Fondúireacht Eolaíochta Éireann
Science Foundation Ireland

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Excellence in Research - Profiles of SFI Researchers

Research for Ireland's Future

Foreword by Minister for Science, Technology & Innovation, Conor Lenihan TD

Excelling in the fields of science and innovation necessitates foresight, determination and a willingness to take risks in order to unearth and discover new models, methods and meanings. It also requires encouragement and support at the highest level.

The Government, through the Strategy for Science, Technology and Innovation (SSTI) 2006-2013, has committed itself to providing the necessary funding and foundations for Ireland to assume a leading position in international scientific research terms. The SSTI's core objectives are that by 2013, Ireland will be internationally renowned for the excellence of its research, and be at the forefront in generating and using new knowledge for economic and social progress, within an innovation-driven culture.

In December 2008, the Government launched "*Building Ireland's Smart Economy: as Framework for Sustainable Economic Renewal.*" The Smart Economy is at the heart of the Government's economic recovery. The Smart Economy framework sets the focus on how the research and university sector can contribute to economic renewal – we must all work together in delivering on the ambition for a future Ireland. We are greatly encouraged by advances so far, and are resolute on continuing in this regard.

Ireland's ever-strengthening community of SFI-funded scientific researchers are pursuing a wide range of exciting projects, and striving to address many of the challenges posed by the Biotechnology, ICT and Energy sectors. Their motivation is to help us better understand the world we live in, to efficiently harness natural resources, and to employ new procedures that provide commercial and practical benefits in our daily lives.

This Science Foundation Ireland 'Excellence' brochure showcases some of Ireland's very best research talent, and illustrates the depth and scope of the extraordinary work that is taking place out of the spotlight, behind laboratory doors here in Ireland. It also chronicles the progress that has been achieved by those individuals profiled, and serves as an incentive for aspiring scientists, engineers and innovators to follow similar career paths.

'Excellence' will help enable Irish-based scientific researchers to reach key new audiences, nationally and internationally, in the educational and commercial spheres and beyond. In establishing new connections, it will increase awareness and convey the message that high-level scientific research in Ireland is relevant and making a profound impact on everyday life. The Government remains confident that breaking through the seemingly impenetrable boundaries of possibility is very much within the grasp of these SFI-funded researchers and their colleagues.

Conor Lenihan TD
Minister for Science,
Technology & Innovation

Introduction by Professor Frank Gannon, Director General, Science Foundation Ireland

Through the Government's Strategy for Science, Technology and Innovation (SSTI) and in line with the Government's Building Ireland's Smart Economy framework, SFI is continually investing in research excellence across the diverse areas of biotechnology, ICT, sustainable energy and energy-efficient technologies.

This book is designed to tell the stories of SFI-funded researchers involved in these areas - what they are doing, why they are doing it and what the consequences of their research will be. A glimpse of each researcher's career path is also presented here, so that the reader can imagine the steps that have lead to the research now being supported by SFI. Placing each piece of research in the context of its impact on society should, it is hoped, bring alive the sense of adventure that characterises scientific research. Each research project also has the possibility of generating novel applications that may end up as intellectual property that is licensed - or even as the basis of a new start-up company.

The ongoing commitment provided by the Government towards this and other research activity has been critically important to the enhancement of Ireland's knowledge economy. Indeed, the Government views the implementation of the SSTI as central to Ireland's competitiveness in key sectors. With this appropriately supported research environment, our research community has genuine potential to make its mark in international scientific circles.

This anthology of short stories should be read and absorbed by frequent visits and random selection. In doing so, any reader - from the casual to the committed - will appreciate the extent and value of the research that is performed in Ireland. The international flavour of the researchers and their wide range of experiences will also be evident.

With SFI funding presently going to over 500 laboratories nationwide, the selected examples here could not possibly, in themselves, convey the full richness of research output being carried out around the country. Instead, this book aims to stimulate a thirst for more descriptive testimonials where the relevance of SFI-funded research for society and the economy shines through.

Prof. Frank Gannon
Director General
Science Foundation Ireland

Case Study

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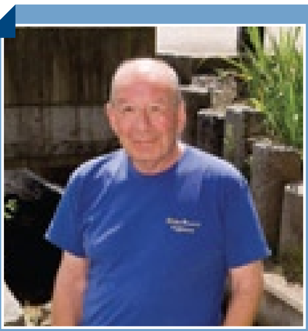

Researcher Prof Mark Achtman

Title *Following a trail of diversity*

Case Study **01**

Bacteria are highly adaptable, so they readily form local populations. As Prof Mark Achtman at University College Cork explained, diversity makes it easier to follow a genetic trail. For a number of years, Prof Achtman has been following the progress of pathogens around the world, and as a result of this research, techniques are being developed to track down troublesome strains.

Prof Achtman's trail-following research began at the Max Planck Institute for Infectious Biology in Berlin. He became interested in the ulcer causing *Helicobacter pylori*, a bacterium that affects about 90 per cent of the world's population. Although globally widespread, *Helicobacter pylori* is genetically diverse, and it is only transmitted by close personal contact.

Because of this, he explained, it became a very useful marker for human migration, and among his findings was that the most isolated native Americans, far up the Amazon, still carry the strains they inherited from their east Asian ancestors.

Helicobacter pylori made the task of tracking a lot easier because it has so much genetic diversity. Even in relatively short sequences tell-tale variations could be detected. Such diversity is far from universal. Other pathogens show little variation, such as *Yersinia pestis*, the cause of plague, described by Prof Achtman as "genetically monomorphic". However, the study of more diverse genomes had shown the value of this approach in keeping track of pathogens.

On making the move from Berlin to Cork, Prof Achtman concentrated on developing techniques to trace the spread of these more stable pathogens, and in this he was helped by the advances made in analysing the human genome. The same techniques that helped unravel the human code could also be applied to bacteria and at one stage the group published a comparison of 17 different genomes. "This attracted a lot of attention," said Prof Achtman, because no one had been able to do this before.

Prof Achtman's work was helped by a software programme developed by one of his research students at Berlin, Dr Daniel Falush. This programme made it possible to distinguish between genetically different populations, be they bacteria, sunflowers or fishes. Dr Falush went on to work as a Wellcome Trust Investigator at Oxford, but he has since rejoined Prof Achtman in Cork.

"This is enabling research", said Prof Achtman, and he sees it leading off into different directions ranging from genotyping of salmon, epidemiology, and yet more tracking of human movement. Prof Achtman is involved in running international databases on pathogen diversity, and he has established an all Ireland collaboration on *Salmonella*.

Prof Achtman explained that "high throughput genotyping has become a very powerful tool, and it could, for example, be used to track down individual strains of a drug resistant pathogen within a hospital. You can see patterns that no one has been able to see before."

» Prof Mark Achtman was born in Kielce, Poland, and following his BSc at McGill University, Montreal, Canada, completed his Masters at the University of Manitoba, Winnipeg, Canada, and his PhD on molecular biology at the University of California, Berkeley, USA. Prior to taking up his position at University College Cork, Prof Achtman led a research group at the Max-Planck Institute for Infectious Biology in Berlin. Prof Achtman was granted an SFI Principal Investigator award in 2007.

» Collaborators: Sebastian Suerbaum, University Hannover; Elizabeth Carniel, Institut Pasteur Paris; Paul Keim, NAU; Gordon Dougan, Wellcome Trust Sanger Institute; Martin Maiden, Oxford University.

» Awards: Main Prize German Society of Hygiene & Microbiology, 2004. Section Editor at PLoS Pathogens since 2007

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Researcher Dr Geraldine Boylan

Title *Helping the helpless*

Case Study

02

When babies are born they cry, but otherwise it is almost impossible to see if they are in distress. Dr Geraldine Boylan, head of the Neonatal Brain Research Group, University College Cork, said "that it is possible for a baby to have a brain seizure without anybody noticing that something is seriously wrong." Not only can this happen, but Dr Boylan believes that up to 85 per cent of the seizures that occur in the newborn may not be spotted, and this may have long term implications for mental health.

Premature babies, and those requiring resuscitation, are particularly at risk, and Dr Boylan's goal is to initiate a programme of careful monitoring to detect brain distress as early as possible. At present we are dealing with a silent injury, and as she admits, no one yet knows how many adult disorders could be traced back to an early, unobserved, seizure.

One of the problems is that most of the research results currently available are based on cases where seizures were detected by visual observation. Dr Boylan said that "more than likely this is just the tip of an iceberg. In my opinion those figures have been vastly underestimated." The real figure could be much higher but without careful monitoring we simply do not know the true extent of the problem. Dr Boylan said she is very reluctant to quote hard and fast figures simply because so few tests have been done.

"What our group is doing in Cork," she observed, "is the most intense work being done anywhere in the world, and the programme of research is still developing." The Cork group intend to launch an intensive monitoring programme for newborn babies using EEG (Electrocephalography) equipment. However, while the testing itself does not involve great expense, very few people have experience in interpreting the results. "In an adult," said Dr Boylan, "it is difficult enough, but with a baby the brain is developing fast, so patterns change. The pattern in a baby of 24 weeks, is very different from a baby of 25 weeks."

The graphs and peaks of an EEG trace form patterns, so Dr Boylan's team have been working with Neonatologists in Cork University Maternity Hospital, and Drs Liam Marnane and Gordon Lightbody of the Electrical Engineering Department at UCC to automate interpretation of these signals. "We have a really good algorithm now," she remarked, "that compares very well with the traditional approach to interpretation but because it is automated, it can process the results faster and more objectively and include other relevant information from vital signs monitoring also."

Research by Dr Geraldine Boylan at UCC aims to detect previously undetectable brain seizures in newborns, as possible indicators for susceptibility to future mental illness.

- Dr Geraldine Boylan has an MSc in Physiology and a PhD in Clinical Medicine from University College London.
- After working as a clinical scientist at King's Hospital, London, she became a lecturer in Paediatrics at University College Cork. She is now a Senior Lecturer in the School of Medicine.
- Dr Boylan received a Principal Investigator Career Advancement Award from SFI to develop an automated seizure detection system. This project involves collaboration between the 15 strong interdisciplinary team in Cork with medical staff and researchers at University College London and St Vincent's University Hospital, Dublin. The research, which has attracted international attention, is also being supported by the Wellcome Trust, the Health Research Board and more recently by European funding under the FP7 Health programme.

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Researcher Dr Gerard Boyle

Title *Monitoring tiny eye movements*

Case Study

03

In many medical situations, such as coma or stroke, it is vital to assess a patient's level of consciousness. This can be done by measuring tiny eye movements, called ocular micro-tremor, or OMT. There is currently no portable, patient friendly machine available to doctors to measure OMT, but Dr Gerard Boyle, a medical physicist and engineer, based at St James's Hospital, Dublin, has SFI funding to develop just such a device.

Many of us would have heard of REM, or Rapid Eye Movements, which are known to occur during dreaming. However, there are also other eye movements going on, and unlike REM these are happening constantly, not just during dreaming. These movements, called OMTs, are so tiny that we are not aware that they are happening.

One reason that OMTs are very important medically is because of the link – which was found by Prof Davis Coakley at TCD back in the 1980s – between OMT and a person's level of consciousness. The more rapid the person's OMT, the more alert they are. The less rapid the movements, the less conscious a person is, and when OMT stops altogether, that is a diagnostic tool to indicate a person is 'brain dead'.

Thus, the measurement of OMT is highly relevant to the work of an anaesthesiologist, as it slows down as a person goes deeper into anaesthesia, and speeds up if a person is becoming alert. As well as stroke and coma, measurements of OMT have recently been linked to neurological conditions such as Multiple Sclerosis or Parkinson's Disease, as the OMT levels have been found to change in people with these diseases.

Building on the work of Prof Coakley, Dr Gerard Boyle became interested in developing a device that can measure OMT. Dr Boyle was involved in the building of a device at St James's based on what are called 'piezo-electric probes' – probes that can measure OMT. The probes are dropped down onto the patient's eye. Eye movement induces a current in the probes and this can be measured. This is not a comfortable process for the patient involved, however.

Device

"The piezo-electric probes work well from a scientific point of view," said Dr Boyle, "but they are not ideal from a patient's point of view." The person's eye must be anaesthetised, and the eyelids taped open before the probes are dropped onto the eye. From the clinicians point of view these probe machines were too large, and not easily transported to where they are needed in the hospital. Furthermore, as the procedure involves contact with the eye, and is, thus, determined to be 'invasive' there are ethical issues to address and permissions to be sought before the device can be used.

Dr Boyle has experience working on a laser-based system, called 'speckle-interferometry', which can measure tiny eye movements in a non-contact manner. The system works by shining a laser at the white of the patient's eye, picking up the light that is scattered from the eye, and extracting the measurements of movement.

"We have a demonstration system of this," said Dr Boyle, "but what SFI funded us for is to look in a little more detail at the scattering process that happens when the laser light strikes the white of the eye. The laser that you use – the power levels are really low. It would be even much less than the laser pointers that are used in lectures, way down below that level, so it's 'eye safe'."

Benefits

The goal for Dr Boyle is to develop a new diagnostic tool for clinicians to measure OMT that would be available at a fairly low cost, compared to say, an MRI machine where €2 million would be invested. The device will be portable and easily transported to theatre to use on people in a coma, for example, or be transported to ICU if an anaesthesiologist wants to determine a person's depth of anaesthesia.

"While a portable device to measure OMT and the use of piezoelectric probes are already quite novel developments," said Dr Boyle, "the laser-based speckle-inferometry system is unique. No one anywhere is doing that."

"However," Dr Boyle said "there is nothing about the demonstration model that has been already developed at St James's that can't be miniaturised. The technology the device will be based on is lasers, and some laser diodes now are the size of a one cent coin."

The SFI grant came on line for Dr Boyle in August 2008 and is a three-year SFI-funded project. The research goal is to have a portable device for measuring OMT that could be used by hospital clinicians – as part of their daily work – all around the world.

Dr Gerard Boyle is developing a machine that can detect tiny eye movements, which indicates a patent's level of consciousness. Photograph, Gerard Boyle.

- Dr Boyle graduated with a BE in Electronic Engineering from NUI Galway.
- Following that he did an MSc in Biomedical Engineering at the University of Aberdeen. He came back to Ireland for his PhD, which he did at TCD/St James's Hospital, and completed in 1998.
- He has worked as a hospital physicist in the fields of medical engineering and clinical engineering at the Meath Hospital, the Adelaide & Meath incorporating the National Children's Hospital (AMNCH), and St James's Hospital. Currently, he is Principal Physicist at St James's as well as a lecturer and course co-ordinator of the MSc Health Science in Medicine course at TCD.

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Researcher Dr John Breslin

Title *On the web: It's good to share*

Case Study **04**

One of the most noticeable trends in recent years on the 'web' has been the growth in the numbers of people using websites that operate as independent online communities. These social websites can be opportunities for people to get advice from others about a particular personal issue, to find people that have a common niche interest, or to use the knowledge of the group to create new information online that we all can access.

For those that might not be sure, an online community could best be defined as a group of people, sharing some common interests, that communicate online. This communication can be done in different ways, for instance, via a mailing list, a social networking website, a message board, or a forum. The interests that people have could be anything, from the architecture of ancient Rome to fossil collecting to windsurfing.

These communities work very well and its members help each other. However, there were, until recently, some issues that prevented individual online communities from linking efficiently with other online communities. It was not easy for someone to easily get an answer to a question, for instance, from several online communities.

Benefits

That technical challenge – to bring online communities together for their mutual benefit – was central to the work of Dr John Breslin, a researcher based at the Digital Enterprise Research Institute (DERI)) SFI CSET at NUIG, and he came up with a tidy solution.

Dr Breslin developed something that is called 'Semantically-Interlinked Online Communities' (SIOC). This initiative brought in standards that govern the way that user-generated content is expressed in social web-sites. In other words, a person in one online community could more easily access information from another community.

"Over the past four years," said Dr Breslin, "we've shown how SIOC and other semantic technologies can benefit users and developers of social web applications. So far SIOC has been adopted in a framework of 50 applications or modules, deployed on over 400 websites." (visit http://sioc-project.org/)

"The SIOC specification is an open-data format," said Dr Breslin. That means it is a definition for how to structure and represent the data from online communities in a common form that can be exchanged and reused across a range of websites.

Communities

People have begun to find that other people online can often give them answers to the specific questions they have. That might be a question from a mother, to other Irish mothers in an online community such as EU mom (see http://www.eumom.com/) about some aspect of a child's health. Or it might be someone looking to find out where the best beaches are in Co Sligo for windsurfing during the summer months.

Dr Breslin co-founded www.boards.ie. This is Ireland's largest discussion forum site with in the region of one million unique visitors per month. The forums for discussion range from things like 'politics' to 'personal issues' to people looking for answers to relatively mundane questions, such as why buses have stopped going through UCD.

There are several other extremely popular online communities in Ireland, such as Bebo – the biggest social networking site in terms of Irish members - P45.net, politics.ie, AskAboutMoney, and the Irish Linux Users Group, for example.

Ireland

The development of the SIOC infrastructure in Ireland can create a hub of interconnected online communities that can, in turn, better link Ireland and Irish people – in the business or personal spheres – to other online communities worldwide.

SIOC has the capability to connect people and discussions across a myriad of Irish online communities. For example, users of mailing lists, readers of forum sites such as www.boards.ie, or third-level students and researchers using portal systems like Drupal (visit http://drupal.org/) – a free website content management system.

People that use social websites benefit from finding people with other niche interests. Or people can form communities around those interests in a much easier manner than was previously the case. For instance, before the arrival of social networking people would just 'happen' across a club or community with a similar interest from reading a magazine, or newspaper or newsletter. These people had been missing out until then.

"For example," said Dr Breslin, "information about a particular club's activities, including archived material from before the person joined, can now be retrieved more quickly. There are less geographical limitations to becoming a member of a social web community, and so there is greater potential to get more people contributing."

The infrastructure has now been laid that should see data being shared across many online communities in new and innovative ways, and Ireland is at the centre of it all.

- Dr Breslin did his undergraduate degree at the Department of Electronic Engineering, UCG (now NUIG), his post graduate work at the Power Electronics Research Centre, NUIG, and his post-doctoral work at the Digital Enterprise Research Institute (DERI). DERI is an SFI funded Centre for Science Engineering & Technology.
- He worked as a research officer with PEI Technologies (1998 to 1999), a lecturer at the Department of Electronic Engineering, NUIG (2000 to 2004) and a researcher and adjunct lecturer at DERI from 2000 to 2004.
- Dr Breslin's research team includes four PhDs and three post-docs. Recently he moved to the Department of Electronic Engineering at NUIG, but he still heads up a research team at DERI.

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Researcher Dr David Clarke

Title *Novel molecules from strange relationships*

Case Study **05**

We are running out of options in dealing with serious infections, and the work of Dr David Clarke, at the Alimentary Pharmabiotic Centre (APC) SFI CSET, University College Cork, is focused on the search for new antimicrobials. Most of our antimicrobials come from bacteria, and while the stock is far from exhausted, the search can lead us into some startlingly strange relationships. One of the reasons for this is that it can take some unusual molecules to maintain a strange relationship, and few could be stranger than the relationship between a bacterium called *Photorhabdus* and a soil dwelling nematode.

Cells of the bacterium, Photorhabdus *(tagged with GFP and, therefore, fluorescing green), can be seen colonising the rectal gland cells of the adult hermaphrodite* Heterorhabditis *nematode. This is the first step in the mutualsitic interaction between the bacterium and the nematode.*

Compound

The bacterium is of interest because it produces beneficial compounds that normally only occur in plants. *Photorahabus* inhabits the gut of a nematode, a small worm-like creature that lives in the soil. The nematode burrows through the soil until it finds an insect larva. Then, bacteria are released into the larva and, as they proliferate, their enzymes break down the insect tissue into a sort of soup upon which the nematode can feed. One of the compounds that seems to help the bacterium is known chemically as 3-5-dihydroxy-4-isopropylstilbene, or more conveniently as just ST. This is an antibiotic, and curious because it belongs to a family of molecules previously known only from plants. These include a two-phenol ring compound, resveratrol, that occurs on the skin of grapes. "Resveratrol," explained Dr Clarke, "has a protective role, and when fed to mice it can extend their lifespan by 20 to 25 per cent. It is not understood why all these benefits occur, but it seems to involve an interaction with proteins that bind with DNA, and this, in turn, affects how cells respond to stress."

Case Study

The fact that a similar molecule has been produced in a bacterium, could be a case of convergent evolution, but it is helpful to the researchers because they can now think of engineering bacteria to produce beneficial compounds in bulk. The researchers have been able to outline a pathway starting with a gene known as *stlA*. This gene codes for an enzyme responsible for producing a compound known as cinnamic acid, familiar to most of us as one of the ingredients in toothpaste, and significantly, the precursor of the two-phenol ring ST. Currently, cinnamic acid is produced from petrochemicals by a process involving high temperatures and toxic chemicals, and brewing up a culture of engineered bacteria would be a much better, cheaper, and cleaner, approach. Earlier this year, Dr Clarke's group published the results from their study of the genes involved in driving the pathway of ST biosynthesis. "About a dozen genes are involved," Dr Clarke explained, "so the next step is to insert them into the workhorse of the fermentation world, *E coli*."

» Dr David Clarke is based at the Alimentary Pharmabiotic Centre at University College Cork. The APC is one of nine SFI CSETs. Dr Clarke is a biotechnology graduate of Dublin City University and following his PhD studies at National University of Ireland Maynooth he conducted post-doctoral work at the IGM, Universite Paris-Sud.

» At the APC his research is focused on biofilm formation and bacterial-host interactions. Dr Clarke's team of four researchers collaborate with the University of Frankfurt in Germany, and the Centre for Ecology and Conservation in the UK.

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Researcher Dr Siobhán Clarke

Title *Providing a foundation for processing on the move*

Communications on the move with seamless integration of services. Graphic: Dr Clarke and Lero.

Case Study

06

Drivers check their speed, occasionally cast an eye on the fuel gauge, and these days many rely on GPS, rather than maps, to find their way. Dr Siobhán Clarke, from the Distributed Systems Group at TCD said that the amount of information we can pick up from the environment while on the move will continue to increase. For example, sensors can already detect some hazardous conditions, and with an on-board processor, toll pass software could be downloaded.

"The ability to pick up and respond to data," said Dr Clarke, "is not just confined to cars, and it is relevant to a whole range of situations where people are on the move." Dr Clarke's research is not so much concerned with the diversity of individual applications, but is focused on developing the underlying technology. As she explained, "what we do is service oriented computing for distributed real time embedded systems."

For some years, Dr Clarke worked as a software engineer with IBM, and then her interest in what is known as object-oriented analysis and design, led her back into research at Dublin City University, and from there to the Distributed Systems Group at Trinity College Dublin. One of the essential aspects of object-oriented programming is that it models how the different elements in a system work together, and as Dr Clarke explained, "the enabling platform has to be constructed based on similar principles. The aim is to achieve the sort of integration that allows users, and their embedded processors, to interact seamlessly with a range of service providers."

One of the possibilities being looked at is downloading software services from different sources. In many situations, a person can have a mobile device without the software installed to complete a specific or unexpected task. For example, when an aircraft is between flights, the software to carry out a diagnostic test might not be in the system. "Downloading this software," said Dr Clarke, "should be possible, and the same could be done for in-car entertainment." Passengers could, for example, download and play interactive games, or when applicable, toll pass software could be made available to the driver. Part of the research by the group involves looking at how installation times can be reduced.

Car manufacturers are well aware of this trend, but they have to proceed with caution. Where safety is an issue, the driver has to be the one making the decisions. However, those decisions can be based on a lot more information, including data about conditions that the driver would not otherwise see.

The group has been studying the possible applications in a variety of situations, and recently they published a paper on accessing medical information in a hospital environment. "In many cases," said Dr Clarke, "where mobile devices could have the capacity to download the information, they could also have the capacity to download the software to process that information."

- Dr Siobhán Clarke graduated in Computer Applications at Dublin City University (1986). She worked for IBM as a software engineer before she returned to academia in 1997 to do a PhD in DCU. She was appointed as a lecturer in Trinity College Dublin in 2000.
- At Trinity College, Dr Clarke leads the Distributed Systems Group and is a Research Area Leader with Lero, the Irish Software Engineering Centre. Lero embraces research activities at the University of Limerick, Dublin City University, Trinity College Dublin and University College Dublin.

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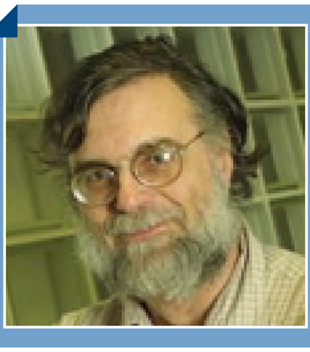

Researcher Prof J.M.D Coey

Title *The magnet man*

Case Study **07**

Magnetism and associated phenomena have been the life's work of Michael Coey, Professor of Physics at TCD. His work in this area is highly cited and he is one of Ireland's genuine world-class scientific performers. In recent years, Prof Coey has become more and more involved in nanoscience and sees in it the means to take another technological leap forward. His research is focused on developing novel ways of utilising nanomagnetic properties in sensors and computers.

Magnets and magnetism are essential to modern computers, involved as they are in the laying down and storage of memory. The hard disk of a computer is packed with tiny magnets that have been crammed into ever smaller spaces in recent decades. The entire content of the internet is stored magnetically. This pressure to pack more and more magnets into ever smaller spaces is akin to what has happened with transistors in computers too.

Roughly speaking, the number of magnets crammed into a given space on the hard disk has doubled every year or two for the last five decades. This has been very important as today people expect to, for example, record entire movies onto their hard disks, something that requires a lot of memory. This would have been unthinkable for the computers of even ten years ago.

Electrons

Electrons are the small, negatively charged particles that orbit or fly around the atom. The manipulation of electrons is the basis for electronics. Electrons can be induced to run down copper wires – the conductors – and movement of electrons creates a current. The electron has, however, another basic property that researchers have only just recently started to make use of. Each electron is a tiny magnet, because something called 'spin'.

Imagine the electron flying in a rapid orbit around a central atom, while at the same time twirling like a spinning top. This is what it does all the time. It is important because whenever a charged particle spins like this, it behaves like a magnet.

Thus every electron has charge and spin. It is a particle that can carry electric current via its charge, but it can also carry magnetism via its 'spin angular momentum', (in quantum mechanics, magnetism arises from angular momentum of charged particles). On a computer's hard disk there are billions of little nanomagnets, and by detecting their 'spin value' we have a way to represent the binary code, as either 1 or 0, the basic language of computers.

Each of these nanomagnets is a small patch of the ferromagnetic layer coating the disk. Until exposed to a magnetic field, patch is not aligned. A magnetic field, however, brings the patch into alignment and the magnetization of the patch can be switched between two clearly defined states, in opposite directions, representing 1 or 0.

The disk is read using a spin valve, which is sensitive to the stray magnetic field produced by the pattern of magnetization on the hard disk. The spin valve is a sensor which produces a voltage proportional to the magnetic field. The bigger the voltage the better, as that means, for example, that there will be less 'noise' to interfere with the quality of information read.

Materials

One of the areas that Prof Coey's group, which is made up of about 18 people, are focused on is the development of new magnetic materials to be used in 'spin devices' – devices that make use of magnetic properties of electrons and thin films of ferromagnetic materials like iron or cobalt. There is a quest for better materials, which must be capable of being made into thin films, and grown into stacks with lots of different layers. This research must be completed before we see real working spin devices. The equipment to do this work is expensive, but when it is in place, it is possible to engage with industry partners, as Prof Coey's group have with Intel.

Memory

Another of Prof Coey's research areas is memory using magnetism, specifically the topic of Magnetic Random Access Memory or MRAM. Under the MRAM system in computers, a binary 1 or 0 is stored in a spin valve which can be switched by passing electric current pulses along a lattice of wires. Where the two pulses coincide at the same intersection there is enough field to switch the element, thus switching 1 to 0 or vice versa. However, this approach has a problem. A better approach is to use the magnetism carried by the electron current to do the switching.

We all know that if you put your laptop on your lap it will warm up after a time, and after a few hours, it can get really hot. One of the biggest problems for electronics is this heat management problem. The heat needs to be either dissipated far more efficiently, or better still computations need to be done to the same high standard without generatating as much heat in the first place. There maybe a way to do this somehow using the spin currents.

Communication

Spin currents, and the associated spin-transfer torque, is the new big idea. However, switching a spin value is not all that can be done with this technology. It is also possible to use those spin polarised currents in suitable spin valve elements to generate microwaves. This opens the door for the development of chip-to-chip communication using microwaves that are generated locally using these spin polarized currents. This will be a great improvement when it comes, as it will allow the different parts of the computer to communicate directly with each other, using microwave radiation rather than traditional electric currents.

This means that chips in future would not just be micro-processors, they could have functionality and intelligence built into them and be specialised for a variety of tasks within the computer system. These future chips should also be more energy efficient.

- Prof Michael Coey was born in Belfast and did a BA in Cambridge University in 1966.
- He followed that up with a PhD working in the area of magnetic oxides at the University of Manitoba, Canada (1971) and a period as a researcher with the CNRS in Grenoble, France.
- He is a Fellow of the Royal Society and a Foreign Associate of the National Academy of Sciences. He is one of the founders and was Deputy Director of the TCD CRANN nanoscience research centre.

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Researcher Prof David Cotter

Title *Leaner and greener telecommunications*

Case Study

08

With growth almost doubling every year, telecommunication networks are coming under strain. Service providers are worried because in meeting the demand for extra bandwidth they face diminishing returns. As Prof David Cotter at the Tyndall National Institute explained, “everyone wants more capacity but they expect costs to remain the same. One result of this is that service providers might start to slow down delivery, just to contain costs.”

“Fibre optics,” he said, “have already made a big contribution to networks,” and he argues “that further developments in photonics can help to solve the growing problem of providing more bandwidth without being burdened by a matching rise in costs.”

Replacing what has become known as ‘the last mile’ would be a major advance, and as Prof Cotter explained, “this substitution of optical fibre for copper, while expensive, could be a good investment.” Optical fibres can carry up to a thousand times the traffic of the copper equivalent, but this is just one of the advantages, and to understand why, we need to take a look at how the local exchanges work. Local exchanges in towns serve about 15,000 lines, and there are a large number of these around the country. Each of these exchanges might have 900 racks of equipment, and simply keeping this equipment cool consumes a lot of power. Prof Cotter’s colleague, Prof Paul Townsend, worked with BT in the UK before coming to Tyndall, and as he remarked, “one exchange can use as much energy as a powerful locomotive, and in the UK there are between one and two thousand local exchanges.” Indeed, telecommunications already consumes a significant fraction of global power generation, and is set to increase further.

Fibre optics

Tyndall researchers, in collaboration with BT and other companies, have prototyped a new ‘extended reach’ technique, that will allow the fibre optic last-mile connections to homes to be extended right into the core of the national network. The impact of this on local exchanges would be enormous. Instead of a big building the local exchange could be packed, with space to spare, into a single rack of equipment, consuming the equivalent power of one light bulb. The resulting energy and cost savings could be very significant.

The Photonic Systems Group have a number of ongoing projects with major companies, including BT, who are providing access to the BT Ireland fibre optic network for advanced experiments, and also with Orange Labs (formerly France Telecom) which recently collaborated with the Tyndall researchers on running a 1,000 km test. One of the goals in this research is to discover how to pack even more into long distance fibre optic lines. Another of Prof Cotter’s colleagues, Dr Andrew Ellis, has developed a new information transmission technique known as ‘coherent wavelength division multiplexing’, in which the near-infrared light used in fibre optics is utilised very efficiently to carry a large amount of data within a narrow optical bandwidth.

Looking further into the future, as bandwidth demands continue to grow rapidly (driven by greater individual usage and the increasing prevalence of video-intensive applications), the energy consumption by telecommunications networks increases at an even faster pace. However, energy limits – both practical and regulatory – will constrain future growth, and Prof Cotter points out this is potentially a significant break on development of the knowledge economy. Tackling this ‘energy crunch’ in telecommunications, through innovative use of photonics and other technologies, is an important research challenge.

» Prof David Cotter is based at the Photonic Systems Group at the Tyndall National Institute.

» Prof Cotter was previously head of Optical Systems Research at Corning UK, and head of Photonics Systems at British Telecom. Born in Scotland of Irish parentage, Prof Cotter received his primary degree, PhD, and DSc from the University of Southampton.

» Before working in industry he held a post-doc position at the Max Planck Institute for Biophysical Chemistry in Germany. Prof Cotter is co-author of two books on nonlinear physics.

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Researcher Prof Christopher Dainty

Title *Shedding light on many subjects*

Case Study 09

Without light, and optics, there would be no life on Earth. Optics underpins solar cell technology, lighting and displays, as well as medical techniques and communications. It is expected that optics, which is also sometimes called photonics, will surpass electronics in the 21st century in terms of the size of the industry reliant on it. Prof Chris Dainty, as Head of the Applied Optics Group at NUI Galway, is involved in applying optics to many fields, including medicine and astronomy.

It has been said that the 20th century was the century of the electron, and the 21st century will be the century of the photon – a photon being a light particle and the fundamental component of optics. From powering the internet through fibre optics (which will eventually go to every home) to new better lighting systems, to advanced new techniques for laser surgery, optics will become ever more central to our lives.

Astronomy

A really big development happening in European astronomy just now is the building of the European Extremely Large Telescope, or E-ELT. This is provisionally scheduled to be a massive 42 metre diameter giant telescope, the biggest in the world, costing €900 million, and placed probably in Chile or Antarctica. Prof Dainty and his colleague, also in the NUIG Applied Optics Group, Dr Alexander Goncharov, were the only Ireland-based scientists asked to join the initial concept design team of 50 people. Prof Dainty worked on the adaptive optics side, while Dr Goncharov worked on the optical design aspects of the project, asking questions like, What will the telescope look like? What will it do? What will be its specifications?

The initial baseline design has been worked out now, and the project has now gone out to teams of engineers to work out the details. The E-ELT will look at fainter and smaller objects in the night sky at better resolution. Its resolution will be 20 times finer, smaller and better even than any space-based telescope currently in existence.

The atmosphere is a barrier that must be overcome, as distortion of viewing through a ground-based telescope can occur due to what's called 'atmospheric turbulence'. The E-ELT will operate in the near infra-red spectrum of light – water absorbs infra-red and this means that very dry sites, where there is little water, and high altitudes, where there is less atmospheric distance to travel, are popular for telescopes.

Vision

Prof Dainty is also concerned with the technical applications of optics in many other areas, and one of these has to do with human vision. Here, he has a collaboration with Alcon Ireland to check the merits of intra-ocular lenses before they are replaced in a cataract operation. Many elderly people get cataract operations when their own lens begins to get cloudy, and a better plastic lens is put in its place.

Those having cataract surgery can potentially attain better eyesight than they ever had, even in their youth. It can also leave them not requiring eye glasses any more. It is the world's biggest surgical procedure, with 14 million operations performed per year. Ireland will see the numbers of procedures grow as the population ages in the coming years.

Prof Dainty's team has built a machine – one of only a handful in the world – called an 'Adaptive Optics Visual Simulator'. This machine is capable of assessing the potential impact of several lenses on a person before they undergo eye surgery. The patient can sit in front of the machine and say whether they see better or worse with a particular synthetic lens. This means that when the lens is actually inserted in the patient's eye during surgery, there is a greater confidence that it will improve sight.

This machine is important for companies that wish to test out new lenses designed for use in eye surgery, such as cataract operations. In the past, what would have to happen is that trials would have to be done with new lenses using real people. These are expensive, and they raise ethical considerations as there are risks to people involved in the trial. With the Adaptive Optics Simulator, field trials are only done at the very end of the process, when the capability of a lens has already been rigorously tested.

In this way, Prof Dainty and his team are working with Alcon Ireland to improve the design of intra-ocular lenses. His collaborations in this field also involve leading eye surgeons, including Michael O'Keeffe and Colm O'Brien, based at the Mater Hospital, Dublin.

» Prof Dainty has a Diploma in Photographic Technology from Regent Street Polytechnic (1968). He did his post-graduate work at Imperial College, London, where he gained at MSc (1969) and a PhD (1972). He worked at Imperial College up to 1984 and remains on an extended leave of absence from there. Prof Dainty has 'significant' interaction with more than 20 companies across many areas where optic technology can be applied, and has been involved recently in the concept study for the €900 million European Extra-Large Telescope, which will become the world's largest telescope when built.

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Researcher Dr William Donnelly

Title *Self-regulation will give networks the capacity needed for the next generation internet*

Case Study

10

The internet is no more than 40 years old, yet still primarily based on the technology of the 1970s. "You could say that it is now operating well beyond its initial design," observes Dr William Donnelly, director of the Telecommunications Software Systems Group at Waterford Institute of Technology.

With the rapid expansion of communications this reliance on relatively old technology has become a serious problem. The telecommunications solutions that has worked well up to now is just not flexible enough to handle an explosive growth in traffic. As Dr Donnelly explains, "convergence is adding to that problem because users now expect a high level of service no matter where they are or how they connect to a network." "Telecommunication engineers," he added, "have helped to create these high expectations because existing telephone services usually have a performance level of 99.99 per cent. Our computers might occasionally crash, but no one expects the phone line to fail."

Congestion

Unless networks can be managed more efficiently, congestion is going to bring everything to a halt. "We now have users communicating with users, users communicating with machines, and machines communicating with machines," said Dr Donnelly, and so it's not just one network, but many. "It's a heterogeneous environment spanning many different network technologies."

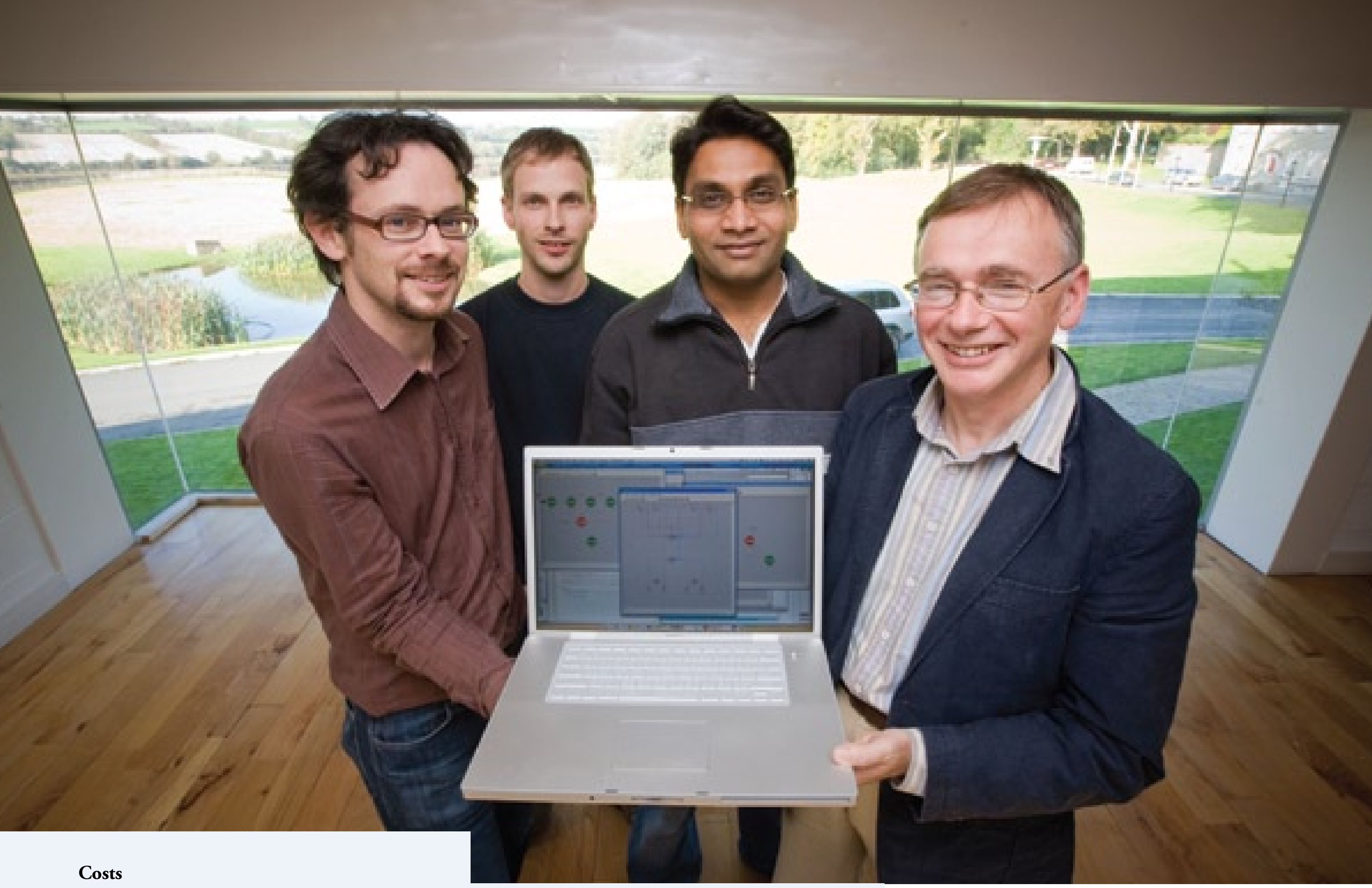
In the past, engineers made predictions, and planned accordingly, but as Dr Donnelly said, "this linear approach no longer works because the operating environment has become a lot more complex, and demand is completely unpredictable."

Dynamic

"What we need now is a more dynamic communications framework," he said, and achieving this is the aim of his SFI-funded research. "If the next generation of networks are to work," he explained, "they have to be self-governing, self-healing, self-optimising, and self-protecting." As he admits, this is quite a challenge, but it is one that has already been overcome. "Nature," he said, "has been able to survive many upheavals, and if we look at how the body works, we have many examples of autonomic control for complex systems."

During exercise we convert glucose into energy, and Dr Donnelly compared this to using bandwidth. If the exercise becomes more intense, and the glucose supply becomes inadequate, the body keeps going by burning up fat. "The fat," said Dr Donnelly, "is like the spare capacity in the telecommunication system, and instead of being localised, that capacity is general. If we look at current management we usually find that there is just one fall back position, and this has been fixed by predictions."

Thus, congestion in Cork might be routed to Portlaoise, but the system has no way of knowing whether or not Portlaoise is already congested. As Dr Donnelly explained "it is possible to replace this simplistic predictive approach with a more sophisticated system with the automatic capacity to balance real-time needs against real-time capacity." Such a capacity can be fine-tuned to distinguish between different levels of demand. Video conferencing demands a lot of bandwidth yet delays in transmission are not acceptable because they cause juddering of images. A slight delay in delivery of data creates no problem, so instead of having fixed allocations, the system could allocate bandwidth as required on the basis of priority.



Dr Brendan Jennings, Dr Sven van der Meer and Dr Sasitharan Balasubramaniam, Senior Investigators with the TSSG and Dr Willie Donnelly, Head of Research and Innovation.

Costs

"Achieving this level of response," said Dr Donnelly, "is not just a matter of getting more efficiency." Autonomic management would also keep costs down, and this has become a huge issue as service providers struggle to deliver more and more with the same resources. "Service providers," said Dr Donnelly, "buy enough bandwidth to satisfy expected demand. Having to buy in extra capacity can eat into organisational profits, but if they can better balance demand, they can squeeze more out of the existing system."

Trying to maintain a high level of service by adding to existing networks would only make costs spiral up out of control, and Dr Donnelly remarked that it's important for us to realise that the way we communicate has changed dramatically over the past few years. We still tend to think in terms of traffic as on roads, where highways are built to accommodate ease of traffic. "Imagine if everyone woke up tomorrow and decided to work elsewhere," said Dr Donnelly, and "this is much closer to the situation faced now by telecommunication managers." Demand is no longer localised, and with the rapid rise in mobile communications no one could possibly make predictions on demand. "Traffic," said Dr Donnelly, "is being driven by user behaviour, and we are getting patterns that we have never had to deal with before, such as virtual communities, geographically separate, but linked by telecommunications."

"Going back to the analogy with fat," Dr Donnelly remarked that "athletes manage to get the balance right, and we could be doing much the same in how we allocate bandwidth." "In calculating the costs," he said, "it's not the fibre, but the inefficient switching that is so expensive. Find different ways of getting into the network and a lot of problems would be solved."

- Dr William Donnelly is Director of the Telecommunications Software & Systems Group at Waterford Institute of Technology.
- After graduating as a physicist, Dr Donnelly worked for 15 years in the telecom industry before going back into research.
- The Telecommunications Software & Systems Group works with a number of industry and academic collaborators, and since 1996 12 spin-out companies have been established, three patents granted and 16 licence agreements signed. The team, funded by the AMCNS PI Cluster Award (04/IN3/1404C) in 2004, led by two SFI Principal Investigators, included six research staff members and six PhD students. As a result of this SFI-funded work, the WIT group is leading a European research programme on Autonomic Network Management.
- In 2008, Dr Donnelly was awarded funding from SFI to establish a Strategic Research Cluster FAME (08/SRC/11403) which that builds on the autonomic communications management work of the previous SFI award, and includes collaboration with industrial partners in Ericsson, Cisco, IBM, Teléfonica I&D, Alcatel-Lucent and HPy and academic partners in UCD, NUI Maynooth, TCD and UCC. HEAnet support the activity with Ireland's academic research network.

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Researcher Prof Linda Doyle

Title *Making better use of spectrum*

Case Study 11

When mobile phones and radios communicate over the airwaves they use part of what people in telecommunications refer to as the spectrum. Spectrum is scarce, and becoming scarcer all the time, because the number of new devices is increasing fast and they all need a share of it. Prof Linda Doyle has been researching ways that the airwaves can be used more efficiently than today and she has come up with a 'cognitive radio' that can find signalling space, no matter where it is located.

The Centre for Telecommunications Value-chain Research, or CTVR, is a national centre - headquartered at TCD - that does research into future telecommunications systems. "The mission of the CTVR," said Prof Doyle, "is to do outstanding research in the telecommunications sphere, to think about what the telecommunications networks of the future are going to be like, and to do this work in collaboration with industry."

The CTVR has researchers based at UL, NUIM, UCC, DIT, DCU as well as TCD. It is one of the nine well funded, prestigious Centres for Science and Engineering Technology (CSET) supported by SFI. There are five research strands within the CTVR and Prof Doyle is the research leader for the 'emerging networks' strand.

Spectrum

One of the key areas for Prof Doyle is what is called 'spectrum'. In telecommunications the word is used to mean all the airwave space that is available for devices to send or receive communications. Every communication device, whether it is a mobile phone, or a radio, needs some spectrum in order to operate. These devices also all need to operate at different frequencies – in a defined 'space'- in order not to interfere with each other. This is becoming more difficult as the number of devices is growing relentlessly, as the amount of available spectrum throughout the world shrinks.

Spectrum is seen by telecommunications people as a scarce resource, as there are a finite number of frequencies that exist. Some of these frequencies, might, using real estate jargon, be considered 'beachfront property' – something everyone wants. The reason that everyone wants these frequencies is that they have good physical properties that make them behave and propagate in a way that is conducive to the kind of communication system that any given entity wishes to introduce or build.

There are tonnes of new wireless devices, requiring spectrum, emerging all the time, and this is putting pressure on the limited amount of spectrum that remains. This is where Prof Doyle comes in. She examines how people are using the spectrum and she has found that people are not using it effectively or efficiently. There are many people around the world, she said, that are looking at ways to better improve spectrum use, and she is one of these. This work can also help prevent spectrum running out in coming years.

Regulation

There are national and international regulators that decide who gets to use precious available spectrum and for what purpose. In this sense the regulators are extremely powerful. In the UK, there is the Ofcom (the Office of Communications), for example, while in Ireland we have ComReg (the Commission for Communications Regulation).

Some of the regulations that cover this area are quite outdated, however. For example, in Ireland, the Wireless Telegraphy Act, 1926, remains the main legislative plank on which decisions on spectrum are made. A long time before the wireless internet explosion.

The sinking of the *Titanic* on 5th April, 1912, was a catalyst for introducing spectrum regulations. On that terrible night some ships close by did not hear the distress signals of the *Titanic* as she sank. The ship that eventually arrived to rescue survivors was the *Carpathian*, but that vessel was further away than nearer ships that didn't pick up the distress signal. The signals weren't heard because of the mess in spectrum back then. The *Titanic* was broadcasting on spectrum that some nearby ships weren't listening to.

The authorities began to clean up the free-for-all that was spectrum usage after the sinking. From that time, almost a century ago, right up to today, there are very strict and stringent rules worldwide on how spectrum can be used. For example, there are a range of frequencies set aside for mobile phone usage.

Cognitive

The regulations governing spectrum make it very difficult for newcomers to the telecommunications scene to secure space to operate. This had led a lot of researchers, including Prof Doyle, to try and find a better way of doing things, and she began to think that a 'dynamic approach' to spectrum was the way forward.

Prof Doyle came up with the idea of a 'cognitive radio', a radio with a 'brain'. "The radios look around and see where they can find empty wide spaces. They hop into the space and then they move out of the space quickly when the owner comes back."

"Think of a car park," she said, "if the owner of a space in the car park is not using the space at that particular time, then someone could use the space until he comes back. A cognitive radio works in the same way. It searches for spectrum space at a given location, finds it, then dashes into the space, and out again when the owner returns."

TV 'wide space' is one good source of un-used spectrum. A cognitive radio must reconfigure itself to make use of any spare space. It changes the frequencies that it operates on and its parameters to 'scope' the signal that it is transmitting to fit into the available wide space 'hole'. "This is a terrific way to make better use of spectrum", said Prof Doyle.

Ireland

Ireland holds many advantages for those that wish to do tests and trials using spectrum. On the continent of Europe, and Britain, the population is denser, and this means that most of the spectrum is being already used. Ireland, which has just one border, and just four million people, has a relatively good spare spectrum capacity.

The CTVR has its own spectrum and it is free to operate in the heart of Dublin city. This would not be possible in other European cities. Prof Doyle and her colleagues, thus, are promoting Ireland as a 'playground for spectrum' – somewhere where leading academic researchers and top flight industry could come to experiment.

- Prof Doyle graduated in Electrical Engineering from UCC in 1989. She worked for Siemens AG, Germany before she returned to academia to do an MSc (1992) and a PhD (1996) – both in TCD.
- She was appointed as a lecturer in the Department of Electronic and Electrical Engineering at TCD in 1997.
- Prof Doyle is leader of the 'Emerging Networks' research strand at the CTVR SFI CSET.

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Researcher Prof Sylvia Mary Draper

Title *A bottom-up approach to building molecular devices*

Case Study **12**

Two-dimensional layers of carbon, just one atom thick, have been found to have remarkable properties. Prof Sylvia Draper at the School of Chemistry in Trinity College Dublin compares these sheets, known as graphene, to chicken wire because all the carbon atoms are neatly arranged in perfect hexagons. However, there the comparison ends, for these tiny sheets are extremely strong and so conductive that electronic engineers believe that they would be ideal for making very fast switching devices.

When the special properties of graphene were discovered, just a few years ago, physicists had a hard time trying to flake-off single sheets from lumps of graphite, but as Prof Draper explained, chemists solved that problem by building from the bottom-up. "Chemists," she said, "are used to starting with single molecules, and that's what I do." At first, all the hexagons are aligned at angles, "like propellers", so Prof Draper uses a chemical reaction to make them lie flat. For Prof Draper the challenge is not in producing molecular graphene, but in finding out how each layer interacts with the next in solution and in the solid and what she can do with it.

"There are other chemists out there working on these carbon sheets," she said. "so I asked myself, what can I do that's a bit different?" Carbons on the outer edge of the sheet offered some opportunities to attach different atoms, and different side-chains. As a chemist, she knew that one carbon and one hydrogen together provide the same number of electrons as an atom of nitrogen. "So, I could take a couple of carbons and hydrogens from the outside edge of my graphene and add nitrogen atoms on instead without perturbing the intra-layer arrangement."

The insertion of nitrogen, she discovered, makes a significant difference. While pure carbon monolayers are hard to dissolve, the addition of nitrogens makes her graphenes very soluble. For micro-electronic engineers planning to use graphene in fast switching transistors, this could be a discovery of enormous importance because it makes it much easier to apply the one-atom thick layer. "Drop and spin," said Prof Draper, and the liquid would spread itself flat.

Another important character of these monolayers is that they interact with light. As molecules absorb photons, electrons move, and light is emitted. "With the nitrogen-containing materials you can go from green to orange to red, and the wonderful thing about nitrogens," she added, "is that they have a lone pair of electrons, so they have a way of attaching themselves to metals." With metals attached, the opportunities to fine tune the behaviour become enormous, and as Prof Draper observed, it's a double whammy - light is captured and fluorescence is seen.

Ruthenium compounds attached to nitrogen, she said, are particularly good at capturing light, and they could become the active part of more efficient solar cells. Prof Draper believes that these flat molecules could make an enormous difference in how we manufacture electronic devices. At present, she said, we use silicon and titanium dioxides. As she observed, these are expensive to make, and, when a computer dies, hard to dispose of. With one atom thick monolayers we might yet be able pack the equivalent of a PC onto a watch, and when it finally breaks down, all we are left with is a little bit of carbon.

- Prof Sylvia Draper went on from a first at the University of Exeter to study for her PhD at Cambridge, and she continued post-doc research at Trinity College Dublin, where she is now Associate Professor and Head of Inorganic and Synthetic Materials Chemistry.
- Prof Draper has a particular interest in the synthesis of novel graphene molecules, and her group of eight postdoctoral and eight postgraduate research students collaborates with other researchers in Ireland, Germany, Italy, Switzerland and the UK.
- Prof Draper was presented this year with the TCD Provost's Excellence in Teaching Award and the NAIRTL award for excellence in the integration of teaching and research.

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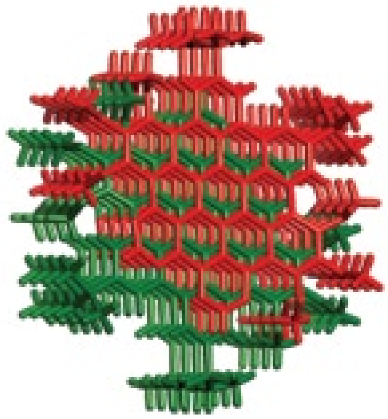

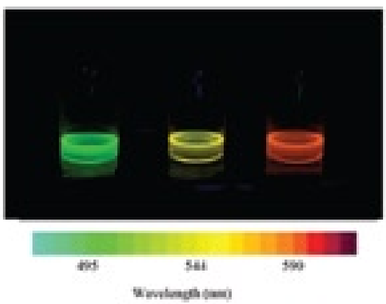

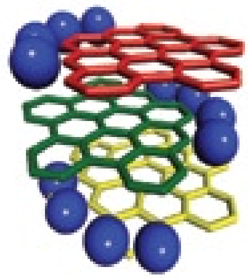

How the N-containing ligand can be used as a link in 3D a chain of metal atoms

Researcher Dr David Finn

Title *Understanding the neurobiology of pain and its modulation*

Case Study

13

Pain can make life miserable, yet in situations of extreme stress we may not even be aware of it at all. Soldiers fight on despite injuries that would normally cripple them, and it's often the same in competitive sports. Dr David Finn at the Department of Pharmacology and Therapeutics and co-director of the Centre for Pain Research, National University of Ireland Galway, observed that perception of pain is quite complex and that an increased understanding of the ways in which pain is modulated during times of fear and stress may aid identification of new therapeutic targets for the treatment of persistent pain.

Warning

Pain is essentially a warning system to let us know that something is wrong, and it is usually produced from areas of the body that are more susceptible to injury. However, once the warning has been given, the persistence of pain can cause more harm than good, and chronic, long-term pain is an enormous and widespread problem. "Pain," said Dr Finn, "is the most common reason people seek medical help." Chronic pain affects 13 per cent of the Irish population and the economic impact is enormous.

"The body," Dr Finn explained, "has a number of mechanisms to deal with pain, and while we know that opiates, such as endorphins, play an important role, they only represent part of the story."

"There is a significant physiological difference between chronic pain and something like a mild headache," he said, and "even acute pain from a cut or burn can be less of a problem than a long term ache because it is usually short lived, with a definite beginning and end."

Chronic pain is more complex and the root cause can be persistent. In addition to the opioid system, one other system that plays a role in pain modulation is the endocannabinoid system. "This is the system that responds to marijuana," he explained, "and while the effects have been known for a long time, little was understood of how the drug actually works until the last 10 to 15 years." Now, we understand that the cannabinoid system is one of a number involved in dealing with pain, and they work synergistically. "Understanding how these systems work together," said Dr Finn, "could help us deal more effectively with chronic pain."

People suffering from multiple sclerosis and arthritic conditions have found that marijuana can help treat their pain, but Dr Finn commented that this is a very crude way to deal with the problem, aside from issues related to the legal status of marijuana. An alternative approach is to isolate and pharmacologically characterise the active components, and target the appropriate components of the endocannabinoid system directly with plant-derived or synthetic cannabinoids. For example, one of the current problems with opiates is that over time, more have to be given to get the same relief, a phenomenon known as tolerance.

One promising approach, however, is to combine drugs. "Animal studies," said Dr Finn, "have shown that a mixture of low dose morphine with a low dose of the active ingredient of cannabis, delta-9-tetrahydrocannabinol, better known simply as THC, is more effective than either drug on its own." Because the drugs work synergistically, lower doses in a mix are likely to be more effective while at the same time avoiding some of the side effects of higher doses of either drug administered alone. How we perceive pain is also important.

"It is quite common for people suffering from chronic pain to also suffer from depression and anxiety," said Dr Finn. The more powerful drugs, such as morphine, can help because they dampen down the whole nervous system, and curiously enough, breaking the pain cycle seldom results in addiction.

» Dr David Finn, a graduate of NUIG has a PhD in Neuroscience from the University of Bristol, and after working as a post-doc research fellow at the Institute of Neuroscience at the University of Nottingham, he became lecturer in pharmacology at NUIG in 2007.

» Dr Finn received the SFI President of Ireland Young Researcher Award, the Weyth Award for research in preclinical psychopharmacology from the British Association of Psychopharmacology, the Pain Research Medal from the Irish Pain Society and The Outstanding Young Person of the Year Award from Junior Chamber Ireland.

» Dr Finn is co-director of the Centre for Pain Research at NUIG and is a committee member of the Neuroscience Cluster at the National Centre for Biomedical Engineering Science. He works with a team of two post-doctorate researchers and five PhD students. Dr Finn collaborates with Agilent Technologies and STI Pharmaceuticals and has a number of academic collaborators in Ireland and abroad.

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Researcher Prof Stewart Fotheringham

Title *Ireland finds its place in space*

Case Study

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Geocomputation is about the capture, analysis, visualisation and modelling of 'spatial data' – data that are linked to points in space. It is regarded as one of three key areas that will change the world, the others being nanotechnology and biotechnology. Ireland is prepared for the geocomputation revolution due to the work of the National Centre for Geocomputation, or NCG, established by Prof Stewart Fotheringham.

Beginnings

SFI provided seed money for the NCG through its Research Professorship scheme, which brought Prof Stewart Fotheringham, a highly respected geocomputational scientist to Ireland. He came in 2004 and set up the NCG from scratch. It is now regarded as one of the top five centres for geo-computation in the world – a remarkable feat for such a short time. From an initial staff of four, there are now 25 people working at NCG, and this is set to rise to 40 during 2009/2010.

More recently, SFI has provided significant further funding for the setting up of a Strategic Research Cluster (SRC) in Advanced Geotechnologies. The cluster is centred at the NCG, but will also involve researchers from electronic engineering and computer science at NUIM, computer science at TCD and UCD, and the Digital Media Centre at DIT.

Geocomputation

The burgeoning field of geocomputation is a very practical science which aims to provide decision makers, in public bodies and private industry, with vastly better information from which they can make important decisions. It is about spatial data, and that means any data that can be linked to points in space, each with an X-Y co-ordinate. The location is linked to other 'attributes', which could be figures for crimes, unemployment rates, incidence of a particular disease, pollution levels – there are infinite possibilities.

Thus, a senior Garda, using geocomputation, for example, could examine the spatial pattern of burglaries in an area over time or track locations of assaults ocurring in Dublin, and at what times, and allocate officers accordingly. This means that precious Garda resources could be used more efficiently. Or, a health official might note that a higher than average incidence of a particular cancer is linked with a town, or part of a town, and initiate an investigation into the possible reasons why this is happening. The list of ways that geo data can be used is endless, limited only by the imagination.

"Spatial data," said Prof Fotheringham, "have special properties statistically, so special techniques are required to handle them. They also lend themselves to display, in the form of various types of maps and 3-D images. The data can be linked with other data and relationships can more easily be seen between variables."

Ireland

People in Ireland have been capturing spatial data for centuries. For example, census data, or health data, has always been spatial, since people are linked to a particular address. So, recordings have been taken, but the processing of the data into something that is useful has not been done, and that is where the NCG comes into play. That's its job.

Think of almost anything in Ireland where spatial data is being used, and the NCG will be interested in it. Where are the problems with coastal flooding? If the sea-level rises in the future by 5cm, which parts of the Irish coast will be flooded? Are there patterns involved with certain crimes? Where is a killer or burglar likely to strike next? In times of limited resources, answers to such questions can be of great help to public bodies and those tasked with making planning decisions for the future. Where should a hospital be located? What location can provide the best service to the most people?

The use of geo data in Ireland has been slower than in the UK, and the UK, in turn, has been slower than the USA. In the USA people in business, as well as government, understand that there are spatial data all around them and they can be very informative. There are technology parks in the USA totally based on spatial data, and there is one in The Netherlands too. Ireland is playing catch-up, but the NCG is keeping us in the race.

Census

The data gained from the census in Ireland is a vital source of information that is used by government agencies for future planning. The census data have been traditionally gathered in units, called 'electoral divisions' and there are just under 3,500 of these across the country. That might sound a lot, but it doesn't provide information on, for example, the socio-economic differences between people living in Maynooth, a town of 11,000 people. The system is, in fact, quite a blunt instrument.

The NCG has generated a mathematical algorithm to generate much smaller spatial units, called 'small areas', of which about 17,000 cover Ireland. These give us much more detail about areas of need within our cities. For example, instead of data being reported for Maynooth in one single electoral division, there will be approximately 30 small areas. Reporting data at this level will produce vastly superior information on which local and national government agencies can base decisions.

The 'small areas' approach will be used by the Central Statistics Office, for the first time, in the 2011 Census for reporting data. "This," said Prof Fotheringham, "will give all local government and national government departments a much clearer picture of the social and economic fabric of the country." "It is going to give them a clarity that is almost unheard of" he said, "So they are going to be able to make much, much better informed decisions about the location of resources and facilities."

Future

The SRC funding will enable the NCG to move more into the field of geotechnologies. This means more work will be done over the next five years into developing spatial sensors, devices and technologies that capture spatial data, as well as finding new and improved ways to process and visualise the data. One of the big challenges is making sense of data in a world where absolutely massive data sets can be generated in seconds. The key is to find new ways to make sense of it all.

"It is hard to assess where the 'next big thing' in geocomputation is going to come from," said Prof Fotheringham. Who would have anticipated, 20 years ago, that mobile phones would be so popular today? Or who would have guessed even 10 years ago that SatNav systems would take off as they have done? A geo-explosion is coming, and the mobile phone is likely to be involved, but nobody is exactly sure where we are headed. "That's why this area is so exciting," said Prof Fotheringham.

The technology is moving so fast that there has been no real debate about how this all can intrude on our privacy. In modern cities today there are CCTV cameras that track people's movements, as well as mobile phones, and other sensors such as RFID tags. But, as with all technologies there is the potential for good and bad. GPS can save people's lives by helping the emergency services get to a location faster. It can also signal a person's location if they are lost on top of a mountain or out at sea. But, on the other hand people probably don't want all their movements tracked so we have to be careful we maximise the good uses and minimise the bad ones.

» Prof Fotheringham did his BSc at Aberdeen University, and went on to do his MA and PhD at McMaster University in Canada.

» Prior to his arrival in Maynooth in 2004, Prof Fotheringham was actively involved in large GIS (geographical information system) based initiatives in the USA, Canada and the UK.

» He has held academic posts at the University of Newcastle, the State University of New York at Buffalo, the University of Florida and Indiana University.

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Researcher Dr Uri Frank

Title *Stem cells: Moving to an invertebrate model*

Case Study

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Stem cell research is mostly conducted on mice and human cells, but work by Dr Uri Frank at NUIG suggests that using an invertebrate model would not only be cheaper, easier, and free of ethical restrictions, but can also provide new insight into the biology of stem cells and their evolutionary origin. This knowledge may be applicable also to biomedical research. The invertebrate he works with is called Hydractinia echinata belonging to the phylum Cnidaria (includes jellyfish, sea anemones, hydras and corals). Dr Frank wants to convince stem cell researchers of the benefits of utilising this model.

Dr Frank, a developmental biologist, explains that stem cell research is driven by two main incentives, one being the great potential of these cells for regenerative medicine, and the other is the role of stem cells in development, adult life and ageing. This is the reason, he says, why most stem cell research is being carried out on mammalians. Dr Frank argues that work on invertebrates may open up new perspectives for stem cell research that are not feasible in mammals.

Pluripotentcy

It has been known for some time that some invertebrates maintain a population of pluripotent stem cells throughout their lifetime. These are cells that are undifferentiated and can develop into any cell type in the body. In humans and other mammals, pluripotent stem cells only exist in very early embryos, at the preimplantation stage. Of course, working on embryos in humans at that stage, or any stage of life, is technically difficult and ethically controversial. Work on mice does not sort out the technical difficulties.

Those invertebrates (like Dr Frank's model animal) that keep a stock of pluripotent stem cells for their entire lives, have an unlimited ability to regenerate parts of their bodies that may have been lost. For example, decapitating a Hydractinia individual isn't fatal and the animal regenerates a new head within days. Furthermore, some cnidarians, such as corals, do not seem to have a limited lifespan. They can live for thousands of years without any sign of senescence. Their pluripotent stem cells can replace any lost cell.

"The immediate question that arises is why do some invertebrates maintain their pluripotent cells throughout life? That question could be turned on its head," said Dr Frank, "Why don't humans keep their pluripotent cells? Why do they lose them?"

Scientists believe that all animals living today, including invertebrates and humans, are the descendants of a single common ancestor that lived hundreds of millions of years before the times of the dinosaurs. If this is true, invertebrate stem cells should be very similar to their human counterparts and studying them may provide information on human stem cells. "Possibly," says Dr. Frank, "this animal maintained its stock of pluripotent cells, like Hydractinia does, but as evolution progressed, for some reason, humans, and some other animals, lost that trait." "There is a theory," he adds, "yet unproved, that the loss of these cells was the price that had to be paid for increasing complexity."

Hydroids

The hydroid animals that Dr Frank works on are morphologically very simple. A quick look at them, and they don't, at a first glance, look like animals at all, perhaps more like plants and they don't have many organs. However, they do have cell types that are specific for animals – nerve and muscle cells – so they are certainly animals.

Cnidaria, to which Hydractinia belongs, is a very ancient group of animals with the fossil record showing that they existed at least 600 million years ago. Given that they have been around such a phenomenal length of time, Dr Frank believes there is a good chance that they have inherited many characters from the common ancestor of all animals. Maintaining pluripotent cells throughout life may be a primitive characteristic that was lost in some, but not all, animals during evolution.

For stem cell researchers, this means that stem cells can be studied at any developmental stage of the animal. Furthermore, Dr Frank argues that working with human or mouse stem cells is mainly restricted to cell cultures. Hydractinia, being small and translucent, enables observing labeled stem cells in the living animal.

A colony of Hydractinia echinata *modelled in glass. Photograph Werner Muller, Zoology Deptartment, University of Heidelberg.*

Projects

Dr Frank has two SFI-funded projects running. One that started about three years ago is centred on characterising the general stem cell population of his invertebrate hydroids. There are stem cells in these animals that can differentiate into any cell type, and others that can differentiate only into particular cells, but not to others. Both types of stem cells look the same morphologically, so Dr Frank is seeking genetic markers for each cell population.

The other project is centred on the function of the Wnt signaling pathway in stem cell decision-making. Wnt is a protein that is used by some cells to signal other cells how to behave. It plays a role in embryonic development but also in stem cells. This protein, Dr Frank has shown, signals the Hydractinia embryo where to make the head, but it also instructs stem cells to self-renew. Wnt signaling is very similar in mammals, and, thus, he wants to further study the role of this pathway in Hydractinia.

- Dr Frank did his PhD in the University of Amsterdam (1995), followed by post-doctoral work at the National Institute of Oceanography, Haifa, Israel (1995-1997), and the University of Jena, Germany (1997-1999).
- He held the position of Assistant Professor at the University of Heidelberg, Germany, from 1999-2005. He took up his post at NUI Galway in October 2005.

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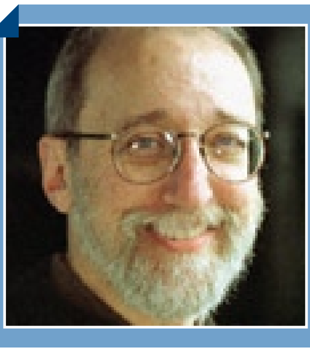


Researcher Prof Eugene Freuder

Title *Helping computers to help decision makers*

Case Study 16

Anybody who has solved a Sudoku puzzle is, whether they know it or not, a constraint programmer. Prof Eugene Freuder, director of the Cork Constraint Computation Centre, 4C, at University College Cork explained that solving the puzzle involves inserting numbers that satisfy certain *constraints:* for example, all the numbers in any row have to be different.

"Constraint programming," he said, "has an important role to play in how we can use computers to solve complex problems." Constraint programming is being used at 4C to "help computers to help people to make better decisions."

Many everyday decisions involve weighing up a variety of options and tradeoffs, and typical examples would include buying a house or a car. Similar problems, but on a broader, more complex scale, often face people in industry. "An engineer tasked with assembling a PCB," said Prof Freuder, "can be faced with a daunting choice of options, and the same applies to a person responsible for scheduling meetings or factory production."

Constraints

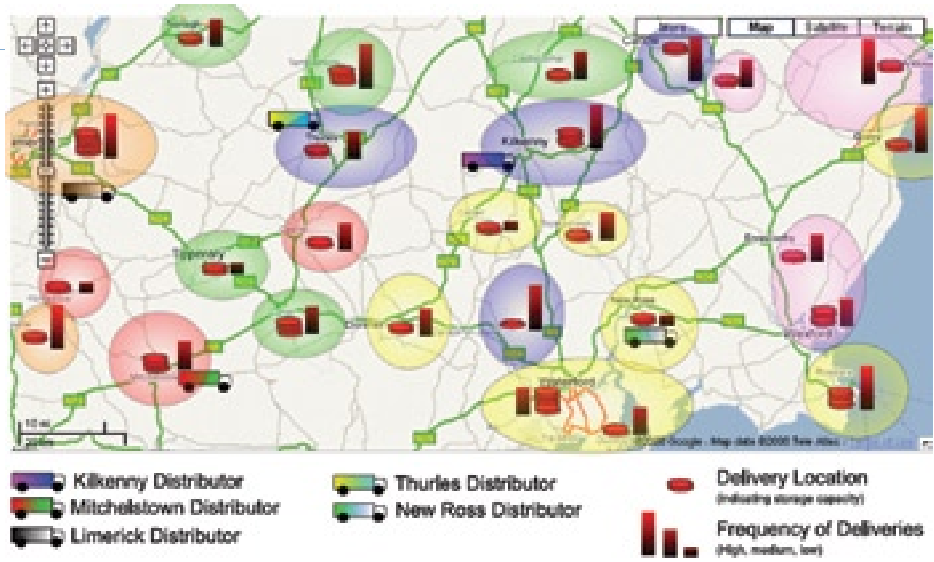
"Real-world constraints," he said, "can involve costs, preferences, uncertainties and change." Constraints arise in design and configuration, planning and scheduling, diagnosis and testing, and in many other contexts. Constraint programming can solve problems in telecommunications, internet commerce, electronics, bioinformatics, transportation, network management, supply chain management and many other fields.

One of the benefits of working with constraint programming is that there are so many possible applications. "One of the projects we are working on," said Prof Freuder, "is to put constraint programming, 'CP inside', into popular software packages." Although constraint programming is generally at the core, the 4C group takes a wide view of how decision making can become part of computerised systems. Prof Freuder said "there have been a number of notable successes, including the development of a more cost effective prototype procurement system for Cork City Council, which utilised software for which Alan Holland of 4C won an Irish Software Association award."

Collaboration

Prof Freuder said, "that the group is very active in industry collaboration, and because of this one of their key players is External Liaison Officer, Dr James Little." "Having worked in the software industry, and being close to the research," said Prof Freuder, "means that Dr Little knows how to initiate collaborative projects." When it comes to technology transfer it is important to have someone with industry experience who can help to generate, fund, manage, implement, and exploit such projects, and the resulting intellectual property.

Constraint programming helps solve complex problems, such as those faced by distributors based in different locations.



"Researchers need to learn how to make the first move," said Prof Freuder, "there is a an Irish proverb that sums this up, "if your messenger is slow, go to meet him." This proactive approach has helped the Centre to establish an Industry Associates Programme with over 50 members and to build up a database of industry and Government contacts with over 400 entries.

While 4C has been working in collaboration with some very large companies, including Alcatel-Lucent and BT, the researchers have also been helping new companies, such as TreeMetrics. "This company," said Prof Freuder, "has some wonderful technology using lasers to measure forestry resources." By developing a way to transform raw data into knowledge, the 4C group shared an it@cork Leaders Award with TreeMetrics, which has exported Irish technology to over a dozen countries.

» Prof Eugene Freuder studied Mathematics at Harvard and has a PhD in Computer Science from the Massachusetts Institute of Technology. He worked mainly in the University of New Hampshire in the USA before coming to UCC in Ireland to take up an SFI Fellow Award and establish 4C.

» Prof Freuder is a Member of the Royal Irish Academy and a Fellow of the American Association for the Advancement of Science, the Association for the Advancement of Artificial Intelligence, and the European Coordinating Committee for Artificial Intelligence.

» Prof Freuder shares an SFI Principal Investigator Award with the Associate Director of 4C, Dr Barry O'Sullivan, and is Deputy Director of the ITOBO SFI Strategic Research Cluster.

» 4C has obtained funding from Science Foundation Ireland, Enterprise Ireland, the Embark Initiative, the European Union, the Southern Health Board (HSE), the Environmental Protection Agency, the Marine Institute, and from industry.

» The UCC Technology Transfer Office reports that 4C technology transfer activities for 2008 included a patent filing, a preliminary patent filing, a patent assignment, three licence agreements and an evaluation licence.

» 4C has worked with the Cork City Council and Cork University Hospital as well as a number of multinational and local companies.

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Researcher Prof John Gamble

Title *Volcanoes: How do they work?*

Case Study

17

A greater understanding of deadly 'super volcanoes', how the Giant's Causeway was formed, and the possible links between two Krakatau eruptions, are just some of the research goals of John Gamble, a top volcanologist and UCC Professor of Geology. For volcanologists the parts of the world that are by far the most interesting are those where volcanic eruptions regularly occur. These are places like Indonesia, Iceland, Japan, the Philippines, the west coast of North America and the west coast of South America. This is where it's at, where volcanoes do their stuff, typically erupting at the boundaries between Earth's 'tectonic plates', where plates collide and subduct (where one plate is pushed beneath the other), and where rocks melt due to the temperature and pressure conditions generated by these huge collisions. Much is known about volcanoes, but much too is still to be learned.

Projects

One area of the globe that Prof Gamble has spent time in, and is a centre of volcanic activity, is Indonesia. He has a current PhD student finishing up a project that involved studying 'Anak Krakatau', or 'Son of Krakatau'. This is the name given to the young cone emerging from the sea at the site of the catastrophic 1883 Krakatau eruption in a remote region between Sumatra and Java. The aim was to establish links between the eruption products of Anak Krakatau and the great eruption 126 years ago.

Another important project takes place much closer to home and involves studying basaltic rocks in Co Antrim. These rocks were formed about 60 million years ago when lava flowed across the surface of Antrim and NW Scotland, including the islands of Skye and Mull, roughly coinciding with the time the north Atlantic Ocean opened. The Giant's Causeway, one of Ireland's World Heritage Sites, was formed during this period and the unusual shape of the rocks there was a result of the way the basalt magma cooled. This is a cross-border study initiative involving Prof Gamble, Dr Paul Lyle in the University of Ulster and researchers based at the Geological Survey of Northern Ireland. It is now into its second year of funding.

'Super volcanoes'

Volcanic eruptions involving basaltic rocks, such as those that occur in Hawaii, are typically not as explosive as those involving andesite and rhyolite rocks – that arise from magma that is many times more viscous and therefore more potentially explosive than basalt. Andesite and rhyolite volcanoes occur around the Pacific 'Ring of Fire' in, or near to New Zealand, the Philippines, Japan and Indonesia, for example. Prof Gamble is investigating the links between andesite volcanoes and what are called rhyolitic 'super volcanoes'. A typical andesite volcano might erupt once every hundred years, or perhaps once every 25 years, and produce a few cubic kilometres of magma – a small amount in volcanic terms. The ongoing eruptions on Soufrière Hills Martinique, in the West Indies, are typical of an andesite volcano. It has been erupting for the past decade or so, but has produced just a few cubic kilometres of magma.

Contrast that with a super volcano. These might erupt only once every 100,000 years, but when they do erupt they can produce vast, almost unimaginable amounts of magma - thousands of cubic kilometres. These have caused a 'volcanic winter' or global cooling in one fell swoop. The enormous eruption that occurred in Lake Taupo, New Zealand about 26,500 years ago is one example of a super volcano. It was massive, around 800 – 1000 cubic kilometres of erupted material.

Landsat satellite image of Lake Toba on island of Sumatra, Indonesia. The lake was formed during the eruption of a super volcanoe 70,000 years ago. The large crater filled with water and a new dome emerged as an island.

Image, NASA and USGS.

Cargo

The 'crystal cargo' that magmas arising from andesite and rhyolite super volcanoes produce are being compared by Prof Gamble and his team. The cargo is made up of crystals and rock fragments that have many sources and origins in the complex volcanic plumbing system beneath a volcano. Using microanalysis methods with lasers, electron beams and ion beams, Prof Gamble and colleagues have discovered links between andesitic and the rhyolitic 'supervolcanoes'. But precisely when an eruption will occur, he can't say. These super eruptions could take place at many locations around the 'Ring of Fire', western USA, western South America, Indonesia, Japan or New Zealand. "If something like this occurs, everyone should be worried," said Prof Gamble, "even if they are living on the other side of the world to where the eruption occurs, as the effect on global climate could be sudden and quite dramatic."

Large eruptions

In recent times there have been no eruptions of super volcanoes dimensions, but in 1815 there was a very large eruption from Mount Tambora on the Indonesian island of Sumbawa. This started on the 5th April that year, but local historical details are sparse, and it involved perhaps 30 cubic kilometres of magma. However, this was the same year as the Battle of Waterloo, which took place in Belgium on the 18th June 1815. The impact of the volcano on climate was such that a month after it erupted, it was reported that the Summer in Europe was very cold, with many soldiers at Waterloo dying of exposure rather than of their wounds.

Another very large eruption, but not a super volcano, occurred in 1783 in Iceland – the 'Laki fissure eruption'. This produced 14 cubic kilometres of basaltic lava and killed 50 per cent of Iceland's livestock and 25 per cent of its people. That was with 14 cubic kilometres, so imagine the impact of a super volcano that produces 1,000 - 2,000 or more cubic kilometers of material. The impact would be almost unimaginable.

Predictions

On the big question, can geologists predict volcanoes? Prof Gamble says "yes and no." In recent decades predictions have become more accurate, but only where sophisticated monitoring equipment is in place. As to when eruptions turn on and turn off – we have some way to go! These predictions cannot be made to the minute or hour, but may be accurate to the day or week in the right circumstances. A clue comes when movement of fluid is detected underground, this can be detected by seismometers and modern instrumentation for measuring Earth deformation, including Global Positioning Satellites (GPS). This indicates that magma is on the move up to the surface.

For example, the climactic eruption of Mount Pinatubo in the Philippines in 1991 erupted within a day of what was predicted. The 'precursor activity' became clear. This pre-eruption activity can involve earthquakes – the result of rocks breaking – or the release of particular gases. Sometimes with small volcanoes - the andesite type volcanoes - eruptions can't be predicted. They just 'go off'. But, with the larger volcanoes, the pre-cursor activity is often clear and indicates an eruption is on the way.

Benefits

"There are a number of benefits to the public that can arise from their support for research into geology, and volcanism in particular," said Prof Gamble. This work can contribute to global efforts to understand more about the interior of the Earth and how volcanoes work, including the nature and timing of the very dangerous 'super volcanoes'.

There are economic benefits too, as scientists can learn more about how ore deposits form, most particularly Irish gold, that was deposited in geothermal systems associated with volcanism in the distant past. Most of Ireland's gold that has been mined to date is of volcanic origin, and understanding more about volcanoes can help with understanding how, when and where gold might have been deposited in Ireland.

Also, by understanding more about volcanoes that erupted in the past, particularly the very large volcanoes, and the super volcanoes, we can learn more about how these volcanoes made a past impact on global climate, and could do so again in the future.

» Prof Gamble is a graduate of Queen's University, Belfast, where he achieved a First Class Honours undergraduate degree and was a Foundation Scholar. He was awarded a DSc.

» After his undergraduate studies he went straight into working as a lecturer in geology at the University of Newcastle, NSW, Australia. He also worked at Victoria University of Wellington, New Zealand, where he was Head of Department for two separate periods, before being appointed Chair of Geology at UCC in 2002.

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Researcher Prof David Clifford Henshall

Title *Improving recovery in brain damage*

Case Study **18**

A little bit of stress can actually be good for the brain. As Prof David Henshall, working as an SFI Principal Investigator at the Royal College of Surgeons explained, the brain, after a minor insult, is much better prepared to deal with injury. Knowing how this pre-conditioning works could help us deal more effectively with serious injuries or long-term disorders, such as epilepsy.

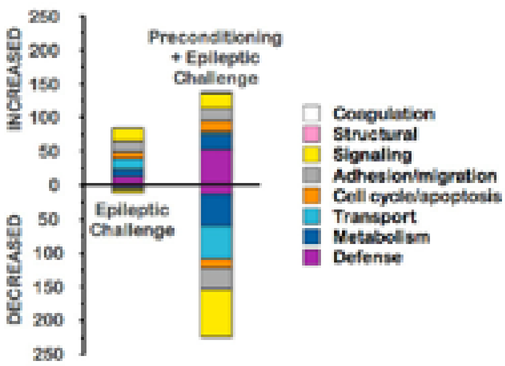
Brain injuries, even if relatively minor, are extremely serious because they disrupt the complex web of neural connections. But, as Prof Henshall pointed out, the brain has some surprising powers of recovery. “Best understood perhaps are the stem cell sites in the brain,” he said, “where new neurons and other specialised cells are produced.” In response to injury, these sites go into overdrive, and if the damage is slight, replacement neurons can plug the gap. However, if the damage is more severe, and vital connections have been lost, the replacements also die.

Repair

The fact that preconditioning gives the brain a better chance of recovery makes Prof Henshall believe that there must be opportunities to make better use of these and other natural repair systems. Of particular interest to him is the damage caused by long term seizures in epilepsy. “Seizures,” he said, “can trigger a close down and death of neurons.”

Programmed cell death is one of the most common processes in the body, and it is nature’s way of cleaning up and recycling waste tissue. “In cancer, the problem is that cells refuse to die, but in the brain,” said Prof Henshall, “neurons do quite the opposite.” Cancer researchers have done a great deal to explain the processes involved, and he has been able to apply this knowledge in reverse.

The genes responsible for triggering cell death are known, so as Prof Henshall explained, these can be knocked out by a process such as RNA interference. Pre-conditioning the brain seems to activate complementary pathways which reduce the amount of cell death following a brain insult. The result is that neurons that would have died, remain alive. In an SFI funded study, Prof Henshall found that preconditioning doubled the number of surviving neurons and dramatically reduced the development of epilepsy. “We think this approach will have real significance for the treatment of epilepsy,” he remarked, but at the same time, he warned that we do not yet know if there is a downside in keeping once-injured cells alive. Furthermore, the cleaning up process can go too far, and undamaged neurons around the core area are dragged into the process. “Saving those,” said Prof Henshall, “could also make quite a difference, and it might also give new cell replacements a better chance of taking up residence.”



The graph shows results from DNA microarray analyses of ~40,000 genes in the mouse brain and illustrates the pre-programming effect that a brief preconditioning seizure can have in terms of the scale and nature of genes responding to prolonged epileptic seizures.

» Prof David Henshall studied pharmacology at the University of Bristol and following a PhD in neuropharmacology at the University of Edinburgh he did postdoc work at the University of Pittsburgh, USA.

» He was associate scientist at the Robert S Dow Neurobiology Laboratories in Portland, USA before taking up his position as senior lecturer in molecular physiology and neuroscience at the Royal College of Surgeons of Ireland.

» His group are supported by the Wellcome Trust, the Irish Health Research Board and the Irish Council for Science Engineering and Technology.

» Prof Henshall’s group of nine researchers have worked with Biovail Technologies (Ireland) on new drug efficacy, and they collaborate with other researchers in Trinity College Dublin, the RS Dow Neurobiology Laboratory in Oregon, USA, and the Lerner-Natoli Laboratory in Montpellier, France.

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Researcher Dr Emmeline Hill

Title *Applying science to Ireland's thoroughbred horse industry*

Case Study

19

Consider this: The Men's 1,500 metres world record fell by some 31 seconds in the 86 years from 1913 to 1999 when the current world record was set by Hicham El Guerrouj of Morocco at 3 minutes 43:13. That's an improvement of about one second every three years. The English Derby, a horse race run over 2,414 metres, was won in 1908 in 2 minutes 39:80, while in 2008, *New Approach* won it in a time of 2 minutes 36:50. That's a far less impressive improvement of about one second every 33 years or so.

Why have human world records been falling rapidly compared to horse race times? The figures above suggest that the men's world records are falling up to 10 times faster than horse races, run over roughly similar distances. The answer lies in science. Science has been increasingly applied to athletics in the modern era – perhaps too much some would argue - while horse racing has maintained a 'traditional' approach.

Dr Emmeline Hill, an equine scientist based at UCD, is starting to change all that. She is helping to keep Ireland at the forefront of the thoroughbred horse breeding industry by applying science to horse performance. She wants to understand, at the genetic level, why some thoroughbred horses will develop into champions, while others will not. Such information could be extremely valuable, when it is considered that the world record price paid for a yearling thoroughbred foal is $16 million (€11.7 million).

Focus

There are three goals for Dr Hill in her SFI-funded project entitled: The genomics of performance in thoroughbred horses. She wishes to better understand the differences at the single gene level – genes that are important for exercise – between winning thoroughbreds and non-winners. From there, she wishes to identify the genes that have been selected for, and propagated from generation to generation in the 400 year plus breeding programme in thoroughbreds. Finally, she wishes to understand the function of these genes that have been selected for.

The Irish thoroughbred horse industry is held in high esteem around the world. Ireland produces the most thoroughbred foals in Europe, and only the US and Australia produce more foals. Despite the spectacular success of the Irish thoroughbred industry down the years and decades there have been few, if any, scientific ideas or methods brought into the breeding and training of horses. This is in contrast, for example, to cattle breeding where, beginning in the 1970s, there was a massive increase in milk yields following the introduction of scientific methodologies. The same thing never happened in the thoroughbred industry, which is known for its traditional and conservative views.

Dr Hill believes that there is massive potential for applying science to the thoroughbred industry in order to both minimise costs and improve the chances for success. The idea is to identify changes in particular genes that are related to exercise performance rates in elite horses – the winners of top races like the English Derby – against thoroughbreds that will not become winners.

The horse genome was sequenced in 2007, in work funded by the National Human Genome Research Institute in the US. This work was done in order to compare a range of mammalian genomes, including the horse, to that of the human. The horse was brought in to this 'comparative genomics' study, because researchers thought it could be a good model to study the genetics of exercise. The horse could indicate what genes are important in exercise, and how these relate to obesity and diabetes.

Breeding

Thoroughbred horses have been selected, however, for exercise-related traits for the last 400 years. The first recording of pedigrees and relatedness was published in 1791 by Weatherbys and it's still maintained by Weatherbys. In the 1600s and 1700s, people in Britain had what were called 'hobby horses'. At some point in the hundred years or so before Weatherbys started keeping records, eastern horses were imported from the Arabia Peninsula and crossed with hobby horses, creating faster local horses.

An elite horse exercising on a threadmill.
Photograph, Emmeline Hill.

In thoroughbreds, over the past 400 years or more, there has been very strong breeding selection among a small group of stallions, and a larger group of mares. For every breeding stallion there are 45 breeding mares. This kind of selection doesn't operate in humans, for example, so it should be easier to find out what genes are involved with exercise in thoroughbreds when they have been bred for that purpose. The 'selection pressures' in the thoroughbred have been exercise-related pressures.

Industry

The experimental work with thoroughbreds is done with the co-operation of one of Ireland's leading race horse trainers. The horses are put through an exercise regime, often on a high-speed treadmill. Muscle biopsy samples are taken from the large hindquarters locomotor muscle before exercise, immediately after exercise and four hours after exercise. This is done to understand the genes responding to the exercise stimulus. The access that Dr Hill and her veterinarian colleague, Dr Lisa Katz, and their graduate students – one of who works full-time collecting physiological data from the horses – have to top-class racing horses is something that is not being done in other countries. She says that the co-operation of the Irish racing industry at the highest level is crucial to her work.

The relationship with the trainer, established over a number of years, is such that the scientists can follow the animals, look at their response to training, look at age effects, and follow them out and see how they perform on the racecourse. This is all helping to identify molecular profiles between muscle in elite animals and muscle in ordinary animals. The goal is to find out what is special about the elite group.

The Irish race horse industry is slowly beginning to recognise the importance of applying the sciences to their practices. It is notable that the most successful operations in the country are also those that are most interested in embracing new technologies. Dr Hill has been working closely with the industry, and ultimately this collaborative work could produce a definitive test that marks out an elite thoroughbred early on.

- Dr Hill obtained her undergraduate degree in Genetics at TCD, and followed this up with a PhD in Molecular Genetics, also at TCD.
- She has worked as a research associate at the International Livestock Research Institute in Kenya, and as a consultant for the Food and Agriculture Organisation of the United Nations, before taking up her post-doctoral work at TCD and UCD.
- In 2004 she was a winner of the prestigious President of Ireland Young Researcher Award, funded by SFI.
- Dr Hill, who is from Wexford, has always had an interest in horses, and her family has bred horses for generations.

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Researcher Prof Kieran Hodnett

Title *Solid State Pharmaceuticals Cluster*

Case Study **20**

Discovering a new drug can mark the end of a long quest by researchers, but for the pharmaceutical industry, this is just one part of the equation. Before anything can be produced, the industry has to work out how to produce the drug in bulk and in a form that can go on the market.

As Prof Kieran Hodnett from the Solid State Pharmaceutical Cluster based at the University of Limerick explained, there can be no tolerance for variation, yet processes can be extremely difficult to control. Crystalisation, phase transformation, and mixing are just some of the stages likely to be involved, and if these processes vary, even slightly, materials may have to be reprocessed, or even discarded. Compared to other industries, the level of reprocessing, he said, is higher, and the main reason for this is that traditionally the emphasis was on monitoring chemical characteristics rather than taking important physical characteristics into account.

The cluster, although based at UL, involves collaboration between Trinity College Dublin, University College Cork, University College Dublin, and the National University of Ireland, Galway, and the aim is to match the wealth of chemical, engineering and other academic knowledge with practical production know-how from industry to solve that problem of getting drugs into the right form.

Most of the drugs we take, usually as pills, are are in powder or crystalline form. Crystals can vary, and although this might only be apparent under a microscope, the differences can influence how a drug is taken up by the body. Although drugs may be chemically the same, how they are presented usually determines when, where, and how they will be absorbed.

Manufacturing

It takes more than trial and error to get all of those processes right, and Prof Hodnett explained that knowing what's involved at the molecular level and understanding the science behind reactions gives industry much more control, and apart from a better end result, there can be a considerable saving of resources.

With more than 80 pharmaceutical companies manufacturing in Ireland the sector is responsible for a quarter of our manufacturing output. One of the main reasons why those companies have done so well in Ireland is because the quality of production is high, and as Prof Hodnett observed, the way to keep this sector healthy is to provide a high level of support from research-based expertise.

Manufacturing pharmaceuticals is a highly competitive business, and likely to become more so as patents are starting to run out on some of the most popular drugs. "Having a competitive advantage in process control," said Prof Hodnett "is becoming more important for companies, and there is a related issue in how launch sites for new drugs are chosen." Patent protection only lasts for a limited number of years, so manufacturers cannot afford any delays in the start up of production. Decisions on where to locate initial bulk production are made on the basis of known track record and availability of expertise. Plants with a reputation for getting it right first time are always going to be the first choice for production of new drugs.

A number of academic researchers are associated with the Cluster, and there is active industrial participation with companies such as Janssen, Schering Plough, GlaxoSmithKline, Merck Sharpe and Dohme, Roche, Pfizer, Eli Lilly, Covidien, Wyeth and Helsinn Chemicals involved.

Mr. Brendan O'Callaghan, General Manager, Schering Plough; Prof Kieran Hodnett, Dean Faculty of Science and Engineering, UL; Dr. Tom O'Ceallaigh, Principal Scientist, Merck Sharp and Dohme and Dr. Liam Tully, Process Development Team Leader, Pfizer at the launch of the Solid State Pharmaceutical Cluster at the University of Limerick.

- Prof B K Hodnett, founding Director of the Materials and Surface Science Institute (MSSI) is Dean of the Faculty of Science and Engineering, University of Limerick.
- He is also Visiting Professor at Eindhoven University, The Netherlands, and Adjunct Professor, Curtin University of Technology, Perth, Australia. Following post-doctoral research at the Université catholique de Louvain, Belgium, and at the University of Waterloo, Ontario, Canada, Prof Hodnett took up his position at University of Limerick.
- His research currently covers polymorphism, crystalisation, silica gel formation and the role of enzymes in mesoproous solids.
- Prof Hodnett is scientific director of the Solid State Pharmaceuticals Cluster, a organisation made up of five academic groupings, and support by SFI under the SFI Strategic Research Cluster Programme.

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Researcher Dr Paul Hurley

Title *Next generation microprocessors*

Case Study 21

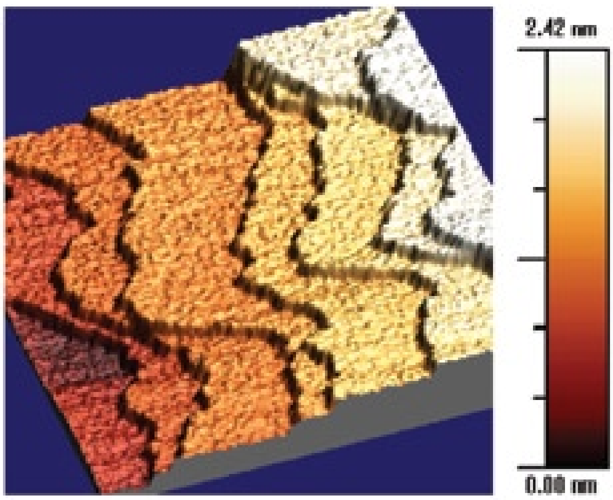
The Device at the Heart of the Information and Communication Age

The last 40 years have seen dramatic developments in computing power, information storage and digital communication technologies. The driving force behind these developments has been in large part due to the on-going miniaturisation of metal oxide semiconductor field effect transistors (MOSFETs), which are the fundamental switching elements of integrated circuits. Silicon has been the dominant semiconductor material used in the fabrication of MOSFETs and other solid state devices for the last 40 years. This is due to its electrical and mechanical properties, the excellent insulating properties of silicon's native oxide (SiO2), as well as it natural abundance. Silicon is the second most abundant element in the earth's crustal rocks.

Miniaturisation

The scaling of MOSFET dimensions from values of around 10µm in the early 1970s to values of around 65nm in 2007 was achieved without changing the basic MOSFET concept or the silicon and SiO2 materials which constitute the device. The reduction of the dimension of the MOSFET results in increased switching speed and a higher integration density, which together allow increased computing power which has enabled the explosion of portable electronic devices. The scaling of the device dimensions over the last 40 years has followed 'Moore's Law', which is named after Gordon Moore, one of the founders of Intel. Moore's Law holds that every two years, the number of transistors that can be placed into a given area of the chip will double. This Law has proved unerringly accurate up to now, and has enabled the high volume manufacturing of digital integrated circuits for information and communication technologies.

Challenges to continued scaling of the minimum size of MOSFETs were encountered in recent years as the scaling of the device dimensions reached 90nm in 2003, and the thickness of the gate oxide was reduced to around 1nm, which is close to the dimensions of atomic structure. At this length scale the insulating SiO2 gate oxide material started to lose its insulating properties, which resulted in increased power consumption in integrated circuits, shortening battery life, which is especially problematic for portable devices. Since 2000, several research teams and industries around the world have worked hard to find a new material that would replace silicon dioxide as the standard 'gate oxide' in MOSFETs. This was a huge task as silicon dioxide has been at the heart of ICs for the last 40 years, and taking it out and replacing it with a new material was akin to open heart surgery for silicon based integrated circuits. But it was achieved, and all the hard work culminated in the latest Intel chip, the Penryn microprocessor, which has transistors with dimensions of 45nm and with a new gate oxide that considerably reduces leakage at this tiny scale. The new processor has improved performance, while using less power, which is very important as we look towards a future where energy efficiency will be paramount.



Surface of InGaAs covered with a thin oxide layer.

Miraculous

The miraculous new material is called hafnium dioxide. The new material had to have a lot of properties, but uppermost it had to be an excellent insulator, and it had to have a high dielectric constant (k), a so-called high-k material. Every material has a dielectric constant k. In the semiconductor industry, 'high k' is important because the higher k is, the more charge a material can store. This allows the gate oxide of the MOSFET to be physically thicker, which cuts down on leakage currents and power consumption.

Dr Paul Hurley has been investigating the defects that might exist in hafnium dioxide, as well as any defects that might be present at the interface between hafnium dioxide and silicon. The aim of the research was to understand the origin of any defects and to explore ways in which these defects could be reduced or eliminated. This is critical for device performance of MOSFETs using hafnium dioxide, as these defects can degrade the performance and reliability of devices. At this point Intel became interested, and this led to an SFI-funded project in 2005 that also involved Dr Robert Barklie at Trinity College Dublin and Prof Greg Hughes at Dublin City University.

Things are moving fast. Hafnium dioxide, experts believe, will suffice for devices down to minimum sizes of 32 nm, but in two to three years time, some new oxide will again be required. Dr Hurley and his team are investigating alternative oxide materials that could replace hafnium oxide.

Silicon Forever?

But, silicon – the semiconductor in the device - itself could also be replaced. Dr Hurley and his group are investigating MOSFETs using compound semiconductor materials which have a higher switching speed than silicon. The compound they are looking at is indium gallium arsenide, or InGaAs. The key to InGaAs is that it possesses a far higher electron mobility than silicon. This means it can be used to achieve a higher switching speed, or more importantly, it could be utilised to achieve the same performance but at a lower power consumption.

The focus of Dr Hurley's work now is two pronged: to develop new high-k materials to replace hafnium dioxide, and to form them on compound semiconductors. This work has led to high level collaborations with the Intel Components Group in Oregon, USA and with Intel in Leixlip, Ireland. This involves exchange of materials and samples between Tyndall and Intel. It's a two-way process.

Future

The semiconductor industry is now moving into the 'materials era' of device scaling, where more and more elements of the periodic table are being incorporated into integrated circuits. In the future, faster and faster chips might not be what it is all about. The use of these new materials will allow chips to offer a range of different functions such as sensing, light emission and energy scavenging among other things. Integrating more functions onto a single chip as opposed to lots of separate chips will also allow smaller portable electronics, while at the same time saving on supplies of precious raw materials. So, looking into the future, perhaps it will be a gradual change rather than a revolution, with future electronic devices being smaller, smarter and most importantly - more energy efficient.

» Dr Paul Hurley obtained his undergraduate degree (1985), and subsequently his PhD (1989), from Liverpool University.

» He then worked for two years as a research associate, also at Liverpool University, before taking up a post at the National Microelectronics Research Centre, the forerunner of the Tyndall National Institute, in 1992. He is currently a Senior Research Scientist at Tyndall as well as a part-time lecturer at University College Cork.

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Researcher Dr Guillaume Huyet & Dr Stephen Hegarty

Title *Quantum dots*

Case Study

22

In fibre optic telecommunications, stability is a big issue, and one of the problems with the lasers used to generate intense beams of light is that they can be sensitive to vibration, heat and photons. If any of their own light is returned, they become destabilised and cease to function. Up to now, the way engineers got around this problem was by inserting optical diodes, devices that only allow light to pass in one direction. Although costs have fallen, fitting diodes is an expensive chore, and researchers at the Tyndall National Institute believe that quantum dot lasers could do the job without the need for diodes, eliminating the assembly cost penalty.

The fabrication of nanometer-sized semiconductors, known as quantum dots, has a huge significance for the whole electronics industry. At Tyndall, the Cork Institute of Technology's Photonic Device Dynamics Group is leading research into their properties and possible application in such areas as telecommunications. The group is led by Dr Guillaume Huyet, with Senior Research Fellow Dr Stephen Hegarty, both of whom are co-PIs on the SFI Principal Investigator (PI) grant.

On a normal scale, the wavelength, and hence the colour, of light emitted by a particular semiconductor is determined by a fixed energy separation, known as the band gap. However, if the semiconductor is brought down in size, this behaviour changes. By going down to the nanoscale, explained Dr Hegarty, the normal band gap behaviour no longer applies. Once the dimensions go below about 20 nanometres, other constraints apply, and a semiconductor starts to behave less like itself and more like an atom.

Because this behaviour is determined by size, a nanometer-sized semiconductor dot can be tuned to emit a whole spectrum of colours. "Nature gave us so many atoms," observed Dr Hegarty, "but now we are not stuck with these, we can make tunable atoms." This means that researchers can embed thousands of these artificial atoms in other semiconductor materials to design an ultra-stable quantum dot semiconductor laser.

Applications

Apart from being more suitable for integrated assembly, Dr Huyet and his team have been able to show that quantum dots are not affected by light return problems, and, like atoms, they emit very coherent light. The impact on photonics is certainly going to be significant, and one of the aims at Tyndall is to investigate so-called mode-locked lasers for generating trains of very short pulses of laser light. Such pulses form the building blocks for signal transmission in telecommunications, with data encoded by turning on or off individual pulses.

These pulses can be created by shining a small amount of light from one laser (the 'master' laser) into a second laser (the 'slave' laser), causing the slave laser to become synchronised, and only emit short bursts of light at regular intervals. At present, such lasers are extremely sensitive to very small changes in any one of a number of conditions, and can quickly become destabilised and stop emitting pulses. Dr Huyet's group have shown that the increased stability of quantum dot lasers makes them ideal for such mode-locking setups, increasing the reliability and wavelength-range of obtainable pulses.

Dr Huyet said "that the technology involved in making quantum dots is now quite advanced, and, since the appointment of Dr Pelucchi as a new SFI PI, Tyndall can now 'grow' their own." The term 'grow' is quite appropriate, as fabrication on this scale is now very much a bottom-up approach. Having quantum dot fabrication facilities on their doorstep gives a huge boost to the PDD group's research, giving a new dimension to their efforts to understand the dynamics of quantum dot devices. "What's most important now," said Dr Hegarty, "is to understand the science behind it. Know the science," he said, "and the applied technology will follow."

» Dr Guillaume Huyet is Senior Lecturer at the Cork Institute of Technology and Head of the Photonic Device Dynamics research group at Tyndall National Institute. He studied at Ecole Normale Superieure de Lyon and obtained his PhD from Universite de Nice - Sophia Antipolis. Dr Huyet conducted post doctorate research at the University of Balearic Islands, University College Cork and the University of Stratclyde, and became a Lecturer and an SFI PI at University College Cork, before joining the Cork Institute of Technology.

» Dr Stephen Hegarty is senior research fellow with the Photonic Devices Dynamics Group. Following his PhD from the National University of Ireland, Dr Hegarty worked on industrial research in the US before joining the group at Tyndall.

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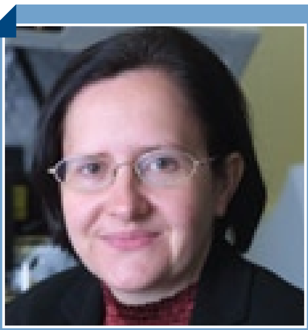

Researcher Prof Suzanne Jarvis

Title *Understanding biology at the nano-scale*

Case Study

23

The development of instruments that can view molecules at the nano-scale; the manufacture of new materials that mimic nature, and are less toxic; and a better understanding of diseases of ageing such as Alzheimer's disease and glaucoma are some of the benefits that can arise from the work of Prof Suzi Jarvis, UCD.

Prof Suzi Jarvis, an Oxford graduate, arrived in Ireland in 2002 and worked first at TCD. She moved to UCD in 2007 and there set up a multi-disciplinary team of electrical engineers, physicists, chemists, biologists, botanists and zoologists.

The engineers and the physicists are developing tools and techniques which enable the other researchers to look at natural materials at the nano-scale, understanding how they work, and possibly developing new materials that mimic the natural materials.

There is so much still be learned at this nano level, and it is a field that is just opening up for study. Specifically, Prof Jarvis and her team have been improving something called 'atomic force microscopy'. This is not something new and has been around for a few decades.

Microscope

However, the technique gained new life, as a means to delve into the nano world in recent years, when an engineer that had been working with Prof Jarvis applied 'noise reduction' methods – already in use in CD and DVD players. The result was an enhanced type of microscope that was up to 20 times more sensitive than any standard types.

This was a crucial breakthrough as it provided Prof Jarvis with a new, tremendously powerful tool with which to examine how biological molecules behave at the nano level. Even the role of water, so common in biological systems, and the role of the lipid layers within cell membranes were not clearly understood. Here was a tool that for the first time allowed researchers to look at how molecules behaved at the nano level.

The great improvements to the atomic force microscope initiated by Prof Jarvis and her team has commercial potential. Anyone studying how molecules behave at the nano scale would be interested in this advance. A collaboration, thus, has been entered into with US firm, Asylum Research, in order to develop a more user friendly version of the microscope that Prof Jarvis is currently using.

Membranes

One of the main areas that Prof Jarvis is interested in studying is biological membranes, as, somewhat surprisingly, not a lot is known about how precisely they operate, and how materials pass in and out of cells across such membranes.

It is known that lipids make up cell membranes, and that water and cell membranes interact, but what was not known was how exactly this happened. Prof Jarvis has looked at the way lipids and water operate using the atomic force microscope, and this has shown that lipids can modify the structure of water, which in turn can have an impact on how easily, or not, something can get across the cell membrane at a certain point.

Prof Jarvis is also looking at molecules such as cholesterol, to see the kind of effect it has when it's present in a lipid, and how much of an effect it has when there are different concentrations of cholesterol in a lipid. For example, researchers have noted a link between the high levels of cholesterol in membranes and certain diseases.

Fibrils

Another area of interest to Prof Jarvis is proteins, specifically proteins that form in clumps called amyloid fibrils, and that have been associated with diseases of ageing such as Alzheimer's disease, diabetes and glaucoma. When these amyloid fibrils form they can cause diseases in the brain, the eye, or the liver, as with diabetes. These fibrils have been always linked with a destructive role in the body, but Prof Jarvis is finding, using the atomic force microscope, that nature also puts this fibrils to beneficial use.

For example, Prof Jarvis and her team have found a natural adhesive made by algae that helps them to stick to walls. Her team, and other teams, have found that amyloid is present in a wide range of natural materials where they are acting as lubricants or adhesives. This means clearly that there is 'good' amyloid, and a 'bad' amyloid. Prof Jarvis is using the atomic force microscope to look at the internal structure of both to try and find out how each type is structured, and the differences between them.

She has found that good, or functional, amyloid fibrils are very useful materials – they are self-healing, very tough and can provide mechanical strength in many directions. In addition, she has found – importantly – that functional fibrils are different from the amyloid fibrils that scientists have been growing and doing research on in a test tube. The fibrils formed in the test tube are very different to functional fibrils, and, it is suspected the 'in vitro' fibrils are also very different to the disease-causing fibrils.

This difference that has been found means that scientists need to find an 'in vivo' source of fibrils. It would be very difficult to obtain fibrils that have come from human brain, or eye tissue, so the best 'in vivo' model might be the algae or plants that use functional fibrils to cling to walls or other surfaces.

One part of the research is to try and mimic natural fibrils, as that could produce new materials that mimic nature and are less toxic. For example, new products that are just as effective, but not as harmful as some existing solvents and glues could be made. She is now working with an Enterprise Ireland funded business partner and her former postdoctoral research fellow, Dr Anika Mostaert, to bring these new materials to market as soon as possible.

Prof Jarvis suspects that there may be a link between the presence of cholesterol in cell membranes and whether amyloid fibrils are functional or pathogenic. In algae and insects that use functional fibrils, for example, there is little or no cholesterol present in the cell membrane. On the other hand, she has noted that in the areas where fibril related diseases occur, like in the brain, the back of the eye, and in the liver with diabetes, these are regions that are lipid rich with a high concentration of cholesterol.

It is interesting, she said, that there are reports where people who take statins – which lower cholesterol – see a reduction in the progress of their Alzheimer's disease.

A greater understanding of how cells actually work at the nano-scale at the cell membrane interface, could lead to more rational drug design as it should provide a better understanding of how things, such as drugs, for example, get in and out of cells. If more can be understood about the processes that go on at cell membranes and why drugs can cross them, it could change the way that drugs are delivered, for instance.

Benefits

Prof Jarvis said that the most immediate impact of her work will be in the commercial area, as the instrumentation that her team is developing, in collaboration with an industry partner, will be useful for anyone that wants to look at the nano-scale and the biomimetic adhesives her team are developing have potential applications as medical adhesives. This in turn has the potential to create jobs here in Ireland.

» Prof Jarvis is a graduate from the University of Oxford, with a BA in Physics and a Kodak sponsored D.Phil. in Materials Science. This was followed by post-doc work in Japan at the Joint Research Centre for Atom Technology, Tsukuba, leading on to a staff position at the Nanotechnology Research Institute, also in Tsukuba.

» In July 2002, Prof Jarvis, with funding from SFI, moved to Ireland and became a research professor at TCD, School of Physics. In 2007, she moved to the Conway Institute at UCD, where she heads up a multi-disciplinary team.

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Researcher Dr Debra Laefer

Title *Faster, cheaper, more accurate urban modelling*

Case Study 24

Better disaster management and planning of large infrastructure projects will become possible thanks to novel data collection, processing, and transformation methods for aerial laser scanning also known as Light Detection and Ranging (LiDAR). New flight paths have enabled the gathering of unprecedented levels of building façade data using a helicopter at 500m over Dublin. The project has focused on this aspect of data capture to enable automated conversion of the data into city-scale computational models appropriate for high-level engineering analysis. Already the work has generated baseline data to assist emergency services to make better decisions on where to deploy resources for disaster management. Critical advances have been made in the automated detection of existing structures, the segregation of that data, and its further conversion into Finite Element Method (FEM) meshes.

LiDAR

This technology is commonly used for digital terrain mapping by geologists, hydrologists and planners, but it has also been used to generate city-scale, virtual models. It operates by firing a light source at something and measuring the time it takes the light to bounce back. Since we know the speed of light, the distance to the object can be determined. Traditionally LiDAR has been collected and processed to generated data in 2.5 dimensions (2.5), where every point only has a single elevation to represent it. Dr Laefer considered that, by flying at 45 degrees to the buildings, with a new approach to flight path overlap, it would be possible to generate vertical data.

This data would be far more valuable than that previously collected in terms of determining building features. A key component is in window detection as this greatly influences a building's stiffness. This characteristic requires gathering high quality vertical data along each building's façade.

Infrastructure

The Dublin Metro project was one of the key motivating factors in trying to come up with ways to assess building characteristics along its proposed route. There is a very high concentration of listed buildings along the route, and so, a way was needed to assess potential damage in advance of any underground construction. More traditional methods had been used in advance of the building of the Dublin Port Tunnel. Despite those efforts, one in eight buildings along its route were damaged, and the city paid out €4.6 million in damages. Clearly a new method that would better assess problems in advance is required. One that is capable of predicting more accurately how individual buildings will respond to a certain amount of ground movement. Given that there are thousands of homes and other buildings along the proposed Metro route, it is not financially feasible to measure, survey and assess every individual building that is along its route using traditional methods.

The best possible method, from an engineering point of view, to assess potential damage to buildings in advance of tunnelling, is by going to the building, measuring it in detail and spending somewhere between two weeks and two months per building generating a data 'mesh' that could be used to make predictions on future scenarios. That just was not financially realistic for Metro North, and some creative thinking was required. Dr Laefer had the idea that aerial data generated from LiDAR could be used to generate the data meshes. This was done using a helicopter to enable the highest possible quality data. The flight paths can be planned in order to best collect vertical façade data on buildings of interest. The data is then 'cleansed' – a process being still worked on and perfected – so that data points related to each building can be identified individually. The various data points can be linked to boundary walls. The next step is to transform the data into a meaningful finite element method (FEM) mesh. This is being done with a breakthrough realisation that the voxelization (see image) a solid model can be generated successfully without any manual intervention.

» Dr Debra Laefer has a BA in Art History from Columbia University, New York; BS in Civil Engineering, also from Columbia; an MS in Civil Engineering (Geotechnical) from Polytechnic University, Brooklyn; MS in Civil Engineering (Structural) from the University of Illinois at Urbana-Champaign (UIUC); and a PhD in Civil Engineering (Geotechnical) also from the from UIUC.

» In the US, she previously worked in general construction and also supervised restoration and preservation construction of historic structures for the US National Park Service. She is the author of over 40 papers related to the protection and repair of historic structures. At UCD, her research team consists of three post-doctoral students, four doctoral, two masters and three undergraduate students.

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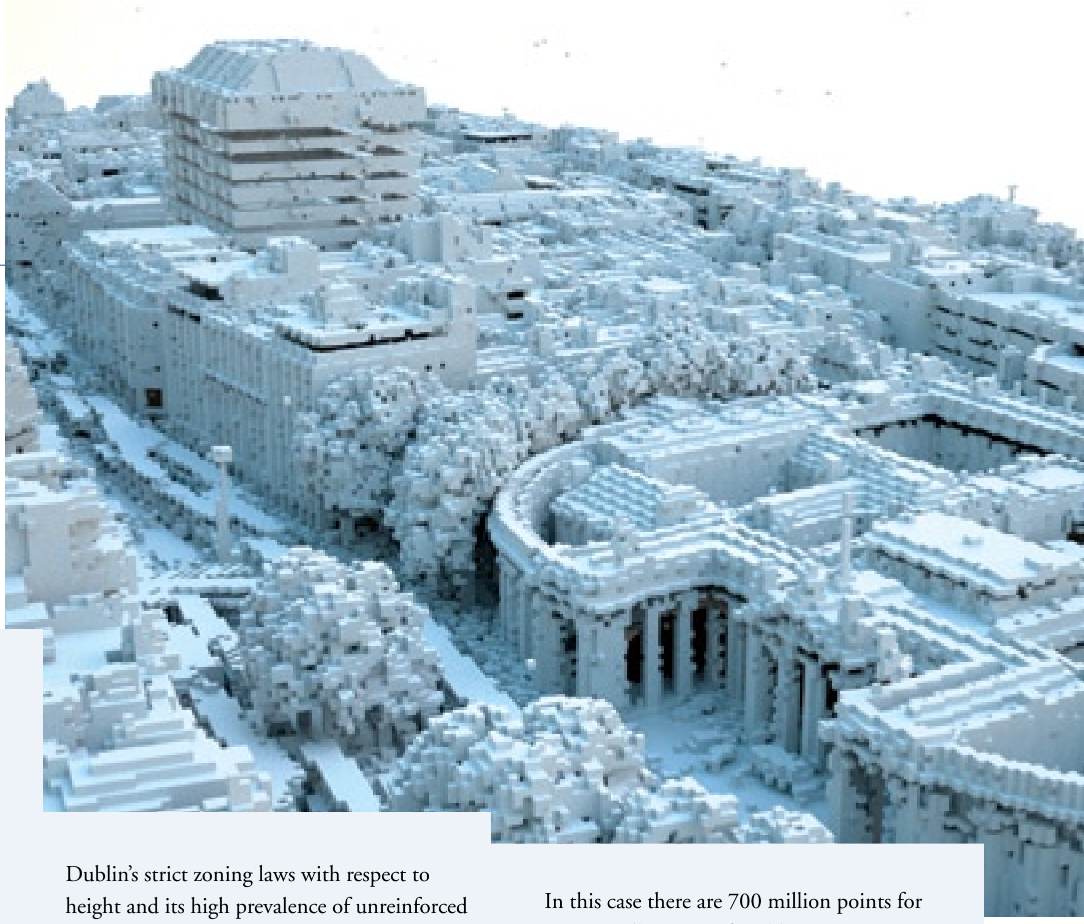


Pictured here is a surface rendering of Dame Street. This is a product – as opposed to a photo – that has been produced by Mr. Tommy Hinks, a doctoral candidate of Dr Debra Laefer and a member of her Urban Modelling Group at UCD. [Credit: GUILD grant]

From such models the response to various ground movements can be predicted. In the past, when people were conducting LiDAR surveys over an urban area they simply flew with the intention of collecting topographical data for flood plain mapping and other surface feature detection. This meant that the vast majority of data being collected was from that directly beneath the survey instrument, namely streets and roofs, with only minimal vertical data being gathered. There was insufficient data to determine where the window openings were, and this meant such surveys were inadequate for understanding how tunnelling might impact existing aboveground structures.

Empirical

The state-of-the-art method for first order predictions of trying to determine the impact of tunnelling on buildings – in the US and around the world – is by old empirical methods because of the financial and temporal bottlenecks of generating large numbers of computational models. This means that only selective buildings of interest along the route are surveyed and further evaluated. From this, an individual data mesh is generated for each building. This is expensive but enables designers to decide in advance if a building is to be structurally reinforced, monitored, or simply left as it is, as the cheaper option might be to allow some damage. As the Metro North line is slated to go through Dublin's highest concentration of listed buildings, there is concern for these buildings. Despite this, it is not financially feasible to generate 'meshes' for each of them. Consequently, the aerial LiDAR approach explained here offers for the first time the opportunity to apply this technology, and the subsequently generated 3D data, to more accurately and cost-effectively determine large-scale, city-wide impacts from tunnelling.

Dublin's strict zoning laws with respect to height and its high prevalence of unreinforced masonry buildings makes this the perfect testing ground for this technology as buildings are not heavily shadowed by each other and their structural features are largely visible, in contrast to a place like New York City, where the combination of short and tall buildings and the prevalence of reinforced concrete and glass-clad steel structures pose further challenges.

Benefits

Given that €4.6 million was paid out in damages following the construction of the Dublin Port Tunnel, it is clear that costs associated with damages from the Metro North project could be much higher. The funding for this project by SFI was €460,000, setting a relatively low damage payout threshold to benefit the taxpayer for damage prevention during Metro North's installation. The other benefits are that this technology can place Ireland right out at the forefront of creating engineering-enabled 3D urban systems, and this can help industry and public bodies to do better work. A patent* has been filed by Dr Laefer for the data processing portion of this work which will enable the point cloud data for a particular building to be automatically selected and segregated out of the larger set.

In this case there are 700 million points for just a small section of Dublin's city centre, so such automated capabilities are at the foremost of interest. To date, such efforts have relied upon heavy manual intervention or have had to make do with a low level of reliability. Conversely the data has had to be overlain on existing maps in conjunction with other data sets, which can often be either unavailable or out of date. The techniques outlined in the patent overcome such difficulties by relying upon previously unexploited latent information in the data. The techniques lay the basis for a new generation of tools that could here help after disasters. For example, in California, aerial LiDAR has already been collected for much of the State in an attempt to try to establish pre-disaster baseline maps. The idea is that if there was a major earthquake, they could fly the state again, and use data matching techniques to compare one data set to the other, and such before and after comparisons could help the emergency services make reliable decisions in a hurry.

With further efforts in this area Ireland could go beyond California and become a leader in 3D LiDAR data capture and processing, thereby providing emergency services with better data to prioritise interventions.

*This patent was made possible by collaborations with computer scientists Dr Hamish Carr, UCD, and Carol O'Sullivan, Associate Professor Computer Science, TCD.

Researcher Dr Caitriona Lally

Title *Results flow from basic research*

Case Study 25

Restricting the flow of blood has a serious impact on health, and stents are often used to keep arteries open. Dr Caitríona Lally at Dublin City University explained that this is not just a matter of sticking in a tube, even though this is essentially what a stent is. There are lots of situations where body fluids have to be kept on the move, so stents can be used, for example, to keep a bile duct or urethra open. In each case the design has to be quite different, so there are a great number of different stents in use. After conducting research on biofluids at the University of Limerick, Dr Lally started to work with an industrial partner, Medtronic Vascular, on stent design. "That was about eight years ago, and at that time," she said, "so little basic research was being conducted in this field that the organizers of the national bioengineering conference struggled to find a suitable category for her presentation." Since then, however, stent design has become a hot topic. "Improved designs," she said, "apart from improving treatments, can be worth a lot to the medical device industry of which Ireland has become an important centre."

Real life

Until recently, design mainly focused on the mechanical aspects of development, and not enough was known about the impact of stents on the body. To mimic real life conditions, Dr Lally uses a bioreactor built from flexible silicone materials. "This has similar mechanical properties to an artery," she said, "but simply looking at the response to fluid flow is not enough to show how living tissues respond to the insertion of a stent."

A common problem is that smooth muscle cells in the artery walls start to grow in response to the stent. Thus, having opened an artery that had been blocked by a build up of fat, smooth muscle growth can close it up again, but for a different reason.

"Our research," she explained, "indicates that this particular problem could be solved by making the stent with less rigid materials." However, the choice of material can depend on where the stent is to be inserted. For example, the carotid in the exposed neck area would represent quite a different challenge compared to the deeply embedded coronary artery. It is now also possible, she said, to study the body's response to medical devices with imaging techniques such as MRI. With this, she explained, "we can find out things like changes in the mechanical properties of live arteries in a non invasive way."

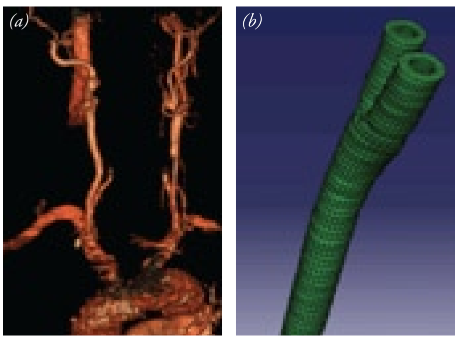
"It's a fast moving field," said Dr Lally, "and while medical grade stainless steel is still the most common material in use for stents. Stents are now also manufactured from materials such as nickel titanium alloys with shape memory, a material originally developed for NASA." Other recent moves are towards biodegradable, and drug delivering stents, which can be left in place to replace something such as a series of regular injections.

Repair

As stent design improves, more opportunities open up to use them in ways that would have been unthinkable just a few years ago. One of the most exciting developments is in tissue repair. "Some of the latest stents with active cells," she said, "are somewhere between a stent and a tissue engineering device."

As Dr Lally observed, "a lot of the practical applications depend ultimately on fundamental research. Basic research also broadens the field, and this has certainly been the case with her own work." Understanding how the body reacts to stents also makes it possible to know how the body will take to a vascular graft. Dr Lally is currently working with Swedish collaborators on using a natural polymer as a scaffold for engineering an artificial artery. Other researchers at TCD and the Royal College of Surgeons, she said, are doing a lot of work in this area, but on cartilage and bone. Dr Lally keeps in close contact with these researchers, and as she remarked, "I am like the vascular arm."

Numerical model of a stented vessel



(a) Reconstructed CT image of human carotid arteries, (b) Numerical model of a carotid artery bifurcation generated based on CT images

» Dr Caitríona Lally is a graduate in Mechanical Engineering from the University of Limerick, and has a PhD from Trinity College in cardiovascular biomechanics and finite element modelling. Dr Lally was awarded an Enterprise Ireland Innovation Partnership grant in 2005, and SFI Research Frontiers Grants in 2006, 2007 and 2008.

» Dr Lally works with a number of academic and industrial collaborators including Medtronic Vascular in Galway, the Trinity Centre for Bioengineering, Western Vascular Institute, Trinity College Institute of Neuroscience and Chalmers University of Technology.

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Researcher Prof Marina Lynch

Title *Maintaining the older brain*

Case Study **26**

As the brain ages it changes in ways that make it more susceptible to stress. Prof Marina Lynch at the Institute of Neuroscience at Trinity College Dublin explained that her research into this began when she was investigating the influence of age on what is known as long-term potentiation, LTP, an electrophysiological characteristic of the brain which has been shown to utilise synaptic processes which appear to be required for storing memories and during learning. With age the process becomes less efficient, and Prof Lynch wanted to know why, and if a cause could be found, would it be possible to modulate it?

Ageing

What she found is that as the brain ages, highly polyunsaturated acids in membranes are gradually replaced by less saturated molecules, and this appears to be sensed by defender cells as a mild form of attack. Certainly this change is accompanied by activation of microglia, the immune surveillance cells in the brain. These cells are constantly on the alert and respond to stressors by producing proinflammatory cytokines. Under controlled circumstances, activation of microglia and production of low concentrations of proinflammatory cytokines are probably beneficial, but when the brain is under prolonged stress, these changes are likely to be detrimental. It seems that the gradual change in membrane composition pushes that defensive response of microglia into overdrive, the microglia cells produce excess proinflammatory cytokines and this, in turn, can further damage the membrane by increasing production of reactive oxygen species. As in most biological systems, where there are promoters, there are also modulators, but, at least in the aged brain, the increase in proinflammatory cytokine production appears to be coupled with a decline in the anti-inflammatory cytokine proteins.

Balance

Prof Lynch's group have been delving into the details of the processes which help to maintain the balance between pro- and anti-inflammatory processes, and what they have found is that activation of a receptor on the microglia, known as the CD200 receptor, plays a key part in keeping microglial activation, and therefore the inflammation response, under control. "What we know now," said Prof Lynch, "is that anti-inflammatory cytokines are responsible for maintaining CD200, which activates the CD200 receptor, at an appropriate level."

Prof Lynch remarked that understanding mechanisms by which microglial activation occurs means that we might be able to do something to modulate it. Therefore identification of a role for this receptor site gives the researchers a target, and as Prof Lynch explained, "we know under what circumstances expression of CD200 is decreased," so the challenge now is to see what would happen if the anti-inflammatory cytokines which increase CD200 could be boosted. "Getting the balance right," said Prof Lynch, "is likely to be very important, because shifting the balance to an anti-inflammatory state could also leave the brain open to attack, and, for example, cancer cells, instead of being eliminated, could potentially proliferate under these circumstances."

At present, however, the biggest problem seems to be the declining ability of anti-inflammatory cytokines to keep the overactive microglia cells under control, at least in the aged brain, where modulating the response of microglia cells could be beneficial. Interestingly, the researchers have proposed that diet could also play an important role. While investigating the declining number of double bonds in polyunsaturated fatty acids, Prof Lynch wondered if diet had much of an influence. By feeding lab animals with Omega 3 and other fatty acid supplements Prof Lynch discovered that the change could be reversed, and importantly microglial activation was reduced so, indeed, what we eat might even delay the need for modulation.

» Prof Lynch studied Physiology at NUI Galway and completed her PhD at Trinity College Dublin before continuing research at King's College, London and the National Institute for Medical Research, London. At Trinity College Dublin she became director of the Institute of Neuroscience.

» Prof Lynch's group collaborates with a number of researchers in Ireland, the UK, Denmark and the USA. Her research has been funded by Science Foundation Ireland, the Health Research Board Ireland, the European Commission, Amarin Neuroscience Ltd, and other bodies. The research, which has resulted in 14 patents, has been widely reported on in the scientific press.

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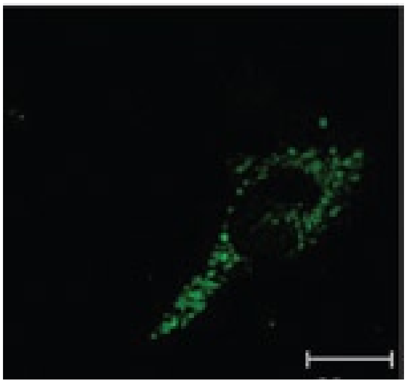
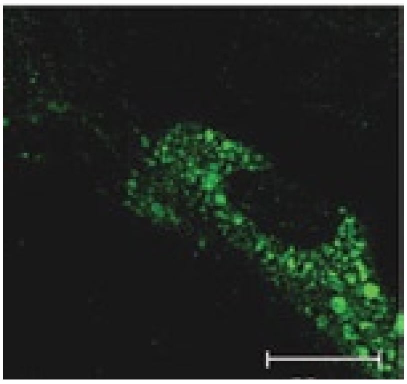
Before and after stained sections showing how anti-inflammatory cytokine, IL-4, increases CD200 expression.





Researcher Dr Celine Marmion

Title *Fighting cancer with precious metals*

Case Study **27**

Platinum is more precious than gold, and not just in money terms. The metal is a killer of cancer cells, but as Dr Celine Marmion at the Royal College of Surgeons in Ireland observed, so far only three platinum-based drugs have been approved for world-wide clinical use. "Platinum is effective because it latches onto the backbone of DNA, and that stops it replicating. Tumour growth is brought to a halt, but unfortunately, platinum does not discriminate between cancer and normal cells, so treatment has to be carefully focused on the tumour itself." "The trade off," said Dr Marmion, "involves killing the cancer while leaving enough normal cells for recovery."

Objective

One of Dr Marmion's objectives is to make delivery of platinum drugs more selective. "Already," she said, "it's known that different platinum compounds are more selective than others, and that cancer cells can develop resistance. There is some sort of self-defence mechanism at work." There is also another serious barrier in that platinum likes to bind to sulphur-containing biomolecules thus making them unavailable to bind to the DNA of cancer cells. The cell has no shortage of these, so most of the platinum gets mopped up before it ever reaches through to the DNA. "It is believed", said Dr Marmion, "that only about one per cent of a platinum drug actually reaches its intended target, and that means higher doses are required which can lead to serious side effects".

Targeting

With SFI funding, Dr Marmion has been looking for ways to get around these problems. One of her approaches has been to find out if platinum compounds could be attached to something else that targets cancer cells. "We think we have found that hook," she said. Her group have developed a new class of platinum-based compounds that have been shown to be very effective at killing cancer cells but are much less toxic towards normal cells. These are currently being tested on a whole range of cancer cells.

Ruthenium

Another precious metal that researchers are looking at is ruthenium, and among Dr Marmion's collaborators are two leading experts in this field, Prof Enzo Alessio and Prof Gianni Sava at the University of Trieste, Italy. "Ruthenium compounds," she said, "are of great interest because some have been shown to be highly effective against metastasising cancer cells." These are the cells that break away and spread cancer, and as Dr Marmion explained, "we can treat a tumour, but once a cancer starts to metastasize, we really have very little defense." One of Dr Marmion's research students has been working in Trieste with Prof Alessio's group. Prof Alessio is the leading chemist responsible for the development of a ruthenium-based cancer drug due to go into the second phase of clinical trials.

- Dr Celine Marmion graduated from the University of Surrey where she also completed her PhD.
- She lectured in chemistry at St Mary's University College, Twickenham before becoming a lecturer at the Royal College of Surgeons in Ireland in 1997. She was promoted to senior lecturer in 2003. At RCSI she has a team of one post doc and two research students. She also has a Visiting Professor from the University of Khartoum, Sudan working with her team at present.
- Her research concentrates on the development of metallodrugs that show selectivity for the cancer cell nucleus. Dr Marmion is a member of the Centre for Synthesis & Chemical Biology, a UCD/TCD/RCSI research consortium. She is also one of two national delegates on the Management Committee of EU COST D39 entitled 'Metallodrug Design & Action' . Her group works with others in Hungary, Italy, Germany and the Czech Republic as well as with groups in IT Tallaght and NUI Maynooth.

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Researcher Prof Mary McCaffrey

Title *Traffic control for cells*

Case Study

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Transporting materials into, through and out of the cell requires significant energy and biological control. There are many triggers and switches and groups of proteins that control these processes in the many specialised cells of the body. As Prof Mary McCaffrey at the Molecular Cell Laboratory, University College Cork, observed, traffic control has a big influence on our general health. Many disorders, such as cystic fibrosis, Huntingtons disease, and diabetes can occur due to critical proteins not being located correctly in the cell.

Proteins which control intracellular trafficking – the Rabs

Prof McCaffrey explained that "there are several protein families which regulate and control the transport of a plethora of proteins in our cells". One prominent such family of proteins, involved in the control of intracellular trafficking, are the RabGTPases. The suspected role of these traffic regulators first became apparent through the study of secretory mutants of yeast. Prof McCaffrey said "she had been lucky as a Post-Doc to be working at L'Institut Pasteur in Paris in the late 1980's when a group of researchers there decided to concentrate on the study of these Rab human-equivalents of the yeast mutants." Thus began a major area of biological study (now Worldwide) into these master regulators of intracellular trafficking. We now know that there are about 70 different Rabs in humans and they are involved in controlling distinct trafficking steps from one organelle to another within our cells.

Going downstream of the Rabs – the Rab11-FIP's….

One of the major approaches taken by Prof. McCaffrey and other Rab researchers has been to identify new proteins which function under the control of Rabs in their activated state. This approach led Prof. McCaffreys group to the discovery of a new family of proteins – now called the Rab11-Family Interacting Proteins. The first such protein discovered, about ten years ago, by Mary's group was the Rab Coupling Protein(RCP). Additionally, her group discovered and studies the other members of the Rab11-FIP's including FIP2, FIP3, FIP4 and Rip11.

The critical physiological importance of these proteins has become more and more apparent in the past couple of years with the demonstration that RCP functions in cell motility by mediating the passage of both growth factor receptors and integrins to the cell surface. The consequences of this are increased cellular growth and motility. This explains why Rab11c(Rab25) and RCP are strongly implicated in metastatic breast and ovarian cancers, for which there is a poor prospect of recovery.

Furthermore, FIP3 functions in the late stages of cell division, while Rip11 is necessary for the transport of the Glucose transporter GLUT4 to the cell surface in response to insulin signaling. Very recently FIP2 has been shown to be necessary for the transport of ion channel receptors in neurons. This calcium dependent event is fundamental to a physiological process called long term potentiation (LTP) more commonly known as memory.

A good decade for the Rab11-FIP's….

Prof McCaffrey explains that the first decade of work on the Rab11-FIP's has been both rewarding and revealing, uncovering their importance in a wide range of critical physiological events. No doubt the coming decade will be just as fruitful. By understanding the molecular players and events underpinning processes such as cell division, cell motility, memory and blood sugar control, research in this field has very broad ranging and fundamental implications for human health and the potential for development of more specific therapeutic interventions in a range of diseases.

- Prof McCaffrey graduated from National University of Ireland Galway before studying for her PhD at the University of London.
- She has conducted research at the Centre Nationale de Recherche Scientifique, France, L'Institut Pasteur & L'Institut Curie, Paris and the European Molecular Biology Laboratories in Heidelberg.
- At University College Cork, Prof McCaffrey leads a team of eight full-time researchers working on the methods employed by cells to transport materials. The team collaborates with several other research groups in UCC, UCD, TCD, London, Paris, Glasgow, and Bristol.

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Researcher Prof Kingston Mills

Title *Controlling the immune response to tackle disease*

Case Study

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The identification of molecules that are capable of enhancing or suppressing the human immune response, and thereby provide the means of designing new treatments for a range of human diseases, is the research goal of Prof Kingston Mills, Chair of Experimental Immunology, TCD. This research goal, if achieved, can lead to the development of new or improved vaccines against infectious diseases, as well as new therapeutics to deal with autoimmune disease.

The primary aim of Prof Mills' research is to look at the methods used by pathogens - bacteria, viruses or parasites - to modulate immune responses. The approach is to learn from the pathogens that have spent millions of years evolving mechanisms to protect themselves against destruction by the human immune system, and to apply that knowledge to develop new therapies for autoimmune diseases and cancer, for example.

The pathogens operate by evading, or suppressing the immune response. This, in turn, enables them to prolong their survival in humans. The tactics adopted by pathogens can include changing their structure, or life cycle, as well as the production of molecules that are capable of inhibiting key cells of the immune system.

Immunology SRC

Prof Mills, as well as being funded as an SFI Principal Investigator (PI), is Director and one of nine PIs involved in a recently approved SFI Strategic Research Cluster, or SRC, which funds the Immunology Research Centre at TCD. This involves a collaboration with NUIM and two industry partners, Schering Plough and the Irish TCD-campus startup Opsona Therapeutics. The start-up was founded by Prof Mills as well as fellow TCD based researchers Prof Luke O'Neill, Prof Dermot Kelleher, as well as Mark Heffernan, who is now the CEO.

The overarching aim of the SRC is to discover new activators or inhibitors of innate immunity. The innate immune system is the immune system's first line of defence against infection. It doesn't need to be mobilised and responds to an infection within an hour or two of that infection being detected. This is in contrast to the other arm of the immune system, the adaptive immune system, which kicks in more slowly, over several days.

The innate immune system is being targeted for study because it is so vital to the overall immune response. The cells of the innate system constantly patrol the body watching out for infection or damage, and when they see a problem, they rush to the site. In addition, the innate cells then direct the slower adaptive response. This means that essentially everything that happens in the immune response is controlled by the innate immune system.

The researchers within the TCD immunology SRC, including Prof Mills, want to discover new molecules that can activate the innate response. This includes the products of pathogens and dead or dying cells, which are known to be capable of activating an immune response. These activating molecules could help provide new treatments for a number of diseases.

Therapeutics

For example, in cancer, the treatment goal is to 'up-regulate' the immune response because a strong immune response is needed against the person's own cells, which have become cancerous. On the other side of the coin, with auto-immune diseases, such as rheumatoid arthritis, multiple sclerosis, type 1 diabetes, or lupus, the aim is to tone down the immune response, as the person is responding too strongly to some of their own cells.

The aim with autoimmune disease, thus, is to turn off the immune system as it is out of control. The SRC researchers, including Prof Mills, understand that – not surprisingly – viruses, bacteria and parasites are a very good source of molecules that can turn off the immune response, as this is what they have evolved to do over millions of years. These immune-suppressing molecules could then be used as therapeutics against autoimmune diseases.

Cancer

Prof Mills is working on a new approach to treating cancer called 'dendritic cell therapy', an approach that is being tested in animal experimental models at the moment. The way it works is that surgery is performed on people with cancer, a tumour is removed, and this tumour is used as an antigen [something that provokes a response from the immune system] to active normal cells which have also been taken from the same patient. Thus, the patient's immune system is primed to respond to the cancer, and once that has been done in the normal cells, these cells are infused back into the body to fight the cancer.

This up-regulating of the immune response in people with cancer is vital, as many people with cancer – and other chronic or long term infections, such as Hepatitis C – are very immune suppressed. It is difficult to generate an immune response in an immuno suppressed environment, so if normal cells are taken out of that environment and exposed to tumour cells and then re-infused there is a far better chance that they will develop an effective response. "There is evidence," said Prof Mills, "that this approach is working in the animal models."

Ireland

The standard of immunology research in Ireland is very high thanks to the work of Prof Mills and others. According to the citation impact analysis of scientific papers, taking population into account, Ireland ranks second in the world in immunology, only behind Switzerland. "The SFI SRC will help to maintain Ireland's leading role," said Prof Mills, "as will a new Bioscience Institute being built in TCD." The Institute will further help to bring top-class immunology researchers together, which can only help to raise standards. Prof Mills and his colleagues have the ambition of ultimately further raising the bar for the standards of immunology research in Ireland, and to encourage development of Irish-based companies.

Adaptive

The adaptive immune system has memory, unlike the innate system, which performs a sentinel type role. The adaptive system lays down memory cells that can survive in the body for decades, so that, for example, a person that has received a measles vaccine at age 7, could, at the age of 47, have the capability of rapidly mobilising an immune response should they encounter measles again at that stage.

Generally what happens with infection is that the innate system responds rapidly to the site of infection, and keeps the infection under some kind of control. However, this innate response is often not enough to rid the body of the invaders, so a rearguard action is needed from the adaptive system to clear out the infection. There are some infections, however, such as TB, that even the adaptive system can't clear.

Prof Mills and colleagues in the SRC are studying TB – a very successful pathogen. Success as a pathogen means that it can survive long enough in the host in order to be passed on to another host. This ability means that TB must have developed a sophisticated armoury for evading immune systems. The aim is to study TB to identify molecules that have potential as suppressive molecules that can turn off the response that causes auto immunity.

» Prof Mills did his undergraduate degree at TCD, graduating with a BSc in biochemistry.

» He also did his PhD at Trinity, working in the area of immunology. He did his post-doctoral work at University College London, and the National Institute for Medical Research, Mill Hill, London.

» He worked as a senior scientist at the UK National Institute for Biological Standards and Control before returning to Ireland in 1993 – taking up a post of Director of the Institute of Immunology at NUIM.

» He was appointed chair of Experimental Immunology at TCD in October 2001 and is currently Head of The School of Biochemistry and Immunology and Director of the SFI-funded Immunology Research Centre.

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Researcher Prof Patrick Nixon

Title *Building the future web*

Case Study

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In the not-too distant future, our homes will be full of hundreds, if not thousands, of tiny almost invisible sensors, as well as some larger portable, mobile devices. The sensors and the devices will all be individually connected to the web, and each other. How this is done is the core research theme being tackled by Prof Paddy Nixon. The idea of ubiquitous computing – that computing is all around us – has been around for a while now. Prof Nixon recalls that in the early days of this field people talked about 'smart buildings' and 'intelligent environments'.

Strategy

Prof Nixon is interested in tackling the job of building an infrastructure that could support hundreds, thousands, millions even, of sensors, all connected to the web, as well as mobile devices. Many people have connected small numbers of sensors to the web to perform particular tasks, but what Prof Nixon is about is developing a system, a next generation web, which would continue to work at whatever scale it was asked to work at. The number of devices, or sensors, involved, would not be an issue.

His ambitious plan was to invent an infrastructure for the 'sensorised world' where we would all have hundreds, maybe thousands of sensors in our homes, cars and workplaces, all helping humans to, for example, better monitor their blood pressure, remember to take the bins out, or turn the heat on a hour before people arrive home.

But, for the sensor revolution to happen it would require a totally new infrastructure. It was very important too that the new infrastructure was designed so that the privacy of people regarding the ownership of their information was protected. It was essential also that trust was built up from the very start, to ensure that people regarded the new technology as providing a helping hand, rather than opening the door to 'Big Brother'.

The title of the project that is funded by SFI is 'Secure and Predictable Pervasive Systems'. It is very important when building next generation Internet that it is secure, and that privacy of individuals is respected, that it is predictable, in that it works no matter where a person is located physically, and that it is pervasive, in other words, that it exists everywhere on the globe, and that it is always turned on, and works fast.

Adaptive

Today there are in the region of 600+ million Internet users in the world. If we take that figure – even though it will no doubt grow in future – and imagine that all of these users will have sensors in their homes, in addition to sensors outside the home. This adds up to tens of billions of sensors that will be in place all around us, into the future.

The questions for Prof Nixon are how will all of these sensors communicate with each other? How can this be done in such a way as it's manageable? What happens if one sensor, or several sensors, break down, will it affect the working of other sensors? How can the network be designed so that it's self regulating and can 'heal' itself? There is a term in medicine called 'autonomic', which refers to the system in the body that enables the body to repair itself, following say, an injury from a cut to the hand. Another example of this is when a person starts running. The body responds by automatically increasing its heart rate to deliver more oxygen which is required. When the running stops, and the body is at rest, then the heart automatically slows.

Prof Nixon wants to take this 'autonomic' idea and apply it in the technology world. For example, battery power is a limiting factor for sensors as it limits their lifetime. Could the system be designed so that batteries would be turned off when the sensor is not required to function? This would be an adaptive response to increase sensor longevity. What other decisions can be made to further increase sensors' life-spans?

Vision

The notion of the 'sensor web' is something that Prof Nixon has been advocating for some time, along with his UCD colleague Prof Barry Smyth. There is talk about web 2.0 and web 3.0, but Prof Nixon asks what is going to happen in the real world?

The reality, he believes, will be the setting up of an infrastructure that will facilitate the connection of sensors, mobile devices and the Internet into a 'Central Nervous System' (CNS) for planet Earth. This technological CNS will, for example, monitor the environment and help people predict and then fix problems. This CNS will help the individual in areas like healthcare, entertainment and their social lives.

"My vision is that world and how do we achieve that it," said Prof Nixon, "it won't be easy, and there are some basic technical problems that must be overcome." There are very simple technical limitations [with today's internet], like the number of IP addresses. How do you address a sensor when there isn't enough IP addresses to label them all?

These technical problems should be overcome in time, but one thing that Prof Nixon is firm on, is that this future will not be simply about millions of people sitting down at a computer and diving into the virtual world. It's about people taking an active part in the 'real world', and having their active lives "augmented by technology", he said.

» Prof Nixon became the youngest full Computer Science Professor in the UK when he was appointed as Professor of Computer Science at the University of Strathclyde at the age of 32. He headed up research groups at TCD and Strathclyde before setting up the Systems Research Group at UCD in 2005. While in Scotland, his research group received funding of €22 million from the European Commission, one of the EU's largest ever basic research grants.

» Prof Nixon did his undergraduate degree at Liverpool University and followed that with a PhD at Sheffield University. His research team consists of four academics, six post-docs and 22 PhDs.

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Researcher Prof Stefan Oscarson

Title *Sugar markers for vaccines*

Case Study

31

We take table sugar for granted and use it by the kilo, yet if it had to be produced synthetically rather than from plants, a spoonful might be worth its weight in gold. Prof Stefan Oscarson at University College Dublin said that making ordinary cane sugar had become the holy grail of carbohydrate synthesis. For more than a century chemists had tried to mimic the natural molecule, but as he remarked "we managed it". At the time he was Professor of Organic Chemistry in Stockholm, and news of his success became one of the chemical highlight of 2000.

Prof Oscarson's group is now based at the Centre for Synthesis and Chemical Biology at UCD, and there he continues to look at the detailed structure of carbohydrates. As he explained, nature abounds in sugars, and of particular interest to him are the oligosaccharides that occur on the outer coats of bacteria. In the oligosaccharides, the simpler sugars are joined in chains and often there are links to other chemicals.

One of the reasons why these oligosaccharides are being studied is that they serve as targets for our immune system. Our immune system can identify a bacterium as an invader by the particular oligosaccharides on its coat. A number of vaccines have been developed using these oligosaccharides. As Prof Oscarson explained, "a saccharide is taken from the bacteria and it is joined to a protein to make a vaccine."

This works quite well, but harvesting natural oligosaccharides from bacteria is not always easy and the results are not always good, so Prof Oscarson's group have been applying their carbohydrate skills to synthesising alternatives.

Synthetic

"Natural oligosaccharides," said Prof Oscarson, "occur in many different forms, and this raises some difficulties." The natural compound may not be chemically consistent or stable, it can be expensive to harvest, but these are not the only problems. "Bacteria," he said, "are very good at using these variations to fool the immune system." With synthetic oligosaccharides, there can be a lot more control, and by gaining more understanding of the processes involved, it is possible to focus on the point of interaction with the receptor.

"Synthetic glycoconjugate vaccines," said Prof Oscarson, "have a good future. The first of these, developed by a Cuban group is now a successful commercial product, it is just as effective as the one produced using natural oligosaccharides, and it is cheaper."

This sort of research involves a lot of collaboration, and while his group can come up with the oligosaccharide protein conjugates, they depend on others to do the immunological evaluation. The group is looking at the oligosaccharides on a number of bacterial types, including Neisseria meningitidis, one of the bacteria causing meningitis, and they are looking at opportunistic fungi because these also present the immune system with oligosaccharide hooks.

Glycosides remain the core concern of Prof Oscarson's group, but a number of other researchers are now working in the broad area of carbohydrate chemistry. Carbohydrates are involved in a vast array of biochemical processes, so expertise in this area is of enormous importance. Prof Oscarson said "that in UCD alone, three groups are working on carbohydrates." Other groups are active in Galway and elsewhere, and Prof Oscarson said "they are all beginning to work together as a carbohydrate cluster."

- Prof Stefan Oscarson is a chemistry graduate from Stockholm University, and following his PhD there he worked in industry before becoming Professor of Organic Chemistry at Stockholm and later at Göteborg.
- His main research interest is in synthesis of biologically active natural products, particularly oligosaccharides and glycoconjugates. Prof Oscarson heads a team of five postdocs, five PhD students, two ERASMUS students, and two fourth year project workers at the Centre for Synthesis and Chemical Biology in University College Dublin.
- The Centre collaborates with a number of groups in the US, the UK, Canada, India, Sweden, South Africa, Germany, and Belgium.

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Researcher Prof Jochen Prehn

Title *Controlling cell death*

Case Study 32

Apoptosis is the name given to the process that triggers a cell to die. This is a natural process that exists to protect the body, when, for example, it needs to get a rid of a mutant cell that could be a danger to other cells. There are several different 'apoptotic pathways' in the body. Prof Jochen Prehn, RCSI, and his team want to better understand and control these. Better control, for example, could enable scientists to 'signal' cancer cells to die, or 'signal' neurons in an Alzheimer's patient not to die.

The over-arching aim of Prof Prehn's research is to understand the pathways involved in the initiation of the various cell death, or apoptotic, programmes in the body. How are these pathways triggered? How can the trigger be stopped from working? Or how can the trigger be enhanced so that it works even better? These questions are crucial for understanding immune responses, and diseases like cancer.

There are many treatments for cancer, such as drug therapies and gamma-radiation, but some people respond better than others. It is important to know why this happens. Also, in situations such as stroke, heart attack, or neurodegenerative diseases, apoptosis is triggered, and cells – that are needed by the body – can die *en masse*.

Damage

When cells are damaged for some reason, such as in the aftermath of stroke, or with neurodegenerative disease, the body then attempts to eliminate those cells that are not working properly. This appears to be an in-built safeguard mechanism, so that cells, in cases where something has gone wrong, are killed off before they damage other cells.

When this happens, a couple of different 'cell death' programmes are activated.

Prof Prehn and has team are working to find out what exactly are the cell death programmes that are activated when cells are damaged? How are they activated? What can be done to stop them being activated? Or, how can we increase the activation of these programmes? In the latter case, greater knowledge would help hugely with cancer treatments, as cancer cells could be triggered to commit suicide.

There are two teams of investigators at his lab. One team investigates apoptosis from the point of view of how can it can be enhanced, so that it could be applied to treat cancer, and other conditions where it would be useful to trigger cells to die.

The other team looks at preventing apoptosis from becoming over-activated following neurological injuries or with neurodegenerative disorders. In these cases, it is crucial to save neuron cells in the brain that would otherwise have been triggered to die.

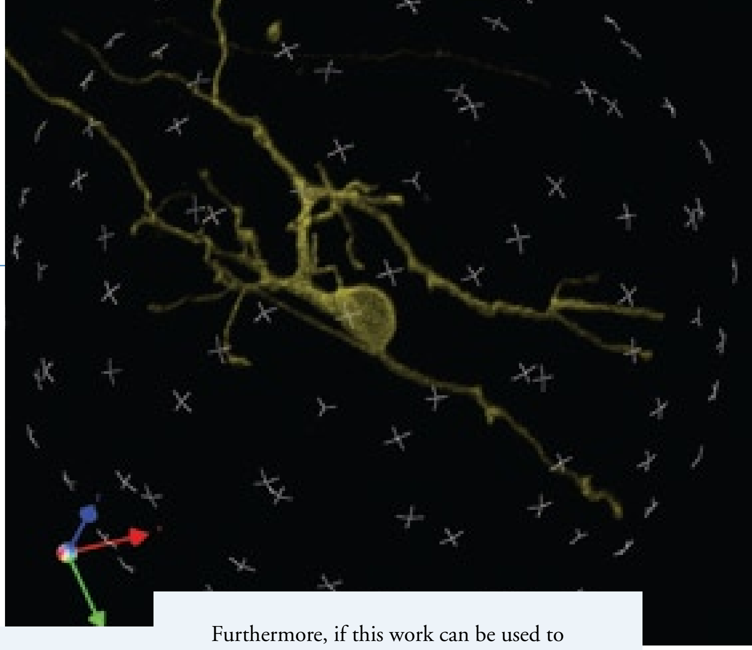
Systems biology

Prof Prehn's lab has the capability of looking at single cells in detail thanks to availability of top-class microscopes in the lab. Cells are followed over time to see how they behave. The goal is to quantify or measure the important pathways involved in apoptosis in 'real time'. This information is fed into a mathematical model and this provides a way to describe the process of apoptosis.

SFI provided an industry supplement for this work, which enabled Prof Prehn to employ a software engineer, Heinrich Huber, whose background was in nuclear physics. This engineer has been working at RCSI since 2004. He has brought a new mind-set through the application of maths to biological questions.

The 'systems biology' approach was adopted and this involves looking at organs, or cells, from the point of view of a 'system', in the way engineers would look at a manufacturing plant as a 'system'. Each functioning part is analysed in detail to figure out its role in overall functioning of the cell or tissue. The application of this approach to studying apoptosis involves looking at each component of the pathway that triggers apoptosis in greater quantitative detail.

How can the molecular switches that turn apoptosis 'on' and 'off' be explained? What genes are 'up' and what are 'down' at particular points in time during apoptosis? The expression of the genes can be inferred from the presence of certain proteins in the cell, as proteins are the product of gene expression. The amount of protein and the type of proteins can be quantified at any point in time by feeding data into a computer programme developed with the collaboration of mathematicians and engineers. This gives an overview of the 'system' in action, rather than looking at things in isolation.



A 3D rendering of a living nerve cell from a mouse brain. Image: Manus Ward and Heiko Duessmann.

Viewing the system in this way, the questions become; do cells undergo apoptosis? Do they not undergo apoptosis because protein X is missing? Or because protein Y is elevated? This situation can be more complex, but the answers to such questions help to predict how cells will behave in certain situations, and under certain conditions.

The ability to predict how cells will respond, in terms of apoptosis, can have very important clinical applications. For example, if it was known that a particular cancer cell type is unlikely to undergo apoptosis in response to a given treatment, then the question for the clinician is, is it ethically correct to go ahead with this treatment?

The use of single cell imaging technology at RCSI and computer modelling and systems approaches, thus provides the means to explain if a cell will respond to apoptosis or not, and what kind of genes and other factors are important. Some of the models, which are based on simple differential equations, will provide a clear outcome. Other models are more complex, and based on probability.

Benefits

The prime benefit of Prof Prehn's work is that it can supply the tools that enable others to predict the likely responses of cells or organs to a number of situations.

This has the potential to have a huge impact on drug testing, as it provides the means to enable scientists to improve the efficiency of many existing drugs on the market.

It also can impact on the drug discovery process itself, as it would make it more streamlined. Experiments, for example, that can be predicted to be highly negative from the point of view of drug discovery, would simply not be conducted because they would be a waste of time.

Also, in terms of the emerging area of personalised medicine, this provides a tool for clinicians to predict in advance whether a patient is likely to benefit from a treatment.

If the treatment is expensive, there is an economic as well as human benefit. For example, if an expensive anti-cancer treatment is not likely to work, should it be used in the treatment of the patient? Thus, doctors have the tools to make better decisions.

Furthermore, if this work can be used to develop greater understanding of the apoptosis signalling cascade, then it might be possible to develop a drug that is an 'apoptosis inhibitor' for instance. This might be something useful for treating stroke.

"The work in this area has also underlined the benefit," said Prof Prehn, "of engineers and mathematicians working with biologists to understand biological questions."

» Prof Prehn studied Pharmacology at the University of Bonn (1984-1989) and followed that up with a PhD in Pharmacology at the Philipps-University Marburg, Germany (1989-1992). He did his post-doctoral research at the University of Chicago (1993-1994).

» He was a lecturer in Pharmacology at the University of Marburg, an award winning researcher at the Westphalian Wilhelms-University Muenster, and Prof of Experimental Medicine at Goethe University, Frankfurt, before taking up the post of Chair of Physiology at RCSI in 2003.

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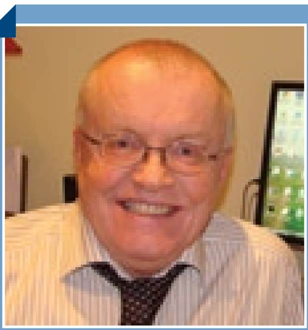

Researcher Prof Michael Scott

Title *Winning the 'hacker' wars*

Case Study

33

The safety of the Internet as a place to do business, and the protection of financial and medical data - these are two key functions that cryptographers play today. These mathematicians and their codes are all that stands between us, and the 'hacker'. Once a new code, or cipher, is designed, then the hackers will try and break it. This means cryptographers like Prof Michael Scott must constantly design new and harder ciphers.

Cryptography on one level is quite glamorous as it has been a main subject in many books and films, such as *The Da Vinci Code* (2006), and *Enigma* (2001). The core of these stories usually focuses on an important code, and how people managed to 'break' it. In reality, however, cryptography is far less glamorous. It is characterised by hard work, centred on the building and implementation of new codes, or ciphers.

This is a field that dates back to Roman times. Julius Caesar, for instance, is regarded as one of the first people to use cryptography when he invaded Britain. He wanted to ensure the integrity of messages sent with couriers back to Rome. Should a courier be captured, the captors would have to break the message code to read it. A 'Caesar Cipher', as it's known, involved shifting letters up the alphabet. A message reading T-H-E, might shift up the alphabet by three letters and read W-K-H instead – simple.

From Caesar's time right up to World War II and into the modern era, cryptography become central to military conflicts. It is said by some that the capture of the German enigma machine and its accompanying codebook shortened the war by two years. It was particularly valuable that the Germans were not aware the code had been broken, and so did not take any action to ensure their encoded messages were not being read.

Internet

Cryptography moved centre-stage with the arrival of the internet. In the modern age, information, as well as information protection, is an important issue. There have been some serious breaches of security online where credit card details have been stolen, shaking the system of e-commerce. Hackers have also broken into bank or hospital databases, gaining access to people's financial or medical details. This also affects confidence. The only thing protecting us from such ciber criminals is cryptography.

"There are certain things that individuals can do to protect themselves, but most chose not to do so," said Prof Scott. For example, take the www.amazon.com website, which sells books. This offers a one-click purchasing facility where people that feel they may come back to the site later and buy more, can leave their credit card details with the website. Many people do so.

"But, if someone hacks into the server, all the card details of all the customers that are held by amazon.com can be easily stolen. It is safer, though more tedious," he said, "to input the credit card number with each purchase." That ensures that the number is not left lying around in cyberspace. "It's like leaving a credit card lying around in somebody else's house and just trusting them to look after its integrity," said Prof Scott.

Mathematics

There is no getting away from it, however, cryptography is very mathematical and 'hard'. In order to encourage more mathematical research, and to encourage research in 'the mathematics of communication', SFI funded the Claude Shannon Institute (see http://www.shannoninstitute.ie/) of which Prof Scott is an academic member.

Cryptography is a very competitive field. It is also becoming ever more important as more and more devices are designed so they can 'talk' to other devices. For example, in the future, car sensors will communicate with each other. One sensor might want to say to the other close by: "the direction I just came from, there is a roadblock three miles up ahead" or "there is fog up ahead" or "there is an accident up ahead" or they might say to each other "you are two feet away from me, back off". If a hacker 'broke' these wireless communications, they could easily cause a major car pile-up.

Wireless sensor networks are a huge coming technology and, unless it is all properly secured, there will be major problems. For example, if an employer were able to hack into sensors that are on the body, such as a heart monitor, they would be aware that a prospective employee coming for interview has such a monitor and might not employ him.

There are great efforts made to protect the internet today, and crucial data sets, but there is no perfect system of cyber security. As soon as someone designs a system that seems un-breakable, up pops a genius somewhere that can break the code. This cat and mouse game is constantly played out between cryptographers and hackers, with the cryptographer using heavy-duty mathematics to make life difficult for the hacker.

Strategy

The tactics used by cryptographers designing a new security system is to first work out the 'threat model'. What is the problem that is being faced by the bank, hospital or individual, for example? Who is going to attack the system and why? What is the likely strategy of the attacker going to be? What is the best way to counteract that?

These questions form much of the basis for the type of work that Prof Scott does and his research team are interested in inventing and implementing new cryptography.

"One of the big problems with protecting the internet," said Dr Scott, "is that there were no cryptographic security systems built into it at the start." If cryptographers were allowed to start from scratch and design the internet today, then there certainly wouldn't be the same number of major security breaches as we've had.

Ireland

In other developed countries, such as the USA and the UK, information security, in terms of protecting the national interest, is looked after by designated, very serious, well-funded bodies - the National Security Agency in the case of the USA, and GCHQ in the case of the UK. France, Italy and German also have bodies dedicated to this task.

On the plus side, Ireland has an improved computer infrastructure through the Irish Centre for High End Computing, or ICHEC. Things have improved to the point where continental mathematicians are seeking Irish help with some big computations they wish to do, and this computer resource is a great help to cryptographers' work here.

SFI

Prof Scott has two sources of SFI funding, one through the Claude Shannon Institute, and the other through SFI's (RFP) Research Frontiers Programme. The RFP enabled him to bring in two PhD students that are working on cryptanalysis. This means that the students are working on strategies to 'attack' existing ciber protection systems to determine how strong they are, and where any potential weaknesses might lie?

One problem being attacked by the students is called 'the discrete logarithm problem'. A lot of cryptography is based on the premise that this problem is 'hard' up to certain limits. Dr Scott and his team, however, are attempting to show that even up to a higher limit, the problem is not hard, and systems must go beyond that to remain secure. The team wants to work out the number of bits required to secure the problem.

Prof Scott has made a major contribution to what's called 'pairing based cryptography'. He discovered a new 'pairing system' that is twice as fast as any other known pairing system. This is called the η_T pairing and it was discovered in DCU. There is a standard algorithm for implementing 'pairings' called the BKLS algorithm. S at the end stands for Scott. An algorithm named after him? It's a cryptographer's dream!

- Prof Michael Scott did his undergraduate work at QUB and his did post-graduate work at TCD (MSc) and the University of Dundee (PhD).
- He worked for two computing consultancies in England, Robin Hills (Systems) Ltd in Exeter as well as Digital Applications International (DAI) in London. Then he worked for a year with the Medical Research Council, also in London before taking up his current post in 1983.

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Researcher Prof John Sweeney

Title *Soils, uncertainty, and climate*

Case Study 34

Predicting and assessing the impact of climate change on Irish soils, and attempting to overcome the uncertainties is an SFI project, led by Prof Sweeney, a climate researcher at NUIM.

Soils

The soils of Ireland are varied, from the peatlands of Mayo to the mountains of Wicklow and the arable Golden Vale of Munster. These soils are a national resource, but they are likely to be impacted by climate change in coming years. Exactly how the soils will change, is the focus of research work by Prof John Sweeney, Professor of Geography, at NUIM.

The ongoing changes in rainfall intensity, and temperature is likely to have an impact on our soils, influencing both soil formation and soil erosion. Prof Sweeney's goal is to try and quantify exactly what the resilience and resistance of Irish soil will be to changes in climate, and to understand how soils will change over time.

National productivity is linked to our soils, and this means an understanding of how our soils will change is of key economic importance, as well as academic interest. There is also a requirement to fit in with the EU strategy on soil protection, and this requirement was proposed under the EU Soil Framework Directive earlier this year. This proposed Directive requires all member states to take action to prevent soil degradation.

Prof Sweeney and his team are attempting to predict how soils will change in future using a technique called 'statistical down-scaling'. This is a method for bringing a finer resolution to the relatively coarse outputs that are provided for future climate projects by the big global climate models. When climate scientists talk about models they are talking about the complex maths involved in predicting future climate.

The big models make predictions based on grid squares of 300 or 400 km^2, which is not a fine enough resolution to tell scientists what is happening in the soils of Tipperary against those of, say, Donegal.

A downscaling method has been developed, using the Irish meteorological network, which provides for predictions at a scale of around 10 km^2. The predictions for the present using this method have proved accurate at small scales. This has provided the researchers with confidence in making future predictions using the same method.

In order to look at how the different soil types in Ireland will respond to climate changes, it is necessary to input lots of parameters into the predictive model, including land usage, the slope of the land, altitude and future rainfall patterns, for example. This is not the first time that a 'downscale' approach has been taken. It has already been used to 'drive' water and flood-related models for hydrology and to look at forestry and issues of biodiversity, for example. It's a powerful technique, and it's well proven.

Planning

It is essential for planners to have a handle on how Irish soils will change into the future. For instance, in the area of forestry, it might be the case – without the work of people like Prof Sweeney – that in 50 years time a climate type might not be suitable for a tree type that is being planted today. People that are planning right now for future water supply needs to our towns and cities need to understand what is going to happen to Ireland's climate in future, and so do farm managers, and people planning for infrastructure, for example.

If the predictions are proved right, planners will have planned correctly and the taxpayer will not be burdened. Perhaps if the climate predictions are very accurate, with the right planner, Ireland could emerge as a net economic beneficiary from climate change, rather than a net loser.

Temperature changes into the future can be predicted with significant confidence by scientists, but rainfall is far more difficult to predict, as, in Ireland it can be raining in one location and not raining a few miles down the road. The trend, the evidence shows, will be for increased winter rainfall in the west, and decreased summer rainfall generally, but most particularly in the east. Despite two wet summers, in 2007 and 2008, Prof Sweeney is confident that these were 'aberrations' from the model norm and indications from summer 2004 would seem to confirm this.

Uncertainty

Predicting the future involves a level of uncertainty, of course, no matter how good climate models are. Another project that Prof Sweeney is heading up involves trying to tackle the question of uncertainty. The goal of the project is to deal with the complexity of hydrological models and get a stronger 'signal' or end product.

It is all about getting consistency from climate models. Currently, the situation with models is that if one climate model is run twice in a row, with the same parameters, or variable factors, there will be two different answers at the end. Overcoming this problem is important in order to make better and more consistent predictions.

Skills

One issue that Prof Sweeney states is important for the whole area of climate research into the future in Ireland is the need to overcome a skills deficit in this area. There is a lack of people, he said, that are skilled at modelling, atmospherics and mathematics, and such people are essential for Ireland to build research capacity in these areas.

NUIM has just started a Masters course in Climate Change, another positive move towards ensuring that Ireland has a conveyor belt of home-grown talent in climate research into the future.

» Prof John Sweeney has been a lecturer at the Department of Geography in NUI Maynooth since 1978.

» He did his BSc at the University of Glasgow where he achieved First Class Honours, and was awarded his PhD, also from Glasgow in 1980.

» He has taught and conducted research at a number of universities in North America and Africa, and been involved in various national and international bodies. As one of the contributing authors and review editors of the recently published Fourth Assessment Report of the Intergovernmental Panel on Climate Change, John Sweeney shared with several hundred other climatologists the 2007 Nobel Peace Prize.

» He is interested in the impacts of climate change in Ireland, and in the production of climate scenarios for Ireland for the middle and end of this century.

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Researcher Dr Daniela Zisterer

Title *Adding value to anti-cancer drugs*

Case Study 35

A few years ago, Dr Daniela Zisterer, an SFI Investigator working at Trinity College Dublin, began looking at protein receptors. Her attention was focused on one particular receptor whose biological function was unknown. At the time Dr Zisterer was working at with the University of Sienna in Italy, where she had contact with a group of chemists, headed by Giuseppe Campiani.

The chemists had synthesized a compound, pyrrolo-1-5-benzoxazepine, otherwise known as PBOX, that could bind to these little understood receptors, and would help in uncovering their biological role. “The receptors,” she said, “occur on the outer surface of mitochondria, the tiny power houses present in every cell, and it was thought all that was known about them is that they are somehow involved in controlling cell growth.”

“We tested the PBOX compound on some cancer cell lines and found that it was quite an effective killer,” she said. Oddly enough, however, it also worked on cells that did not have that particular receptor. This roundabout way of making discoveries, is often a feature of fundamental research, and it gave her a valuable lead for her current work at Trinity College Dublin.

Cytoskeleton

The PBOX compound is now known to disrupt a fine structural framework in the cell known as the cytoskeleton. The cytoskeleton gives the cell its shape and is important in cell division, and by attaching itself to one component of this, tubulin, the cell, detecting that something is wrong, goes into programmed death.

As Dr Zisterer explained, “there is a chain of command, so the drug by binding to tubulin causes the disruption of the cytoskeleton that, in turn, triggers a cell death cascade.”

“A number of anti-cancer drugs, such as taxol, work this way,” said Dr Zisterer, “and the reason they are effective is not because they are specific to cancer cells, but because cancer cells are more prolific.”

Dr Zisterer would like to achieve better targeting to single out the cancer cells and there have been significant improvements in this over the last few years.

Until quite recently the only curative treatment for chronic myeloid leukaemia was bone marrow transplantation. Now, with Gleevec, a ‘wonder drug’ from Novartis, a mutant protein in the cancer cell acts as a target, and normal cells are unaffected. However, as with performance of many other drugs, cells ‘learn’ how to fend off attacks, and over prolonged use, cancers become harder to treat. Some chronic myeloid leukaemia patients have become resistant to Gleevec.

Added value

“One of the techniques used to overcome that kind of resistance,” said Dr Zisterer, “is to change or combine drugs, and her group is working on a combination of PBOX and Gleevec.” When the combination was tested on a particular resistant cancer cell line it was found that the addition of PBOX overcame resistance to the other drug.

Cancer cells have a remarkable array of defensive mechanisms. “Some of these defences,” said Dr Zisterer, “work like a pump, ejecting the attackers, and this is the cause of multi-drug resistance.” The PBOX compound appears to be able to bypass some of these defences.

Having found a way of adding value to anti cancer drugs, the follow-up is likely to be in the form of a goal-directed research project. “The important thing,” she said, “is that a valuable discovery has been made.” However, the compounds at present, are not water soluble, and it will take chemical expertise to overcome that problem. “That’s going to be a project in itself,” said Dr Zisterer, and her immediate concern is to stay with the fundamentals. “We are trying to make crystals of the tubulin bound to the PBOX,” she said.

By x-raying these crystals, the fine details of how and where binding occurs may become clearer. “If you were able to characterise the binding site,” she remarked, “then you could design new compounds that would bind even better.”

» Dr Daniela Zisterer received her primary and postgraduate degree in biochemistry from TCD. At TCD Dr Zisterer heads a group of two post-doc researchers and a PhD student.

» Dr Daniela Zisterer is an SFI-supported Principal Investigator and in recognition of the quality of her research she was awarded Fellowship of Trinity College Dublin. Dr Zisterer’s group collaborates with researchers in the US, Italy and in Dublin with St James’s Hospital.

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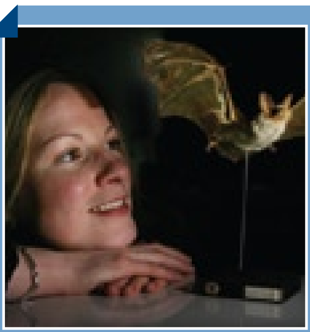

Researcher Dr Emma Teeling

Title *We can learn a lot from bats*

Case Study 36

Many of the problems that humans face – viruses, age-related illness – have been successfully tackled at the genomic level by other animals. The science of comparing such solutions to the situation in humans is called comparative genomics. This is the field of Dr Emma Teeling who is using the amazing bat as her comparative model.

The field of comparative genomics is all about learning from Mother Nature. The world is full of amazing animals and plants, and many of them have found ways to tackle diseases, or do things that humans can't do. One of the most incredible of all species is the bat, the only mammal that can fly, change its metabolic rate in response to temperature, resist viruses, develop echo-location to navigate, and live for a very long time.

Dr Teeling said that she has had the good fortune to work with bats for the past 10 years – a creature that she said is probably the most unusual of all mammals. A creature with a very high metabolic rate that burns huge amounts of energy flying, yet has longevity, and is more resistant to oxidative stresses than humans. Little is known about why bats fly, or why they evolved other remarkable abilities, like echo-location, but if we find out, Dr Teeling said, this could be very useful for humans.

It is not just Dr Teeling that has identified bats as a potential solver of human problems. Leading researchers such as Prof Mario Capecchi, Nobel Prize winner in 2007, have recognised that humans can learn from bats. This has led some to take big chunks of bat DNA and insert them into transgenic mice to test if the mice will live longer, or have an improved ability to fight disease or cope with oxidative stress.

Unique

Bats operate at a very high metabolic level, something necessary for flight, but they can also go into a state of torpor when the temperature drops. In this state of 'true hibernation' they reduce their breaths to a few tiny inputs of air every 40 minutes. Again, it is not fully understood how bats go into torpor, or why they do it? Yet, it might be a survival mechanism that provides a key to longer life, or better health.

The bats are unique among mammals primarily because of their ability to perceive their environment using 'laryngeal echo-location'. This means that they have an ability to produce very high frequency energetic sounds from their larynx, at frequencies that humans can't hear. These sounds bounce off various obstacles in their environment and back to them, providing navigation clues like the way a submarine uses radar.

Bat ears tend to be big, as they need big ears to pick up the returning echo sounds. Meanwhile, their eyes have shrunk in size because they are no longer as reliant on them, as say, we humans are. The feat of echo-location is dazzling, as for it to be effective, neurons in the bat brain have to fire at a speed that is currently beyond the scope of how scientists and neurologists now understand how neurons actually fire.

Comparisons

If a gene is 'highly conserved' over evolutionary time, meaning that it has remained the same for a long-time in a given species, then chances are that if there is a mutation in this gene it will lead to an illness. This information from the bat genome can help to determine whether a human has a mutation that could result in some kind of disease. It also then offers the possibility of scientists targeting the mutation, and correcting it.

The solutions that Mother Nature has found to common problems, such as disease and ageing, in bats and other creatures can be 'mined' and applied to humans. That is the idea behind comparative genomics – to try and better understand how genes evolve, are used, and function, and the role of mutations in causing things to go wrong.

A better understanding of that in the animal world could be of great help in humans. It could, for example, lead to an identification of genes that are known to cause various diseases. Once that is done, a human population could be 'screened' to see if they are susceptible to a list of diseases, and preventative measures could be taken early on.

At the moment, Dr Teeling is focused on identifying the genes in the bat that are involved with sensory perception. Once that work is complete the next stage would be to look at genes that are important for the immune system, and then a bit later on again, the target will be to look at genes that slow down, or perhaps speed up, ageing.

Dr Teeling has done research on the world's smallest mammal, pictured here, the bumblebee bat, Craseonyctiers thonglongyai. *Photo: Emma Teeling.*

Bumblebee

The smallest mammal in the world is the bumblebee bat. It was originally found in a small population in Thailand. It was the only species of what was thought to be a whole family of bats, which was separated from other mammals for 50 million years. It was discovered back in 1973 and people then assumed this bat was endangered.

Then in the 1990s a bat that looked the same as the bumblebee bat was found in Burma, or Myanmar. It turned out that this was the same species, but it was using a different echo-location signal – at a higher frequency – than the Thailand bat. Dr Teeling was funded, under the SFI Frontiers Programme, to determine what was happening here? How, and why were two species, which looked alike, separated?

Dr Teeling, thus, got involved in a huge research group working on bats, based in Thailand, Myanmar and the UK, all of them collaborating on sorting out the species divergence of these two similar, tiny bats.

DNA samples were taken and analysed. It was found that these bats, which were thought endangered, were actually more plentiful than researchers had believed. It was also found that - more than likely - the bats in Myanmar had come from Thailand and that they were two separate species.

The question was did the change in echo-location cause the species to diverge? A change in echo-location, it has been argued, means bats can feed on different prey, but it also means that bats operating on different frequencies can't hear each other and become socially isolated. The findings raised more questions that needed answering.

Benefits

Some might argue why would SFI get involved in supporting obscure research into why two bat species on the other side of the world diverged? Dr Teeling said that there are many reasons why this work can be of benefit to us all here in Ireland.

The techniques used in comparing the Asian bats – through molecular markers – can be applied to learn more about our own Irish bat population. How many bats do we have? How many species are there? Where did our bats originally come from? These are the type of questions that can be addressed using the same kind of techniques.

Direct benefits too can accrue to millions of people everywhere from this work, she said, if it means that scientists better understand how inherited deafness and blindness, something that is common in bats, occurs in animals and humans. There are an estimated 250 million people, she said, in the world that are hearing impaired, and by 2010 there will be 80 million people in the world that will be entirely blind. Ageing too may one day be tackled, and the long-living bat might, said Dr Teeling, one day provide the secret of eternal youth!

» Dr Emma Teeling did a B.Sc. in Zoology at UCD, graduating in 1995. Following that she did an MSc in Animal Behaviour and Animal Welfare between the University of Edinburgh and Cochrane Ecological Institute, Alberta, Canada. Her PhD in Molecular Phylogenetics, which she completed in 2001, was done at QUB, Northern Ireland and the University of California, Riverside. Emma did her post-doctoral work at the Laboratory of Genomic Diversity in the National Cancer Institute, USA. In January 2005 she was appointed as a lecturer in Evolution and Genetics in the School of Biology and Environmental Science, at UCD.

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Researcher Prof Gary McGuire

Title *Keeping our best kept secrets*

Case Study 37

Want to hear a secret? All our personal data, financial, health or legal, is stored on computers somewhere, and it's not totally safe from prying eyes. The security of the data depends on the quality of cryptographers that 'encrypt' data before it is sent over the Internet, and then 'decrypt' data so it can be read at the receiving end. Our unsung cryptographers have also been designing - for many years – 'error correction' techniques that ensure we have good TV pictures and sound quality from our CDs.

Prof Gary McGuire, School of Mathematical Sciences, UCD, and Head of the Claude Shannon Institute for Discrete Mathematics, Coding, Cryptography and Information Security, is one of these unsung mathematical heroes. He has been working for years on problems involving cryptography and error correction. Then SFI came calling.

The protection of data, whether it is being transmitted, or stored somewhere, is of crucial importance to industry, especially those industries where a lot of business is being done on the Internet. The system must be trusted, and that means the data must be protected to a high level. The Shannon Institute was set up in 2006, under SFI's mathematics initiative. They are now the recognised experts in this area in Ireland.

The mission of the Institute is to support Irish-based research in the mathematics of communication, most specifically in the fields of cryptography and error correction. Cryptography is concerned with the protection of data as it is transmitted through an insecure channel, or medium. Error correction involves preserving the reliability of information when it is transmitted through a 'noisy' channel of some sort. There are engineers and computer scientists working with mathematicians at the Institute, and there are people from four universities, UCD, DCU, NUIM and UCC, with the HQ at UCD.

Examples

An example of where cryptography comes into play these days is when a purchase is made on the Internet with a credit card. If the website is a 'secure' website, a little lock symbol will appear in the corner of the web browser as the purchase is being made. The appearance of the lock symbol means the card number is being encrypted.

That means that the credit card number digits are converted into 'gobbledegook' that cannot be 'read' by an eavesdropper listening on the transmission channel. When the number arrives at its correct destination, the gobbledegook is decrypted back into the number.

The credit card industry is very interested in new cryptographic methods, and several companies came last year to UCD for a conference on 'elliptic curve cryptography'. This kind of cryptography is the standard maths behind many security systems today.

A major issue for the big credit card companies is how their cards can be read and authorised faster, while also becoming more secure in transmission. This latest method of cryptography, they felt, might be the answer. Nobody wants to have to wait for a long time at a restaurant while a machine attempts to authorise a credit card. People want to have the transaction done almost instantly, and also for it to be secure.

Approval

The delay in approving a credit card can, said Prof McGuire, be quite long sometimes, and this has the potential for embarrassment to the card holder. This field is all about speed, and the speed of the transactions depends on how fast the cryptography is. However, greater speed often comes at the expense of security, so there's a trade-off.

If speed is pursued at the expense of security this can lead to problems. For example, in London, wireless Oyster cards were introduced for the Underground. This is a smartcard that contains a certain amount of credit that users have placed on their card. There is a wireless reader that subtracts credit off the card when it is held up to a reader. The card doesn't have to be swiped, just held up. The drive for speed, however, meant the card had low security, and the encryption code was broken. This has opened the door to possible abuses, such as people making and selling fake cards.

However, there are situations where speed is absolutely essential. For instance, there is talk about putting intelligent sensors in cards that can 'sense' if a car is too close, meaning that avoiding action must be taken immediately to avoid a collision. If the encryption of the command to 'avoid the car in the next lane' takes five seconds, for example, that is not quick enough, as by then a crash will have already occurred.

Error correction

The other aspect of the work at the Institute, is the writing of mathematical algorithms that work to 'correct' data that has been distorted in transmission. An example of this today would be the TV reception via satellite. Lots of people get their TV signals these days from a satellite. That signal must travel through the Earth's atmosphere, and depending on the weather and other factors, the signal receiver can pick up high or low levels of interference. The receiver has inbuilt mathematics that acts to de-code the signal and get rid of the interference. Hence a consistently good picture, which would not be the case in the absence of the maths.

The same principle applies to CDs and DVDs. These disks don't produce scratching noises, or other unwanted sounds, like the old LPs used to. If there is dust on a CD, for instance, a CD player will still play the music with perfect sound. This is because of an in-built error correction code. The information on the CD is digital, and this information is run through the correction code before the music is played. That is why there is a slight delay between pressing the play button and the CD actually producing sound.

New maths

Prof McGuire has lately been working on the implementation of some very new mathematics. There are new types of mathematical elliptical curves, which are known as 'Edwards Curves'. These curves might provide a way to do encryption faster. It's a very new area, said Prof McGuire, as the Edwards Curves were only published in 2006. Since then it has been a very active area in mathematics, and people at the Institute have been involved in progressing the field and working with engineers in coming up with a hardware 'real world' implementation. A patent too is on the way.

Think of the huge online security issues facing Irish banks, such as AIB and Bank of Ireland, said Prof McGuire. They might have thousands of people going online, all at the same minute of the day, looking to do some online banking. The name for the time spent by each person during a transaction, or transactions from start to finish, is a 'session'. If the person logs out and logs in again, that is another session. Each session requires a cryptographic key and must be encrypted and decrypted by the bank's computer. This has to be done thousands of times per minute, potentially, so the system requires very fast encryption and decryption, as well as very fast response times to these processes. The Edwards Curves provide a way of doing all of these security actions much faster.

Ireland

Given that cryptography comes into almost every area of business and industry today, it is strategically important that Ireland has an independent capability in the area. The fact that the Shannon Institute exists, with its expertise, could help to attract foreign companies that might want to do some, or part of their cryptography work here. One issue that needs to be looked at, said Prof McGuire, is that Ireland does not have a government agency responsible for security and cryptography, unlike most other developed nations. Government documents, he said, and communications need to be secured and safely stored. Almost all important data is now digital - residing in computers - and it needs to be encrypted and protected. Then there is the field of communications, such as email and telephone calls. These need encryption too.

It is in our national interest for Ireland to have its own agency responsible for these matters, said Prof McGuire, because otherwise it would have to be out-sourced to a private company, which represents a security risk, and the company could go bust.

In the UK, this area is controlled by MI5 and MI6, and in the USA it's under the control of the National Security Agency. In other countries, such as France, the national cryptography function is under the control of the Ministry of Defence.

This issue is going to get bigger, he said, as the world is getting more computerised all the time, and more security is required as a result. For Ireland it would make sense perhaps to have a cryptology unit based within some arm of government such as the Department of Defence or the Department of Justice, Equality and Law Reform.

» Prof McGuire did his undergraduate degree at UCD and followed that up with a PhD at California Institute of Technology (1995). Next, he went to the University of Virginia where he completed two years of post-doc research and was a 'Whyburn Research Instructor'. He was a member of staff at NUI Maynooth before taking up his current position at UCD at 2006. He has collaborations with the University of Virginia; University of Turku, Finland; the Technical University of Copenhagen; the University of Toulon; the University of Aachen, Germany; and the University of Leiden, the Netherlands. His research team is made up of two post-docs, and two PhDs.

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Researcher Prof Noel Lowndes

Title *Damage control*

Case Study

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Every time a cell divides there is another chance for errors to be made. There are about 10^{13} cells in our body, and during our lifetime about 10^{16} cell divisions. Even if mistakes in copying our genetic material, DNA, are extremely rare, said Prof Noel Lowndes from the Centre for Chromosome Biology at the National University Ireland, Galway, our bodies are replacing tens of millions of cells every day. It is amazing, he said, that in spite of the huge potential to make mistakes, that so few errors actually occur. Even so, mistakes do happen, so, strictly speaking, there is no such thing as a true clone.

The main reason why we are not overwhelmed by an accumulation of errors, he explained, is that the body is not only extremely good at copying DNA but also at making running repairs. Prof Lowndes and his research group are particularly interested in how potentially lethal mistakes in DNA are detected and corrected when they occur.

Cancer

"Errors," he said, "are a lot more frequent than most of us realise, but the cell has evolved a remarkable array of strategies capable of fixing quite serious problems." Those tools are very important to us because when they fail, cells can go out of control and we get cancer.

A lot of cancer research concentrates on killing off the tumours, but in one way this is like shutting the stable door after the horse has bolted. Making sure that the natural repair systems are working at full efficiency has the potential to prevent or at least delay cancer.

Prof Lowndes believes that this deeper understanding is essential if we are to defeat cancer. "Clinical research," he said, "is mainly based on the application of prior knowledge to patients, so it can only do so much. Besides, most current interventions are based on basic research that might already be 20 years old."

Just how good those tools are for repairing damaged DNA is illustrated by our reaction to something like the ultra violet rays from sunlight. The repair system recognises the damage, and cleaves out a chunk that might be 30 nucleotides in length. Then, using the matching strand as a template, a perfect copy is made and spliced back in to the gap. There are many different types of damage, and just as many tools. "One of the most dangerous types of damage," said Prof Lowndes, "is when both strands of DNA are broken. There are two fantastic mechanisms that can repair this damage but even so, these occasionally fail, and those loose ends can be very dangerous as they are capable of fusing with other parts of the genome, sometime causing cancer."

Stem Cells

Cancers, explained Prof Lowndes, originate in stem cells rather than in differentiated tissue, and this has huge implications for targeting of treatment. Once cells have differentiated, he said, they are unlikely to cause problems, but every group of differentiated cells has the support of a much smaller underlying stem cell population. "It is from these stem cell populations," he said, "that cancers come, and a big problem is that they can keep on coming." A tumour might be killed off only for the cancer to reappear again because there are some stem cells somewhere that are no longer obeying the rules.

The surprising thing is that tumours survive at all. The cells in tumours are out of control, starved of oxygen and nutrients, and without replenishment, he argues, a tumour would eventually die.

"The repair mechanisms," he said, "work extremely well, but eventually the sheer number of divisions stacks the odds against us." Errors slip through and accumulate, and this is why cancer is almost, but not quite exclusively, a disease of middle and old age. The median age for people getting cancer is 65 to 70, and as Prof Lowndes observed ironically, it's actually a sign of success. We are living long enough for the mistakes to overwhelm the repair processes. "In humans," he said, "there are at least six types of genes involved in mechanisms that prevent cancer developing. In mice, which seldom live longer than a year and a half, there are just two."

» After studying genetics at Trinity College Dublin, Prof Lowndes received his PhD from University of Glasgow before working as a post-doctoral researcher at the National Institute for Medical Research, London, and then as a Principal Investigator at the Cell Division Cycle Laboratory of Cancer Research UK.

» He was appointed Professor of Biochemistry at National University of Ireland Galway in 2001, and he is one of just four Irish-based scientists to have been elected to the European Molecular Biology Organisation.

» Prof Lowndes heads the Centre for Chromosome Biology, a group composed of ten independent laboratories, most of them funded by SFI at Principal investigator level. His laboratory consists of one senior researcher, three postdocs, one technician and eight PhD students.

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Researcher Prof Douglas Leith

Title *Finding solutions to wireless 'bottlenecks'*

Case Study

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Our homes of the future are likely to be wireless, if technology roadmaps are correct. The phone, TV and internet, and all the services that go with them, will be provided wirelessly. But, before that can happen there are at least two technological bottlenecks that must be overcome, in the area of bandwidth and signal interference. A race is on worldwide to solve these problems, and Prof Douglas Leith, director of the Hamilton Institute, located on the campus of NUI Maynooth, believes his research team is well placed to beat all competition.

The Hamilton Institute is a purely research institute, set up in 2001. It was funded by SFI with the goal of focussing on doing good mathematics and using this to solve important problems. The focus normally at institutes and universities around the world is either on pursuing good mathematics or developing good applications. Hamilton stands on both pillars.

Out of nothing, it has grown over seven years to be home to 50 researchers, and nine full-time faculty members, with a growing international reputation in many areas.

Networking

Prof Leith's own area of research is in networking. Most people today using the internet have wireless antennae attached to their DSL modem. This is standard now. The reason that this technology became ubiquitous so quickly is that it is cheap and simple to use, but the downside, said Prof Leith, is that people have started to use it for applications that it wasn't designed for.

An example of this is where Skype, or other software, is being used for making very cheap, if not free, phone calls over the internet. The signal to make the Skype call is via the wireless Internet, which means the phone call is transmitted by a radio signal. However, the problem is that this is a lot less reliable than traditional phone cabling and this can create problems in terms of transmission delays and break up of signals.

The Skype call is transmitted from caller to caller, through the air to a DSL modem situated somewhere in the home, and then over the Internet. If the distance between the phone and the modem is too great, it could cause reception problems. Further, if there are other wireless services being used in the house this could also be a problem.

Future

In coming years, it is likely that TV is going to be provided over the Internet, down the DSL phone line – competing with satellite and cable TV providers. The way it will work best is for TV signals to come into the house via the phone line. Once inside it will be distributed to a number of wireless access points, where the signal will then be sent to the TV.

For most homes today, the wireless access points – where a device will be plugged in – would correspond to the existing phone points. These phone points might be in the hallway, for example, and upstairs in one bedroom, and far from where the family wish to view the TV – the downstairs living room, for example. This is a problem, given that bandwidth drops with distance. The further a TV set is from a wireless access point, the weaker the signal is, and TV needs a lot of bandwidth to work.

The only choice for prospective DSL TV customers at this stage is to re-wire the house, and insert new wireless access points where they are needed, close to the TV, or TVs. The practical issue here is that this is expensive, and creates a lot of hassle too, so it would seem unlikely that many people would chose to go down this route.

A wireless solution is required, and this is the area that Prof Leith works in.

Roadmap

The telecommunication industry technology roadmap in this area envisages lots of 'plug-sized' wireless access points around the house, one in each room at least, as well as an Internet connection. This kind of set up would ensure that bandwidth is sufficient throughout the home and no matter where TVs are, reception would be good.

But, it is not all about bandwidth. The other significant technical issue in this 'space' is interference. With so much wireless being used in the future, there is a potential problem of wireless services interfering with each other in each house, and with services in next door neighbours' houses. There is only a certain amount of radio spectrum available, and this must be managed very well to have space for everyone.

This is a huge issue in the wireless services area, and it's a problem not yet solved.

The situation is totally different than the traditional 'wired' house. In the latter, if a person wants an extra connection for some reason, a wire is run to provide that connection, for whatever purpose, and there is no interference with other wires. Also, as many wires can be run as the householder wants, and it won't affect other wires.

With wireless, if there is an extra wireless access point added somewhere in the home – say in a bedroom to allow a student to have Internet and DSL TV services – this could, if not properly managed, interfere with other wireless services in the house.

The wireless signals are transmitted through the air and signals interact with each other.

Solution

The solution that will provide for better management of wireless services, and ensure consistency of quality of those services will ultimately come from algorhythms. This involves the use of mathematics to solve a problem, in a step-by-step fashion.

Prof Leith believes the Institute has the capability of being first to solve the wireless technological 'bottlenecks' of bandwidth and interference, because of the combination of skills that reside 'in-house'. The presence of mathematicians and people focused on the applied side makes for a strong and unique research team.

There are teams working all over the world on solving these bottlenecks, as they are 'hot topics' in communication, but Ireland, represented by the Institute have a real chance of winning this technological race. "I think the thing that gives us an edge in competing is this combination of these really strong mathematical skills, and down in the trenches applied skills – it's very rare to get that combination," said Prof Leith.

» Prof Leith achieved his undergraduate degree and PhD at the University of Glasgow, in his native Scotland. He followed this up with post-doc work at the University of Strathclyde, where he went on to become a senior lecturer in the Department of Electronic and Electrical Engineering. He is a Royal Society Research Fellow.

» He founded the Hamilton Institute, which is based at NUI Maynooth, in 2001 with his colleague Prof Robert Shorten. This is a multi-disciplinary research institute that seeks to use mathematics to solve a number of 'real world' problems. The Institute has 50 researchers, with nine full time members of staff. It has collaborations with Intel Communications Europe, Cisco Systems, Eircom, DaimlerChrysler and Nokia.

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