

When does more
give less in the
olfactory system?

Q&A: *PN* speaks
to Dr Kevin Fong

Making the first
leap into public
engagement

The Biomedical Basis of Elite Performance

News from the event announcing the
winners of our schools competition,
The Science of Sport: How to Win Gold.



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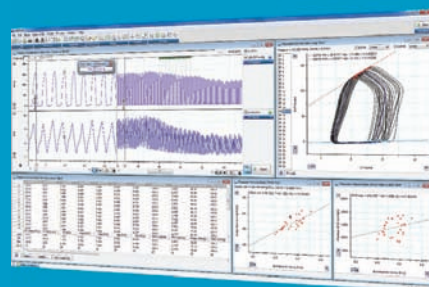
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© 2012 The Physiological Society
ISSN 1476-7996 (Print) ISSN 2041-6512 (Online)
The Physiological Society is registered in England as a
company limited by guarantee: No 323575.
Registered office: Peer House, Verulam Street, London WC1X 8LZ
Registered Charity: No 211585.

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A photograph of Edinburgh Castle, a large stone fortress, perched on a rocky hill. The castle features multiple towers, battlements, and a prominent cylindrical bastion on the right side. The entire image is overlaid with a semi-transparent blue filter. The text is positioned in the upper right corner.

Physiology 2012

2-5 July
Edinburgh International
Conference Centre
United Kingdom

Key dates

Apply for a travel grant by 31 May 2012

Reduced rate registration closes 1 June 2012

Prize lecturers

Cori Bargmann – Rockefeller University, New York, USA

Gareth Leng – University of Edinburgh, UK

Diane Lipscombe – Brown University, Providence, USA

Jere Mitchell – UT Southwestern Medical Center, Dallas, USA

Peter Ratcliffe – University of Oxford, UK

Holly Shiels – University of Manchester, UK

www.physiology2012.org

Welcome to the new-look *Physiology News*. I am delighted to be taking over Editorship of a magazine that has established itself as a valued, authoritative and highly readable publication among the membership, and hope you enjoy reading this spring issue.

Written by
Mike Collis

The diverse content of *Physiology News* is testament to the hard work, dedication and high standards of the previous Editor, Austin Elliott and his editorial board. I see my role and that of the new editorial board to build on this solid platform of success.

In taking on the role of Editor I also feel that it is my responsibility to challenge assumptions and question the status quo. What can a quarterly magazine add and what will make Members of The Society want to read it? If a magazine such as *Physiology News* is to prosper in today's world of information overload, it must complement other, more immediate forms of communication and add a distinctive value of its own. As one of the new editorial board succinctly put it 'Why should I pick up *Physiology News* to read when I have a pile of scientific papers to plough through?'

The refreshed magazine has kept the best of old style publication, with additional features. Views and comment articles will reflect the controversy and disagreements that are part and parcel of scientific debate; The magazine will also address the long term strategic issues – such as what The Society should be doing in the next decade to support its Members, and what the big questions are in Physiology? As well as drawing on expert articles and opinion from the wider community on issues relevant to physiology. Most importantly, we will continue to recognise the human nature of physiologists; reporting on Members' involvement in the usual variety of Society activities as well as the innovative individuals who have dedicated themselves to understanding how biological systems work and the underlying stories behind great discoveries.



Features: Opinion

Accreditation – will it make a difference without increased funding?

Written by Mike Collis

What's your view?

What are your views on accreditation? Please send them to editor@physiologynews.org or via our online survey at www.physiologynews.org/survey

Many of you will know that the Society of Biology is running a pilot scheme to accredit its courses in the UK. The Physiological Society has been working with the Society of Biology specifically on the accreditation of degrees that have a significant to do with research component. The aim of any accreditation system must be to set high standards, so that those undertaking the course in question receive a training that equips them for their future careers and makes them attractive recruits for both industrial and academic employers.

A key feature of the Society of Biology accreditation scheme is that the student has a significant (minimum of 6 months) 'hands on' exposure to laboratory research.

To what needs to change to allow the UK to have courses that provide the in vivo experience that would meet the criteria for accreditation? As with most things, it all comes down to money. Courses that involve a significant time in the laboratory are expensive to run. This is particularly the case when the laboratory work is done by the student. The added costs of personal protective equipment for the students, the costs of housing equipment staff providing close supervision and the costs of animals and animal facilities all make course involving in vivo work expensive. In fact, they cost more than most academic institutions are willing to pay without additional financial support that has come to receive a pretty thin flow these days.

The emphasis of accreditation on practical laboratory experience is in response to the concerns expressed by many employers that today's graduates are not ready to work in a research lab and in fact require training in even the most basic of techniques. The current lack of practical laboratory experience in the new graduate is probably also one reason why the standard PhD is now taking 4 rather than 3 years.

But when we see the PhD courses that can offer this type of practical experience without many industrial sponsors can guarantee an in vivo placement for students? The answer is very few. Of only two MPhil courses both of these are primarily for research and involve an industrial placement – which is not guaranteed to be in vivo. There are a few excellent academic institutions that offer a small number of students the opportunity to experience some in vivo research, but they cannot offer the kind of exposure required for accreditation. Sometimes something changes, there will be no course that can guarantee to provide the in vivo skills required for accreditation within the Society of Biology framework. I don't think this is a desirable situation and an additional concern is that the scenario will not help the few courses that do provide some limited in vivo experience to matter support from their institutions, particularly in a time of reduced budgetary input.

Currently, the majority of students will only get the practical training envisaged by the accreditation system if they take a further degree such as an MSc or MPhil. The Society of Biology has not excluded higher degrees in its accreditation framework, probably because of concerns that the quality of the first degree cannot be guaranteed. It will be interesting to see if this position changes and accreditation is extended to post-graduate courses. On the one hand, it would recognise the value of some of the excellent post-graduate courses that are available and would help students select them and consequently enhance their career prospects. On the other, such an extension of the boundaries of accreditation could not necessarily facilitate extra funding for MPhil courses and could be seen as an endorsement of the status quo rather than a lever to improve standards and stimulate new courses. Potentially, the MPhil is not regarded as equivalent to a Masters degree in the Bologna Accord, as the next academic year of the MPhil does not provide an equivalent number of credits. In fact, there is anecdotal evidence that a number of universities on the continent refuse entry to PhDs to students with the MPhil. The response students who wish to attend these courses to take an additional Masters, which is at odds with one of the key aims of accreditation is to produce 'research-ready' graduates.

What is clear is that accreditation has to be linked to enhanced funding if it is to achieve its aim of improving the standards of its courses, particularly those involving in vivo research. The Society of Biology and its member organisations (such as the British Ecological Society and the British Pharmacological Society) are supporting an MPhil in Integrated Pharmacology and Physiology for Research at

'Hands on'

A key feature of the Society of Biology accreditation scheme is that the student has a significant (minimum of 6 months) 'hands on' exposure to laboratory research

Physiology News / April 2012 / Issue 68

There is clearly an important role for the magazine, which differs from the more immediate and data heavy forms of electronic communication now available. However, this doesn't mean that the magazine should not evolve and move with the times. I hope that during my tenure as Editor we will continue to integrate the magazine with other aspects of The Society's communication, particularly the website. *Physiology News* has tended to be predominantly inward looking, focussing on the world of the academic physiologists – not unreasonably, as they are the majority of our membership. However, in its new incarnation, the magazine will broaden its content to reflect The Society's work with external organisations and groups that are important to us as

Physiologists, such as the major research funders and the science teachers in schools who are nurturing the discipline's next generation. I am lucky to have an editorial board who are at different stages in their scientific careers with a diverse set of interests and experiences (their bios can be found in the News Section) and as a team, we will work hard to deliver a vibrant, readable and informative magazine.

Finally, *Physiology News* is your magazine and I encourage you to contribute to its pages. As Editor, I see my role as encouraging diversity, debate and ensuring the views of the membership are reflected in the magazine your input – as always – is incredibly valuable to achieve this.

“My research is driven both by curiosity but also my clinical background — the work explores important things we don’t understand but which we know must be going wrong in disease. I have always regarded *The Journal of Physiology* as the primary place to publish such work — even if the manuscript is rejected, I hope to get some insightful comments.”

Simon Gandevia

Undergraduates invited to present at The Society Main Meeting

For the first time we are inviting students to present their undergraduate physiology research project as a poster at Physiology 2012. The Rob Clarke Undergraduate Abstract and Presentation Awards, named in honour of the late Dr Rob Clarke, will be awarded for the best abstracts and posters presented. Louise Robson, Chair of The Society’s Education and Outreach Committee, commented “I am thrilled that we now provide undergraduates with the opportunity to not only attend The Physiological Society’s Main Meeting, but to also present their research. I am really looking forward to talking to the students and would strongly encourage all our Meeting visitors to pop along and talk to them too. After all, they are the next generation of Physiologists.”

All successful students will receive one year’s free membership of The Society and eligibility to apply for £200 to support attendance at the Meeting. Application information can be found on The Society’s website under the Education and Resources tab. Alternatively, you can email education@physoc.org.

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“I am thrilled that we now provide undergraduates with the opportunity to not only attend The Physiological Society’s Main Meeting, but to also present their research.”

Louise Robson
Chair of The Education and Outreach Committee

Aussie scores a century!

‘My research is driven both by curiosity but also my clinical background – the work explores important things we don’t understand but which we know must be going wrong in disease. I have always regarded *The Journal of Physiology* as the primary place to publish such work – even if the manuscript is rejected, I hope to get some insightful comments.’ Simon Gandevia

In 1976, Simon C. Gandevia and D. I. McCloskey published a paper in *The Journal of Physiology* on Joint sense, muscle sense, and their combination as position sense, measured at the distal interphalangeal joint of the middle finger (*J Physiol* 260, 387–407). This was the first of a long series of papers in which Simon, in collaboration with a succession of co-researchers, investigated

questions about how our proprioceptive senses contribute to control movements and postural adjustments, how the brain drives the motoneurons and muscles, particularly under circumstances when the muscle’s performance changes, such as during fatigue, and how human breathing is controlled. In December last year Simon published his 103rd paper in *J Physiol* on Dynamic changes in the perceived posture of the hand during ischaemic anaesthesia of the arm (*J Physiol* 589, 5775–5784). This remarkable record of fundamental research into human neuromotor control over more than 35 years is celebrated on *The Journal of Physiology*’s Century Citation Club web page (<http://jp.physoc.org/site/misc/century.xhtml>). We wonder how many other physiologists can claim a similar achievement.

How much does your MP know about scientific research?

The answer – maybe not much; however, The Society is hoping to change this by increasing the interaction between researchers and parliamentarians through its new MP-engagement scheme.

One of the most pressing policy issues requiring our collaboration with MPs is the transposition of EU Directive 2010/63/EU (on ‘the protection of animals used for scientific purposes’) into UK Law. It is a crucial time for scientists to engage with their MPs to explain their work, the importance of science and the need to ensure harmonisation of legislation across Europe. As a result,

the first phase of The Society’s MP-engagement scheme is focusing on increasing awareness of the issues surrounding scientific research using animals. Working with Understanding Animal Research, the scheme will cover the substantial benefits such work has upon the UK public; whether it is fundamental research, or for eventual medical or veterinary benefit. We are here to support Society Members to raise these issues with their MP so if you would like to get involved, please contact The Society’s Policy Manager, Michelle Brook on policy@physoc.org or see <http://www.physoc.org/mp-engagement-scheme> for further information.

Research Excellence Framework update

At the end of January 2012, the Higher Education Funding Council for England (HEFCE) released a long-awaited document entitled Panel Criteria and Working Methods. Whilst not sounding enticing, this missive finalises the assessment criteria and working methods of the four main panels for the 2014 Research Excellence Framework (REF), which oversee 36 sub-panels.

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...defined reductions in the number of required submissions from researchers (both female and male) taking parental leave, and the ability for institutions to submit a 'reserve' output, to be assessed if a sub-panel refuses the request from an institution to give double weighting to a specific output.

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Panel Criteria and Working Methods was produced in the latter half of 2011 following a lengthy consultation (to which The Society responded) on proposed draft criteria. The amendments include a number of clarifications and improvements on previous guidelines, including defined reductions in the number of required submissions from researchers (both female and male) taking parental leave, and the ability for institutions to submit a 'reserve' output, to be assessed if a sub-panel refuses the request from an institution to give double weighting to a specific output.

Other statements of interest include the fact (emphasised by its inclusion not only in the general criteria, but also in statements in every panel criteria), that 'No sub-panel will make use of journal impact factors, rankings or lists, or the perceived standing of publishers in assessing quality of research outputs' – something of significance, considering many institutions appear to have policies dictating that research must be published in journals with certain impact factors!

The Society will be producing a statement about REF in the near future to ensure Members are informed about the contents and implications of Panel Criteria and Working Methods and other documentation relating to REF – please check The Society website for updates.

Recognising the next generation of physiologists

The Society places great importance on recognising the work of undergraduates and encouraging them to pursue a career in the discipline. In addition to the Rob Clarke Undergraduate Abstract Presentation Awards (see news item on previous page), The Undergraduate Prize for Physiology recognises outstanding final-year physiology students. Forty-five prizes were awarded to undergraduates at the end of 2011, who each received £100 and a year's free membership to The Society. A full list of the winners can be found on The Society website (www.physoc.org) as can more information on the prize scheme, which will run again in 2012. A call for nominations for students across the UK and abroad will open later in the year.

What do you get if you cross a physiologist with a comedy night?



Mark Kerrigan pondering how many cow's knees you can get in a mini.

The answer is Bright Club: Bodies. On a chilly February night three Society Members and a member of the Phys Soc office team took to the stage to joke about their research and experiences as scientists. The audience was far from cold, however, giving all the scientists turned-stand-up comics a very warm reception.

The sold-out event was supported by The Society and took place as part of Brighton Science Festival. Lewis Dean, Higher Education Officer at The Society and evolutionary biologist; Nicole Slavin, undergraduate Member (University of Westminster); Mark Kerrigan, the Society Rep at the University of Greenwich; and David McAlpine, auditory neuroscientist at UCL each took to the stage with aplomb. Mark made cows' knees hilarious (rather than slightly disgusting) and Nicole wowed the audience with her wonderful, operatic voice.

Bright Club is an award-winning public engagement project that was set up by the UCL Public Engagement Unit and One Green Firework comedy agency in 2008. It aims to break down barriers between universities and the public, raise awareness and change perceptions of science and scientists through laughter and entertainment. As part of The Society's commitment to public engagement it is supporting four Bright Club: Bodies evenings in 2012; these are at Edinburgh in April, Cardiff in July and Manchester in October.

If you think you can talk about the lighter side of your research, for example, any humorous anecdotes about the time you discovered you can fit precisely 21 cows' legs into a Mini, please get in touch with our Outreach Manager, Louise Crane (outreach@physoc.org), to have your moment in the limelight.



Northgate High School wins gold

We are delighted to announce the winners of our schools competition, The Science of Sport: How to Win Gold. The gold medal prize went to Northgate High School in Suffolk for their poster 'The effect of video imagery on sports performance'. Joint silver went to Danny Foster at Moulton College in Northamptonshire, and Harriet O'Connor at Ringwood High School in Hampshire, and Bronze went to Sophie Sibley of South Wilts Grammar School.

The competition was designed for A-Level students to complete a 30-hour sports physiology project and present their findings to The Society. Judging took place at our scientific Meeting, *The Biomedical Basis of Elite Performance*, in London on 20 March. Lead judge, Valerie Gladwell, said: "This was an inspirational competition. My fellow judges and I were blown away by the quality of the ideas and the students' presentations. They were able to express their scientific

understanding not only to the judges, but also to the eminent scientists that visited their stands. I would like to congratulate the winners as well as thank all those who were involved in the competition in some way; namely, the teachers of the participating students, the scientists who mentored the students."

At the presentation ceremony, each of the winners received a medal and certificate as well as prizes for themselves and their school. Northgate High School landed a Train Like a Champion Day at an English Institute of Sport High Performance Centre, with various other prizes awarded to the medal-winning teams (full details are available at www.understanding-life.org).

The Society would like to extend its thanks to Valerie, for her invaluable contribution to the development and success of this competition, as well as the judges and the mentors who gave up their time for the competition.



Gold, silver and bronze medal winners of the Science of Sport: How to win gold

Designer Athletes debate

To coincide with *The Biological Basis of Elite Performance* meeting and The Cambridge Science Festival, The Society ran two public events, which explored enhancement in sports for a non-science audience.

Former England cricketer Ed Smith chaired the London event, which was fittingly held at The Oval, and New Scientist's Linda Geddes chaired the Cambridge panel of experts. Both events generated a fascinating and lively discussion.

In London, panel member Cristiana Velloso gave an insight into the development of gene-doping in mice and how this might one day be applied to humans. Maria Kavussano, expert in morality of sports, explained why athletes cheat, and Steve Ingham, Head of Physiology at the English Institute of Sport, provided a perspective on what might be perceived as "natural" doping – training athletes in such a way that their physiology is enhanced in a similar way to the effects of illegal substances. Ron Maughan's encyclopaedic knowledge about drug-dopers and sports nutrition complemented the panel by posing fascinating questions about where the line between natural dietary enhancement and doping is drawn.

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"Should coaches and medical professionals be punished if their athletes are caught cheating?"

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The following evening, Steve Ingham journeyed to Cambridge to continue the discussion with Steve Haake, a sports technology expert, and Chris Cooper, who further explored drug doping. Both events had a large element of audience discussion, with some fascinating questions such as, "Should coaches and medical professionals be punished if their athletes are caught cheating?"

The Designer Athletes event will be held at the Edinburgh International Science Festival on Thursday 5 April and Glasgow Science Festival in June. A podcast capturing the discussion will be available on The Society website in due course.

Meeting notes

Vascular & Smooth Muscle
Physiology themed meeting



When the call for a Vascular and Smooth Muscle Themed Meeting was circulated, it seemed a great opportunity to propose a symposium based on the idea that processes as diverse as contraction, migration and gene expression without membrane–membrane junctions providing for segregated calcium signalling. The proposal was accepted and The Physiological Society's Events Team seamlessly engaged and delivered what proved to be a very successful programme of events.

The symposium, which took place at the University of Edinburgh on 6–8 December 2011, began with Casey van Breemen who introduced the concept with the first identified cellular nanospace, the 'sarcoplasmic reticulum' – 'plasma membrane' junction. I provided supporting evidence for this and the concept of lysosome–sarcoplasmic reticulum junctions within a segregated cytoplasmic space calcium-dependent contraction. Mike Zhu added the Two-Pore Segment Channels, David Beech the TRP channels and Ian Parker the IP3 receptors. Nicola Fameli then blinded everybody with mathematical 'proof' that only nanospaces, and not microdomains, could support compartmentalised calcium signalling.

Graeme Nixon then escorted us through the plasticity of proliferating smooth muscle cells, ably assisted by John McCarron, Maria Gomez and Teresa Perez-Garcia. Casey then rounded things off with an integrated model of nanojunctions within smooth muscle – Martin Bootman suggested that "...smooth muscle may be more complicated than cardiac muscle..."

The oral and poster presentations were of the highest standard and added to what was a vibrant meeting. The prize winners were as follows:

Oral Communication Competition

Winner: Junxi Wu

University of Strathclyde

Runner up: Thomas Jepps

St George's University of London

Poster Competition

Winner: Lynn McKeown

University of Leeds

Runner up: Oluseye Ogunbayo

University of Edinburgh

New editors join the Society journals

Experimental Physiology



Joseph Bruton

Joseph Bruton obtained his PhD on malignant hyperthermia at Trinity College Dublin in 1985.

Following a spell studying shoulder pain in stroke patients, he switched to research on striated muscle using rodent models. Much of his research has focused on warm-up and muscle fatigue. Currently he is investigating the adaptations in muscle to a range of muscle diseases.



Ulf Simonsen

Ulf Simonsen is Professor of Pharmacology at the Department of Biomedicine, Aarhus University, Denmark.

He obtained a medical degree from Aarhus University and a PhD on cholinergic and endothelial regulation of coronary resistance circulation from the Universidad Complutense, Madrid, Spain in 1994. His research focuses on developing novel pharmacological approaches to improve endothelial function in cardiovascular disease. Endothelial dysfunction plays an important role in the development of pulmonary hypertension, which affects survival in patients with chronic obstructive pulmonary disease and interstitial lung disease. The aim is to target signal pathways in the lungs and heart involved in the pathophysiology of these diseases. Another focus is to improve endothelial and erectile function in patients with diabetes.

The Journal of Physiology



Peiyong Fong

Peiyong Fong earned baccalaureate and PhD degrees from Yale University and the University of

California, San Francisco, respectively. After postdoctoral studies at the University of California, Berkeley, she expanded her repertoire as a Long Term Scholar of the Human Frontiers Program Organization, working at the Center for Molecular Neurobiology, Hamburg. Peiyong has integrated structure–function analysis into many aspects of her research, which is broadly directed at understanding epithelial ion transport in health and in genetic and acquired diseases. Currently Assistant Professor at Kansas State University, Peiyong focuses primarily on functional interactions between ionic channels and transporters in thyroid epithelium.



Louise Robson

Louise Robson is a senior lecturer in Biomedical Science at the University of Sheffield, moving from Leeds where she obtained

her PhD and completed postdoctoral research in renal physiology. Louise's current research looks at the processes that regulate CFTR, the Cl⁻ channel mutated in cystic fibrosis. She has chaired the Education and Outreach Committee at The Society since 2008, and sat on Council and the Executive Committee. She teaches a wide range of physiology topics at Sheffield, across all levels, and is also passionate about taking physiology out to the public, lecturing for the Royal Institution and during National Science Week.



Derek Bowie

Derek Bowie studied at Strathclyde University in Scotland before completing a PhD in Neuropharmacology at

the University of London. He then spent two years as an Eli-Lilly postdoctoral fellow at the Universities of Strasbourg and Zurich before moving to the USA for eight years to work at the National Institutes of Health and Emory University. He is currently a tenured Professor at McGill University and recipient of the Canada Research Chair award in Receptor Pharmacology. His research focuses on understanding the role of glutamate and GABA-A receptors in neuronal circuits.

Making your first leap into public engagement

Written by

Emily Robinson

Whether it is called public engagement or science communication, funding bodies and universities alike are requiring researchers to engage the public with their work more and more these days. These interactions with the public aim to humanise research and to increase public understanding of the scientific method – and the whole process is also extremely rewarding for the researchers involved. However, as a researcher how do you start engaging this elusive ‘public’?

I am a final year neuroscience PhD student in the Brain Inflammation Group (BIG) at the University of Manchester. The focus of my PhD is to investigate the mechanisms of action of the pro-inflammatory cytokine interleukin-1 in acute brain injury – or in terms that I might use when talking to the general public is ‘to look at how our immune system can often cause brain injuries to become worse’. Throughout my PhD I have become heavily involved in organising and taking part in numerous public engagement projects. The wide range of activities, audiences and delivery methods I have used to do this highly impressed the judges at the Society of Biology and led them to name me the New Researcher Science Communication Award winner 2011.

We all want to make a huge impact with our science and we may have the same aspirations about public engagement, but just as we have learnt from experiments – we may need to start small and wait for some preliminary results before we can claim to have changed the world! I am not dissuading people from thinking big, but

“We may need to start small and wait for some preliminary results before we can claim to have changed the world!”

Emily Robinson

if you are new to public engagement organising your first event on your own can seem very daunting. It is also worth remembering that there is no benefit from an idea that never becomes reality. Therefore, initially you may want to find some support to help you get your event off the ground.

The first event I organised was called ‘Meet the Neuroscientist’ at the Manchester Museum of Science and Industry (MOSI). This was part of a family-orientated programme of day activities held monthly to allow the public to meet different researchers. I successfully applied for an Outreach grant from The Physiological Society and I was also in contact with a very supportive science communication officer at the museum. With this help and funding I was able to create the type of event I had envisaged, which would have been impossible to achieve on my own.

I wanted to show that neuroscience is all around us in our everyday lives. To demonstrate this I provided simple hands-on activities based around the brain and the senses. To explore the content of my own research I set up a brain

injury case study area, which displayed anatomical models and information about stroke, to illustrate what can happen when the brain is damaged. A group of my colleagues kindly helped out to give simple, yet scientific, explanations for all the activities and they were also on hand to talk through their research.

With an estimated one thousand visitors interacting with the activities I felt that my first event had been a real success. Brilliant feedback left on our ‘Comments Carpet’ said: “I thought the experiments were awesome” and “Erie is now a norosintist [sic]”. I also received feedback praising the event for catering for “all the members of the family” regardless of age or their knowledge of science.

On a personal level, the most profound part of the day came from a conversation I had with a visitor recovering from a haemorrhagic stroke. Talking to this lady made me realise the importance of conveying how cutting-edge research is trying to reduce the devastating effects of brain disorders such as stroke. I have since then been involved in events aimed at explaining our research to stroke patients. Therefore this experience was not only very enjoyable and rewarding, but it also influenced how I approached future outreach projects and contributed to me being recognised for my science communication work. So sometimes the first few tentative steps can be the start of an important journey.





Report: Young Life Scientists Ireland Symposium

Written by
Keith Siew

Affiliate Representative, Keith Siew reports his experiences of organising a YLS symposium.

Although well over a year and half ago it seems like only yesterday that I and my co-chair, Naadiya Carrim, were strolling home from a class get together at the Trinity College Dublin science gallery. It was there that we had the then seemingly crazy idea of running our own symposium dedicated to the often overlooked young scientific community of Ireland. Fresh out of our undergraduate degrees we had already attended numerous YPS meetings but we found ourselves part of an audience that was without a communal forum or outlet on our own shores for peers to meet, present work and share in our passion for science. With this need in mind we set out with the help of many a friend drawn from a plethora of peers, academics, societies and industry partners across multiple disciplines to form the inaugural meeting of the Young Life Scientists' Ireland (YLSI) Symposium.

The objective of our meeting was to unite the life science disciplines under a single banner to promote an ethos of integrative and collaborative research in the young scientists of tomorrow's community with the hope of building bridges and stimulating new ways of thinking. Our intervarsity organising committee was representative of the diversity in Irish Life Sciences, drawn from postgraduates and undergraduates across the country both North and South of the border, with a range of backgrounds in physiology, biochemistry, genetics, microbiology, neuroscience and pharmacology.

YLSI took place on the 12 November 2011 at University College Dublin, attended by over 110 scientists from Ireland and abroad, presenting over 24 oral communications run in six parallel themed sessions and well over 50 poster communications in a keenly contested moderated poster session. The symposium also offered attendees the opportunity to part-take in a range of interactive workshops, giving tasters of novel techniques in imaging, insider insights into how to write successful grant applications or debating the hot topic of bioethics. However, it was the motivation and inspirational keynote speakers who were the highlight of YLSI.

Jennifer Mitchell from University College Dublin, a scientist who has conquered so much in such a short time, truly set the tone in the morning, inspiring us all to follow in her footsteps with her exceptional work on 'The role of CD36 as a platelet receptor for Gram-positive pathogens'. Our other guest speaker, Prem Kumar from University of Birmingham, taught us all to not judge a book (or in this case a journal) by its cover, with an equally inspiring talk on 'Fact and artefact in chemoreceptor physiology: can everyone, or even anyone, be right?'. Prem not only reminded us why we entered careers in science but, indeed, motivated us to continue research with his passionate and very motivating talk.

Finally, with thank you speeches given, many well-deserved prizes awarded and the scientific festivities truly concluded for the day, we topped off our symposium with a wine reception where everyone could mingle and discuss the day's events with one another, keynote speakers, guest lecturers and industry partner alike.

On behalf of all the committee we wish to extend our sincere thanks and appreciation to all our sponsors, universities and societies – especially The Physiological Society – for their support and advice, and of course all the attendees that made YLSI 2011 possible.



Walking around an animal facility and talking with scientific staff, gave science teachers a much greater insight into both why and how animals are kept and cared for.

Teachers find out how and why animals are used in research

Last summer, a group of science teachers met in York to produce ideas for explaining why and how animals are used in research. The two-day session included a trip around the University of York's animal house – the first time that most of the teachers had ever been in an animal facility.

The result was a group of resources aimed at Key stage 3–4, which you can now find on our School Zone website: www.understandinganimalresearch.org.uk/schoolzone.

In School Zone, we have an area for teachers and an area for students. The teachers' zone provides downloadable lesson-planning resources, such as The war against malaria and Animals in space, matched to the curriculum. We also cross-link to relevant materials on our main website.

The student area has a series of interactive activities of the drag-and-drop and matching variety as well as a quiz that gets over some of the main points around the use of animals in research.

We explain the vital role of animals in making medicines, talk about what animals are used and why, and go through one exercise – Rights and wrongs – that takes students through some of

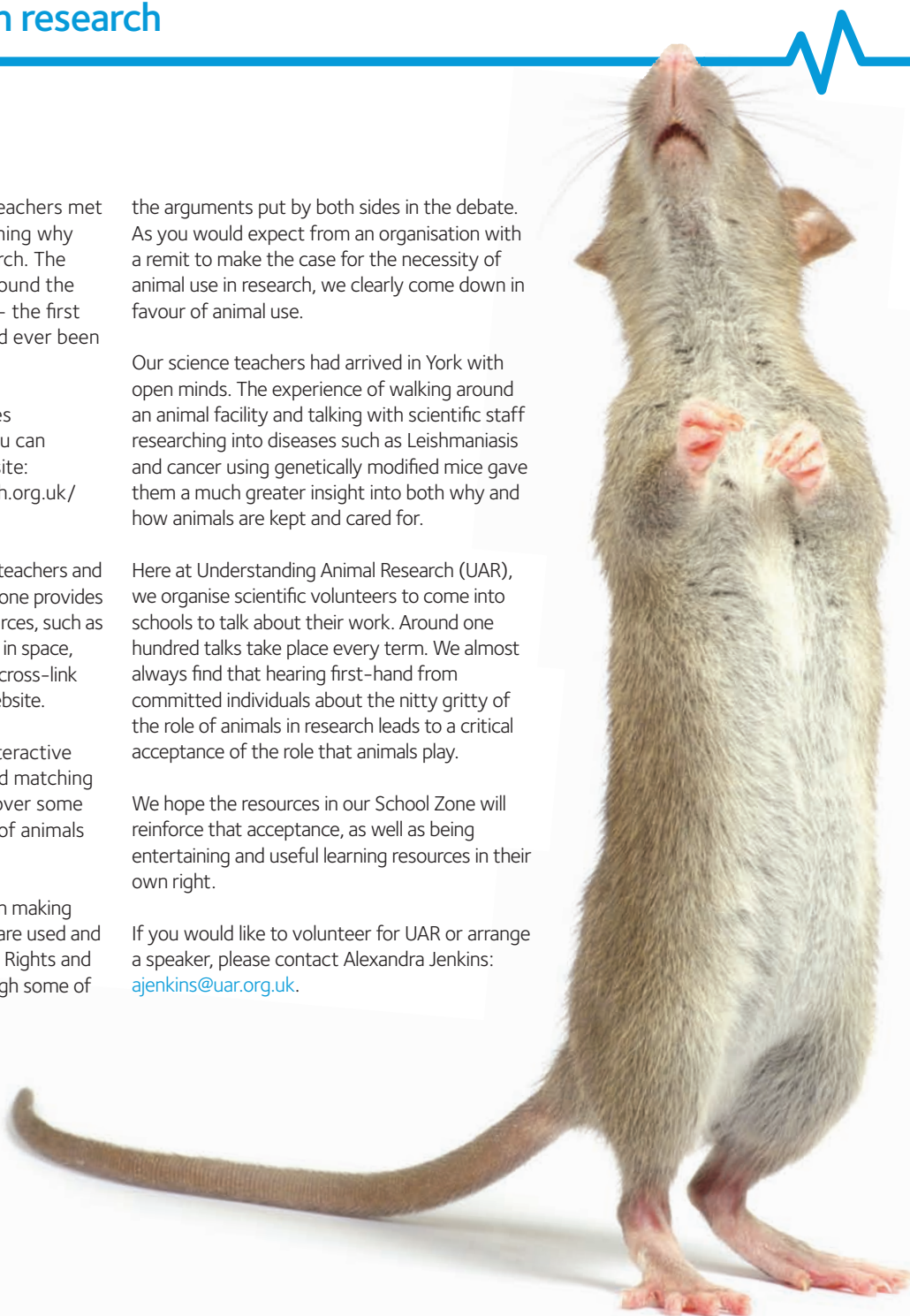
the arguments put by both sides in the debate. As you would expect from an organisation with a remit to make the case for the necessity of animal use in research, we clearly come down in favour of animal use.

Our science teachers had arrived in York with open minds. The experience of walking around an animal facility and talking with scientific staff researching into diseases such as Leishmaniasis and cancer using genetically modified mice gave them a much greater insight into both why and how animals are kept and cared for.

Here at Understanding Animal Research (UAR), we organise scientific volunteers to come into schools to talk about their work. Around one hundred talks take place every term. We almost always find that hearing first-hand from committed individuals about the nitty gritty of the role of animals in research leads to a critical acceptance of the role that animals play.

We hope the resources in our School Zone will reinforce that acceptance, as well as being entertaining and useful learning resources in their own right.

If you would like to volunteer for UAR or arrange a speaker, please contact Alexandra Jenkins: ajenkins@uar.org.uk.



Meet the new editorial board

The new-look *Physiology News* is brought to you by the following team, who comprise some new faces with long-serving editorial board Members. Their expertise spans a wide range of areas and they each bring a wealth of experience to inform what goes into the magazine.



Mike Collis

I trained in physiology and pharmacology and have conducted my own research in both academia and in industry. My personal

research areas were cardiovascular, tissue repair processes and adenosine receptors. I have also been responsible for the academic collaborations of Pfizer in the UK. More recently I spent four very enjoyable years as CEO of The Physiological Society, during which time I gained both an understanding and affection for the way The Society operates. I am now semi-retired and spend some of my time working to support integrative (*in vivo*) physiology and pharmacology research and training in the UK. I am a Member of The Physiological Society, the British Pharmacological Society and serve on BBSRC and MRC funding panels.



Sarah Hall

I have been a member of the editorial board of *Physiology News* since 2007. I have always enjoyed the magazine's eclectic combination of

research, news and opinion and I am confident that the new editorial board will continue to provide our readers with something to think about. I am an electrophysiologist by training, with main interests in cardiac cell physiology and ion channel regulation. Over the last decade, I have undergone a gradual evolution towards more teaching-focused activities, and now spend much of my time explaining the joys of physiology to Cardiff University students on science, medical and dental degree schemes. I am also involved in a variety of outreach activities and have recently been associated with the Wellcome Trust 'In the Zone' exhibition which will tie in with the London Olympics to outline the physiology of exercise to the general public.



Michael Evans

I was elected to Council last July and I sit on The Society's Policy Committee, so my role on *Physiology News* Editorial Board is to lead on policy

matters, quite a big task given the seeming complexity of such matters. Previously, I was a member of The Journal of Physiology Editorial Board (2004–2011). I am excited at the prospect of contributing to the magazine and hope that we as a board can continue to develop it as a sounding board for current topics and issues in the field and of relevance to The Society and its Members. My background is as a cellular physiologist focusing since the mid-1980s on cochlear hair cells. I am a Senior Lecturer at Keele University, where I am Course Director for Neuroscience.



Jamie S McPhee

I hold a lecturer and research position in the School of Healthcare Science at Manchester Metropolitan University. It is also my

privilege to be an Affiliate Representative for The Physiological Society. I sit on Council meetings and am a member of the Meetings Committee involved in planning of scientific meetings. My main research and teaching interests are in physical activity and health, with a major focus on the ageing neuromuscular system leading to sarcopaenia and frailty in old age. Our interdisciplinary group try to understand the fundamental processes underlying sarcopaenia and whether there is anything we can do to maintain muscle function into old age.



Keith Siew

I have been a Member of The Physiological Society since 2010, initially joining as an undergraduate Associate Member and continuing

on to become one of the elected Affiliate Representatives serving on The Society's Council, Education and Outreach and Membership and Grant Committees. I am proud to represent my fellow Affiliate Members at the highest levels of The Society. My love-affair with physiology began back in my native city of Dublin while undertaking a BSc in Physiology & Pharmacology at UCD. After attending my first Main Meeting of The Society in Dublin, 2009, I was well and truly bitten by the research bug. I attended Physiology 2010, presenting my undergraduate research at the YPS meeting (successfully obtaining second prize for oral communications) where I also met my current supervisor. I have since completed an MSc in Imaging & Microscopy at UCD and commenced studies for a BHF-funded PhD in Medicine at Cambridge University. My research interests include renal salt handling, hypertension, osmoregulation and novel 3D imaging techniques.



Samantha Passey

I completed my undergraduate degree in Biochemistry with a Year in Industry in 2003 at the University of Bristol. I went

on to do a PhD in Biochemistry in the field of actin dynamics and Rho GTPase signalling. Since completing my PhD in 2007 I have worked as a postdoctoral researcher in a range of academic and industrial research environments including the London School of Hygiene and Tropical Medicine, Syntaxin Ltd, the Bristol Heart Institute and most recently on an NC3Rs-funded project at the University of Bedfordshire using tissue engineering approaches to grow skeletal muscle *in vitro* with a functional neuronal input. In this work I am co-culturing motor neurons with skeletal muscle cells in 3D *in vitro* models to build a neuromuscular junction.

Update



As Sam will now be taking up a new post in Australia, this edition of *PN* will be her last as an editorial board member. Sam has been a fantastic contributor to the magazine and a very active member of the editorial board, who all thank Sam for her hard work and valuable contribution to the success of the magazine over recent years. We wish her every success with her scientific career 'down under'.

Forthcoming meetings & events

Legislation around the use of animals is changing. Learn more about what this means for you at *Time for Change*, an event organised by The Physiological Society, Understanding Animal Research, the British Pharmacological Society and the Society of Biology.



2012 Forthcoming events

27 Apr

Time for Change event
at the Wellcome Trust,
Euston Road, London

26 Jun

Cardiac & Respiratory
Physiology abstract
submission

4–6 Sep

Cardiac & Respiratory
Physiology themed
meeting at the University
of Manchester

Time for Change

You may be aware that legislation around the use of animals in research is changing. This work is currently governed by the Animals (Scientific Procedures) Act of 1986, but following transposition of the European Directive 2010/63/EU, changes to UK legislation will come into force from January 2013.

The Physiological Society is collaborating with Understanding Animal Research, the British Pharmacological Society and the Society of Biology to hold a one-day event to provide Members with the opportunity to learn more about the proposed legislation.

Time for Change is taking place on the 27 April at the Wellcome Trust, Euston Road, London. With representation from the Home Office, as well as presentations from those working in industry, academia and contract research organisations, this event will be a great opportunity for Members to learn more about the proposed changes, consider how the changes may affect their own practices and to raise areas of concern.

For more information and to sign up to this event please visit: www.bps.ac.uk/details/meeting/1662261/Time-for-Change.html or contact our Policy Manager, Michelle Brook on policy@physoc.org.

Microelectrode Techniques for Cell Physiology, 5–19 September 2012, Plymouth, UK

The workshop, run by the Marine Biological Association, provides intensive practical tuition of a number of microelectrode, patch clamp and optical techniques applied in cell physiology. It is intended for postgraduate students, post-doctoral workers or established scientists wishing to apply these techniques in their research. The workshop covers lectures and practicals in electronics, microscopy, data analysis and computing, bilayer recording, flash photolysis, multi-electrode arrays and *in vivo* patch clamp recording. It also covers the following techniques as three-day experiments:

Two-electrode voltage clamp
Patch clamp – single channel,
whole cell, slice recording
.....
Single-electrode voltage clamp
.....
Dye injection
.....
Ion-selective microelectrodes
.....
Fluorescent indicators and
fluorescence imaging
.....
Amperometry and capacitance
measurements
.....

Daily lectures are given by teachers and visiting lecturers to cover the basic techniques and specialised topics. A copy of the Plymouth Microelectrode Handbook will be provided.

Twenty places are available and the course fee is £1200. This includes accommodation, meals and tuition. Participants are responsible for their own travel arrangements. For further information please contact Alexa@mba.ac.uk. The closing date for applications is 30 April.



Meeting notes

Cardiac & Respiratory Physiology
Themed Meeting



This event will feature a focused symposium on 'New Insights into the molecular basis of cardiac arrhythmias: from animal models to computations' and takes place on 4-6 September 2012 at University of Manchester. Abstracts submission and registration opens on 26 June.

The Meeting will bring together scientists working on cardiac arrhythmias in a variety of research fields. It represents a broad range of interests that will encompass not only experimental, most recently genetic model, systems, but also clinical applications. These will involve an interdisciplinary range of biophysical, physiological, genetic and computer modelling approaches.

Invite to the next FEPS meeting: Santiago de Compostela

The next meeting of the Federation of European Physiological Societies (FEPS) will be held in Santiago de Compostela, Spain from 8 to 11 September 2012.

This will be a joint meeting of FEPS with the Spanish Physiological Society and also the Endocrine Society of Portugal. Many Members of The Physiological Society will have been to joint meetings with the Spanish Society and will know that these events are both scientifically stimulating and socially fun. The meeting will begin with a Young Physiologists' Symposium and will then continue with symposia and poster sessions designed to cover a broad range of physiological topics. The major scientific highlights will include the plenary lectures. At this stage three are confirmed. The meeting will begin with Francis Ashcroft (Oxford) giving the Annual FEPS Lecture entitled 'ATP-sensitive K channels, from molecule to disease'. Rafael Yuste

(Columbia, New York) will lecture on 'Dendritic spines and distributed circuits'. Finally, the meeting will close with Ramón Latorre (Valparaíso, Chile) giving the Juan Negrin lecture of the Spanish Physiological Society 'Spying the molecular workings of ion channels using fluorescence'.

As a UNESCO World Heritage site, Santiago de Compostela is a beautiful place to visit and it is immediately clear why it has become a focus for pilgrims for the last thousand or so years. The university is right in the middle of the town next to the old cathedral and accommodation for the meeting is within easy walking distance. Do come and join us in September.

President, FEPS

David Eisner

Meeting website

www.feps2012.org

Deadline for abstract submission

7 May 2012

Deadline for early registration rate

31 May 2012

Update on IUPS 2013

The Congress is now a very short sixteen months from this issue of *Physiology News*. By the time you read this article, the International Scientific Programme Committee (ISPC) will have met in Birmingham and have selected the symposia to form the heart of the Congress.

Planning is progressing well and as the Congress nears, excitement is mounting. Registration, abstract submission and accommodation booking will all open on 1 September 2012, so mark this date and tell your friends, colleagues and collaborators. Bookmark the website www.iups2013.org for all the latest news and updates. Stage two of the website (the science), will be launched in May 2012.

We are also delighted to be able to formally announce our partnership with both the European Society for Microcirculation (ESM) and the European Vascular Biology Organisation (EVBO) who have agreed to join the IUPS Congress in 2013. We look forward to working closely with both organisations over the coming months.

An impressive line-up of plenary and keynote speakers has been confirmed.



Support IUPS 2013

We would like to invite all members of the physiological sciences community to contribute to the success of the 37th Congress of the International Union of Physiological Sciences through your attendance.

IUPS 2013 will attract many graduate students and postdoctoral fellows seeking knowledge of the latest research findings. Many of these physiologists do not have adequate funds for travel to the UK and need to be supported with travel grants in order to attend and present their data and learn about you. To make their participation

How you can get involved in IUPS

• Suggestions for topical and controversial Point-Counter-point sessions or as we like to call it 'Fight-Club' are sought. These mini-sessions of a maximum of 15 minutes in duration will consist of two individuals debating a specific topic. Please submit your contentious issue that has perhaps polarised current thinking (or might do in future), along with the names of two individuals who might be prepared to speak on the topic from opposite ends of the spectrum. Each session will have a moderator with the audience voting on the overall winner at the end.

• Top predictions in the physiological sciences – what can we expect in the next 100 years! We would like to solicit some of your predictions of where we will be 100 years from now (scientifically speaking that is). The prediction should be in the form of a one-line headline statement and be aimed at a general public audience. Selected predictions will be judged by a panel of experts as to the likelihood of coming true and will form part of an on-line discussion forum, prior to and during the meeting. Those submitting should be prepared to comment further and be available for media enquiries if asked.

• Official congress bloggers wanted. Are you an established blogger? Fancy reporting on the congress as it happens? Please RSVP to info@iups2013.org telling us who you are and providing a link to a previous blog. Official bloggers will be offered a 50% discount on their registration fee.

Suggestions for 'Fight-Club' and 100 year predictions should be sent to info@iups2013.org by 1 May 2012.

possible, we ask for your financial assistance to make it an exciting and dynamic Congress. Please take an active role in ensuring the success of the IUPS 2013. Take a few moments now to make a donation.

You can donate online using the JustGiving website; all major credit cards are accepted. Visit <http://www.iups2013.org/support.html> for further details. UK taxpayers may gift-aid donations.

Our thanks to those who have already donated!

Society Prize Lectures at IUPS 2013

Opening Lecture
Roger Y Tsien
San Diego, USA

Public Lecture
Russell Foster
Oxford, UK

IUPS and ADInstruments Education Lecture
Olusoga Sofola
University of Lagos, Nigeria

The Paton Lecture
Geoffrey Burnstock
London, UK

Michael de Burgh Daly Lecture
Peter Carmeliet
Leuven, Belgium

Sharpey-Schafer Prize Lecture
William A Catterall
Seattle, USA

Bayliss-Starling Prize Lecture
Graham J Dockray
Liverpool, UK

Annual Review Prize Lecture
Eric Gouaux
Oregon, USA

Joan Mott Prize Lecture
Eleanor A Maguire
London, UK

IUPS President's Lecture
Denis Noble
Oxford, UK

August Krogh Lecture
Patrik Rorsman
Oxford, UK

Hodgkin-Huxley-Katz Prize Lecture
Erin M Schuman
Frankfurt am Main, Germany

GSK Prize Lecture
Mala Shah
London, UK

FEPS Lecture
Juleen R Zierath
Stockholm, Sweden

For a full list of lectures visit
www.iups2013.org



I|U|P|S|2013

**37th Congress of the
International Union of Physiological Sciences**

**International Convention Centre (ICC)
Birmingham, UK**

21–26 July 2013

www.iups2013.org

When does more give less in the olfactory system?

Written by

Johannes Reisert
and Alan Gelperin

Monell Chemical Senses Centre,
Philadelphia, PA, USA

Our senses are exposed continuously to sensory stimuli from our surroundings. We can choose to close our eyes or ears, avoid touch or move away from hot or cold, and we can change voluntarily the perceptual quality of stimuli to some extent (for example, the Doppler effect in audition created by moving quickly towards or away from a sound source or defocusing our eyes to blur an image).

Recent results suggest a mechanism by which an olfactory percept can be changed by altering the stimulation rate of the olfactory system due to voluntarily changing breathing or sniffing patterns.

The sense of smell begins with the inhalation of odorants into the nasal cavity. Volatile odorant molecules are carried by the air into the nasal cavity to activate olfactory receptor neurons (ORNs) embedded in the olfactory epithelium (Fig. 1A). Loss of access to the nasal cavity results in reduced olfaction, a phenomenon experienced by reduced flavour perception during a cold. Inhalation is under voluntary control and can change both in frequency and in the volume of inhaled air. Until recently, it was unknown whether and how ORNs in the nasal cavity and second order neurons, mitral cells in the olfactory bulb, encode for such inhalation-based changes in the stimuli. Recent work is



The sense of smell begins with the inhalation of odorants into the nasal cavity. Volatile odorant molecules are carried by the air into the nasal cavity to activate olfactory receptor neurons (ORNs)

beginning to clarify how these changes in the pattern of stimulus delivery to the olfactory epithelium affect responses of both ORNs and mitral cells. In rodents and also in human subjects odour-guided decisions can be based on the information gleaned from a single sniff.

Rodents can vary their breathing (sniffing) frequency from 2 Hz at rest to up to 12 Hz during high-frequency sniffing bouts. Figure 1A shows a sagittal view of a rat head with a thermocouple probe inserted into the nasal cavity to measure the temperature changes caused by inhalation and exhalation. Periods of low breathing rates can change abruptly into bouts of high-frequency sniffing (Fig. 1B), thus changing the delivery of odorant to the olfactory epithelium and the stimulation patterns of ORNs equally abruptly. This active olfactory exploration has been implicated in such diverse functions as directing odorant flow to different parts of the olfactory epithelium, promoting behavioural odorant discrimination, enhancing discovery of new odorants and adaptive filtering of olfactory information.

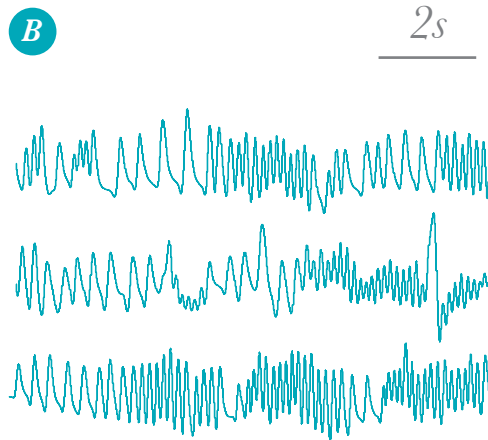
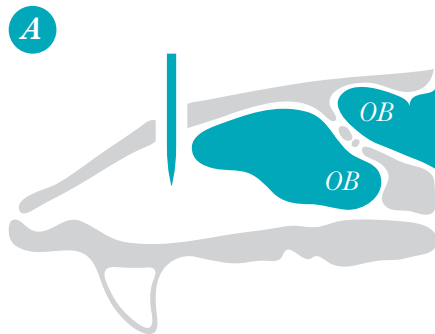
When mice are asked to perform a simple behavioural discrimination task between very dissimilar odorants, they typically require 250 ms

of odorant sampling time, the equivalent of one to three high-frequency sniffs, to determine the identity of the odorants. When confronted with a task to discriminate very similar odours, mice must be forced to extend their odour sampling time to achieve a high level of accuracy. When allowed to make their own decisions about odour sampling time, mice spent the same amount of time sampling odours independent of the difficulty and therefore made less accurate odour discriminations as task difficulty increased (Rinberg *et al.* 2006). The rapid (few sniffs) decisions mice make when free to do so may relate directly to the decrease in information content of sensory input with sniff number at high sniff sampling rates. On the other hand, the sensory information content clearly does not fall to zero after a few sniffs, as forced prolongation of sniff sampling leads to higher accuracy of odorant discrimination.

But how do ORNs respond to such repeated stimulations at varying frequencies and are those responses dependent on the odorant concentration? Olfactory signal transduction begins with the binding of odour molecules to odorant receptor proteins (ORs) located in the membranes of olfactory cilia and ultimately leads, via a G protein-coupled biochemical

Fig 1.

Fig 1A shows a sagittal view of a rat head with a thermocouple probe inserted into the nasal cavity to measure the temperature changes caused by inhalation and exhalation. Periods of low breathing rates can change abruptly into bouts of high-frequency sniffing (Fig. 1B).



cascade and opening of transduction channels (for review see Kleene, 2008), to the generation of action potentials (APs) that are carried to the olfactory bulb via olfactory axons.

The suction pipette recording technique (Lowe & Gold, 1991) can be used to record simultaneously the odorant-induced receptor current and APs produced by ORNs.

Figure 2A shows such a recording, in which a mouse ORN was exposed repeatedly to the odorant cineole at a frequency of 2 Hz.

The first exposure generated a large receptor current with only a few APs fired during the rising phase of the receptor current. The AP train was cut short because the AP amplitude collapsed quickly (see also responses to the third and fourth stimulation) due to inactivation of voltage-gated Na^+ channels during strong depolarizations. Subsequent stimuli reliably generate short bursts of APs upon each stimulation and the repeated application of cineole is faithfully conveyed to the olfactory bulb. This is not the case when the stimulation frequency is increased to 5 Hz (Fig. 2B). After the first odorant exposure, the ORN only generated APs sporadically to subsequent stimuli and hence this ORN continued to provide information, albeit less precisely, for each stimulation.

Furthermore, this stimulation-frequency-dependent reduction of AP firing is dependent on the odorant concentration. In a modified stimulus protocol designed to simulate the rapid switch from low- to high-frequency sniffing, an ORN was exposed to heptanal first at 2 Hz followed by 5 Hz stimulations (Fig. 3) (Ghatpande & Reisert, 2011). For these

recordings a mouse line was used that also expressed green fluorescent protein (GFP) in ORNs that expressed the heptanal-responsive I7 OR protein (Bozza *et al.* 2002) for identification. At 1 μM heptanal the ORN generated APs with every stimulation at 2 Hz and did so reasonably reliably at 5 Hz. But an increase to 3 μM heptanal entirely abolished AP generation during 5 Hz stimulation, even

Additionally, during the higher frequency stimulations (Fig. 3C) a temporal shift between the odorant exposure and the ORN response is introduced. But it should be pointed out that a set of ORNs expressing a different, less sensitive OR for heptanal might display similar response characteristics but a higher overall odorant concentration (equivalent to a shift of the data in Fig. 2B & C to higher odorant concentrations).

a single sniff

In human subjects, odour-guided decisions can be based on the information gleaned from a single sniff.

though the ORN still faithfully responded during the 2 Hz stimulation. Thus, from the view of this particular ORN and what information is being relayed to the bulb, an increase in stimulation frequency and concentration greatly reduced the information content. Figure 3B shows that ORNs can respond with AP firing to 2 Hz odorant exposures with nearly 100% accuracy at intermediate odorant concentrations and only begin to fail at high concentrations. In contrast, accuracy never reached levels higher than 60% at 5 Hz stimulation, and failed entirely at concentrations higher than 10 μM heptanal.

Thus, the presence of or change to a higher heptanal concentration might still be relayed to the brain, although through an entirely different set of ORNs and thus mitral cells.

In conclusion ORNs do not simply report the presence and concentration of an odorant but they also modulate their output depending on the stimulation frequency. These results give further impetus to the need to parse olfactory adaptation at the level of intact organisms between peripheral sensory events and central processes (Dalton, 2000)

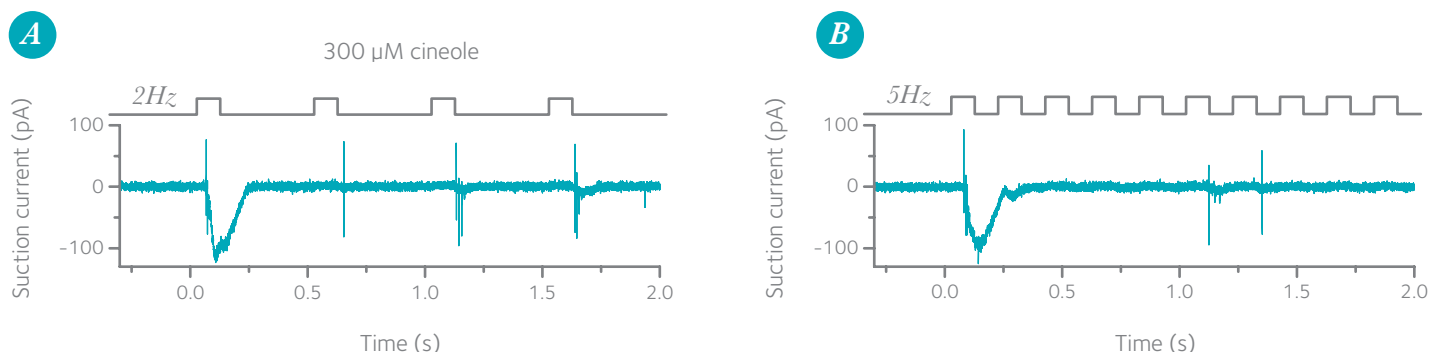


Fig 2.

Acknowledgments

The work was supported by a Morley Kare Fellowship and an NIH grant (DC009613). This material is based upon work supported by the US Army Research Office (grant number W911NF-11-1-0087). The authors would like to thank Drs K. Field and G. Lowe for fruitful suggestions and discussion of the manuscript.

So why sniff if it apparently leads to loss of information?



Periods of low breathing rates can change abruptly into bouts of high-frequency sniffing, thus changing the delivery of odorant to the olfactory epithelium and the stimulation patterns of ORNs equally abruptly.

A requirement for APs to be generated during a subsequent stimulation is that the receptor current from the previous stimulation has terminated. This allows the ORN to hyperpolarize so that voltage-gated Na⁺ channels can recover from inactivation. A mutation in the cyclic nucleotide-gated channel that causes subtle prolongations of the receptor current (Song *et al.* 2008) further reduces the likelihood for AP generation during repetitive stimulation with an equivalent reduction in odorant-induced local field potentials recorded from the olfactory bulb. Also, recordings from mitral cells of artificially ventilated mice or rats (to experimentally control the ORN stimulation frequency) showed that an increased odorant exposure rate leads to reduced firing of mitral cells although, unlike the case in ORNs, mitral cell firing does not seem to be entirely suppressed at high stimulation frequencies (Bathellier *et al.* 2008; Carey & Wachowiak, 2011). A possible reason for the difference in ORN vs. mitral cell responses might be the high convergence of more than 1000 ORNs expressing the same OR to around 25 mitral cells receiving input in a single glomerulus.

So why sniff if it apparently leads to loss of information? A tantalizing interpretation of these results is that it provides the animal with the possibility to selectively suppress its responses to continuously present odorants by voluntarily increasing its odorant sampling frequency (as in Fig. 3A, 3 μM trace). This mechanism has been described as adaptive filtering (Verhagen *et al.* 2007). A novel odorant experienced during a high-frequency sniff that activates previously unstimulated ORNs can still generate responses, at least during the first odorant exposure (see Fig. 2A). This can be sufficient for odorant identification as the discrimination task only has to be performed in the presence of a background activity that had been reduced due to previous high-frequency sniffing. While adaptive filtering seems to function at the ORN and bulb level, where less AP firing could indeed mean more, it remains to be seen how such a frequency-dependent modulation of ORN activity contributes to odorant discrimination at a behavioural level.

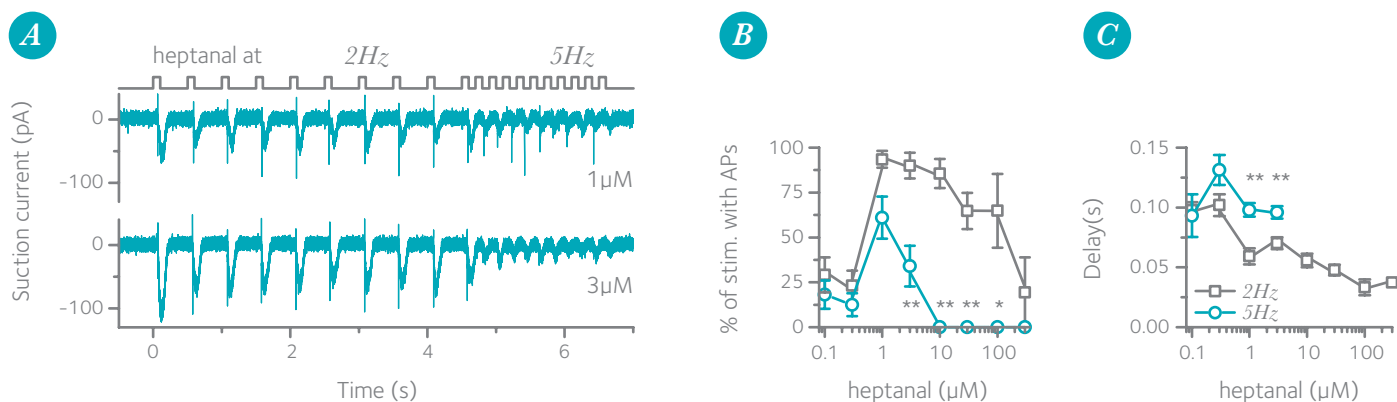


Fig 3.

Figure 1. Breathing pattern in a freely behaving rat. A, sagittal view of a rat head, showing the nasal cavity with the olfactory epithelium (OE) and the olfactory bulb (OB). A thermocouple has been implanted into the nasal cavity to monitor temperature changes following inhalation and exhalation. B, recording of a freely breathing rat that shows the variability in breathing patterns ranging from low-frequency sniffing bouts. Upstrokes in the recordings represent phases of inhalation. Modified from Kepecs *et al.*, *Journal of Neurophysiology* (2007) with permission from the authors and the American Physiological Society.

Figure 2. Changes in stimulation frequency alters action potential generation in mouse olfactory receptor neurons. A, suction pipette recordings from an isolated mouse olfactory receptor neuron (ORN), that was exposed to the odorant cineole at a frequency of 2 Hz as indicated by the top line. Each stimulation lasted 100 ms. B, same ORN as in A, but now stimulated at 5 Hz; again each stimulation was 100 ms. While action potential are always generated by the first cineole exposure (at $t = 0$), the likelihood of action potentials being generated during each subsequent stimulation is reduced. Thus, the ORN failed to encode each stimulation.

Figure 3. Concentration dependence of action potential generation during changing stimulation rates. A, suction pipette recording of a mouse ORN that expresses the heptanal-responsive I7 odorant receptor. The ORN was first stimulated at 2 Hz followed by a 5 Hz stimulation sequence. Action potentials were generated during the 2 Hz and also quite reliably during the 5 Hz stimulation at low (1 μM) heptanal (upper recording), but failed to be elicited during the 5 Hz, 3 μM recording (lower trace). B & C, analysis of the recordings from a cohort of 17 ORNs. Per cent of stimulations that elicited action potentials at 2 and 5 Hz and delay of action potential firing averaged over all 2 and 5 Hz odorant stimulations in a given sweep. Data points are mean \pm SEM of 3–17 ORNs. * $P < 0.05$ and ** $P < 0.005$, two sample t test. Modified from Ghatpande & Reisert (2011). ♦

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Accreditation – will it make a difference without increased funding?

Written by
Mike Collis

What's your view?

What are your views on accreditation? Please send them to pneditor@physoc.org so that they can be included in a future issue of *Physiology News*.



laboratory experience in the new graduate is probably also one reason why the standard PhD is now taking 4 rather than 3 years.

But where are the MBIol courses that can offer this type of practical *in vivo* training and how many industrial sponsors can guarantee an *in vivo* placement for students? The answer is very few. I know of only two MBIol courses: both of these are primarily in pharmacology and involve an industrial placement – which is not guaranteed to be *in vivo*. There are a few excellent academic institutions that still offer a small number of students the opportunity to experience some *in vivo* education, but they cannot offer the level of exposure required for accreditation. So unless something changes, there will be no courses that can guarantee to provide the *in vivo* skills required for accreditation within the Society of Biology framework. I don't think this is a desirable situation and an additional concern is that this scenario will not help the few courses that do provide some limited *in vivo* exposure to muster support from their institutions, particularly in a time of increased budgetary rigour.

London, which has a significant *in vivo* component. But this funding is only for the first year and there needs to be more sustained funding of this targeted nature if we are to see a paradigm shift in graduate training and reap the benefits of an accreditation system.

Currently, the majority of students will only get the practical training envisaged by the accreditation system if they take a further degree such as an MSc or MRes. The Society of Biology has not included higher degrees in its accreditation framework, probably because of concerns that the quality of the first degree cannot be guaranteed. It will be interesting to see if this position changes and accreditation is extended to post-graduate courses. On the one hand, it would recognise the value of some of the excellent post-graduate courses that are available and would help students select them and consequently enhance their career prospects. On the other, such an extension of the boundaries of accreditation would not necessarily facilitate extra funding for MBIol courses and could be seen as an endorsement

Many of you will know that the Society of Biology is running a pilot scheme to accredit bioscience courses in the UK. The Physiological Society has been working with the Society of Biology specifically on the accreditation of degrees that have a significant *in vivo* training component. The aim of any accreditation system must be to set high standards, so that those undertaking the course in question receive a training that equips them for their future careers and makes them attractive recruits for both industrial and academic employers.

A key feature of the Society of Biology accreditation scheme is that the student has a significant (minimum of 6 months) 'hands on' exposure to laboratory research, either as part of a 4 year Master of Biology (MBiol) course or through an extramural year in industry. The emphasis of accreditation on practical laboratory experience is in response to the concerns expressed by many employers that today's graduates are not ready to work in a research lab and in fact require training in even the most basic of techniques. The current lack of practical



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'Hands on'

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So what needs to change to allow the UK to have courses that provide the *in vivo* experience that would meet the criteria for accreditation? As with most things, it all comes down to money. Courses that involve a significant time in the laboratory are expensive to run; this is particularly the case when the laboratory work is *in vivo*. The added costs of personal Home Office licences for the students, the costs of having experienced staff providing close supervision and the costs of animals and animal facilities all make courses involving *in vivo* work more expensive. In fact, they cost more than most academic institutions are willing to pay, without additional financial support that has come in recent years from industry or from a learned society. If accreditable *in vivo* courses are to become a reality, then there clearly needs to be extra funding available to run them. HEFCE has a budget for Strategically Important and Vulnerable Studies (SIVS) that could be used in this way. To their credit, HEFCE are supporting an MSc in 'Integrated Pharmacology and Physiology for Research' at King's College

of the status quo rather than a lever to improve standards and stimulate new courses. Paradoxically, the MBIol is not regarded as equivalent to a Masters degree in the Bologna Accord, as the extra academic year of the MBIol does not provide an equivalent number of credits. In fact, there is anecdotal evidence that a number of universities on the continent refuse entry to PhDs to students with the MBIol. This requires students who wish to attend these courses to take an additional Masters, which is at odds with one of the key aims of accreditation i.e. to produce 'research-ready' graduates.

What is clear is that accreditation has to be linked to enhanced funding if it is to achieve its aim of improving the standards of bioscience degrees, particularly those involving *in vivo* education. Shouldn't the Society of Biology and its member organisations be lobbying for a link between accreditation and enhanced funding if accreditation is going to make a difference? ♦

Q&A

Physiology News speaks to Dr Kevin Fong for his views on the health of physiology as a discipline, how it informs his day job as an anaesthetist at University College Hospital in London, and why it's important to get out there and engage the public on the importance of physiology.

Q&A: *PN* speaks to... Dr Kevin Fong

Kevin Fong is an anaesthetist and honorary lecturer in physiology at University College London (UCL). He holds degrees in medicine and astrophysics and is co-director of the Centre for Aviation Space and Extreme Environment Medicine at UCL. Appointed a Wellcome Trust Engagement Fellow in 2012, he has fronted several BBC Horizon documentaries on aspects of physiology and most recently BBC 2's *To Boldly Go...*, a series exploring the body's physiological adaptations and limitations for survival at the extremes.

How healthy do you feel physiology is, as a discipline?

I get the impression that we are seeing the disappearance of physiology departments proper in the UK over recent years. They are becoming part of wider disciplines – which is strange really, given this country's huge history in whole-body, integrated physiology. I think physiology is still alive and well but somewhat hidden – it is buried under other things; cardiac physiologists are subsumed within cardio-thoracic or cardiological research teams and pulmonologists are subsumed within respiratory teams. A lot of people don't recognise it as a discipline in a way that perhaps they did 20 or 30 years ago. To say 'I'm a physiologist' in any public environment is to invite the question 'What is physiology?' so in that sense, I think its public profile is not what it could be.

Do you think that it is important that physiology is promoted as a discipline specifically, or do you think it is more important to create an interest in science more generally?

I think it is important to ensure that there is a new generation of capable physiologists to continue investigations within physiology. There is this sense that the future of medicine is simply molecular in nature – of course, this is the exciting, leading edge of it – but at the end of the day, the genomes make proteomes, the proteomes make organ systems and they, as an

integrated whole, make physiology. I remember going through medical school thinking, 'They must have answered all of those questions because everyone seems to have moved on to this other game; we must understand everything about the macroscopic properties of the heart, or a pair of lungs or bone or muscle', and actually far from it – there are many, fundamental unanswered questions that are of huge practical, medical, scientific importance. After decades and decades of understandable focus on the molecular side of things – which, in a sense is still physiology just on a different scale – eventually I think it will come full-circle and we will begin to appreciate again that our nuanced understanding of integrated physiology is essential to everything we do in science and medicine.

In your view, what part does physiology play in modern medicine?

As an anaesthetist it's obviously central to my everyday clinical job; that's what we do in anaesthesia and intensive care, we manipulate whole-body physiology in real-time and try to balance it against injury or illness, or the system as a whole from pharmacology. The core speciality of the anaesthetist is really being able to fly a person's physiology in real-time against assembled threats – and that is what attracted me most to it. It's not just a picture in a text book or an equation about gas exchange, it's happening in front of you, levels are going up and down and the only thing preventing the situation heading too far in the wrong direction is you and a syringe

full of drugs, or a machine. Physiology is central to anaesthetists, but every doctor has to have an intrinsic understanding and appreciation of the impact of what they are doing upon the patient's physiology – not just on the organ in which they are specialising. Whether it is appreciated or not, a fundamental understanding of physiology is absolutely central to modern medicine.

How does physiology inform your job/research?

Medicine doesn't work if you don't treat the whole. Ultimately the more you work in medicine and with the human body, the more you realise that it is very hard to deal with any part of it in isolation. What happens in one area tends to have impacts throughout – it's almost so obvious as to be not worth stating and yet, because the trend in medicine is towards super-specialisation, we can get a little bit siloed in our view. That's one of the things that attracted me to anaesthesia – it is still a general speciality, you have to understand the human body as a whole and that is what I enjoy, the childhood wonder that I had about the way things worked is about the whole human body. No-one goes to a bookstand, opens up a book of the human body and says 'that lung bit is fascinating' – you look at the whole thing – all of it is amazing.

“Medicine doesn't work if you don't treat the whole. Ultimately the more you work in medicine and with the human body, the more you realise that it is very hard to deal with any part of it in isolation.”

Dr Kevin Fong

You work on space medicine. Can you tell us about your research on the effects of zero gravity on human physiology?

Before I studied medicine I studied astrophysics. With those two qualifications I was really, really lucky and got the chance to go and work at NASA's Johnson Space Center – in their human adaptation and countermeasures office. It's the home of astronaut training and I was asking the questions of how you protect astronauts' physiology



Photograph: KevinFong by AnthonyCullen®

against microgravity and long-duration weightlessness. I got very interested in plans to send humans to Mars – not only because of the science that might lie there waiting to be discovered, but for physiologists it's the boundary condition mission, it's taking the effects of weightlessness and extrapolating them – these are missions that maybe last up to 1000 days so if you are thinking about what the ultimate effect of long-duration weightlessness is on the body, then you really have to think about a mission to Mars, because that is the longest one on our books at the moment.

It's fascinating that when you look at the history of it, people readily predicted what would happen to the body. They predicted that bones and muscles would waste, they predicted that it would have some sort of effect on your sense of balance, but there was a whole bunch of other stuff that came as a surprise – it has an effect on your immune system, it seems to affect haemopoiesis, you get space-based anaemia and really profound problems, not just with your balance, but with your hand-eye co-ordination, your ability to track moving objects. The more you look, the more you see – weightlessness has a multisystem impact. You need to understand the physiology of spaceflight before you can develop protection against it. The best thing about it was that I was there in the front row seats as these questions that were almost science fiction but on the borderline of becoming science fact, were being tackled.

You are becoming a regular on TV and have been appointed a Wellcome Trust Engagement Fellow. How important do you feel it is as a scientist to get 'out there' and communicate what you do to a general audience?

It is hugely important – it is difficult to overstate it – but it is worth overstating because it is so important for the public to have a much clearer understanding of what we do and why we do it. I think you have a duty to share the fascination that you have with science otherwise, if you don't share it, it's like being the curator of an amazing museum of rare and beautiful artefacts that you never bother to show anybody else. There is just no point. I think it is also important to bring the next generation through, because certainly I know what it was that brought me to science – it was hearing people communicate it when I was growing up. I still remember some of the seminal science documentaries I watched, I remember James Burke doing Connections on a beach somewhere and using a spiral shell to demonstrate the Fibonacci series. If those memories endure and have driven me to a career that I have really loved, then you feel like you should return that. It is lovely to have the opportunity to do that [communicate what I do]. I think it is fundamentally important. ♦

Tanycytes emerge as hypothalamic chemosensors

Written by

Nicholas Dale
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The brain, and in particular the hypothalamic region, contains neural circuits that control feeding and energy expenditure. Although the inexorable rise of obesity has driven intense study of these neural circuits, the possible roles of non-neuronal cells in this region have not been extensively studied. There is now increasing evidence that hypothalamic tanycytes, cells that lie at the interface between the ventricular cerebrospinal fluid and the brain parenchyma, could be active participants in these hypothalamic networks.

Everyone who has worried about their weight and diet has an intuitive understanding that somehow the brain controls body weight. This control is not just associated with the conscious 'shall I shan't I' internal debate over a tasty and usually highly calorific food item, but is also autonomic i.e. controlled beneath the level of consciousness. The first evidence for this emerged from very early studies that showed that lesions of the ventromedial hypothalamus of rats led to over-eating and obesity (Hetherington & Ranson, 1940) whereas more lateral hypothalamic lesions led to a dramatic drop in food intake (Anand & Brobeck, 1951).

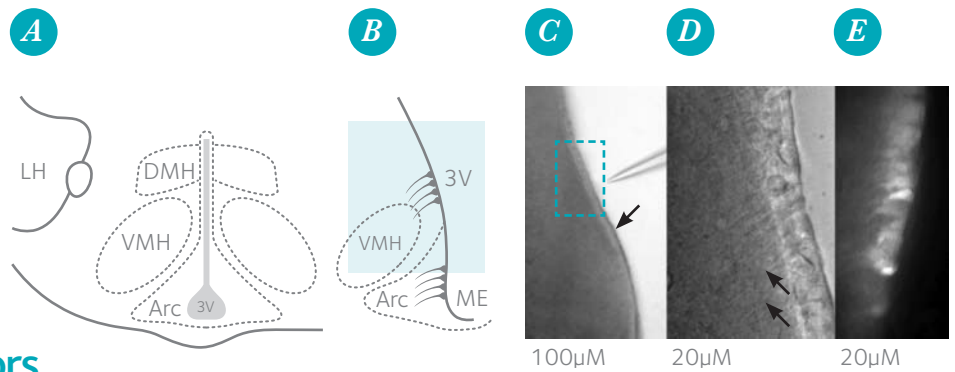


Fig 1.

Neuronal nuclei within the hypothalamus are in effect multivalent chemosensors and integrators of information that control: appetite and food intake, the burning of energy and the deposition of fat.

Everyone who has worried about their weight and diet has an intuitive understanding that somehow the brain controls body weight. This control is not just associated with the conscious 'shall I shan't I' internal debate over a tasty and usually highly calorific food item, but is also autonomic.

We now understand that neuronal nuclei within the hypothalamus (Fig. 1) are in effect multivalent chemosensors and integrators of information that control: appetite and food intake, the burning of energy and the deposition of fat (three factors that collectively determine energy balance). Physiological control of body weight requires the monitoring and integration of many signals that circulate in the body and provide information from the periphery (stomach, pancreas, fat stores etc.) to the brain (Morton *et al.* 2006). These key signals include not only circulating metabolites such as glucose, free fatty acids and amino acids, but also specifically secreted hormones such as leptin, ghrelin and insulin. Understanding how hypothalamic networks respond to, and integrate, these signals to alter their output is an exciting and highly active area of neuroscience that is extremely relevant to the rapidly increasing incidence of obesity and related illnesses now evident in nations with advanced economies.

At the border of the hypothalamus, lining the wall of the third ventricle, are a group of enigmatic glia-like cells called tanycytes (Fig. 1). These cells have a soma that contacts the ventricular fluid, and a single process that penetrates into the brain parenchyma. They

are found from the very ventral part of the ventricle wall at the median eminence β tanycytes) and progress dorsally to about mid-way up the ventricle wall (α tanycytes). The very ventral tanycytes have been of great interest in the context of the regulation of gonadotropin-releasing hormone (GnRH) secretion. The functions of the more dorsal tanycytes remain less clear. The processes of these tanycytes project into the arcuate nucleus and ventromedial hypothalamic nucleus, two key areas associated with



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Fig 2.

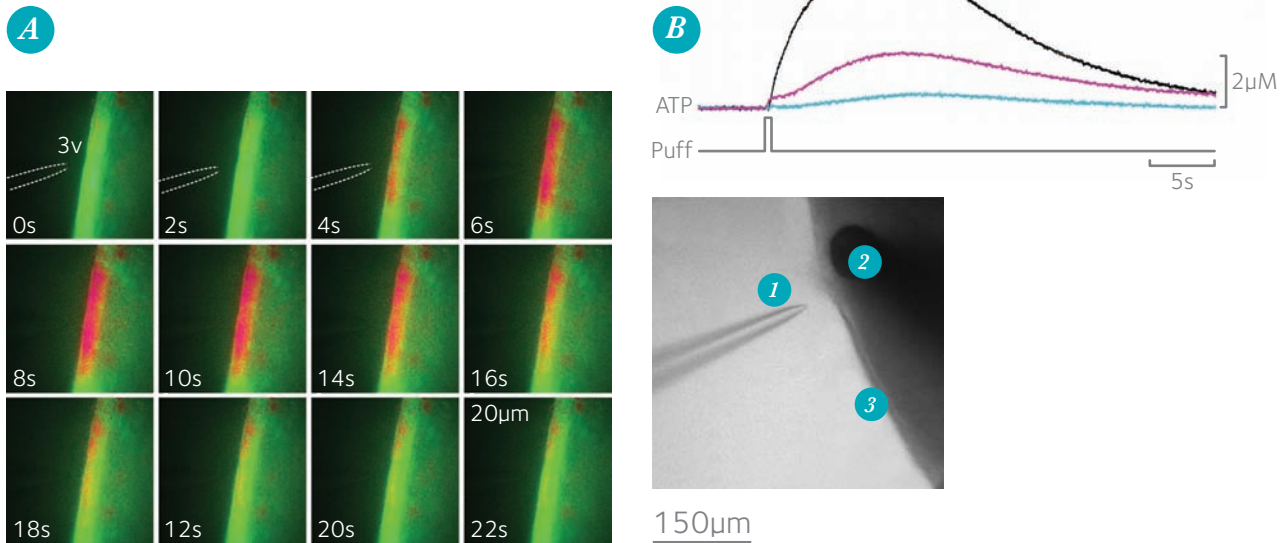


Figure 1. The neuroanatomy of the hypothalamus and location of tanycytes. A, diagram showing the key nuclei; lesions to the Arc and VMH result in obesity, whereas lesions to the LH (location of orexinergic neurons) reduce feeding. B, tanycytes are located at the boundary with the ventricle and have cell bodies that contact the cerebrospinal fluid and a single process that projects into the brain and into nuclei such as the VMH and Arc. C, picture of a hypothalamic brain slice, roughly corresponding to the area of the dotted box in B. The tanycytes are evident as a translucent strip at the edge of the slice (arrow); a puffer pipette is also visible. D, higher power image from dotted box in C. The tanycyte cell bodies are visible as are the processes extending into the brain (arrows). E, Fura-2 fluorescence (excitation at 340 nm) showing loaded tanycytes; both the cell body and processes are evident. C–E from (Frayling *et al.* 2011). Abbreviations: LH, lateral hypothalamus; VMH, ventromedial hypothalamic nucleus; DMH dorsomedial hypothalamic nucleus; Arc, arcuate nucleus; 3V, 3rd ventricle; ME, median eminence.

Figure 2. Tanycytes respond to selective stimulation of their cell bodies with glucose. A, Fura-2 ratio images demonstrating an increase of intracellular Ca^{2+} in the tanycyte cell body layer in response to a brief puff of glucose (at time zero) from a pipette (dotted outline shown). B, tanycytes release ATP in response to glucose. Inset, recording arrangement showing ATP biosensor and glucose pipette. The numbers indicate the positions of the glucose pipette. Traces: ATP release evoked by the three positions of the puffer pipette, indicated in the inset, relative to the timing of the puff.

Figure 3. How tanycytes may integrate into the hypothalamic networks that control appetite and energy homeostasis. Five major nuclei in the hypothalamus form an interconnected network that regulates energy homeostasis: Arc, arcuate nucleus; VMH, ventromedial hypothalamic nucleus; DMH, dorsomedial hypothalamic nucleus; LH, lateral hypothalamus;

and PVN, periventricular nucleus. The Arc contains two mutually antagonistic cell types – the neuropeptide Y (NPY)-containing and the pro-opiomelanocortin (POMC)-containing neurons. Activation of the NPY neurons stimulates feeding whereas the POMC neurons have the opposite effect. Both the Arc and VMH contain glucosensitive neurons. Tanycytes project into the Arc and their processes come into close apposition with those of the NPY neurons (Coppola *et al.* 2007). More dorsally located tanycytes also project into the VMH where their processes come close to the cell bodies of glucosensing neurons (Levin *et al.* 2011). Glucose from the cerebrospinal fluid in the ventricular fluid can activate tanycytes, which are also sensitive to acetylcholine (ACh) and histamine (His). Tanycytes therefore integrate a number of different signals and may constitute an active part of the metabolic sensing network in the hypothalamus.

energy balance (Fig. 1). This has led to irresistible speculation that tanycytes could be participants in the neural networks that control feeding and energy balance via sensing circulating glucose/nutrients in ventricular cerebrospinal fluid.

There is some indirect correlative evidence that tanycytes may have a physiological role in responses to glucoprivation. Injection of alloxan (an inhibitor of glucokinase) into the third ventricle kills a large number of glial fibrillary acidic protein (GFAP)-positive cells,

many of which are tanycytes. These cells eventually regenerate. The glucoprivic response disappears and recovers with a time course similar to that of the disappearance and reappearance of the GFAP-positive cells including the tanycytes (Sanders *et al.* 2004).

The hypothesised role for tanycytes as glucosensors has been predicated around their possession of the glucose transporter involved in this role in pancreatic β cells, along with K^+ -ATP channels (KIR 6.1) and the associated sulfonylurea receptor (SUR) subunit as well as

glucokinase. This has led to the idea that tanycytes sense glucose via the same mechanism as that of pancreatic β cells. However, the mere presence of these components does not mean that tanycytes are indeed glucosensors; a demonstration that tanycytes respond to variations in glucose concentration over a physiological range is required to strengthen this hypothesis. In a wider context, we can regard tanycytes, placed at the border of the 3rd ventricle, as potential chemosensors able to respond to a variety of signals in the cerebrospinal fluid.

Funded by the MRC via a Milstein award to perform somewhat risky science, we decided to enter the field of tanycyte signalling. Our approach was influenced by the revolution in astrocyte biology that came about through application of intracellular Ca^{2+} imaging. This demonstrated that astrocytes signal via variations of intracellular Ca^{2+} rather than membrane potential. Given that tanycytes express glial cell markers and have electrophysiological properties characteristic of glial cells (Jarvis & Andrew, 1988), we decided to apply Fura 2 Ca^{2+} imaging methods to the investigation of rat tanycyte signalling (Dale, 2011; Frayling *et al.* 2011).

Our initial investigation of the glucosensitivity of tanycytes was disappointing – when we changed the bathing glucose concentration of our hypothalamic slices, the tanycytes remained stubbornly inactive, although under certain conditions, notably in the presence of modulatory transmitters (5HT and acetylcholine), small intracellular Ca^{2+} signals in response to alteration of bath glucose concentrations could be observed in tanycytes (Frayling *et al.* 2011). The revolution in our understanding came when we selectively stimulated the tanycyte cell bodies with glucose by focal applications (an approach that mimics their selective sensing of the cerebrospinal fluid) via a patch pipette. We were then able to see rapid Ca^{2+} responses to glucose puffs over likely physiological concentration ranges (3–8 mM, Fig. 2A) (Frayling *et al.* 2011). Interestingly, even non-metabolizable analogues of glucose (2-dexoyglucose and methyl- α -D-glucopyranoside) were able to evoke these



Our data also show that tanycytes do much more than respond to glucose. They can be strongly and reliably activated by ATP and neuronally derived transmitters such as histamine and acetylcholine, which are associated with wakefulness and the drive to feed.

Ca^{2+} responses in tanycytes; however, puffs of saline or sucrose did not evoke responses indicating that these were specific Ca^{2+} responses to glucose and its analogues. These data suggest therefore that the mechanism of glucosensing in tanycytes may differ from the model of pancreatic β cells, as this model requires the phosphorylation of glucose to glucose-6-phosphate and subsequent metabolism in the Krebs cycle to generating ATP. The resulting alteration of the ATP:ADP ratio ultimately results in closure of the K^+ -ATP channel and consequent depolarization. Instead the mechanism of glucosensing in tanycytes seems more similar to that in lateral hypothalamic neurons, which can also respond to non-metabolizable glucose analogues (Gonzalez *et al.* 2009).

Even more interestingly, the tanycyte responses to glucose depended upon ATP signalling via P2Y1 receptors. This observation of ATP receptor-dependent glucosensing has recently been confirmed in primary cultures of

tanycytes (Orellana *et al.* 2012). In keeping with the role of ATP that has been described in other chemosensory processes (Gourine *et al.* 2005), we were able to use biosensors (Fig. 2B) to show that tanycytes release ATP in response to stimulation with glucose (Frayling *et al.* 2011). Why tanycytes should respond to selective stimulation of the cell body rather than more general changes of glucose in the bathing medium is unclear and requires further investigation. Nevertheless our data support the idea of tanycytes as polarized chemosensory cells specifically sensing the composition of the cerebrospinal fluid.

Our data also show that tanycytes do much more than respond to glucose. They can be strongly and reliably activated by ATP and neuronally derived transmitters such as histamine and acetylcholine, which are associated with wakefulness and the drive to feed. It is an intriguing question whether tanycytes may also be able to communicate with neurons (Fig. 3). This seems quite plausible

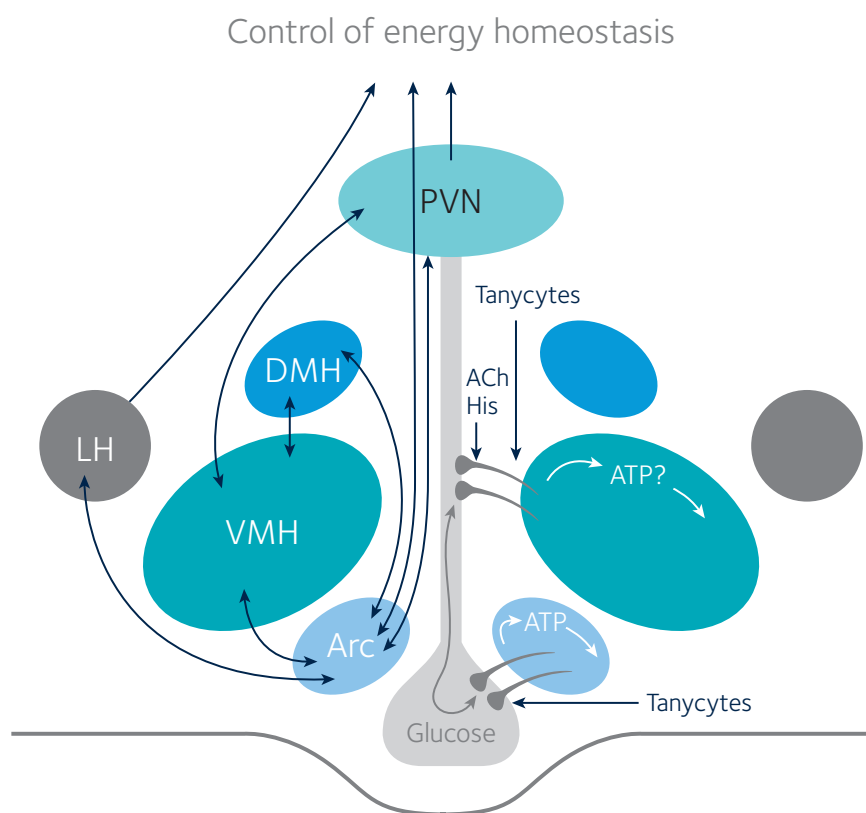
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Fig 3.

Five major nuclei in the hypothalamus form an interconnected network that regulates energy homeostasis: Arc, arcuate nucleus; VMH, ventromedial hypothalamic nucleus; DMH, dorsomedial hypothalamic nucleus; LH, lateral hypothalamus; and PVN, periventricular nucleus. The Arc contains two mutually antagonistic cell types – the neuropeptide Y (NPY)-containing and the pro-opiomelanocortin (POMC)-containing neurons.

as tanycyte processes come into close contact with neurons in the arcuate and ventromedial hypothalamic nucleus (Coppola *et al.* 2007; Levin *et al.* 2011) (Fig. 3). Furthermore, tanycytes release ATP, which could potentially activate P2 receptors on the dendrites of neurons (Kittner *et al.* 2006). Indeed there is some evidence that P2Y1 agonists and antagonists, when injected into the 3rd ventricle can alter food intake (Kittner *et al.* 2006). While this does not demonstrate either a role for tanycyte–neuron communication or of tanycytes in the regulation of feeding, it is consistent with the idea that tanycytes may contribute to these important hypothalamic networks, a possibility that seems well worth testing directly. ♦



Acknowledgments

We thank the MRC for support.

Unravelling the processes that underlie the everyday activity of tracking moving objects

Specialised mechanisms have developed in the brain to allow us to follow moving objects. Our recent work has shown that exposure to only brief visual motion can be assimilated and used to guide eye and head tracking movements, even when an object disappears.

In our everyday lives, we follow moving objects automatically with our eyes. This is called smooth pursuit and it is difficult to generate smooth pursuit eye movements with no moving visual stimulus. When an object moves, we are quickly able to estimate its direction and speed to track it in space (Carl & Gellman, 1987). In addition, we generate an internal representation of the object's velocity, from exposure to the motion combined with cognitive factors such as previous



If a bird flies behind a tree and disappears from sight, we can still continue to pursue its trajectory as we can match our eye velocities to the bird's flying velocity by using only our internally generated response.

experience, prediction, expectation, learning and memory. This means we can continue tracking the object if it disappears from sight. In this situation, we are able to switch from using a combination of visual and internally driven feedback to produce the tracking response, to just using our internal representation. However, this tracking response can only be sustained if we can predict the movement trajectory of the object. If we expect the object to re-appear, smooth pursuit can continue for some time but if we believe it will not reappear, the tracking response decays (Becker & Fuchs, 1985).

For example, if we see a bird flying, it is easy to pursue when you have visual feedback. As well as the direct visual feedback, the pursuit response has an internally generated element so pursuit can become more automatic and you can do other things at the same time, like hold a conversation. This means we are using

prediction to make assumptions about near-future events. If the bird flies behind a tree and disappears from sight, we can still continue to pursue its trajectory as we can match our eye velocities to the bird's flying velocity by using only our internally generated response. This enables us to continue to move our eyes until the bird reappears from behind the obscuring object because there will be a reasonable expectation of when and where the bird will reappear. However, if the bird flies behind a large building, the expectation for future motion would be much lower and the tracking response would be more likely to decay. Recent work has shown that at least 100–150 ms of prior visual motion is required to drive pursuit when a moving target disappears (Barnes & Collins, 2008). In that paper, subjects either pursued a moving target with an expectation that it would disappear totally or reappear. In trials when subjects

expected the target to reappear, smooth pursuit eye movements were continued at a velocity near to the velocity of the unseen target for up to 600 ms. These were guided solely by their internal velocity representation of the target. The internal velocity representation driving the eye pursuit was updated on a trial-by-trial basis, as eight randomised different velocities of target motion were used and the eye movements were scaled to the specific trial velocity.

The situation is more complicated when we track a moving object with our eyes and head together. When we rotate our heads, the vestibulo-ocular reflex (VOR) is invoked, which drives the eyes in the opposite direction at a near-equal rate to the head rotation (for a review of vestibular mechanisms, see Angelaki & Cullen, 2008). This fast reflex allows us to maintain



Figure 2. In further experiments, motion stimuli came in pairs of identical velocity; subjects were able to use the brief motion information in the first to make a pursuit response in the second, where there was no initial motion to drive a pursuit response. Average responses from all subjects for head-fixed eye velocity and head-free gaze velocity (with corresponding head velocity on the right).

fixation on an object when our head moves. However, if we want to follow a moving object with our eyes and head together, we need to countermand this reflex to move our eyes and heads in the same direction. The mechanisms that allow this countermanding to take place are principally the same as those that control pursuit eye movements, although other non-pursuit mechanisms are thought to operate in some circumstances. But previous attempts to examine the role of pursuit in this context have not been able to segregate the visually driven and internally driven components and it was with this in mind that we (Ackerley & Barnes, 2011) investigated the mechanisms involved in the pursuit of a moving target that disappeared from view at specific times, using the eyes and head together.

This series of experiments was designed to uncover features of the internal pursuit response

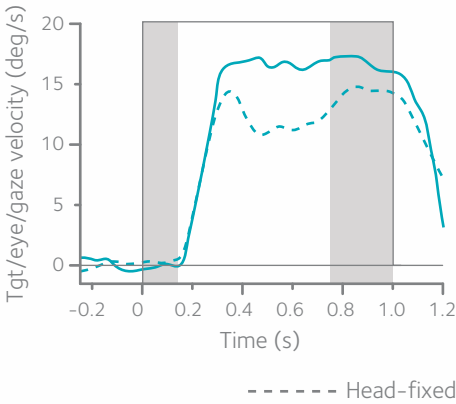
under more natural circumstances. The experiments used a novel protocol that allowed the visual and internal components of pursuit to be segregated, during head-fixed (with eyes only) and head-free (eyes and head) pursuit. In the experiments, the subjects viewed the beginning and/or the end of the visual motion trajectory, using different, randomised velocities, and were instructed to try and pursue the moving target when it disappeared. In experiments where the subjects viewed the first 150 ms and the final 200 ms of visual motion, with an intervening 600 ms period of target extinction, they were able to continue eye or gaze (eye + head) movements during the period of unseen, but predictable motion (Fig. 1, mid-ramp extinction). In contrast, when the subject viewed only the first 150 ms of visual motion and had no expectation that the target would reappear at a later point, eye and gaze velocity decayed after an initial tracking

response (Fig. 1, short-ramp extinction). During pursuit using the head, the subjects were able to obtain a higher pursuit velocity throughout periods where the target was unseen than in trials when they only moved their eyes.

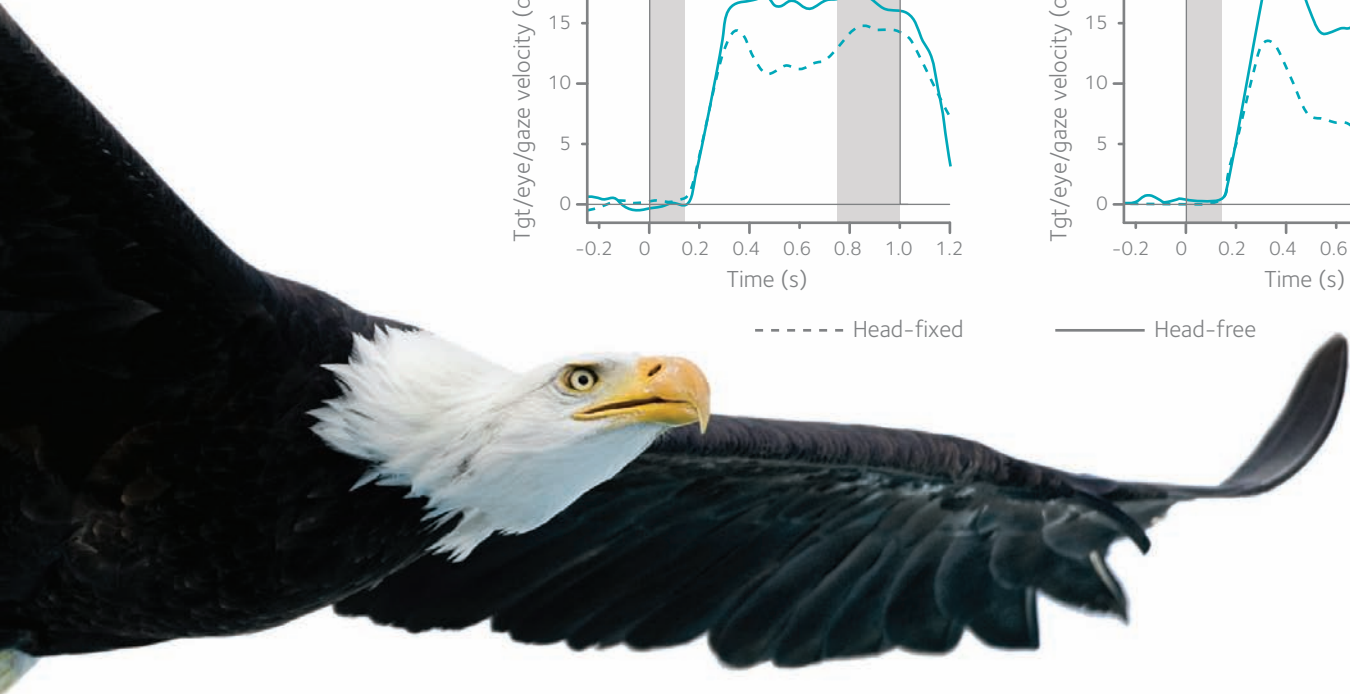
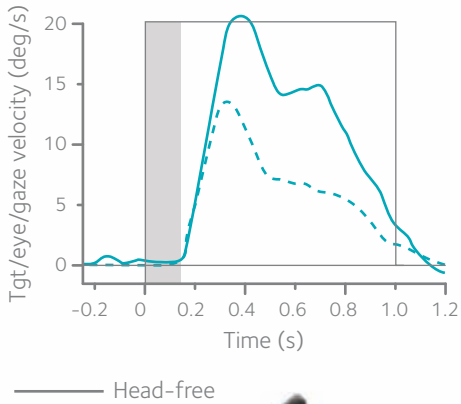
Figure 1. An example of head-fixed (eyes only) and head-free (gaze; eyes and head) average pursuit responses to brief visual motion (grey boxes) from a subject. The mid-ramp extinction condition shows brief motion, with a period of target extinction; the subject had an expectation that the target would reappear later and could continue pursuit. In the short-ramp extinction condition, there was no expectation for target reappearance and pursuit decayed.

Fig 1.

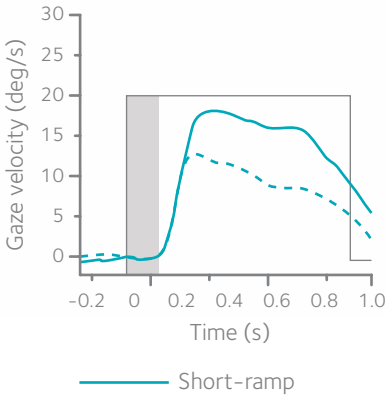
Mid-ramp extinction



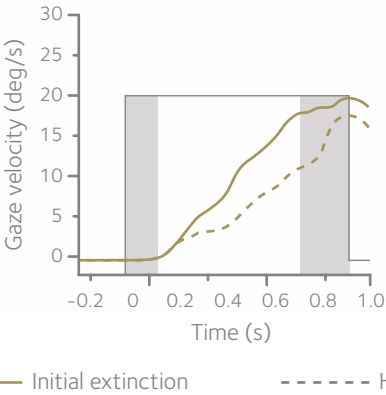
Short-ramp extinction



Eye/gaze velocity



Eye/gaze velocity



Head Velocity

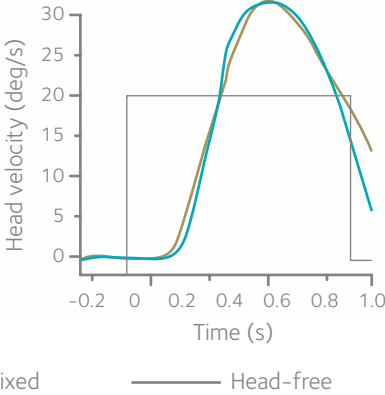


Fig 2.



The brain is constantly using internal predictions to aid us in our everyday lives, rather than having to rely on sensory feedback, which has an innate delay.

In further experiments, the mid-ramp extinction condition was split into pairs of identical randomized velocity stimuli, where the first presentation was 150 ms motion (equivalent to the short-ramp extinction); it was followed by a short break where the target was stationary in the centre of the screen. In the second of the pair, the target disappeared from the centre, which signalled the onset of (unseen) target motion and only the last 200 ms motion was seen (initial extinction). Subjects had to use the motion information in the first of the pair to make an attempt to pursue the second of the pair.

Figure 2 shows that subjects were, indeed, able to successfully make smooth pursuit movements using only the previously remembered motion. This pursuit to the second stimulus was solely driven by internal mechanisms and showed that the brain was using expectations about the future target movement to predict the trajectory, thus doing so with no direct visual motion. Again, the gaze response velocity was higher in the head-free condition than when the head was fixed.

The results show the internal mechanisms for pursuit are similar in head-fixed and head-free conditions. This internal drive is also able to countermand the effects of the VOR, even under conditions when there is no visual stimulus. Detailed analysis revealed that the VOR itself remained active throughout the period of target disappearance, but that, because its gain was slightly less than unity, it resulted in the observed increase in gaze velocity in the head-free condition. In summary, the findings support the view that cognitive mechanisms, such as expectation, can modify smooth pursuit when objects disappear from sight. Furthermore, if we use our heads to attempt to track an unseen object, we can achieve better pursuit, which is of relevance to wider areas, for instance clinical rehabilitation strategies. All of this reveals that the brain is constantly using internal predictions to aid us in our everyday lives, rather than having to rely on sensory feedback, which has an innate delay. ♦

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Acknowledgments

The work from the authors was supported by a grant from the Medical Research Council, UK.

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Q&A

Physiology News speaks to Steve Ingham, Head of Physiology at the English Institute of Sport (EIS).



Q&A: PN speaks to... Steve Ingham

As Head of Physiology at the English Institute of Sport (EIS), Steve Ingham's job is to apply physiological knowledge to the elite performer. He has previously worked towards the Sydney, Athens and Beijing Olympic games with the likes of Sir Steve Redgrave and Sir Matthew Pinsent as an applied practitioner, before taking over the Head of Physiology role where he and a team of 16 hands-on physiologists work to hone the performance of athletes across a variety of sports from track and field athletes, rowers and cyclists.

Which sports do your team focus on and why?

The EIS has a whole host of science and medical teams working with almost 1700 athletes across many sporting disciplines. From the judo team, which, as a contact and combat sport, prioritises physiotherapists and strength coaches, to archery, which depends heavily upon biomechanists to look at technique. My team work predominantly with the 'top five' physiological sports – swimming, athletics, triathlon, rowing and cycling. We focus on these, as our ability to have an impact and improve performance is far greater than for sports that are determined by technical skill or strength, or that are relatively low intensity.

What was the Institute of Sport set up to achieve?

Sports science delivery has been around for 25 years or so. The forefather of the Institutes of Sport was the British Olympic Medical Centre at Northwick Park Hospital, which was set up by Craig Sharp and Mark Harries – the Centre was established in response to the Los Angeles games in 1984, where it was deemed that the medical support for athletes was insufficient. By the mid 90s, there was a systematic review of the UK's provision towards performance sport, which identified that our provision for high-performance sport lagged behind a number of other nations. After a wave of political discussions the Institutes of Sport were set up, first in Scotland then Wales and Northern Ireland, and last online was the English system which has networked sites across the country, the three main sites being Bisham Abbey, Loughborough and Manchester.

How has sports science or exercise physiology research, and how you apply it, changed over the years?

Sports science is a relatively embryonic discipline that is progressing and evolving very quickly. There have been a number of system changes over the years; at the beginning it was very much research oriented, where Olympic athletes were seen as somewhat of a curiosity, with unusual physiological function behind their ability. We weren't really geared up to apply physiological research at this time as the basic knowledge was lacking. Sports-specific ergometry and testing systems soon followed in order to acquire ecologically valid and meaningful data.

It hasn't been until very recently that we have really found our feet and that the sports themselves are recognising the innovations and the real performance differences that can be made with our input. The EIS had to really prove itself when it first started out in 2002, which it did in the run-up to the Beijing games where 100% of the UK Olympic gold and silver medallists were supported by us.

How has the focus changed from understanding the basics of athletes' bodies to application of that research knowledge?

The balance between research and out-and-out support has shifted over the years. Physiological knowledge as it is published in the literature and reported in exercise physiology textbooks, is not based upon elite observations and so what might work as a training intervention for sedentary people or diseased groups won't necessarily translate to someone who is already doing 20 plus hours of training each week. Applying what seems to be fundamental knowledge blindly or incorrectly to these groups is where scientists became unstuck very quickly in the early days.

You really need to work with an athlete, to understand the nuances of what, for example, high-intensity, low-intensity training, recovery or adaptation can do for them. Things have changed a lot, we [exercise physiologists] are now embedded within sports and are able to talk with a greater degree of confidence. We don't necessarily call on a swathe of 'elite literature' in the decision-making process – we are much more dependent upon our own measurements. But these observations provide really good, objective data which enable us and the coaches to evaluate progress, and through deductive reasoning or first-principles physiology, to change strategy.

You say you are now 'embedded' within sports – do athletes welcome the possibility you offer them in improving their performance?

We have to make the case for ideas. If you have somebody who is on a course for an Olympic games, the pressure associated with performing in a final and perhaps potentially achieving a medal-winning performance is very high. Athletes, through time and learning, become very selective. Through the inevitable series of wins and losses, comes a predilection on what has been performed in the past that led to previous performances. In the past we, the scientific community, have been guilty of throwing up ideas which have no real relevance or that haven't been tested with elite athletes and pushing them in front of coaches – 'It's the next big thing, it's the next breakthrough' – but they have not always come to fruition, so there is an understandable degree of cynicism. I don't think it's overly arrogant for an athlete to say 'I'm the only one in the world who can triple jump 18 metres or throw my body over a bar 2 metres high, so is this idea going to work for me?'.

We have to have a good idea: for example, when telling an athlete to stay hydrated when they want to stay light, does not necessarily make sense. The concept of threshold training is one particular example (the point at which lactate and associated acidosis begins to accumulate in the blood, with increasing exercise). According to the research done on this area, this intensity is very potent at improving fitness. For years and years sports scientists have been prescribing this type of training – but the reality is that elite athletes use threshold training very little indeed – if you do too much of it, it can lead to excessive fatigue. Before introducing an idea to athletes we ensure that we have really explored their application. Have they worked in other sports? Is evidence anecdotal or are there field-based measurements? Then you take it to the coach and the athlete – that's when the discussion and brainstorming can begin.

These days, most coaches are equipped and educated to understand our world; however, communications skills are key in order to describe our proposals in very basic terms and then progress the technical explanation if needs be. There is no guarantee though, even for the most legitimate idea. We need to be prepared for a coach or athlete to reject it if it does not fit in with their programme.

There's also a time and a place. Right now we are in the last phase of the Olympics and Paralympics, so this is not the time to say 'Let's scrap that and try this!'. Change and innovation are best placed in the post-Olympic period – when we have two years where we are trying and testing new ideas. The third year is refining these plans and in Olympic year there should be very few changes in strategy – just a bit of fine-tuning.

How do you develop your ideas? Do you cherry pick published research to see how it may work for elite athletes?

There are two approaches to it: the interpretation of new breakthroughs and the testing of coach's ideas. It has been described in Darwinian selection terms where a coach and athlete are continually trialling and testing, accepting and rejecting practice and developing their system through trial and error. If they do a session too many times or if they over-work a certain component, that idea gets rejected from the practice pool fairly quickly, as they start to fail. If a coach says 'what about this?' we can go back to biological first principles to assess whether it makes sense or not, is it stressing the body in different ways? Then we can trial it for a period of time to get some measurements and reassess to see whether it has improved certain physiological capabilities.

The other approach is the interpretation of new breakthroughs, new data that are reported. There may be a nugget of information that might make sense – it might have some emerging responses from sedentary or recreationally trained athletes,

so we can trial that. Looking beyond the *P* value is another aspect of using research. It is unconventional but it is actually at the very heart of applying knowledge to elite athletes. Just because *P*, for example, might equal 0.08, it doesn't mean that it not relevant, it just doesn't comply with pre-set alpha levels of probability. We need to interpret results and see whether we could use it as a concept; for example, scientific studies are looking for a large percentage change, but in elite athletes, we are looking for very small percentage changes, but we are looking for those changes to aggregate over time.

Has funding increased to reflect the increased dependence in sports science and what it can offer?

Following the announcement in 2005 that London would be hosting the Olympic and Paralympic games, £600m was made available for the preparation of the teams. The last cycle (four-year period running up to the games) for 2012 has had £300m invested; an unprecedented level of funding in the UK – but this doesn't just cover science provision, this covers everything from athletes equipment, to their training facilities and everything in between. We traditionally work in cycles, working up to a games and then afterwards we stop, re-breathe and go again, but now we are starting to plan much longer term, which is the first time in my experience we have been able to do that.

The good news is that UK Sport – in looking for a legacy to the London Games – has secured similar levels of funding towards Rio 2016.



“Very little if any real funding is looking at elite groups. For us, it is a shame that no one is properly funding this, as it means we don’t have the knowledge base, which is essential to drive our high-performance agenda.”

Steve Ingham

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This will hopefully prevent the ‘drop off’ in performance seen by host countries such as Australia and Greece in previous years.

Do you think London hosting the games has inspired more to take up exercise physiology?

Sports science is one of the most popular courses at university. Approximately 15,000 undergraduates come out with a sports science or related degree each year. It is a very multidisciplinary degree combining science, mathematics etc., and graduates are very employable.

The funding that comes in to sports and exercise departments is predominantly around exercise sciences – looking at diseases, cardiovascular risk factors etc., in order to see how exercise can improve the outcomes for these groups. Very little if any real funding is looking at elite groups. For us, it is a shame that no-one is properly funding this, as it means we don’t have the knowledge base, which is essential to drive our high-performance agenda. It also means that sports science graduates aren’t necessarily equipped to become sports scientists – so we certainly have trouble recruiting (although admittedly we are looking for a very small proportion of people from the overall pool), we struggle to find scientists with the vocational skills of working with athletes. Most courses aren’t really developed to be vocational which is something to be lamented.

Do you think this might change after the Olympics?

I don’t think it will be the Olympics that initiates a change – employability and student fees will drive it. A number of universities have approached me to look over their courses as they re-validate them to make them more applied, but that is three, four, five years down the line.

What discovery has changed sporting performance the most?

There isn’t a single discovery that has changed the landscape. There are many areas of interest that we think could have a large impact on

performance; however, for whatever reason – logistical issues or means for testing – they just haven’t, yet. In some cases it can take a long time: one example that we’ve been working on for about ten years now is the concept of manipulating warm-ups prior to an event. At the beginning of the 2000s, it was clear that ‘priming’ the system could improve performance. However, coaches and athletes were and are very protective of warm-ups – they don’t really want to be tinkering around with them. There was a reluctance to change their practice.

We then observed what different groups were doing and found that sprinters were warming up in similar ways to endurance athletes – which didn’t make sense. We received some funding to do research – to trial different warm-ups. We were able to study high-calibre elite athletes in a performance setting – a time trial – coupled with measurements of the underlying physiology. The data really spoke for themselves; priming improved 800 metre running performance by about 1% – which is a very large margin for a high-performance athlete

“Yes, we are focused on sporting achievement, but in doing so we are not only advancing the boundaries of human performance, in doing so we are understanding how the body and mind respond to work and stress. That, as a celebration of what we know and how we are progressing, I think, is just as meaningful as us going to the moon – as a means to discovering many other things.”

Steve Ingham

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group. We put that in front of coaches and they immediately responded primarily due to the respect of the calibre of athletes involved. The practice of priming the warm-up is now embedded in all of the physiological sports – cycling, swimming, rowing, etc. As a practice change, it was held off and resisted for a long time – but just that one study has led to a much higher-level conversation with coaches. Our job is sometimes a tricky sell, but with some good data behind it, we are able to apply it.

Is scientific intervention spoiling the concept that sporting achievement is based on natural ability?

There is something that appeals to us about pure effort as opposed to over-engineered sports. At the heart of any sport, athletes are running and jumping about, and we are cheering about it. It’s fair to ask whether we should be ploughing the resources into something more worthwhile. It is an idea I wrestle with.

I think we have a natural impatience for progress – that is the heart of it. We have a yearning for progress and continual improvement. Humans have this inner tendency to want to see our tribe do better than the next tribe. There will always be a natural competitiveness between groups, which is probably why we, as nations, are so immersed in it.

Yes, we are focused on sporting achievement, but in doing so we are not only advancing the boundaries of human performance, in doing so we are understanding how the body and mind respond to work and stress. That, as a celebration of what we know and how we are progressing, I think, is just as meaningful as us going to the moon – as a means of discovering many other things.

In the future, I think you will undoubtedly see a much greater ‘performance culture’ coming to Olympic and Paralympic sports, and this will filter down to all sports.

I think the notion of sporting competition with a purely level playing field is a redundant point – attempting to ensure everybody is treated with the same conditions in each country, in a sterile environment, give athletes the same shoes and the same running surfaces and so on. It is both unfeasible and undesirable to most, and as much as science can give advantages there is also an element of levelling the playing field with science. Ultimately, you will always get people who dominate and they will dominate independent of science. When I had the honour of working with Redgrave and Pinsent, they were just phenomenal – they were going to get a gold medal independent of science input, I am sure. Usain Bolt doesn’t need an aerodynamic suit, he doesn’t need that level of advantage, he will still win with a flappy vest! And that is the beauty of it. People can transcend human performance with pure natural talent.

For more information on the EIS, visit: www.eis2win.co.uk. ♦

In lasting memory of: Brian James Whipp

1937

Tredegar,
South Wales

1960

qualified as a
teacher at
Loughborough
College

1984

elected a Member
of The Physiological
Society

1994

started as Editor
on the Board of
Experimental
Physiology

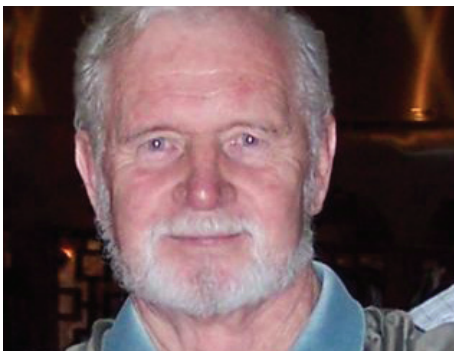
2001

retired as Emeritus
Professor in 2001.

2011

died on 20 October,
at the University of
Wales Hospital after
a short illness.

Obituary Brian James Whipp 1937–2011



Written by Susan A Ward

Brian Whipp was born and grew up in Tredegar in the South Wales Valleys. His first love was sport and, after qualifying as a teacher at Loughborough College in 1960, he was a Lecturer in Physical Education at Dudley Technical College and then at Prince of Wales College in St Johns, Newfoundland, Canada. The award of a Danforth Graduate Fellowship allowed him, however, to consider a research career. Following a BSc (1963) and MA (1964) in Physical Education at the University of Florida in Gainesville, he gained a PhD in Physiology from Stanford University in 1967 under the tutelage of Karlman Wasserman and then moved with him to the Division of Respiratory Physiology and Medicine at Harbor-UCLA Medical Center,

“Brian and his collaborators produced defining research in muscle energetics, pulmonary gas exchange and ventilatory control during exercise. His early recognition that control systems analysis and mathematical modelling provided a means of remotely interrogating physiological system function has proved highly influential.”

Susan A Ward

Torrance, California. Following a brief period as a Lecturer in the Department of Physiology at University College Cardiff, he became an Assistant Professor of Physiology and Medicine at UCLA, later to become Professor of Physiology and Medicine and Vice-Chairman of the Department of Physiology. He returned to the UK in 1992 as Head of the Department of Physiology at St George's Hospital Medical School, retiring as Emeritus Professor in 2001.

Brian and his collaborators produced defining research in muscle energetics, pulmonary gas exchange and ventilatory control during exercise. His early recognition that control systems analysis and mathematical modelling provided a means of remotely interrogating physiological system function has proved highly influential not only because of its impact on experimental technique, but also because it has provided a valuable slant on homeostatic operations as diverse as ATP status in skeletal muscle and arterial blood pH

regulation and how these are challenged at the limits of tolerance. Indeed, his research undertaken at St George's with John Griffiths in the late 1990s allowed the kinetics of intra-muscular high-energy phosphate turnover and pH to be quantified with high fidelity in concert with oxygen uptake kinetics while subjects exercised inside a 'whole-body' NMR magnet, a technical feat others have yet to reproduce.

Brian was elected a Member of The Physiological Society in 1984 and regularly presented at Meetings. He served on the Committee (1993–1997) and was an Editor on the Board of Experimental Physiology (1994–2000).

Brian was also a scholar of Shakespeare, and intensely interested in philosophy, literature and music but, above all, he was a family man. He died on 20 October, 2011 at the University of Wales Hospital Cardiff, after a short illness.

In lasting memory of: David George Shirley

1947

Born in Hull,
England

1972

appointed Lecturer
in Physiology

1973

joined The
Physiological Society

2009

diagnosed with
acute myeloid
leukaemia

2011

Dave died peacefully
at home on 20
October

Obituary David George Shirley 1947-2011



Written by
Steve Walter

Dave Shirley was born in Hull, which explains his lifelong devotion to Hull City FC. He obtained his degree in Physiology from Sheffield University and his PhD at Chelsea College under the supervision of Sebastian Dicker. In 1972 he was appointed Lecturer in Physiology at Charing Cross Hospital Medical School. His research thereafter was based on *in vivo* renal micropuncture and, in collaboration with Robert Unwin, microperfusion. These techniques allowed widespread investigations into segmental renal function, most notably, perhaps, clarification of the value (and shortcomings) of renal lithium clearance measurements as a non-invasive method for determining separately the function of the proximal and distal segments of the nephrons.

Dave was a perfectionist. His surgery was meticulous and great attention to detail was applied to everything. He was also a gifted, popular and enthusiastic teacher; whenever students were questioned about the merits of the teaching staff, he invariably came out on top. It is a measure of the esteem in which he was held that, on hearing of his illness and treatment, some 400 UCL students added their names to the register of bone marrow donors.

The merger of Imperial College and the Charing Cross and St Mary's Medical Schools was not to Dave's liking and, not being a man to compromise, he resigned his position as Senior Lecturer. However, he had just been awarded a grant to study the renal handling of aluminium. He got round this problem by arranging for the grant to be transferred to his fellow researchers and applying for a part-time post at a much reduced salary – nominally as a junior research assistant; however, there was little doubt who was driving the research.

Dave joined The Physiological Society in 1973. He was a founder member of the Renal Group that met following Society Meetings during the 80s and which was a forerunner to the Special Interest Groups and, more recently, Themed Meetings.

Dave continued his collaboration with Robert Unwin but now at the Royal Free and University College Medical School, investigating, in particular, the renal purinergic system, a field in which they made a widely acknowledged contribution. His efforts were rewarded by an Honorary Readership. Sadly, in 2009, he was diagnosed with acute myeloid leukaemia and, despite a bone marrow transplant, he died peacefully at home on 20 October. He will be greatly missed by all who knew him, worked with him or were taught by him.

The Society also regrets to
announce the deaths of:

Alan Chipperfield

Paul Richardson

and Rolf Niedergerke.

Full obituaries for Alan Chipperfield,
Brian Whipp and Dave Shirley can be
found on The Society website at:
www.physoc.org/late-members

“His surgery was meticulous and great attention to detail was applied to everything. He was also a gifted, popular and enthusiastic teacher; whenever students were questioned about the merits of the teaching staff, he invariably came out on top.”

Steve Walter

Experience: Balancing research aspirations against teaching duties

Written by

Jamie McPhee

I recently made the switch from post-doctoral researcher to academic staff in the School of Healthcare Science, Manchester Metropolitan University. My research focuses mainly on understanding the way in which our skeletal muscles change as we get older and the benefits of exercise to maintain health throughout our lifespan. I also teach physiology to undergraduate and postgraduate students.

On the face of it, the transition to academic staff would appear to be straightforward because I remained in the same department in which I was a post-doctoral researcher. I therefore did not have to relocate my family, establish myself within new research labs or enter new social circles. But I have come to appreciate that the directives for academic staff differ from those for research staff and this has taken a little time to get used to. Academic staff must balance research interests against the need to deliver teaching and support to undergraduate and postgraduate students, while it is the privilege of a post-doc to be able to manage their own time and concentrate almost exclusively on research activities.

As a post-doc, I worked on an EU-funded FP7, multi-centre collaboration and my main tasks were to coordinate research activities across different test centres as well as manage our own specific part of the study. I had the freedom to manage my efforts in a way I thought fit, develop new skills and to follow up my own interests and lines of enquiry. The work was demanding, but as long as the deliverables were being met, all was well.

“There are the obvious scientific interests in trying to measure the physical capability of older people, determine why muscles become smaller and weaker in old age and, importantly, find out whether there is anything we can do to slow the deterioration.”

Jamie McPhee

The research area is the ageing neuromuscular system in humans. Whether we like it or not, from middle-age onwards, physical function does deteriorate. The progressive deterioration in muscle size, strength and neural control can lead to mobility problems in later life and, consequently, to loss of independence and social isolation.

Research into ageing and other related projects remains my main area of academic interest, but since November 2011, my time has been filled with teaching undergraduate students (some of whom are anxiously trying to complete their final year dissertations) and supervising postgraduate students who are running their own research projects, while trying to continue my own research. There are benefits of lecturing and supervising students. First, it's a chance to catch up on the textbook physiology, things that I really should know, but have long since forgotten. There's also the reward of pitching a lecture at the right level and seeing the enthusiasm in the faces of students when they come to understand difficult concepts. In the longer term, the keen MSc and PhD students will also help out on specific research projects.

Indeed, as I begin to plan research projects and to delegate tasks I can see that less and less of my time will be dedicated to data collection and more to teaching and project management. But for now, I intend to enjoy my time in the research labs.

My research into ageing is rewarding in many ways. There are the obvious scientific interests in trying to measure the physical capability of older people, determine why muscles become smaller and weaker in old age and, importantly, find out whether there is anything we can do to slow the deterioration. We have established in our research laboratories numerous techniques to be able to characterise the ageing neuromuscular system. A typical sequence of tests in my ongoing studies includes measurements of mobility to gain an insight into the extent to which older people are impaired in their daily lives, such as walking speed, stair negotiation and rising from a chair. We would then perform more controlled measurements of skeletal muscle strength, power and fatigue resistance. During these assessments we would typically monitor neuromuscular activation using a combination of voluntary as well as



Master sprinters competing at the European Master Athletic Championships

electrically stimulated muscle contractions and electromyographic recordings. We also use various imaging techniques to assess muscle size and contractile characteristics, including ultrasonography to record the movement of muscle fascicles during contractions; dual-energy X-ray absorptiometry to measure whole-body and regional lean mass and body fat; but perhaps most revealing of all in terms of characterising structural changes within skeletal muscle, is magnetic resonance imaging. We are privileged to have an MRI dedicated solely to our research purposes. Comparing cross-sectional, transverse images of young and elderly thigh muscles has shown the extent to which skeletal muscles deteriorate.

The quadriceps muscles of an average 70 year-old are around 30% smaller than those of the average 25 year-old of the same sex. This loss of muscle mass with ageing is known as sarcopenia. MRI scans have also shown extensive infiltration of adipose tissue in and around the muscles. Adipose tissue, of course, also accumulates in other parts of the body as we get older. Another technique that we use rather more sparingly is the muscle biopsy. From the small, precious samples of vastus lateralis muscle (about the size of two grains of rice) we assess muscle fibre type composition, fibre cross-sectional area, mitochondrial proteins, mRNA profiles, capillary density, single fibre contractile properties and other characteristics of the muscle. It also gives the opportunity to measure localised inflammation and oxidative stress, which might influence the ageing process. It is apparent that the combination of reduced muscle mass, strength, power and control, coupled with increased body fat levels,

contributes to mobility problems in later life. The muscles of older people are smaller for two main reasons: atrophy of muscle fibres – mainly the type II fibres, as well as a loss of muscle fibres so that older people have fewer muscle fibres overall. All of this raises the question of what can we do to stop, or at least slow, the deterioration.

Currently, the most effective and widely applicable intervention for ageing is exercise. Maintaining a good diet and possibly increasing the consumption of amino acids might also help, and these are two of the research projects I'm currently working on. People who exercise or maintain high levels of physical activity are usually better off at all stages of life than those who are less active or sedentary. I believe this message is clear and well known to the general public, but the statistics make for sorry reading. In England, around two-thirds of people do not meet minimum recommendations for physical activity levels. There are certain groups of people, however, who are highly physically active and engage in competitive sports. Over the years our research group has been attending the European and World Master Athletics Championships to take measurements of skeletal and neuromuscular characteristics, and we are currently planning new studies for this summer. The athletes are aged from 40 to over 90 years and are incredibly dedicated to their sports. We have measured physiological characteristics of some of the world's fittest and most mobile people for their age. To give an indication of their capabilities, the world record for 100 m for males aged 75 years is 13.54 seconds. Although these highly active older people maintain excellent mobility, this

type of research has shown that exercise is not a 'magic pill'. From my observations in testing a couple of hundred 'healthy' older people and a similar number of Master Athletes who are highly physically active and dedicated to their sports, it seems that deterioration of muscle mass and function in old age is inevitable. There are biological processes that we do not understand affecting ageing skeletal muscles.

A less apparent facet to this research is that the older people who volunteer for our studies, usually aged 70 years or more, invariably have interesting and unique tales to tell. The anecdotes can offer an insight into social changes, such as one couple in their late 70s who told how they had "stretched themselves as young adults to buy a nice house for £5000 in a quiet suburb of Manchester. The same house was on the market again in 2010 for more than a million pounds". The stories told by older people can also reveal aspects of life that are of scientific interest. A good example is the contrast between the comfortable lives that most of us lived as children and young adults with plentiful supply of (high calorie) food and motorised transport, and the deprivation

30%

The quadriceps muscles of an average 70 year old are around 30% smaller than those of the average 25 year old of the same sex. This loss of muscle mass with ageing is known as sarcopenia.

suffered by many children in war-time and post-war Europe. These secular changes offer an added complication for research into ageing and reminds us that we must be careful when drawing conclusions concerning ageing, especially in cross-sectional studies comparing modern day young with older adults.

In short, making the transition from post-doctoral researcher to academic staff has brought with it a new challenge. I'm sure the story is a familiar one to academics in most other universities: at fixed times every week I must deliver lectures, tutorials and practical classes and guide anxious final year students through their dissertations. Balanced against this is the desire to maintain research aspirations.



The Society's website – looking forward

Written by
Liam McKay

In November 2011 we launched The Society's new website (www.physoc.org). The website has been given a completely new look to reflect the new Society branding and, based on our analysis of usage on the old website, we have completely revised and repositioned all our content to give visitors a more intuitive experience when navigating pages.

As well as providing information to the broader scientific community, the education sector and the general public, the website now comes with a host of features that are designed to deliver content relevant to you. Pages within the website are now categorised by Themes and Tags; we have also fully incorporated our Society Meetings into the website – allowing visitors to filter meetings of interest. You can also opt to 'watch' content. All of these new functions mean that we can flag content, such as jobs, meetings and news items, to you rather than you

having to trawl the site for it. Members are encouraged to update their profile and indicate the Themes they are interested in.

This will ensure that, once logged in, you get the most from the new site and can access the most relevant information direct from your personal homepage.

The website is not yet finished. We have a number of projects in the pipeline that will further enhance the online experience. We plan to completely redesign the *Physiology News* platform into a new online magazine that will incorporate a fully searchable archive of all past issues.

We are also in the process of developing the committees section of the website, providing a place for committee members to obtain information and collaborate together. The Member Directory will see a number of enhancements, including the Member's service(s). We will be revamping our video content with a view to delivering presentations with integrated slides, and also improving the way we present the benefits available to our Members.

“We are also in the process of developing the committees section of the website, providing a place for committee members to obtain information and collaborate together.”

Liam McKay, Head of Technology, The Physiological Society

13,000

We hope you find our new website an improvement. We are encouraged by the 13,000 visits the website receives each month.

We hope you find our new website an improvement. We are encouraged by the 13,000 visits the website receives each month. However, we are constantly seeking to improve the functionality and content provided to visitors. If you have any queries, comments or suggestions we would love to hear from you at membership@physoc.org.

Why not visit...
www.physoc.org

Raising awareness of The Physiological Society at Queen Mary

Written by
Rachel Ashworth

I am one of only a few physiologists within a large biology department and, as you can imagine, this presents some advantages as well as disadvantages. Seminars can prove a challenge as there are many interesting talks but few that directly address topics in physiology. However, closer examination of Queen Mary College reveals a total of 11 Physiological Society Members across many different departments and faculties.

As a Society Rep, I could apply for the departmental seminar scheme if there were 12 Members at Queen Mary. If we could reach this critical mass it would make us eligible to apply for up to £800 to run a series of seminars. The aim of this would be to unite our small group, by attracting visiting speakers and hopefully stimulate wider interest in physiology as a subject.

With this in mind I decided to apply to the Society Rep fund and hold an event to promote The Society and encourage people to become Members. I chose the old library within the medical school as the venue to host the event. Despite the Medical School perhaps being the

most obvious home of physiology, there are actually very few Members in this faculty compared with the number in Science and Engineering. Interaction between these two groups is encouraged but it is often practically difficult as they reside on different campuses. A joint interest in physiology might encourage more communication between these groups.

I called upon the small but enthusiastic gang of postdoctoral and postgraduate student Members (Angus Wann, Clare Thompson and Lise Mazelet) to help with the event. I wanted people to come and hoped that the promise of free tea, coffee and cakes would prove an irresistible draw. Advertising was important and we produced flyers and posters, circulated information via staff

lists and in eBulletins. On the day it was Clare who managed to coerce one of the Medical School staff into circulating a timely reminder and this was probably the most effective advert of all.

We had more than 30 people drop by, recruited a new Affiliate Member and are in the process of generating an undergraduate group. I am not sure as yet that we have hit critical mass for my original seminar application but I am still working on that.

I did meet several members of the British Pharmacological Society who dropped by to support the event (and have tea and biscuits). As a networking event I would consider this a success and I will continue to build towards hosting future Physiological Society events.

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“As a networking event I would consider this a success and I will continue to build towards hosting future Physiological Society events.”

Rachel Ashworth



Reminder: Election to the Council of Trustees – call for nominations

Following the AGM that will take place in July, six trustees will be stepping down from The Society’s Council. Nominations are therefore being sought to replace these trustees, and proposals should be received by 1pm on Tuesday, 1 May 2012.

Trustees are legally responsible for the overall governance, management and policy of The Society, ensuring that the charitable objects for which it has been set up are met. The Trustees are also the Directors of The Society. For more information, please click here: www.physoc.org/nomination.

Lab profile: The University of Manchester's Centre for Integrative Mammalian Biology (CIMB)

Written by

Sarah Fox

The John Gigg Lab is part of the Systems Neuroscience Research Group within the Faculty of Life Sciences at The University of Manchester. The Faculty has a global reputation for research excellence, being named in the top three UK Biology groupings in the 2008 RAE. In line with the Faculty's drive towards cross-disciplinary research we encourage inter-lab collaboration. This allows us to explore the function of the mammalian hippocampal formation through a mixture of techniques including *in vivo* electrophysiology, immunohistochemistry, information analysis and novel behavioural paradigms.

The hippocampus and other medial temporal lobe structures are crucial for both memory acquisition and the formation of spatial maps of the environment. They are also a target for several brain pathologies and may, in particular, play a critical role in the cognitive deficits experienced by Alzheimer's disease (AD) sufferers. Our current work uses rodent AD models to investigate how AD pathology modulates the flow of information within medial temporal lobe structures and what effect this has on learning and memory.

The majority of our current research is conducted by three postgraduate students: Katherine Davis, Daniel Squirrell and myself. Katherine's work, in collaboration with researchers from the Department of Psychology at the University of Durham, explores how a test for episodic-like memory (autobiographical memory for past events) can be used in mice to dissociate hippocampal performance from that of other cortical regions. Her work with transgenic mice expressing AD-like pathology is highlighting the central role played by hippocampal pathology in specific episodic-like memory loss. She has also been able to track how the deficit develops over time as pathology worsens. Katherine also uses *in vivo* recording methods to assess how Alzheimer's pathology in transgenic mice influences hippocampal synaptic physiology.

Daniel Squirrell recently completed a Masters project in our lab and is now embarking on a PhD with us. He works in collaboration with another Manchester-based group, headed by Marcelo Montemurro, who specialise in computational neuroscience and information theoretical analysis. His research combines *in vivo* multi-channel recording methods with cutting-edge computational analyses, allowing quantification of information transfer across different regions of the hippocampus. These techniques are being applied in both healthy and Alzheimer's transgenic animals with the hope of providing a greater understanding of how Alzheimer's pathology alters information flow. Daniel and our current Masters student Michael Howarth have also pioneered

signals using custom-designed (MATLAB, MathWorks) software to differentiate periods of oscillatory activity and assess how different frequency bands interact. It is hoped that this research will provide insight into how Alzheimer's pathology influences network activity, possibly laying the foundations for the use of such analyses as a diagnostic tool.

The lab is now beginning to move towards the use of optogenetics for targeted activation of specific neuronal populations. In this we are attempting to control the activity of both ionotropic and metabotropic receptors expressed by neurons, in collaboration with the laboratory of Rob Lucas at Manchester. This will allow us to not only control neuronal activity

"My work focuses on how theta and gamma oscillatory activity (brain rhythms) can be modulated by Alzheimer's pathology. The purpose of these rhythms is widely believed to be the orchestration of activity across widespread neuronal populations in order to encode, represent and store information."

Sarah Fox

immunohistochemical studies investigating the spread of both amyloid β 1-42 plaques and interleukin (a marker of inflammation and possibly a key trigger in development of AD and other neurodegenerative disorders) in Alzheimer's transgenic brain tissue.

My work focuses on how theta and gamma oscillatory activity (brain rhythms) can be modulated by Alzheimer's pathology. The purpose of these rhythms is widely believed to be the orchestration of activity across widespread neuronal populations in order to encode, represent and store information. There is currently intense interest in how these rhythms might break down in AD and other brain pathologies. I use *in vivo* multi-channel recording techniques to simultaneously monitor both spontaneous and evoked oscillatory activity within the hippocampus and prefrontal cortex. Following recording, I analyse these

instantaneously but also to adjust the long-term excitability of targeted neurons. It is hoped that this exciting new technique may be used to activate specific sub-populations of hippocampal neurons and may in future enable us to shed light on how different neurons contribute to field oscillations and mnemonic encoding.

Our lab is part of The University of Manchester's Centre for Integrative Mammalian Biology (CIMB). The CIMB is funded by the BBSRC, the Higher Education Funding Council for England, Medical Research Council, Scottish Funding Council, the British Pharmacology Society's Integrative Pharmacology Fund and receives donations from AstraZeneca, GlaxoSmithKline and Pfizer. Continuing support from the CIMB has facilitated the excellent research conducted within our lab and ensures we are able to offer highly sought-after opportunities to future research students.

The last word and finally...

Dame Nancy Rothwell is a longstanding member of The Physiological Society. She is President and Vice Chancellor of the University of Manchester and delivered The Society's public lecture in 2010, entitled "Tracking down killers in the brain: possible new treatments for brain disease".

Nancy Rothwell appointed as co-chair of the Council for Science and Technology

Prime Minister David Cameron has appointed Professor Dame Nancy Rothwell to the Council for Science and Technology (CST) as its new co-chair. The Council advises the Prime Minister on strategic science and technology policy issues that cut across the responsibilities of individual government departments.

Announcing Dame Nancy's appointment, the Prime Minister said: "The UK's outstanding research base together with its strong entrepreneurship gives it immense potential as an innovation economy. Nancy Rothwell's understanding of science and its relationship to business will enhance the Council's high calibre expertise and ensure that science and technology continues to drive UK growth."

Dame Nancy is a longstanding member of The Physiological Society. She is President and Vice Chancellor of the University of Manchester and delivered The Society's public lecture in 2010, entitled 'Tracking down killers in the brain: possible new treatments for brain disease'.



Podcasts

Look out for a new set of podcasts from the *Biological Basis of Elite Performance* meeting, held in March. The series of interviews, will be appearing on The Society website in April.

Contributors

PN is always looking for contributors for future issues, and feedback on our content. If you would like to get in touch, please send an email to pneditor@physoc.org

Erratum

In a previous issue of *Physiology News* (PN85, pp. 9–10), the interview with Roger Tsien contained an error. Roger Tsien has no children. The children referred to on p.10 are those of his brother, Richard Tsien. We apologise to all concerned for this error.

Introducing...



Cornelia Schnelle

I joined the Society as Director of Publications in March, initially sharing responsibilities for Publications with Carol Huxley who is planning to retire in the autumn of this year. My focus will be to work with the Publications Committee and the Task Force to review the Society's publishing strategy, renegotiate the publishing contract and develop the Society's publishing portfolio. Previous roles have included Managing Editor for BioMed Central's BMC series of journals and Editorial Director at Faculty of 1000. Most recently, I was responsible for digital product development at the British National Formulary, a joint venture between the Royal Pharmaceutical Society and the BMJ Group.

Early Career Author's Prize 2011 Winners – just announced!



The winner of the 2011 Experimental Physiology Early Career Author's Prize is **Adam P Mecca** of the Department of Physiology & Functional Genomics, University of

Florida, USA, for his paper Cerebroprotection by angiotensin-(1–7) in endothelin-1-induced ischaemic stroke by Adam P. Mecca, Robert W. Regenhardt, Timothy E. O'Connor, Jason P. Joseph, Mohan K. Raizada, Michael J. Katovich, and Colin Sumners. *Exp Physiol* 96, 1084–1096; doi:10.1113/expphysiol.2011.058578



The runner-up is **Charles C T Hindmarch** at The Henry Wellcome Laboratories for Integrative Neuroscience and Endocrinology, University of Bristol, UK for

his paper, The transcriptome of the medullary area postrema: the thirsty rat, the hungry rat and the hypertensive rat by Charles C. T. Hindmarch, Mark Fry, Pauline M. Smith, Song T. Yao, Georgina G. J. Hazell, Stephen J. Lolait, Julian F. R. Paton, Alastair V. Ferguson, and David Murphy. *Exp Physiol* 96, 495–504; doi:10.1113/expphysiol.2010.056515

Both these papers can be freely accessed from ep.physoc.org as can details of how to enter for the 2012 prize. The awards will be presented on Tuesday 3 July at Physiology 2012 in Edinburgh.

What our Members say

“Joining The Physiological Society has exposed me to cutting-edge research in areas I had only previously learnt about in lectures. It is also a great way to meet the academics whose work I study in detail as part of my course. The Society offers subsidised joining rates for undergraduates, generous travel grants and free attendance for undergraduates to scientific conferences – I would highly recommend it.”

Undergraduate Member