the element boron – boron 10 and boron 11 – in the calcium carbonate of shells and skeletons of fossilised plankton-like organisms called foraminifera. The ratio of the boron isotopes indicates the pH that the shells originally grew at.

"By measuring the boron isotopic composition of these ancient fossils we can get an idea of what the ocean pH, or acidity, was like millions of years ago," says Gavin. "That is important because the acidity of the ocean is determined by the amount of carbon that is dissolved in it, and, on long timescales, the amount of carbon in the ocean will determine the amount of carbon in the atmosphere. So we get a measure of the $CO_2$ variability in the oceans and atmosphere through time."

The advantage of looking at marine carbonates is that sediment cores from the sea bed give us at least 65 million years' worth of data, Gavin explains. Drill ships take samples in the deep ocean as part of the Integrated Ocean Drilling Program, an international consortium of which the UK is a member, and this provides a valuable archive that researchers can study. The challenge is analysing these samples to reveal atmospheric $CO_2$ in the past.

"We used the boron isotopes to look at the relationship between $CO_2$ change, sea level change and global temperature to give us an idea of how the Earth's system behaved in the past, which helps us hone our predictions of how the warm climate of the future might play out," says Gavin.

## Warming world

By analysing the boron content in the foraminifera, Gavin and his team have reconstructed the atmospheric $CO_2$ during the Pliocene. They found that the climate sensitivity was the same during the warmer Pliocene as during colder glacial periods that had previously been measured from the ice cores, once they had allowed for other factors such as reflective ice sheets covering large parts of the world during glacial periods.

The finding is exciting because it helps us understand how today's climate is responding

to rising $CO_2$ levels. "As the climate warms, you might expect more temperature change for a given $CO_2$ change because of amplifying factors such higher atmospheric water vapour content as the world gets warmer," says Gavin. "Lack of understanding of these feedbacks leads to all the uncertainty around what the temperature of the future is going to be because we don't yet know how all the feedbacks are going to play out. What we showed was that as the Earth got warmer or colder in the past, the feedbacks were operating at the same level."

Getting an accurate measure of climate sensitivity is crucial for predicting the future climate. Climate sensitivity is thought to be around three degrees every time $CO_2$ is doubled. "If we continue to burn fossil fuel at the current rate, by 2100 we are looking at about four degrees warming – perhaps a little more. If we are way off on our climate sensitivity estimate, by the time we get to 2100 it might well be more like five, six or seven degrees," says Gavin.

"Our findings use the geological record to support the climate sensitivity quoted by the Intergovernmental Panel on Climate Change (IPCC) based on different observations, for example the modern climate system and the more recent geological record," says Gavin, who was a contributing author on the last IPCC report. "The temperatures we see in the Pliocene are probably going to be reached on earth by around 2080 if we carry on producing $CO_2$ at the current rate," he adds.

## World-leading expertise

This study is a particularly important contribution to the knowledge on past climates because of its high resolution: 100 data points were collected in a painstaking process, each of which took about two weeks to complete.

"Here at the University of Southampton we have the largest boron isotope group in the UK – we are one of the few labs in the world that can do this type of analysis," says Gavin. Having the capability to achieve such high-resolution data is crucial because the more data available, the better the reconstructions of past climates can be.

"It's not just the change in $CO_2$ between the modern and the Pliocene that we are interested in," says Gavin. "52 million years ago there was the Eocene climatic optimum – where global temperatures were 12 to 14 degrees warmer than today – so by looking further into the past we are looking further into the future of our climate."

For more information, visit **www.descentintotheicehouse.org.uk** and **www.southampton.ac.uk/gavin-foster**

# The compassionate duke

To mark the 200th anniversary of the Battle of Waterloo, *New Boundaries* talks to historian and archivist Karen Robson, who explains how the Wellington Papers, a unique resource held at the University, sheds light on the type of leader the Duke of Wellington was.


An engraved nautilus shell depicting Wellington as a national hero; he is shown on one side, with St George slaying a dragon on the other. Produced in the 1850s by C H Wood and now part of the University's Wellington collection

**Q** *What happened at the Battle of Waterloo?*

The Battle of Waterloo was fought on Sunday 18 June 1815, in what is now Belgium. An Anglo-allied army, commanded by the Duke of Wellington, combined with Prussian forces to defeat a French army led by Napoleon, ending his rule as Emperor of the French. Some 200,000 men fought, with around 50,000 casualties.

**Q** *What are the Wellington Papers?*

The Wellington Papers are among the most prestigious collections of primary documents relating to British history in the first half of the 19th century. The unique collection, comprising over 100,000 items dating from 1790 to Wellington's death in 1852, catalogues his military career, his campaigns, and tactics, his political life, and also includes letters showing his more human side. It is an important primary resource for researchers across the globe studying this period.

**Q** *What does it tell us about Wellington's role at Waterloo?*

In the build up to the Battle of Waterloo, Wellington had to be more than a military leader: he was also a politician and diplomat. Britain couldn't fight this battle on its own so this was the coalition of several powers. As the commander of the allied army, as soon as he arrived in Brussels, Wellington was responsible for negotiating with representatives of various powers to ensure they provided the numbers of troops they had agreed to.

We hold several complex treaties of subsidy at the University, including one signed by Wellington and on behalf of the King of Sardinia agreeing how many troops will be supplied and how the command chains will work. This shows first-hand that Wellington had a diplomatic role rather than being purely a military strategist.

**Q** *What can we glean about the type of leader he was?*

Notes and letters that we hold from soldiers – from both during and after Waterloo – show that Wellington's troops had a great deal of loyalty to him but that he was seen as quite aloof and unapproachable, rather than a leader who was loved by his men. This is in contrast to Napoleon, who we know was far more a 'man of the people' who made his way up through the ranks.

Saying that, one letter in particular stands out as showing his compassion. This is a letter from Wellington to Lord Aberdeen, following the death of Aberdeen's brother, one of Wellington's staff officers at the Battle of Waterloo. There is real warmth in the way he sends his condolences and writes about the achievements of the deceased soldier, which counterbalances the view that Wellington was a cold and distant leader.

Another trait revealed in the Wellington Papers is that he was a very 'hands-on' leader. He didn't write much down for his officers before the battle; instead of writing strategic documents he wrote short orders as notes. We know that, rather than delegating, he was generally a leader who was around the battlefield seeing what was going on and that he preferred to talk directly to the commanders in charge of certain parts of the battlefield.

**Q** *What about his later life?*

Wellington had a towering reputation as a soldier and was widely known as the 'saviour of Europe' in the wake of Waterloo. However, his popularity dropped when he took political office on his return to Britain in 1819.

He was still a person everyone wanted to write to; we have a vast number of letters addressed to him on a raft of subjects as Britain developed in the first half of the 19th century – from recipes to cures for earache, to political issues about the Empire. He replied to them all. He was also very interested in technology and inventions: his archive contains material relating to inventions such as a calculating machine designed by Charles Babbage, designs of bridges by Marc Isambard Brunel (the father of Isambard Kingdom Brunel) and the steam carriage created by Sir Goldsworthy Gurney.

When he died he was rediscovered as a great national hero. He had a state funeral; newspaper articles from 1852 show that London was at a standstill, with people arriving from across the country by rail.

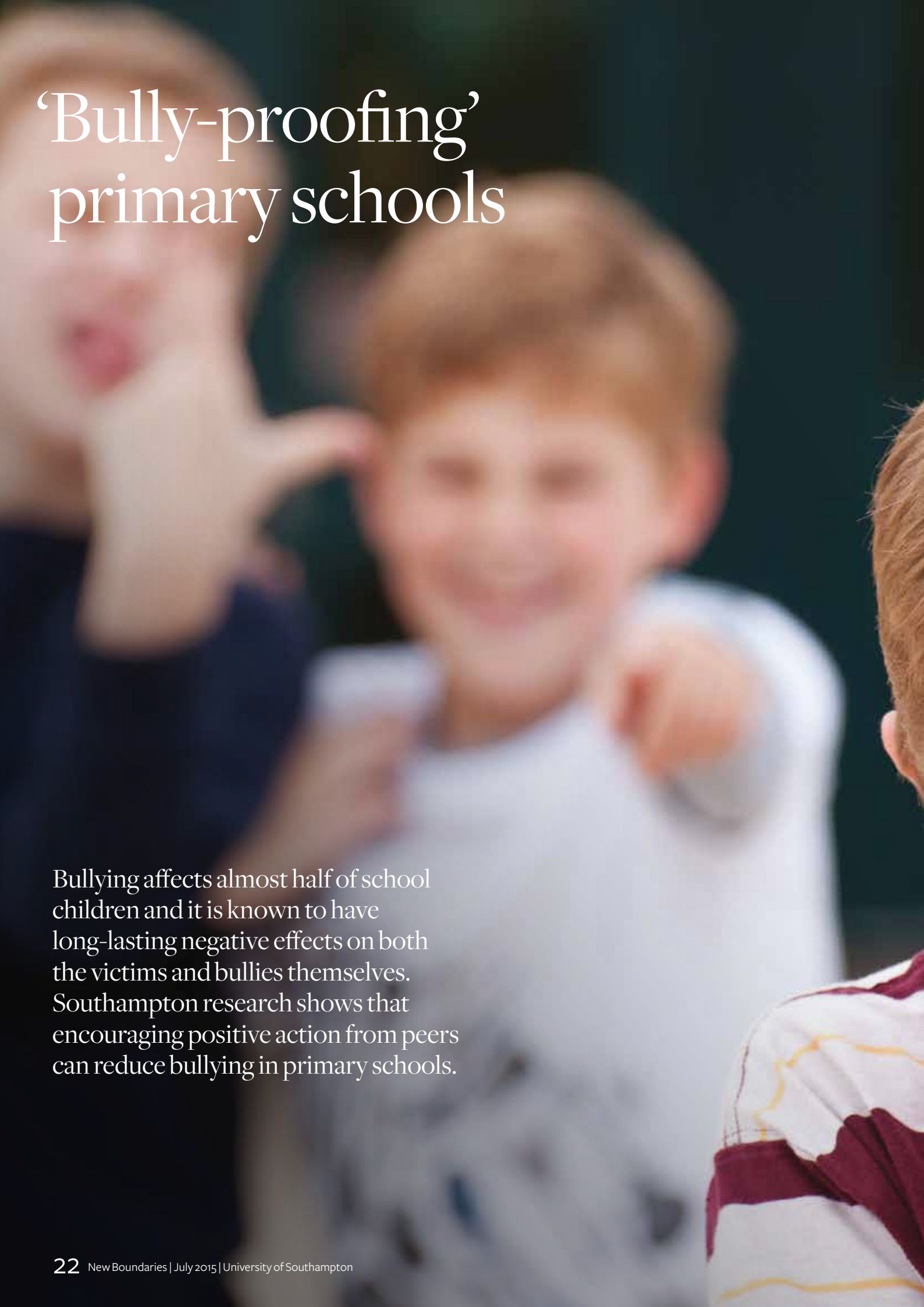
Wellington fitted into Victorian concepts of national pride and identity. The carved nautilus sea shell we hold in the archives illustrates this perfectly: carved after Wellington's death, it represents him as an English hero, with him depicted on one side and St George on the other. This is interesting, as he was of Irish descent.

**Q** *Please can you tell us more about the Wellington Papers Massive Open Online Course (MOOC)?*

In June this year we ran a three-week online course, which enabled anyone to explore the Wellington Papers through a series of videos and articles. We covered topics such as why the Battle of Waterloo was fought, the lead up to the battle, Wellington's Waterloo despatch and people's accounts of the battle – showing the battle from Wellington's perspective. The course is likely to be repeated later this year.

For more information on the Wellington Papers and how to access the archive, visit **www.southampton.ac.uk/archives**

# ‘Bully-proofing’ primary schools



Bullying affects almost half of school children and it is known to have long-lasting negative effects on both the victims and bullies themselves. Southampton research shows that encouraging positive action from peers can reduce bullying in primary schools.

Southampton researchers are part of a European team that has created a set of activities to encourage children to reflect on the effects of bullying through collaborative group work. The programme has been trialled in 16 schools, with promising results.

"There are already a lot of anti-bullying programmes in existence, so what we wanted to do here was to build the resilience and skills of children that broadly address interpersonal skills to help prevent bullying rather than solving problems as they occur," says Professor Daniel Muijs, Director of Research at Southampton Education School.

"We know from our previous research that bullying is not just a relationship between a bully and a bullied person, but is something that involves the whole peer group," Daniel explains. "Bystanders are very influential: they can encourage, for example by laughing at the bullying behaviour, discourage, by telling the bully to stop, or in many cases they can be passive in what happens. There is also a cultural element involved, with the extent of bullying depending on the approach of individual schools."

### Social and emotional learning

Part of a European Commission Daphne III project, this study is a collaboration between researchers in Spain, Italy, Denmark, Latvia, Romania and the UK, with the University of Southampton leading the UK trial of the programme.

The researchers developed the Social and Emotional Early Development (SEED) programme, which consists of 10 activities that aim to help children think about their relationships and interactions with their peers at school. The activities are open-ended: a scenario is presented, for example through a cartoon, and the children are asked to discuss the scenario, come up with ideas of how to deal with the situation and then devise a slogan that encompasses what they talked about. There are also games in which the children can score points for their answers and how well they engage with the group.

"We hope that this intervention will build a basis for skills such as empathy and sociality, which will help to form a defence against occurrences of bullying in these schools in the future,"

Professor Daniel Muijs,
Director of Research,
Southampton Education School

"The aim is to develop children's thinking skills and get them to reflect on the way they think about certain situations and interactions," Daniel explains "This is the first programme of its kind to integrate social and emotional learning, developing thinking skills and gaming. At Southampton we have a strength in interdisciplinary working so we can get people together to address the psychological, educational and technological aspects that come with this type of intervention."

Daniel's team tested the programme in reception, year one and year five classes of 16 UK schools. In a quasi-experimental design, the schools were divided into two groups, half using the programme in the first 10 weeks and the second half using it in the second 10 weeks. In this way, the second group acted as a control group for the first.

The team used three measures to quantify the impact of the programme on the children's behaviour. "First, we used an established child behaviour scale to look at various behavioural factors like aggression, pro-social behaviour, whether a child is withdrawn and so on," says Daniel. Teachers completed this scale about every child in their class before, during and after the programme.

"The second measure was specifically developed for the project to look at a number of things we were trying to develop with SEED," says Daniel. "This was a measure of personal and self-development, emotional literacy, empathy, tolerance, assertiveness, communication and conflict management skills." This was completed at a classroom-wide level so after every session, the teacher would complete this scale for their class as a group.

Finally, they used a sociometric measure, where the children themselves select who their best friends are. "This helps us to identify how many linkages there are inside a classroom, so how close-knit the network is," Daniel explains. "Obviously what you want to see is a lot of linkages and in particular what you don't want to see is too many children who are isolated, unpopular or disliked."

### Impact on behaviour

The results showed a significant improvement on all measures during the 10 weeks that each school took part in the programme. The team repeated the child behaviour scale another 10 weeks after the end of the study, and saw a continued improvement. "So although we don't yet have enough data to say this programme has long-lasting effects, we are seeing continued improvements, which is promising," says Daniel.

"We hope that this intervention will build a basis for skills such as empathy and sociality, which will help to form a defence against occurrences of bullying in these schools in the future," Daniel adds. "Instilling these skills at an early age is important: we know that bullying is a problem in both primary and secondary schools and there is a lot of research that shows that the harm that is done to kids when they have been bullied is persistent over time, so we need to get in as early as possible to try and prevent it."

The team is now aiming to roll this programme out into more schools, and will be making the materials freely available online for schools to use.

For more information, visit **www.southampton.ac.uk/daniel-muijs**

**Key facts**

- Bullying affects almost half of school children
- More than 16,000 young people are absent from school due to bullying
- Children bullied during their early years are up to three times more likely to self-harm than their classmates when they reach adolescence
- Young people who bully are more likely to have a criminal record by the age of 30

# Lighting up the world

Photonics has a huge impact on our day-to-day lives, from navigating airlines to powering the internet. It is a crucial technology for the economy; around 30,000 jobs and 3,000 companies are dependent on photonics in the UK alone. To mark the International Year of Light, *New Boundaries* asks two leading researchers in photonics what Southampton is doing to drive the field forward.

Professor Sir David Payne, Director of the Optoelectronics Research Centre

**Professor Sir David Payne, Director of the Optoelectronics Research Centre (ORC) at the University of Southampton.**

Here at the ORC, we have been at the forefront of photonics for the past 40 years. Our research connects the planet: the global internet relies on our invention of erbium-doped amplifiers that boost optical signals, allowing fast telecommunications. When you travel by plane, you are being navigated by our optical fibres.

We are incredibly fortunate here at Southampton in that we can go all the way from electrons to enterprise; from photons to production. In other words, we can make new fibres, emitters and circuits, develop a new device based on those components, test this in a system and start a company. Very few universities have this capability to go from end to end. This is thanks to our magnificent clean room complex, which is one of the best in the world.

Ten companies have spun out of the ORC so far, all of which are manufacturing businesses, and we are very proud of that. Our drive to innovate and capitalise on our research means there are more special fibre drawing plants in Southampton than any other city worldwide.

So what's next? If the internet continues to grow at the current rate – 30 to 40 per cent each year – it will soon reach its limit. To address this we are working on a new field, silicon photonics, that marries the parallel technologies of electronics and optics to get the best of both worlds. Optics has a major part to play in the 'internet of things' of the future, and is paving the way for a new generation of sensors with unforeseen capabilities. Imagine a sensor that could run hundreds of kilometres along a railway track, giving real-time information on a train's location, speed and the condition of its wheels; this is just one of the new sensors we are developing here at the ORC.

My strategy and research direction has always been to notice what it is that is different in a new invention. Thanks to fibre lasers, which we pioneered here, for the first time we can combine many thousands of individual lasers together to create an energy density that exceeds that on the sun. The energy density this produces inside a vacuum could be high enough to rip it apart and create something: exactly as is believed to have happened in the big bang – a crazy idea that just illustrates the potential of photonics. Practical applications could include making the next accelerator for CERN or creating a capability to shoot space debris out of the sky.

The International Year of Light, within what is the Century of Light, is a huge opportunity to raise the profile of photonics, especially to young people. We need bright young people to take these ideas forward and bring into reality a new generation of technology that was unimagined a decade ago.

**Dr Steve Norman, Technical Consultant and Director, SPI Lasers UK Ltd**

SPI Lasers' products, all of which are based on fundamental inventions from the ORC, are used to make a broad range of consumer products that affect nearly everyone in society. Examples include medical stents for alleviating heart attacks, mobile phones, laptops, solar cells, batteries, automotive components and large sheet metal products. SPI Lasers manufactures in the UK, employs 350 staff in the UK (around 250 in the Southampton area) and exports 95 per cent of its products, with over 35 per cent going to China.

Success in highly technological industries derives from the ability to take groundbreaking research inventions, to carry them through to product design and development, and on to full commercialisation. The UK is justifiably renowned for its creativity and its ability to innovate, and the University's ORC has excelled in the photonics research field since long before the word 'photonics' was coined. Moreover, in this field, the ORC's track record in downstream commercialisation of major technological innovations is among the best in class. For example, the development of optical fibre manufacturing technologies in the 1970s, the invention of the erbium-doped fibre amplifier (EDFA) in the late 80s, the use of optical fibres as high-performance sensors, and importantly the invention of the optical fibre laser in the 90s were all breakthrough inventions that have evolved into multi-billion-dollar markets in which Southampton-linked companies are important players.

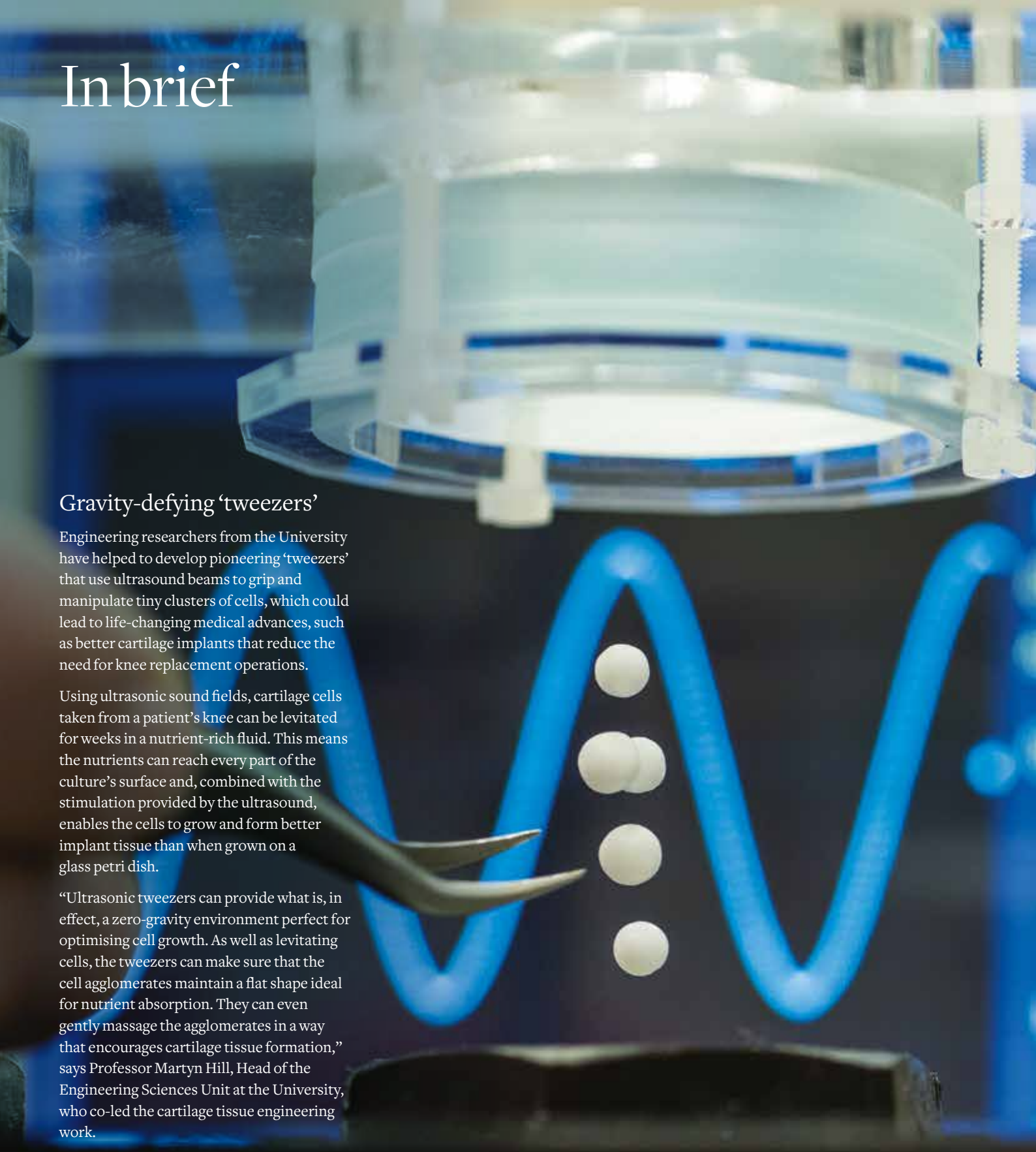
What characterises these successful developments? Firstly, good alignment between the research team's interests and the business strategy of the industrial partner is essential; this can be fostered either through staff secondment, or through tightly linked research collaboration in a relevant field. Secondly, industrial foresight and investment in early-stage technology-watch activities can enable rapid commencement of first-stage (high-risk) embryonic product development. And lastly, entrepreneurial risk-taking attitudes, coupled with an enthusiasm to take research to real product, are essential to drive innovative technologies.

In all these respects, SPI Lasers is proud to have taken many of the ORC's innovations to market over the 15 years since our formation as a 'spin-out' from the ORC. We have very successfully reinforced our technological linkages to the ORC by establishing and co-locating an advanced R&D group at the University, with SPI and ORC staff working together. We have ongoing interactions and exchanges on joint projects and can frequently support researchers with commercial-off-the-shelf (COTS) devices to facilitate their research. The critical element of trust exists between academic researchers ready to put industry challenges at the centre of their work, and industrial developers willing and capable of absorbing innovative ideas from academic research.

With its major impact on society over the last 40 years, Southampton can be very proud that it has such a world-class centre. It is well placed to be a catalyst and technology driver for the future growth of UK photonics-enabled manufacturing industry.

For more information, visit **www.southampton.ac.uk/orc**

# In brief



## Gravity-defying 'tweezers'

Engineering researchers from the University have helped to develop pioneering 'tweezers' that use ultrasound beams to grip and manipulate tiny clusters of cells, which could lead to life-changing medical advances, such as better cartilage implants that reduce the need for knee replacement operations.

Using ultrasonic sound fields, cartilage cells taken from a patient's knee can be levitated for weeks in a nutrient-rich fluid. This means the nutrients can reach every part of the culture's surface and, combined with the stimulation provided by the ultrasound, enables the cells to grow and form better implant tissue than when grown on a glass petri dish.

"Ultrasonic tweezers can provide what is, in effect, a zero-gravity environment perfect for optimising cell growth. As well as levitating cells, the tweezers can make sure that the cell agglomerates maintain a flat shape ideal for nutrient absorption. They can even gently massage the agglomerates in a way that encourages cartilage tissue formation," says Professor Martyn Hill, Head of the Engineering Sciences Unit at the University, who co-led the cartilage tissue engineering work.

With funding from the Engineering and Physical Sciences Research Council (EPSRC), the tweezers were developed by researchers from the universities of Southampton, Bristol, Dundee and Glasgow as well as a range of industrial partners.

## £1.6m to safeguard water, energy and food resources

The University of Southampton is leading one of three major research projects that make up a £4.5m investment from the Engineering and Physical Sciences Research Council (EPSRC) to safeguard the UK's water, energy and food security.

With the world's population due to grow to eight billion by 2030, humanity is facing a crisis, with predictions of increasing demand and shortages of water, energy and food. Water and energy are needed to produce food; water is required to produce energy and with the advent of biofuels, energy and food are increasingly competing for land. This means that any shortage or disruption of one resource will impact on the other two. The unbreakable link between all the resources is known as the water-energy-food nexus.

Research into the water-energy-food nexus will be conducted by interdisciplinary groups of scientists based at 19 universities and research institutes, with support from the Science and Technology Facilities Council's Scientific Computing Department, to tackle these challenges.

The Southampton team will be investigating how nexus 'shocks', such as extreme climatic events that cause flooding or drought, energy shortages, or unsustainable infrastructure development, may help inform the development of more environmentally sustainable and secure systems.

## Genes for post-traumatic stress disorder identified

Southampton researchers have discovered that some soldiers are genetically predisposed to post-traumatic stress disorder (PTSD) and that some are more severely affected by also experiencing adverse immunological reactions.

In collaboration with the University of California, San Diego, the researchers examined 190 US Marines who had donated blood before and after their deployment. They used whole transcriptome RNA sequencing on blood samples of individuals with and without PTSD to identify genetic markers associated with PTSD that are also linked to the body's innate immune system.

"Our findings suggest that it may be possible to identify individuals at risk of PTSD by measuring gene expression from a simple blood sample," explains Dr Michael S Breen, Southampton researcher and lead author of the study. "The question that remains is what's causing an immune response prior to PTSD development. This could be due to increased anticipatory stress prior to deployment, or something more complex, for example individuals having a higher viral load. This is something future studies should focus on."

Michael and his team are now starting a new meta-genomics study to investigate differences in gut bacteria and their relationship to PTSD from both service members and civilians around the globe.

## Family of starfish named after Southampton professor

A newly discovered family of starfish has been named after the University's Professor Paul Tyler MBE.

Recent expeditions involving University scientists to volcanic vents on the ocean floor near Antarctica led to the discovery of the new starfish family, named the 'Paulasteriidae', to honour the work of deep-sea biologist Paul, who recently retired from the University. The new family includes the first starfish species known to thrive at deep-sea volcanic vents. Paul led the Antarctic research programme that discovered these deep-sea vents.

The research, published in the *Zoological Journal of the Linnean Society*, involved Ocean and Earth Science researchers Dr Jon Copley and Dr Leigh Marsh. The analysis was led by Dr Christopher Mah of the Smithsonian Institution and Louisiana State University in the USA using museum specimens and archived data.

"Quite a few people have species named after them, such as Beyonce, John Cleese, Kate Winslet and Prince Charles, but having a whole family of species named after you is a rather more exclusive club," says Jon. " We are delighted to celebrate Paul's contributions as a world-leading deep-sea biologist and inspiration to so many students over decades in this way."

# In brief


## Shifts in consumer behaviour fuel high street revival

Convenience culture and the rise of omnichannel shopping are driving a once-in-a-generation shift in shopping habits that is helping to revive UK high streets. This is highlighted in one of the most exhaustive evidence reviews into high streets and consumer habits ever conducted in Britain, led by researchers at Southampton.

Funded by the Economic and Social Research Council (ESRC) and commissioned by the government's policy advisory group, The Future High Streets Forum, this new report entitled *'British High Streets: from Crisis to Recovery?'* comes at a time when radical shifts in consumer culture and practices are becoming increasingly apparent and widely discussed in public debate.

"Over the past decade a growing number of consumers have reassessed the time-cost savings commonly attributed to large, 'one-stop' out-of-centre stores," says Senior Research Fellow Dr Dionysia Lambiri, a lead author of the report. "Particularly since 2008, a growing number of consumers have adapted their behaviour to the economic crisis and austerity in a way that is supportive of a neighbourhood conception of convenience, favouring 'little and often' shopping patterns over the large 'weekly shop'. The transformative power of these shifts is clearly reflected in the problems of out-of-town superstores widely discussed in the media recently."

## Wearable robotics

Rehabilitation technologists from seven UK universities, including the University of Southampton, will join forces to produce prototypes of soft robotic trousers to transform the lives of those with mobility impairments.

This is the first time soft robotic technologies have been used to address rehabilitation and healthcare needs in a single piece of clothing, enabling our ageing population to live with greater independence and dignity.

The Engineering and Physical Sciences Research Council (EPSRC) has awarded the team £2m for this project. The wearable technology will include trousers and socks that are comfortable, adaptable and meet each user's individual mobility needs.

Dr Chris Freeman, Reader in Electronics and Computer Science, who leads the Southampton team, says: "We will develop fundamental technologies that will transform independent living for the disabled and infirm."

This intelligent clothing will use artificial 'muscles' made from smart materials and reactive polymers, which are capable of exerting great forces. Smart trousers could help vulnerable people avoid falls by supporting them whilst walking, give people added bionic strength to move between sitting and standing positions, and help people climb stairs. They ultimately have the potential to free many wheelchair users from their wheelchairs.

## Breast cancer discovery

Southampton researchers have found that women who are diagnosed with breast cancer and have a family history of the disease face no worse a prognosis after treatment than other women with breast cancer.

About one-quarter of breast cancer cases in developed countries are thought to be related to hereditary factors. The researchers, funded by Cancer Research UK, analysed records from 2,850 women under the age of 41 who were diagnosed with breast cancer and treated in the UK. They recorded the patients' personal characteristics, tumour characteristics, treatment and family history of breast or ovarian cancer over a 15-year period. The results, published in the *British Journal of Surgery*, found that there were no significant differences in cancer recurrence rates after treatment for women with a history of breast cancer in their family versus those without.

"This information will potentially help in planning preventive surgical options at the time of breast cancer treatment. Many genes have now been identified that contribute to a family history of breast cancer in different families so the next step is to investigate whether specific breast cancer genes lead to differences in the effectiveness of anticancer treatments," says study lead Professor Diana Eccles.

## Understanding maritime futures

The Southampton Marine and Maritime Institute has received a £1.05m award to fund 15 doctoral studentships, for research into understanding maritime futures.

The doctoral scholars will address key global issues, such as access to resources, safety and security, the effects of rising sea levels, technical advancements and autonomy, our responses to natural and human disasters and the impacts on people, and the ways people living by the sea understand their experiences and cultural heritage.

The vision for the programme is to develop interdisciplinary thought leaders and researchers, who have a unique human-centred approach to understanding, living, and working with the sea. The programme aims to facilitate a different, more creative and holistic way of problem solving to address marine and maritime societal challenges.

"What's particularly exciting about this award is its focus on creating a transdisciplinary community of innovative and daring doctoral scholars," says Dr Fraser Sturt, Associate Professor in Archaeology at the University. "The scheme has been designed to disrupt our usual working practices to encourage novelty and innovation. Understanding the opportunities and challenges of the marine environment requires people who can engage with viewpoints and data from a range of sources, social as well as scientific."

To find out more about our research and its impact on society, visit **www.southampton.ac.uk/research**

www.southampton.ac.uk/research
newboundaries@southampton.ac.uk
+44 (0)23 8059 8312