PN
Physiology News
Issue 103 / Summer 2016

Numberism

when science and art come together

H³ Symposium

Novel Approaches to Hormone Sensing
(The Inaugural Bayliss-Starling Symposium)

14 September 2016
Hodgkin Huxley House, 30 Farringdon Lane,
London EC1R 3AW, UK

Organised by
Timothy Wells, Cardiff University, UK
Paul Le Tissier, University of Edinburgh, UK

www.physoc.org/novelapproaches

Speakers

Martin Champion
EPSRC, UK

Becky Conway-Campbell
University of Bristol, UK

Monica Cracium
University of Exeter, UK

Julian Davis
University of Manchester, UK

Kurt Gothelf
Aarhus University, Denmark

Andy Harvey
University of Glasgow, UK

John Kopchick
Edison Biotechnology Institute, USA

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Heptares Therapeutics, UK

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Tokyo, Japan

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NC3Rs, UK

Aravind Vijayaraghavan
University of Manchester, UK

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Cardiff University, UK

The Physiological Society

Physiology News

We welcome feedback on our membership magazine, or letters and suggestions for articles for publication, including book reviews, from Physiological Society Members. Please email **magazine@physoc.org**

Physiology News is one of the benefits of membership of The Physiological Society, along with reduced registration rates for our high-profile events, free online access to The Physiological Society's leading journals, *The Journal of Physiology* and *Experimental Physiology,* and travel grants to attend scientific meetings. Membership of The Physiological Society offers you access to the largest network of physiologists in Europe.

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Welcome to the Summer 2016 edition of *Physiology News*

Introduction

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Membership

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Cover image: 'Physic Tears' by Sienna Morris

Limits of Perception: Advances in Bioimaging

Enhancing the impact of imaging science in physiology & medicine

8 – 11 August 2016
University of Warwick, UK

Organisers
Mark Lythgoe, Daniel Stuckey & Tim Witney
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www.ucl.ac.uk/cabi

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www.physoc.org/bioimaging2016

The Physiological Society

Roger Thomas

Editor, *Physiology News*

This issue will be published just before the 2016 main meeting of The Society, held jointly with the American Physiological Society in Dublin. To link with this we publish descriptions of Dublin physiology departments, and I have also asked several distinguished physiologists to remember their transatlantic postgraduate or postdoctoral experiences. Only three of them have met the deadline. I have the impression that such periods abroad were once more popular than they are now, perhaps because young physiologists are concerned that it may be more difficult to find a position back in their home country once they are abroad.

The Wellcome Trust has a scheme that gets round this problem, but it only covers a few fellows. Everyone I have contacted who did spend a year or more abroad seems very happy to have done so, if reluctant to write about it. There is an article about a numerical approach to Physiological Art, and more seriously, calcium and magnesium standards. We also publish a fascinating analysis of Darth Vader's respiratory problems arising from a near-death experience on the volcanic planet Mustafar.

Perhaps it is relevant to outline my own experience. As one of the last (in 1958) to be liable for two years military service in the UK I had chosen to defer call-up in the hope that rumours of its abolition were true. I went to the University of Southampton (I was rejected by Bristol and St Andrews) and ended up in 1964 with a BSc, a PhD and a wife. (I still have all three) Call-ups for National service did indeed end in 1960. I next spent two very valuable years working at the Rockefeller University in New York. Ironically, since I had an immigrant visa, I was liable for military service in the USA after a one year residence! Being married and also too old I luckily escaped this. My laboratory PI was Victor Wilson, who has contributed an article to this issue about his year in Cambridge. While there, he met Gerald Kerkut, who later was my PhD supervisor at Southampton. Once my PhD work was finished it was Gerald who wrote to Victor and secured my position at RU. Remarkably, a few weeks after he wrote I received a letter signed by the President of the Rockefeller offering me a job at a salary, as I recall, of $7,000. I had filled in no application form, nor been interviewed by anyone. Gerald must have written an extraordinary letter. Apparently, it arrived just as the Dean was thinking it would be good to expand the course on basic neurophysiology. While there, I worked on cat motoneurones and Renshaw cells, and taught two short courses on invertebrate neurophysiology. The students were all graduates registered for a PhD, and many were older and better-informed than I was. I returned to the UK in 1966 to a postdoc at UCL with EJ Harris. The two years in New York were the highlight of my early years, and completely spoilt me for the seedy and dilapidated environment at UCL. Three years later, I became a lecturer in Physiology at the University of Bristol.

This issue also has a note about changes to the Society's Articles of Association, to be approved at the Dublin AGM. One of the points made is described as follows: 'Until recently, voting members could raise motions to be discussed at the AGM. This has not occurred in recent years and it was felt important to restore it. From 2017, voting members will be invited to submit such motions.' It is ironic that this is for the Dublin meeting, since it was in the run-up to the 2009 Dublin meeting that the Trustees decided that motions could only be on the agends if supported by 5% of the membership instead of the two members as allowed previously. One member did obtain support for a motion from the required 5%, but his proposal to lower the required support from 5% to 5 members was defeated after the Trustees argued that such a low number might allow The Society to be hijacked by hostile elements. I always found that actual votes on motions enlivened AGMs, which too often seem organised to avoid any serious discussion of the Trustees' decisions. Before 2009, any votes with which the Trustees disagreed were usually ignored anyhow.

Readers of The Society's emails will have noticed that annual general meetings in the British Isles will soon be biennially detached from the main meeting. 30 years ago, they were always held in March at University College London, then they were moved to the summer and a wide variety of meeting sites. Now it has been decided that the main meeting in 2020 will be held in Germany, and the 2022 somewhere in Scandinavia. This is a consequence of an agreement between The Physiological Society, the Scandinavian PS, the DPG and FEPS to co-host a series of biennial joint meetings, starting in London in 2018. Meanwhile we have the 2017 AGM to look forward to. I believe it is to be held somewhere in Great Britain, rather than in Rio de Janeiro (where the IUPS meeting will be held instead of The Society's annual main meeting), in a country whose president is being impeached as I write.

Some readers kindly enquired after my recovery from my downfall at the end of January. It is almost complete, thank you. The photo above was taken recently, and I can report that the stairs concerned are now fully carpeted and much better lit.

Errandum: We apologise for an error in our PN102 edition. The article Eat.Poo.Sleep was written by Sai Pathmanathan, who is a Science Education Consultant and Public Engagement Grant Awardee, and not Outreach Officer at our Society, as incorrectly stated.

Changes to the Articles of Association: the governance review

Although The Society was established 140 years ago, in 1876, its primary constitution (which also included a Memorandum of Association until 2011) was formed in 1937 upon incorporation as a limited company. These articles have been regularly updated, most recently in 2011 as a result of the 2006 Companies Act. The Society has a responsibility to ensure that its governance not only accords with current legislation and best practice but is fit for purpose in facilitating the proper and smooth running of its operations.

Following the new strategic plan, an external review was commissioned in 2013 to report on The Society's governance structure. Oversight of the review and the subsequent recommendations was delegated, by Council, to a Governance Review Steering Group comprising Phil Aaronson, Sue Deuchars, Lucy Donaldson, Blair Grubb, Lucia Silvilotti, Rachel Tribe and initially chaired by Jonathan Ashmore (President) and then succeeded by David Eisner (Deputy President) from July 2014. The external review was conducted by Anne Moynihan, a specialist charity governance consultant. Considerable assistance from Keith Lawrie, the Learned Societies' Liaison Officer for The Foundation for Science and Technology, was also received in respect of constitutional changes.

The Steering Group has, to date, met five times and has drafted the changes which will be put to the voting members for approval at the 2016 AGM. The current and revised Articles can be found at **http://www.physoc.org/AGM-notice2016**. The rest of this article describes the more important changes.

Simplification of the Articles

The Society's wider constitution comprises, in order of precedence, the Articles, the Domestic Rules and the Standing Orders. Changing the Articles requires approval by 75% of voting members. By modern standards, the Articles are overly long. The proposed changes reduce the length by half and transfer some of the information to Regulations, the appropriate place for secondary matters.

Empowering the AGM

In the past, voting members had the right to raise motions to be discussed at the Annual General Meeting. This has not occurred in recent years and it was felt important to restore it. From 2017, voting members will be invited to submit such motions.

Reduction in size of Council

Council is currently made up of 18 Trustees, all of whom are Society members. Two points were made in this context. (i) It was suggested that a smaller Council might operate more efficiently. Indeed there were suggestions to reduce the size of Council to 12. A counterargument, however, is that the various Committees of Council (Meetings, Policy, etc.) which carry out much of The Society's work draw much of their membership from Council. It was felt that a large reduction in size of Council would result in fewer Trustees being available to join these Committees. In the end, the compromise proposal is to reduce Council to 15 member Trustees. (ii) It has been argued that Council would benefit from adding some Trustees who are not members but bring other skills. For many years the Finance Committee has included one or two people who are not members of The Society but bring financial skills. By the same token, it might be useful for Council, itself, to include people with, for example, legal, financial or HR backgrounds. The number of such non-member Trustees is being limited to a maximum of two so that member Trustees remain in the majority.

Role of Affiliates

For many years, two elected Affiliate Representatives have been permanent invitees on Council. As the business of Council has evolved to more strategic discussions and there is a desire to reduce the size of the meetings, it is felt that this convention should discontinue. We value engagement with Affiliates at committee level and will also explore the establishment of formal Affiliate grouping that can help direct The Society's strategy at this level.

Change of Executive Committee to Chairs Committee

The Executive Committee comprises the President, Deputy President, Honorary Treasurer and the chairs of the major committees. It was felt important to emphasise that this committee is not the body that takes decisions for The Society and that Council has ultimate responsibility and power. The Executive Committee will therefore be renamed as 'Chairs Committee' with oversight and coordination responsibilities. Another change is that the Chair of Membership and Grants Committee, who is not currently a member of the Executive Committee, will be a member of the Chairs Committee.

Adoption of revised articles

The revision will be presented at the 2016 AGM in Dublin. Approval of the new Articles will require the approval of 75% of the members voting.

More information about The Society's governance structure, including the most recent committee organogram, can be found at **www.physoc.org/governance**

Physiology Friday! Friday 14 October

It's never too early to start planning for the annual celebration that is Biology Week (8-16 October); so get your brain hats on and start planning your activities! We've commandeered the Friday of Biology Week as a day to celebrate physiology, and we want as many Members to get involved as possible.

Last year Dr John Mackrill at University College Cork, together with his department, planned an action packed week of festivities for Biology Week topping it off with a Physiology Friday extravaganza with staff, students and some visiting year 11 pupils. The event included a #biobakes cake sale, and a world-record attempt to register the greatest number of ECG traces in 5 hours (280 were taken, included that of a government minister) as well as a host of other activities.

Dr Charlotte Haigh, The University of Leeds, has also previously put on events as part of Physiology Friday and encourages other Members to follow suit: '*Putting on an event for Physiology Friday was something I really wanted to do as a Physiologist. It is important we share our discipline widely. I used undergraduate students to promote [physiology] by running a public engagement event and then following this up with a social activity for the students. The students engaged with this and put together some fantastic resources to allow the general public to understand what physiology is and why it was important. I would encourage others to do something similar*'.

If you would like to engage with more school students, put on a community event, or like University College Cork, try and break a world record as part of Biology Week and Physiology Friday get in with the Society for an informal chat and we'll see how we can help! Remember to note it in your diary!

Health of Physiology Report

After a long gestation period, the Health of Physiology report will be released at our main meeting, Physiology 2016, and following the event, will be available on our website. The report sets out the state of physiology as an academic discipline in the UK in 2016, and gives recommendations on how The Society and the academic community of physiologists could take it forward to strengthen its future.

The wellbeing of physiology must be assured by effective training of the next cadre of physiologists who will take the discipline forward and continue to play a central role in biomedical research. This requires a robust training route and continued support through the Research Councils and other sources of funding. The scientific importance of physiology will also continue to be emphasised to the general public via The Society's media outlets, its scientific meetings, publications, and policy and outreach initiatives. All these activities will be strengthened by enhanced collaborations that are now being developed with The Society's partner organisations, most notably in the UK, Europe and the United States. The recommendations in Health of Physiology will focus the work of The Society in order to ensure its future strength.

Science in George Osborne's Budget

The bulk of the government's plans for science funding were laid out (as a framework, if not with much detail) in last year's Comprehensive Spending Review. However, further information and policy of note to the scientific community came out in the recent spring Budget.

Government plans to continue converting schools in England to academy status, eventually achieving full conversion. There is a concern that the change to academies will disconnect student learning from the National Curriculum, potentially reducing students' exposure to science subjects and practical experience of science due to funding and expertise shortfalls.

A more positive change for education came in the form of loans for postgraduate study all the way up to PhD level. These should enable more people to continue their studies after their undergraduate degree, thereby gaining research experience as well as qualifications. They also provide a route for adult retraining in a highly-skilled scientific career later in life. Loans of up to £25,000 will be available, with a projected 9% repayment rate.

The Budget included announcements related to science capital funding, with some specific projects in the life sciences being supported. These include research into ovarian and mesolithiomal cancers, and the Quadram Institute which will study food, health, the human digestive system and the microbiome.

Research Excellence Framework review

While the Comprehensive Spending Review set out the overall size of the science funding pot, we were required to wait until March for the details of the split of that funding among the individual Research Councils and other governmental bodies. Research Councils UK responded by saying 'allocations may have an impact on some existing commitments [and] may necessitate some difficult decisions.'

Resource allocations for most Councils fall in cash terms from 2015/16 to 2019/20 with money instead being allocated to the Global Challenges Research Fund, awards from which must meet international development criteria as well as the scientific criteria normally mandated by the councils. Inflation will progressively diminish the value of science resource budgets towards the end of this Parliament. Full details of Research Council allocations can be found in the government's document at http://tinyurl.com/jk2wuuo

Interested in these or any other policy related issues? Please contact us via policy@physoc.org

Bringing you snippets of the latest intriguing research

Teaching neurons to respond to placebos

Scientist have discovered a way to make neurons respond to a placebo (a medically ineffective treatment), in the same way as they would to medically effective treatment. They found that it is possible to turn a neuron which previously hasn't responded to placebos (placebo 'non-responder' neuron) into a placebo 'responder' by conditioning Parkinson patients with apomorphine, a dopaminergic drug used in the treatment of Parkinson's disease.

DOI: 10.1113/JP271322

Junk for a reason

A junk food diet can cause as much damage to the kidney as diabetes, according to a study published in *Experimental Physiology*. In their study, researchers used animal models of diabetes and models of diet-induced obesity and insulin resistance to see how insulin resistance and too much sugar or fat affect glucose transporters in the kidney. The rats were fed junk food consisting of cheese, chocolate bars, biscuits and marshmallows for 8 weeks, or a rodent chow high in fat (containing 60%) for 5 weeks. They found that certain types of glucose transporters (GLUT and SGLT) as well as their regulatory proteins were present in a higher number in type 2 diabetic rats. But a high fat diet and junk food diet caused a similar increase in those receptors.

DOI: 10.1113/EP085670

Serotonin a clue to understanding Sudden Infant Death Syndrome?

Serotonin, a neurotransmitter in the brain, shortens periods of apnoea and promotes inspiration, according to a study published in *Experimental Physiology*. The researchers found that when injected into the brain stem, serotonin shortens apnoeic events by interacting with the 5-HT3 receptor, which, in healthy babies, is highly expressed in a region of the brainstem associated with the control of apnoeas and regular breathing. Although safe sleeping environments and reduction of behaviours associated with an increased risk of Sudden Infant Death Syndrome (SIDS) have reduced the number of events, SIDS and Asphyxia remain among the most common causes of infant deaths between the age of one month and one year. There is currently no effective treatment for SIDS or Asphyxia.

DOI: 10.1113/EP085716

Physiology at the Royal College of Surgeons of Ireland, Dublin

Jochen Prehn

Chairman & Head of Department of Physiology and Medical Physics, Royal College of Surgeons of Ireland, Dublin, Ireland

The Department of Physiology and Medical Physics is situated in the main college campus on 123 St. Stephen's Green and at the RCSI Research Institute, York House, York Street, Dublin 2. The Department has an outstanding record in both teaching and research. It has always had a strong commitment to undergraduate teaching and is involved in teaching and examining in five different programmes: Junior Cycle Medicine, Graduate Entry Medicine, Pharmacy, Nursing and Physiotherapy.

Academic staff

The department has four full professors and five other academic staff. Prof Jochen Prehn, the Head of Physiology and Medical Physics has been Professor and Chairman, of the Department of Physiology and Medical Physics, at the RCSI since 2003 as well as lecturing students, he is also the co-ordinator of two Centres of Research in the Department, the Centre for Systems Medicine (CSM) and the Centre for the Study of Neurological Disorders (CSND). His research is focused on four areas with a particular emphasis on bioenergetics, mitochondrial physiology, Bcl-2 family proteins and AMPK signaling. Prof David Henshall is a Professor of Neuroscience and lectures to Medical and Pharmacy students. He is also a principal investigator in the Centre for Systems Medicine and his research is focused on cell and molecular mechanisms of epilepsy, in particular the role of microRNA, the modelling and treatment of early-life seizures, ATP-gated receptors as targets for seizure control, and molecular biomarkers of epilepsy. Prof Aidan Bradford is Professor of Cardiovascular and Respiratory Physiology and Vice Dean and Medicine Junior Cycle Director. His research is on airway receptors and reflexes, intermittent hypoxia and sleep apnoea. He has been a member of The Physiological Society for nearly 30 years. Prof Jim Docherty is Full Professor and former Chairman of the Department of Physiology. He has published over 130 full papers in the areas of cardiovascular and autonomic Physiology and Pharmacology. Current main areas of interest: cardiovascular and central actions of stimulants including drugs of abuse; the cardiovascular consequences of portal hypertension. He is a member of The Physiological Society, the BPS and ASPET, and is currently a Senior Editor of BJP.

Centre for Systems Medicine Research Facilities, York House, Dublin

Dr Ian Miller demonstrating how to extract DNA from a banana to secondary school students

Other academic staff include Dr Annette Byrne, who is a tenured Senior Lecturer in Physiology & Principal Investigator in the Centre for Systems Medicine in areas of Tumour Biology/Molecular Imaging. Her research focuses on developing cancer therapeutics and biomarkers with a specific focus on brain, breast, and colorectal cancers. Dr Brona Murphy is a Lecturer in the Department of Physiology. She teaches medical and pharmacy students and co-ordinates the SSC research module for undergraduate medical students. Dr Murphy is a principal investigator in the Centre for Systems Medicine and her research focus is on the activation of apoptosis within glioma. Dr Hans-Georg Koenig is a Lecturer in Physiology and teaches Medical and Pharmacy students. Dr Koenig's research focuses on the regulation of axonal pathology and neurodegeneration. He works on protein interactions and signalling cascades in the axon and axon initial segment with a focus on the regulation of NF-kappaB signalling. These pathways impact profoundly on the pathophysiology of many neurodegenerative diseases, stroke and also developmental disorders of the nervous system. Dr Tríona Ní Chonghaile recently joined the Department of Physiology as a Research Lecturer and she teaches first-year Medical students. Dr Ni Chongaile is a principal investigator and her main research interests are in mitochondrial apoptosis, epigenetic regulation of apoptosis and haematological malignancies. Dr Tobias Engel is a research lecturer to Medical students and Pharmacy students since 2015. Dr. Engel is a principal investigator and the main focus of his research is the study of purinergic signaling (with the main emphasis on the ATP-gated P2X7 receptor), changes in the ubiquitin-proteasome system and apoptosis-related genes and their influence on neuroprotection and epileptogenesis.

Centres of Excellence

The primary research areas of the Department of Physiology includes: Neurological Disorders, Oncology and Diabetes as well as Respiratory and Cardiovascular Diseases. This has led to the establishment of two centres of excellence within the department, namely the Centre for Systems Medicine (CSM) and the Centre for the Study of Neurological Disorders (CSND). The mission of the CSM is to provide a translational research centre that identifies genes, proteins and metabolites implicated in human disease and utilises systems biology and mathematical approaches in order to develop new prognostic tools for the treatment of cancer, neurological disorders and diabetes, and to develop more targeted therapies for patients. The CSND is the only centre in Ireland devoted to the study of acute and chronic neurological disorders. The mission of the CSND is to advance fundamental knowledge of the basis of neurological disorders by conducting cutting edge research and by providing training to the next generation of scientists. The research fields examined within the CSND include, Epilepsy Stroke, Motor Neuron Disease and the Diabetic Brain.

CSM Outreach Activities

The CSM and RCSI is very committed to the development of novel outreach programmes for schools and the general public which will stimulate discussion on new technologies and materials and the role of science in defining how we live our lives. CSM delivers school resources and hosts activities that influence secondary school curricula. We aim to enthuse students about studying science and provide context for job opportunities in Irish-based industry. Our Transition Year work experience programme 'Mini –Science' runs yearly. This week long experience links school students with CSM researchers at the Royal College of Surgeons in Ireland. We also have a steady stream of students that participate on a day trip tour of RCSI and the CSM, who enjoy visiting the labs, talking to researchers and take a tour of the RCSI Medical School.

For information about outreach activities contact Dr Helena Bonner, Education and Outreach, Centre for Systems Medicine.

Further information:

http://www.systemsmedicineireland.ie/
http://www.neuro-centre.ie/

Physiology in Trinity College Dublin

Áine Kelly

Head of Physiology,
Trinity College Dublin, Ireland

Staff and students of the Physiology Department in Trinity College Dublin are delighted to join our other Irish colleagues in welcoming delegates to the 2016 meeting of The Physiological Society in Dublin. The department was established in 1922 and is part of the School of Medicine, which celebrated its tercentenary in 2011. Ten academic staff are supported by nine technical and administrative staff to provide teaching and research training in physiology to almost one thousand undergraduate and postgraduate students. We graduate 18 students in physiology annually as part of the Trinity science degree and teach undergraduate students of medicine and allied health sciences. Our major research expertise lies in the areas of neuroscience and exercise physiology and we run taught MSc programmes in both these areas. Collectively, staff conduct research into the physiological processes underlying learning and memory, the perception of pain, improved sports performance, and the pathophysiology of conditions including Alzheimer's disease, Parkinson's disease, multiple sclerosis, Rett syndrome, type 2 diabetes and Duchenne muscular dystrophy.

Trinity College Dublin last hosted a full Physiological Society meeting in 2003, although we have hosted several Society-sponsored symposia since then. Of course, physiologists visited Dublin in large numbers in 2009, when our colleagues in UCD hosted the annual society meeting, and you may have visited the Trinity campus on that occasion. The intervening seven years have seen many changes in the department in Trinity; personal, physical and academic.

The most obvious recent change in the department has been a change of location. Some of you may remember the beautiful (at least from the outside) granite building, east of the rugby pitch on the main campus, that Physiology once called home. Our new base is on the second floor of the Trinity Biomedical Sciences Institute Building on Pearse Street, a couple of minutes' walk from our old location outside the walls of the main campus.

This 10 story 35,000 m^2 development was opened in 2011. It is a multidisciplinary research building housing 75 PI's from several schools within the university. All of the preclinical training in our medical degree, including physiology, is undertaken in the building. It could be said that what we have lost in historic location we have gained in comfort. While we may feel nostalgic from time to time about our old home, nobody misses the leaky roof of the former teaching laboratory.

Despite being 10 storeys high, space could not be found for our electrophysiologists and exercise physiologists in the new building. Unfortunately, those Faraday cages and metabolic treadmills just take up too much space. After rather a lot of negotiation, an area of the Watts building on campus, just metres from our old home, was identified and refurbished for us. This location also houses the Physiology seminar room. We're a sentimental lot here and very mindful of our history. The seminar room is named in honour of Pat Hartigan, former Head of Physiology who retired in 2001, in recognition of his long and continuing service to the discipline of physiology. We also brought evidence and symbols of our past to the new building; our library holds bound volumes of *The Journal of Physiology* dating back to 1908, while the portraits of our former Chairs of Physiology smile – and in some cases glare – at the viewer from the walls of our new home. With some research activity being located within the Trinity College Institute of Neuroscience, the department is split across three locations. Moving between locations to undertake teaching and research activity keeps the staff fit, if all too often exposed to the Dublin rain.

While our history and heritage is important to us, we are constantly looking toward new teaching and research horizons. The department was instrumental in developing the BSc in Human Health and Disease, a four-year honours degree in biomedical sciences that has a strong foundation in physiology. Established by Veronica Campbell in 2009 and helmed in its infancy by former staff members Neil Docherty and Sarah Harney,

Physiology staff (past and present) at the old Physiology Building

Aedin Minogue and Eric Downer in the TBSI building, Physiology's new home

the programme is now in the capable hands of Eric Downer, who was recruited to this role in 2015. Despite being a very recent recruit to the department, Eric's laboratory is well-established, where he researches the role of the immune system in the pathophysiology of multiple sclerosis.

Marina Lynch has been a cornerstone of the department since 1992. Professor of Cellular Neuroscience and member of the Royal Irish Academy, not only is she a world-leader in the area of neuroinflammation who has published over 200 papers, she is a valued advisor to students and staff alike. Indeed no fewer than four current members of the academic staff spent time as researchers in her laboratory, a testament in itself to her mentorship and guidance, not to mention the excellence of the scientific training she provides.

Veronica Campbell's prodigious academic management and strategic skills, no doubt honed during her time as Head of Physiology (2006-2010), have been recognised by the university. She served as Dean of Graduate Studies from 2010-2013. After a far too brief two-year hiatus back in physiology, she has been nabbed by university management yet again and now holds the position of Bursar and Director of Strategic Innovation of the university. Of course, she remains an active physiologist; her research into the roles of cannabinoids in cell physiology still thrives and we look forward to welcoming her back full-time to the Department in due course. Electrophysiologist Daniel Ulrich, formerly Trinity Physiological Society representative, is presently on leave of absence. Thankfully, the university management recognised that Physiology activity is far too important to leave two academic posts vacant and we were fortunate to recruit two young physiologists, neuroimmunologist Aedin Minogue and respiratory physiologist Deirdre Edge, in September 2015 to step into the breach.

Mikel Egaña is our exercise physiology expert. He has published several key papers on the effects of exercise interventions on vascular and metabolic adaptations and exercise tolerance in type 2 diabetes, obesity and ageing. He runs the MSc in Exercise Physiology and, together with me and led by colleagues from the discipline of physiotherapy, has helped to develop an online certificate course in clinical exercise prescription. Alice Witney researches how different forms of sensory information, including cutaneous, auditory and vestibular afferents, can influence movement. She also puts incredible effort into coordinating the honours degree programme in Physiology, consistently one of the most popular choices among Trinity science students.

Kumlesh Dev brought recent industry expertise and collaboration to the Department when he joined us in 2008. A neuropharmacologist, he researches drug targets for the treatment of diseases including multiple sclerosis and Parkinson's disease. Under his stewardship, the MSc in Neuroscience has grown from strength to strength and was awarded the accolade 'best postgraduate science course in Ireland' at the 2012 Postgrad Ireland awards.

Maeve Caldwell joined us from the University of Bristol in 2014. As former external examiner of our MSc in Neuroscience, she obviously liked what she saw of our department during her visits and we are delighted to have her expertise in stem cell biology as part of our research portfolio.

Sadly, we lost two cherished members of staff in recent years. Chris Bell, the most recent incumbent of the Chair of Physiology, died in 2007 in his native Australia shortly after his retirement, while the energetic, exceptional Tom Connor passed away in 2013. Their academic and personal legacies live on and they are very fondly remembered. We also remember the contributions of our recently retired staff, Roger Luckwill (2009), Alan Tuffery (2010) and Roger Anwyl (2013).

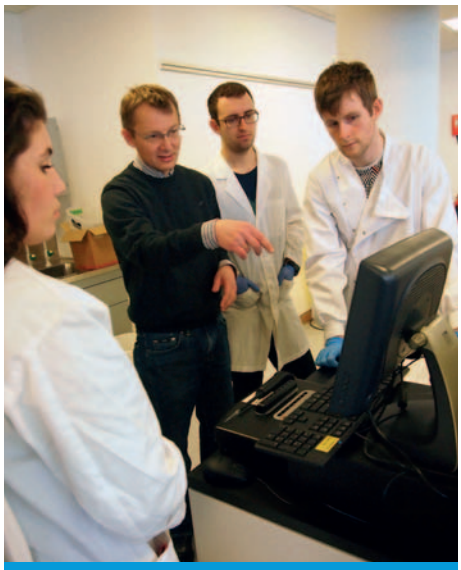
My own six-year tenure as Head of Physiology ends in July 2016 and I look forward to the opportunity to again focus my full efforts on my research into the neuroprotective effects of exercise on the brain. I hope that you will have an opportunity to visit the beautiful Trinity campus during your visit to Dublin and, together with the rest of the members of the department, wish you an enjoyable and successful visit to Dublin.

Veronica Campbell and Pat Hartigan at the newly-named Hartigan Seminar Room

Physiology at University College Dublin

Mark Pickering, Anthony Hyland & Paul Mcloughlin

School of Medicine, UCD, Ireland



Dr Albert Smolenski explains the finer points of platelet aggregation to students during an experimental physiology practical session

Anyone visiting Dublin this year will no doubt notice that the joint meeting of the American Physiological Society and The Physiological Society is not the only major event in the city. 2016 is an important year in Ireland, and Dublin in particular, as it marks the centenary of a key event in Irish history, the 1916 Rising. University College Dublin (UCD) is inextricably linked to this revolutionary period in Irish history, with many students and faculty included amongst the rebels. The university was still relatively young one hundred years ago. In 1908, the National University of Ireland was founded with three constituent University Colleges; Cork, Galway and Dublin. With this act, the Cecelia Street Medical School became the UCD Medical School, and the Professor of Physiology, Denis J. Coffey, was appointed the first president of UCD, a position he would hold for 30 years, spanning the tumultuous period of rebellion that led to the birth of the Irish Republic.

The legacy of UCD in 1916 goes beyond rebellion. The Conway Institute of Biomolecular and Biomedical Research, which opened in 2003 at the UCD Belfield campus, was named in honour of Edward Conway, famous for his work on ion distribution, who would been studying physiology at UCD in 1916. This institute, along with the neighbouring Health Sciences Centre, is the current home of physiology at UCD. While the science and in particular the tools used by physiologists have changed since 1916, many of the same broad questions are still of interest to investigators today. A key strength of physiology research at UCD is the biology of the dissolved gasses in health and disease, a topic that surely would have been of interest to Conway. The current head of physiology in UCD is Prof Paul McLoughlin. His research is broadly focused on the changes in the lung in chronic obstructive pulmonary disease associated with the response to the resulting hypoxia. In recent years this work has highlighted the role of bone morphogenic protein signalling in hypoxia induced pulmonary vascular remodelling and increased pulmonary vascular resistance, revealing a potential new target for therapeutic intervention in this class of diseases.

Other principal investigators in UCD physiology are complementing this research. Dr Christine Costello's group has examined the role of both chemokine signalling and microRNAs in the pathogenesis of pulmonary vascular disease, while Dr. Katherine Howell's group has focused on the role of placental growth factor in hypoxic lung disease and the potential therapeutic application of Erythropoeitin for the treatment of emphysema.

Other research is focused on the cellular response to hypoxia, in particular in an inflammatory context. Prof Cormac Taylor's group has carried out extensive work on the regulation of gene expression responses to hypoxia in epithelial cells. This has led to his demonstration of the effect of hydroxylase inhibitors in reversing symptoms in a model of inflammatory bowel disease. The significance of his contribution to our understanding was demonstrated when Prof Taylor was awarded the 2016 Takeda Distinguished Researcher Award by the American Physiological Society's Gastrointestinal & Liver Physiology Section, the first time that the award had been made to a scientist from outside the United States.

Dr Eoin Cummins' group investigates the role of carbon dioxide in gene regulation in inflammatory disease. Dr Cummins will be chairing a symposium on the topic of the physiological gasses at the upcoming joint physiology meeting in Dublin.

A key strength of research in UCD physiology is its diversity. Dr John Baugh's group's work relates to both inflammation and hypoxia, but has a particular expertise in fibrosis, specifically in relation to the role it plays in the pathology of heart failure with preserved ejection fraction and pulmonary fibrosis. His research has a strong translational and commercial focus, in particular in relation to work on identifying serum biomarkers in these diseases.

Dr Paul Crossey's group has an interest in diabetes, and specifically the function of the insulin, growth hormone, IGF-1 axis in insulin

The Health Sciences Centre in UCD, with the Conway Institute in the background

The stained glass window in the UCD Charles Institute commemorating Kevin Barry, a UCD medical student executed during the Irish War of Independence

deficiency and resistance. His work focuses on genetic mouse models to elucidate these mechanisms, but has involved collaboration with clinicians, specifically looking at foetal placental growth hormone in diabetic pregnancy.

The focus of Dr Mark Pickering's group is neurophysiology, specifically the interaction between neurons and glia and their mechanical environment, as well as the development of new myelin repair therapeutics and research into the evolution of neural coding in simple models of the nervous system. Dr Stuart Bund's research interest centres on smooth muscle. While initially focusing on the vascular smooth muscle, his more recent work has concerned the regulation of ureteral motility by periureteral adipose tissue.

The intracellular signalling networks regulating thrombus formation by platelets is the focus of Dr Albert Smolenski's research group. His work has led to the discovery of new proteins involved in platelet inhibition and regulation of dense granule release. Interestingly, in Dr Smolenski's research we can see echoes of 1916, the year in which anti-clotting properties of heparin were first discovered.

Strong linkages between research and teaching are fundamental to the educational philosophy of physiology at UCD. As in many universities, the academic staff in physiology in UCD are responsible for the delivery of teaching to a diverse range of students. The largest cohort of students are those undergoing medical training. This includes both a graduate entry medical programme, which admits around one hundred students each year, and an undergraduate entry programme, where the two hundred students taught each year also includes students from our international educational partners in Penang Medical College who join us for the preclinical stages of their training.

As well as the medical programmes, physiologists contribute to a wide range of other degree programmes, including radiography, biomedical engineering, and the BSc in Biomedical Health and Life Sciences. Additionally, around twenty students each year complete a BSc in Physiology as part of the UCD science degree programme, another important focus of our teaching activity. It is in this programme that the linkages between research and teaching are perhaps most evident. For example, in the third year of this four-year programme, students undertake an experimental physiology module. This module is entirely laboratory based, and sees the students spend a full day each week in the lab gaining experience of the application of techniques relevant to modern physiology research, ranging from gene expression analysis and tissue culture through to *in vivo* invertebrate electrophysiology and the measurement of platelet aggregation. The skills developed by the students are then utilised in their final year as they undertake their final year research projects.

2016 also marks 10 years of the Summer Student Research Awards (SSRAs), a programme in the UCD School of Medicine which allows approximately eighty undergraduates, in particular medicine students, to gain hands on experience of research by carrying out projects during the summer break between teaching terms. These projects are diverse in scope, and include clinical and educational research in addition to laboratory based projects, many of which are supervised by physiologists.

In both cases, these projects are an important element in the training of our students, as in addition to providing real world research experience, they also allow the students to exercise their critical and analytical thinking skills. Most importantly perhaps, they allow the students the space to make mistakes and learn from them, a process any investigator will understand the value of: as James Joyce, another UCD alumnus, wrote in Ulysses; "A man of genius makes no mistakes; his errors are volitional and are the portals of discovery."

To circle back to where we began, it is interesting to observe how the events of one hundred years ago cascade through history to shape Dublin, UCD, and physiology at UCD today. However, when looking back we should also note another who lived and worked in Dublin one hundred years ago, William Sealy Gosset. While not a physiologist himself, his legacy includes an indelible influence on physiologists (among many others) and some of the fundamental principles on which we build our understanding. While his name may not be familiar to everyone, the pseudonym under which he published (Student, of the eponymous t-distribution and t-test), certainly will be.

Many visitors to Dublin make a pilgrimage to the place he worked for most of his professional life, which is now one of the most popular sites for visitors to Dublin. The fact that his workplace happens to have been the St. James's Gate brewery, home of the most famous Irish back beer, is surely just coincidental.

LifeSciTRC: an international teaching community – now open for Members

Angela Breslin
Education Manager,
The Physiological Society

The Society is pleased to announce that the Life Science Teaching Resource Community (LifeSciTRC) website now has a dedicated portal for Members and is open for resource submissions. The web link is **www. lifescitrc.org**. If you have a teaching or public engagement resource you'd like to share, we'd be delighted to hear from you, at **education@physoc.org**

What is the LifeSciTRC?

The LifeSciTRC is a digital repository, managed by the American Physiological Society (APS), containing over 7,000 peer-reviewed life science education materials. It also provides a platform for online teaching communities, offering users the opportunity to engage with other teaching professionals via blogs and discussion forums. The Physiological Society became a Partner of the LifeSciTRC in 2014 and since then has worked with the APS to set up its own portal, which will enable Members to share resources, peer-reviewed by other Members in their field.

7,000+ free resources

From animations on mitosis to cardiovascular undergraduate practicals; and from career case studies to games on blood types, there is a huge range of resources to choose from, which have been contributed by nine bioscience organisations over the years. [1] Most of the resources are free, accessible to all, and under a Creative Commons Licence. Registration on the site is also free and enables users to share and submit resources, receive recommended items, post comments and serve as a reviewer. To find resources submitted by Members, click on 'Search LifeSciTRC' from the main menu, then 'Advanced Search' followed by 'Partners' and 'PhySoc'.

Online teaching communities

As an international partnership, the LifeSciTRC brings together experts worldwide from across the life sciences, who are involved in education at all levels. Members can tap into this network by registering on the LifeSciTRC, which is free, and joining one of the communities listed. The communities are divided by educational level, and enable users to share resources and teaching ideas via blogs and discussion forums. One community in particular is open to all physiology educators: the Physiology Education Community of Practice (PECOP). Recent discussions have focused on science summer camps for schools and using journals in the classroom.

What are the benefits of sharing a resource on the LifeSciTRC?

Further to reaching an international audience, resources on the LifeSciTRC are also searchable on the BioSciEd Net Portal and National Science Digital Library, thereby expanding the potential reach of your resource with no extra effort. The copyright would remain with you and you would also have the option to publish an abstract describing the resource in the APS journal, Advances in Physiology Education.

How can I submit a resource to the LifeSciTRC?

Once you have registered, you will be able to submit a resource to the LifeSciTRC. Any type of resource (e.g. diagram, video clip, practical) aimed at any age level, apart from whole websites, is welcome. Just click on 'Submit to LifeSciTRC' from the main menu, then 'Submit a Teaching Resource' and select 'The Physiological Society', which will forward your resource to The Society for review. The rest of the submission process will be outlined on the screen and we would recommend setting aside 20-30mins to complete the submission.

Who will review my resource?

The Society recruits a range of volunteers from the membership to review resources submitted to the LifeSciTRC and aims to assign each resource to a reviewer with expertise in around that area. The reviewer will be asked to assess your resource against

the following criteria, which have been agreed by The Society's Education and Outreach Committee, in consultation with the APS: scientific accuracy and/or pedagogic content, age level appropriateness, appropriate level of human/animal use and safety concerns.

Can I become a reviewer?

Any Affiliate or full Member of The Society is welcome to become a LifeSciTRC reviewer. Please email **education@physoc.org** if you are interested.

How can I find out more about the LifeSciTRC?

An introductory workshop will be held at The Society's joint meeting with the APS, Physiology 2016. More details are also on The Society's website, **www.physoc.org/education**, or you can email **education@physoc.org**

[1] Current Partners of the LifeSciTRC are the American Physiological Society, Human Anatomy and Physiology Society, Society for Developmental Biology, The American Association of Anatomists, Massachusetts Society for Medical Research, Northwest Association for Biomedical Research, The Physiological Society, Genetics Society of America and American Society for Plant Biologists.

Win a £50 voucher

The first 10 Members to successfully submit a resource before 1 September 2016 will be entered into a prize draw to win a £50 John Lewis voucher.

Young researchers present to MPs at SET for Britain 2016

Henry Lovett

Policy & Public Affairs Officer,
The Physiological Society

Young researchers can find it hard to make an impact and get their work noticed, especially outside of their specialist field. One excellent opportunity to address this is provided by SET for Britain (SET being Science, Engineering and Technology), an annual event hosted by the Parliamentary and Scientific Committee. This allows early-career researchers to present their work on a poster to a diverse crowd in Parliament. Their research is brought to the attention of MPs, learned societies and fellow researchers in a variety of fields. Prizes are awarded for the three best posters in the categories of mathematics, physics, chemistry, engineering, and biomedical science, with a further overall prize for the category winner who gives the clearest and most effective presentation of their research.

The Physiological Society has been proud to sponsor this event for a number of years, and will continue to do so. This year's SET for Britain was held on 7 March in the Attlee Suite of London's Portcullis House. Three Members of The Society were on the judging panel for the evening's Biological and Biomedical Sciences session: Dr Sarah Hall of Cardiff University, Dr Rachel Tribe of King's College London, and Prof Susan Wray of the University of Liverpool. Our President, Professor Richard Vaughan-Jones, presented the awards and gave an excellent speech on the significance of this event and others like it in communicating to policymakers the importance and vibrancy of current research in the UK. Many prominent political figures attended SET for Britain, including the Science Minister Jo Johnson MP, and the Leader of the Opposition Jeremy Corbyn MP. Other MPs were happy to drop by and express interest in the research being presented, especially if it was being carried out in their constituency.

The Biological and Biomedical Sciences sessions was won by Dr Maeliosa McCrudden of Queen's University Belfast, for her poster about microneedle devices, novel alternatives to regular hypodermic needles for injections.

Two Physiological Society members were amongst the participants: Dr Carrie Duckworth of the University of Liverpool, and Martina Elias of Newcastle University. Dr Duckworth said of the event that *'the opportunity to present my research in this very relaxed forum was an exciting and valuable experience.'* She added that *'I had the opportunity to speak to several politicians at the event including the chairman of the SET for Britain organising group and Parliamentary and Scientific Committee, Stephen Metcalfe MP, who appeared to be very enthusiastic and engaged by my work. The Southport MP, Mr John Pugh, also paid me and my poster a visit, and he asked several interesting questions with regards to the broader applications of my research. I was able to discuss with him some of the intricacies of gastrointestinal function whilst we ate sandwiches!'*

Professor Richard Vaughan-Jones praised the event, saying *'the UK has an excellent biomedical research base for which physiology provides fundamental understanding and direction. SET for Britain provides a unique opportunity for parliamentarians to engage with the scientific research that government funds and recognise the skills of our scientists training and working in the UK. The Physiological Society is extremely pleased to continue its longstanding support for this event.'* He presented awards to the winners of the Biological and Biomedical Sciences session alongside Dr Stephen Benn, Director of Parliamentary Affairs at the Royal Society of Biology, who as Vice-Chair of the Parliamentary and Scientific Committee had been instrumental in arranging and promoting the event.

Preparations are already beginning for SET for Britain 2017, and we hope that The Physiological Society will be well-represented among the participants. Keep your eye on our Society Newsletter for future details on how to apply.

Knitting and physiology in the city of Preston

Caroline Finnigan and Dr Elizabeth Granger with the knitted woolly body

Elizabeth Granger

UCLan and Ri Young Scientist Centre Manager, University of Central Lancashire, UK

In the heart of Preston city centre, we have group of dedicated volunteers who are crocheting colons and knitting neurons as part of our knitted body project. The group meets twice a week and it gives people a chance have a knit and a natter. The aim of the project is to bring older people together and engage them with Physiology. Once we have knitted our woolly body we'll be taking out into local schools to teach 4-6 year old children about the body and healthy living.

The knitted body will be an interactive model once finished. It will have a skin that can be unzipped to show a foam skeleton with the knitted organs inside. Organs include the digestive system that knitted food can be fed through and knitted poo appear at the other end. We also have a squeezable heart, inflatable lungs and reversible kidneys. The model is designed to be hands on and simple to help explain the basic function of each organ.

During the school sessions, we will be teaching children through play using our knitted bodies. The idea is that they can explore the organs of the body whilst having fun. We will be linking the sessions to healthy living and trying to get the idea across that what we do and what we eat affects the insides of our bodies.

The knitting group in action

With rising rates of childhood obesity and the health problems this can lead to, it is more important than ever to encourage children to think about the importance of being healthy from a young age. The sessions will also aim to create an early positive association with science for the children.

Whilst it is really important to engage children with science and the importance of healthy living, bringing people together at the knitting circles is just as an important part of the project. Some of our regular knitters are there to learn new techniques, some are keen to help out and others just come along to socialise. The sessions are led by Caroline Finnigan, a Fibre Artist, and supported by Biomedical and Pharmacy students. There's a great mix of people from different backgrounds. As the project progresses friendships are being made and we are attracting more volunteers at each session. The knitting circles are being held in 'InTheCity', which is a pop-up shop run by the University of Central Lancashire that is hosting a range of community events. The central location makes this accesible for knitters from all areas of Preston.

The next stage of the project involves researchers in the field of Physiology attending the sessions to join in and have an informal chat about their work with the group. This will give researcher an opportunity to engage with the public in a relaxed environment and have a dialogue about their work. If you are based in the North West and would like to attend a session, please contact me via email at **egranger@uclan.ac.uk**. If you would like to have a go at knitting some organs yourself the patterns will be made available on Caroline's website: **http://carryyarnstitching.co.uk/**. To keep up with the project follow the hashtag *#knitbod.*

This project wouldn't have been possible without the generous funding of The Physiological Society through their Public Engagement Grant scheme.

2016 Forthcoming events

29–31 July

Physiology 2016
Joint Meeting of the American Physiological Society and The Physiological Society
Convention Centre Dublin, Ireland

www.physiology2016.org

2 August

H^3 symposium - The cardiac autonomic nervous system: cellular mechanisms to human translation
University of Oxford, UK

bit.ly/cardiach3

8–11 August

Limits of Perception: Advances in Bio-Imaging
University of Warwick, Warwick, UK

http://www.physoc.org/bioimaging2016/

14 September

Novel approaches to hormone sensing (The Inaugural Bayliss-Starling Symposium)
Hodgkin Huxley House, London, UK

http://www.physoc.org/novelapproaches/

Meeting Notes

Biomedical Basis of Elite Performance 2016

6–8 March 2016, East Midlands Conference Centre, Nottingham, UK

Paul Greenhaff

Chair, Scientific Programme Committee (BBEP 2012, BBEP 2016), University of Nottingham, UK

Four years on from the Biomedical Basis of Elite Performance (BBEP) 2012, I was always nervous about how BBEP 2016 would stand up in comparison to the highly successful meeting linked to the London Olympics.

From the outset, however, the signs were at all times positive. Experienced and respected colleagues in the field of human and exercise physiology who made up the Scientific Programme Committee were at all times willing and helpful in suggesting potential high quality speakers and fashioning a world-class scientific programme.

I am very grateful for their contribution as it was the catalyst to success for BBEP 2016. A clear mark of their insight and the scientific esteem of The Society was that with the exception of one individual, every potential speaker The Society approached from across the world, accepted the offer to attend. Furthermore, the majority of the invited speakers actively contributed to the whole three days of the meeting.

Building on BBEP 2012, the 2016 meeting undeniably retained a family feel, which was underpinned by the very welcoming and professional staff of The Society and Ken O'Halloran, The Society's Meetings Secretary. The collegial nature of the meeting was also helped by the close proximity of the conference hotel and the meeting venue, which meant debate and socializing beyond the conference, could continue well into the night.

I am grateful to the exhibition sponsors for their support of the meeting and to the National Centre for Sport and Exercise Medicine – East Midlands who kindly sponsored the Early Investigator Competition to the tune of £1000 for the best oral

communication and £1000 for the best poster presentation. Both competitions were of a very high quality and highly competitive - congratulations to Lauren Skelly, McMaster University, Canada and Fiona Lewis, King's College London, UK.

Finally, I'd like personally to thank the speakers who willingly gave their time and insight, the 270 individuals who registered and attended the meeting and the many thousands of people who watched the presentations online and delivered very positive comments via social media (special thanks go to the AV technical support).

Collectively we delivered a successful event and have now created a flourishing BBEP brand. Onwards and upwards to BBEP 2020!

Report by the winner of the Early Career Investigator Award for Best Oral Communication

Lauren Skelly

McMaster University, Canada

In March, I had the pleasure of travelling from McMaster University in Canada to Nottingham to attend the Biomedical Basis of Elite Performance (BBEP) 2016 Conference. It was my first international meeting and my first trip to the UK.

Over three days, I had the opportunity to interact with and learn from many world-renowned exercise physiologists. The East Midlands Conference Centre provided an outstanding venue, and the small size of the meeting created a warm and collegial atmosphere, which made for a fantastic conference experience. I thoroughly enjoyed attending the symposia presentations that highlighted recent developments in the field, ranging from rodent to elite athlete investigations. I also gained a new appreciation for the history of exercise performance and nutrition in exercise metabolism owing to the outstanding plenary lectures.

Lauren receives the Early Career Investigator Award for Best Oral Communication

I presented research findings from my doctoral work related to sex-based differences in the metabolic and physiologic responses to interval exercise. The oral communication was delivered to the largest audience in my career and was a tremendous platform for me to share my work. I was honoured to receive the Early Career Investigator Award for best Oral Communication in the company of such excellent oral presenters. I am grateful for the support of the National Centre for Sport and Exercise Medicine.

The high quality of the symposia and graduate student oral and poster presentations is a reflection of the passion, continued interest and importance of exercise physiology throughout the world. Thank you to the Physiological Society and the University of Nottingham for hosting BBEP 2016. The experience was a highlight of my graduate career, and I am thankful for the many welcoming and meaningful conversations with the other attendees and for the travel support from the Physiological Society. I look forward to attending future meetings, including BBEP 2020!

Report by the winner of the Early Career Investigator Award for Best Poster Communication

Fiona Lewis

King's College London, UK

I am a post-doctoral researcher at the Centre of Human and Aerospace Physiological Sciences, Kings' College London investigating the effect of ageing on the regenerative potential of cardiac stem/progenitor cells within Georgina Ellison-Hughes's lab.

My research to date has focused on understanding the biology of different sources of stem/progenitor cells, including skeletal muscle progenitors. When I joined King's in 2013 the opportunity arose to collaborate with a fellow researcher, Dr. Agley investigating the role of GSK3 and β-catenin in the differentiation of human myogenic cells.

Fiona receives the Early Career Investigator Award for Best Poster Communication

The Biomedical Basis of Elite Performance 2016 meeting in Nottingham provided an excellent forum to present these findings to experts in the field. The conference itself had an energetic atmosphere with a series of informative talks and plenty of opportunities to network and discuss the exciting research being presented. When it came to presenting my poster, I felt that I successfully highlighted the key findings and their significance, and as a result, I received a lot of positive feedback and insightful discussion. I found this opportunity to receive feedback from peers in a friendly, supportive environment invaluable as we are currently preparing this research for publication and this provided a thought provoking insight.

I would highly recommend this meeting and encourage fellow researchers to attend and enter the poster communication and oral competitions. I would especially like to thank the conference organisers for providing a stimulating environment, the National Centre for Sports and Exercise Medicine for sponsoring this prize and lastly my colleagues and collaborators for their continued support.

About the National Centre for Sports and Exercise Medicine

The National Centre for Sport and Exercise Medicine (NCSEM) is a partnership with founding members in the East Midlands, London and Sheffield. It was established with a £30m grant from the Department of Health as an Olympic Legacy project to deliver education, research and clinical services in sport, exercise and physical activity, that can be translated into improved health outcomes for the nation.

http://www.ncsem-em.org.uk

Meeting Notes

Meeting report: The Biophysical Society's 60th Annual Meeting

27 February – 2 March 2016,
Los Angeles Convention Center,
Los Angeles, USA

Sally Howells

Managing Editor,
The Journal of Physiology

The Los Angeles city skyline

Coming from sub-zero weather in London to the balmy (but rather smoggy) climate of LA was a welcome way to ensure our vitamin D levels were fully restored.

LA was this year's host to the Biophysical Society's 60th annual meeting. Located in downtown LA, we were far away from the glitz and glamour of Hollywood (and the Oscars), but the area was much more pleasant than we had anticipated.

Our *Journal of Physiology* (*JP*) booth was well located in the large exhibition hall, and we had a steady stream of loyal journal supporters visit our booth. Each year we attend this meeting, our reputation grows and delegates come back to talk to us to learn about our new plans and developments. It was also important for us to engage with the younger generation of physiologists. We were proud to inform them that some of the seminal papers for the biophysics community were published in *JP* – we even had a cabinet displaying some of these articles to prove it.

We conducted a raffle to win an iPod touch that encouraged people to come to our stand and learn more about what we do. We were pleased to be able to highlight a special issue on calcium transport proteins and promote a 'Call for Papers' on potassium channels and cardiac electrophysiology. We hope that this will show people our commitment to publishing the best biophysics papers. We were interested to hear than many people were conducting computational and modelling research and were able to let them know that this is an area that we are keen to expand.

Several Editors, past and present, were at the meeting, and this was another excellent opportunity to talk to them about *The Journal* and the discipline as a whole on a more informal basis.

We learned from a more experienced researcher who had published with us in the past that his students weren't that interested in publishing in *JP*, and favoured some newer, 'more exciting' journals. Convincing younger researchers who perhaps haven't grown up with *JP* that we are the true home of biophysics papers and the best outlet for their research will be challenging, but it is something we are committed to achieving. Hopefully the fact that it is still completely free to publish in *JP* might convince some of them.

We promoted a collection of our top biophysics content in a virtual issue, which was a good way to convey the scope of *The Journal* and allowed delegates to see how their research would fit within our broad scope.

Alas, we didn't pick up any awards at the Oscars, but perhaps they just didn't realise we were in town...there's always next year.

We have already booked our spot for the next meeting in New Orleans. We hope to see some of you there.

Nick Boross-Toby (right) and conference attendees

Ken O'Halloran and Sally Howells

From the Archives

From the Archives: minutes of meetings 50 years ago, written by the then Meetings Secretary, EJ Denton

Transcribed by Roger Thomas

The Physiological Society Louvain Meeting, 22–23 April 1966

At the invitation of JP Bouckaert, a joint meeting of The Physiological Society and the Belgian Physiological Society was held in the Department of Physiology, Louvain University, on the 22 and 23 April 1966.

Beginning at 2.30 pm on the Friday, with Professor M Seghers in the chair, 13 communications were given by members of the Belgian Physiological Society, all, including two with French titles, in fluent English and followed by a lively discussion. The Scientific Meeting was followed by a Reception in the University Hall given by the Rector Magnificus, and by a most excellent and leisurely Dinner at Arenberg Castle. After dinner, H Blaschko warmly thanked the Rector Magnificus and Professor Bouckaert on behalf of The Society for their hospitality and for the excellent arrangements which had been made for the meeting. He reminded those present of the last joint meeting of the two societies in Louvain thirty-six years before, and observed that of those present only three - Sybil Creed, JP Bouckaert and himself - had been at that earlier meeting.

In his reply, JP Bouckaert welcomed The Society most cordially to Louvain and adopted the customary pose of a head of department in disclaiming all responsibility for the smooth organisation of the meeting, and redirected The Society's thanks to his secretary, Mademoiselle Pelgrims, and to Dr Casteels. Recalling, in his turn, the meeting in Louvain in 1930, he proposed, to warm applause, sending greetings to those members of The Physiological Society who were at that meeting, and he looked forward to the next meeting in Louvain.

On the Saturday morning, an excellent start was made with coffee. This was followed by 14 demonstrations, with plenty of time for discussion. Lunch was by invitation of the Belgian Physiological Society, and in the afternoon, the British physiologists had their say in twenty-five communications given in two theatres under the chairmanships of JP Bouckaert, JE Desmedt and ZM Bacq.

Before tea, VC Abrahams presented results suggesting that, like iatrogenic disease, the electrical records of the physiologist might in some instances be self-produced, or at least computer-produced. A very similar suspicion must have occurred to many physiologists.

After tea the reflective atmosphere was maintained by MH Pirenne, who, beginning with an analogy from St. Augustine between evil and blackness, moved quickly from the theological to the experimental, and was soon able to convince The Society that blacker than dark was an experimental possibility. Questioners' attempts to re-apply these results to evil were cunningly countered on the theological plane by a further quotation from St. Augustine. The meeting ended at 6.40 pm.

Signed: GL Brown

The Physiological Society Oxford Meeting, 4 June 1966

At the invitation of GL Brown, a meeting of The Society was held in the University Laboratory of Physiology, Oxford, on the 4 June 1966.

Beginning at 11 am, with GL Brown in the chair, eighteen communications were heard, eight before and ten after lunch. In paper 1, the Chairman's impression from the recirculated abstract that the rabbits in the Regius Professors of Medicine's Department were so well trained as to be able themselves to carry out the modified Monnier & Gangloff technique described was unfortunately found to be due to a hanging particle. After tea twenty-one demonstrations, including four extra ones, were given.

After Dinner, which was held in Rhodes House, W Feldberg thank the Chairman for again entertaining the members of The Society so well, accepting in advance GL Brown's assurances that the arrangements were all the work of his secretary, Mrs Richards, to whom the thanks should go. He went on to entertain members and guests with an account of early collaboration with GL Brown during which his eyes were first opened to the possible value of electrophysiology.

GL Brown, in reply, thanked W Feldberg for his very kind remarks and added that this meeting marked the beginning of his own rehabilitation as a physiologist after two years' preoccupation with another matter, but after seeing some of the demonstrations that day he felt that there should be no lack of interest in future development.

Lunch 156, Tea 231, Dinner 102.

Signed: Adrian

The Physiological Society University Cambridge Meeting, 15–16 July 1966

At the invitation of AL Hodgkin a meeting of The Society was held in the Physiological Laboratory, Cambridge, on the 15 and 16 July, 1966.

On Friday morning, members and guests put in a very active two hours among the 31 demonstrations presented at the ARC Institute, Babraham. The visit ended with an excellent lunch in the library, where sherry was generously provided by the ARC.

Beginning at 2:15 pm at Cambridge, with AV Burgen as chairman in one theatre and AL Hodgkin and EN Willmer alternating in a second theatre, 16 communications were heard before and a further 12 after tea. This was followed by sherry party very kindly given by the University in Christ' s College which, to the surprise of everyone present, had to be held indoors. Dinner was in Trinity College and members were delighted to see Lord Adrian in the chair. After dinner, DW Whitteridge thanked AL Hodgkin on behalf of The Society for arranging such a pleasant meeting and the Master and. Fellows of Trinity College for allowing The Society to use their Hall.

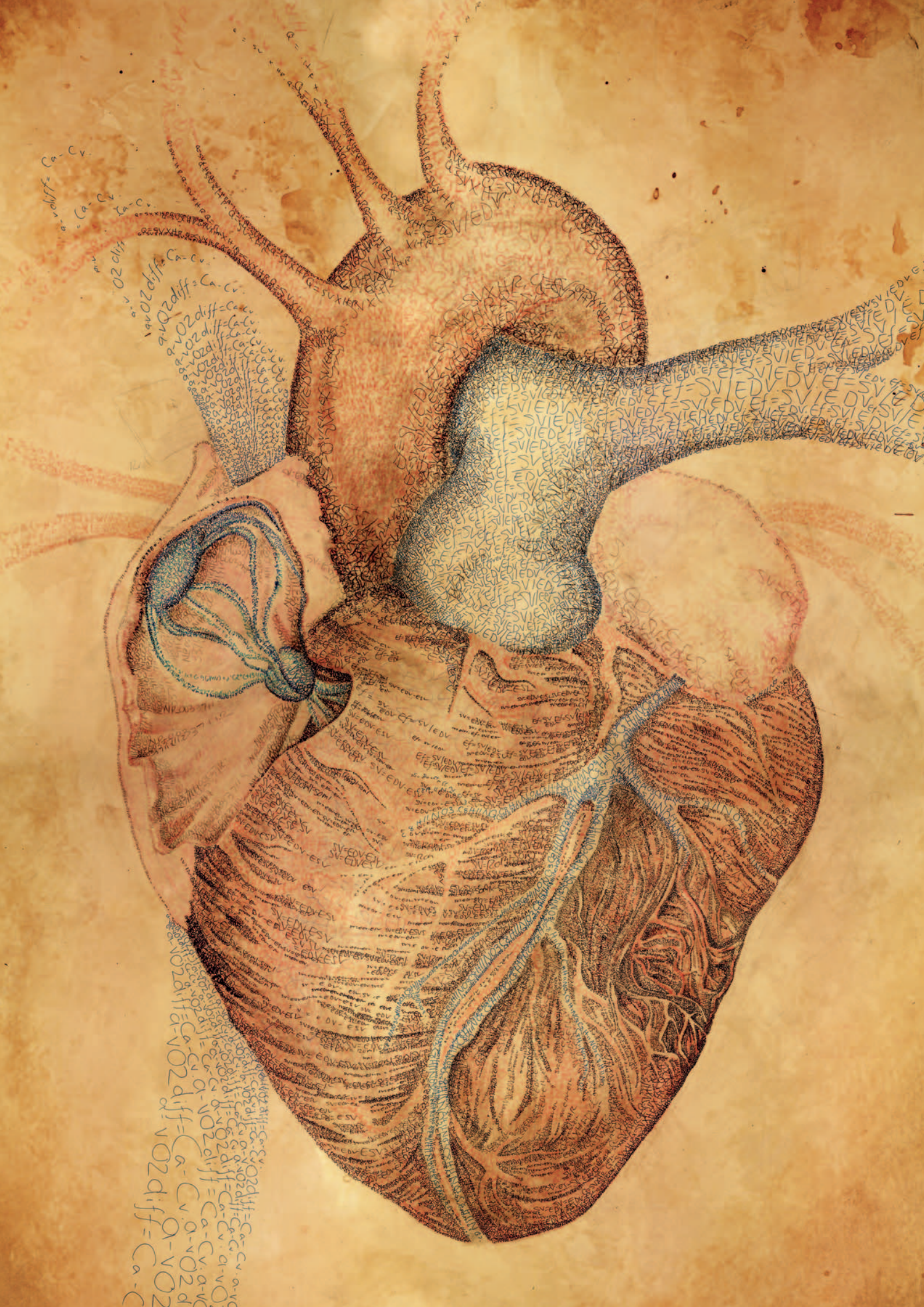
In reply, AL Hodgkin welcomed members and their guests and paid tribute to Miss Sylvia Elton who had so efficiently made the arrangements for the meeting. Trinity College, he pointed out, was a most appropriate place for The Society's dinner, as it was in this college that an earlier Master, Richard Bentley, had against some opposition, established in the college what was perhaps the earliest experimental laboratory. AL Hodgkin ended by proposing the health of the chairman, Lord Adrian, to which members responded with enthusiasm.

Lord Adrian extended the link with Trinity College when he spoke of the old laboratory at Downing Street, a gift of that college, and of the many distinguished physiologists who had worked there, beginning with Michael Foster and including the names of JN Langley, AV Hill and HH Dale, to which his own must surely he added.

On Saturday, beginning at 10 am with EN Willmer as chairman in one theatre and ASV Burgen in the second, a further 10 communications were heard and 20 demonstrations examined before lunch, and the remaining 11 communications after lunch. Communication 24 was withdrawn. The meeting ended with tea at 4 pm.

Friday: Lunch (Babraham) 140, Tea 262, Dinner 183. Saturday: lunch 178, Tea 200.

Signed: RC Garry



Numberism: exploring science through art

Sienna writes about her work as an artist using 'Numberism' – a technique in which she draws realistic images entirely with tiny numbers and equations by hand, using pen, pencil or as etchings on scratchboard, metal or glass.

Portrait illustration: Monique Alcott

Sienna Morris

Artist

Figure 1. (Left) Structures of the 'Heart' are illustrated with the following physiological equations. Great coronary vein: $C_8H_{11}NO_3$ (noradrenaline). Vena Cava: a - vO_2 diff = C_a - C_v (arteriovenous oxygen difference). Cardiac muscle: SV = EDV – ESV (stroke volume). Pulmonary artery: EF = (SV/EDV) x 100% (Ejection Fraction). Aorta: Q = SV x HR (cardiac output). AV Node: 40-60 per min (firing rate). SA Node: $E_m = g'K^+$ [-96 mV] + $g'Ca_2+$ [+134 mV] (membrane potential).

I am a self-taught scientific artist in Portland, Oregon. I started using my drawing technique 'Numberism' as a learning device in 2008. This is similar to pointillism, which uses dots; however, my pieces tell a story of the subject using the scientific and mathematical language of their own structures to more clearly depict them. For me, the illustrations are more realistic and complete because they are drawn with mathematical representations of themselves. While my method utilises tools of academia, my process is visceral and driven equally by love and logic.

When I first started this series, I expected it would put people off, and prepared for the onslaught of 'I hate maths' comments to come my way. Instead, I found that by and large, people loved the excuse to celebrate the inherent beauty of math and science even if they themselves had no natural affinity for it. I describe my work as 'drawing math where it lives', a concept that strikes a chord with most people.

On average my pieces take around 200 hours to draw and upwards of a year to research. The 'Heart' (Fig. 1) took me seven months to draw, which was somewhere around 500 hours of 'numberisming'. It is drawn with physiological equations such as stroke volume in the main body, cardiac output in the aorta, oxygen difference in the superior and inferior vena cava and oxygen content in the pulmonary veins. The remarkable 'electric system' of the heart is highlighted in the right atrium with the atrioventricular node drawn with its average firing rate and the sinoatrial node drawn with its membrane potential. This is part of an ongoing series on the body I am producing with a long-term goal of understanding the brain.

My latest work is 'Fire Dol' (Fig. 2), a story about the very first moments of experiencing the pain of heat. This is not the complex and largely unknown manner in which our brain processes pain, but rather the first reaction to the noxious stimulant, and how this information is transmitted from nociceptors in the spinal cord. It is drawn with the TRPV1 protein, chemical formulas for Substance P, Glutamate, Acetylcholine, reaction time for a reflex arc and equations relating to how action potentials from the dorsal and ventral horns are transmitted along myelinated axons to the brain and periphery. I have used Cable Theory, the GHK equation and Ohm's Law to illustrate this, as well as The Nernst Equation and Membrane Potential for the initial Action Potential.

This piece in particular illustrates the personal mission of my work, in which I emphasise the beauty in systems often first seen as gross, scary, tedious or dull. I personally had the average American school experience with science and mathematics. The one that leaves you running and never looking back, full of sweaty palms and embarrassment. So, my work is aimed directly at those who have the most reason to despise it. 'Fire Dol' was my most difficult in this respect and perhaps the most rewarding.

‘My path isn’t very academic, although I embrace its virtues and methods. It is visceral and full of boundless admiration’

Figure 2. ‘Fire Dol’, (Dols; the unit of pain), illustrates the spinal cord response to thermal noxious stimulus. Fire: 1571 °F or 855 °C (temp of campfire). Grey Matter: NP_061197 (TRPV1 protein), $C_{63}H_{98}N_{18}O_{13}S$ (Substance P), $C_5H_9O_4$ (Glutamate), $C_7NH_{16}O_2$ (Acetylcholine). White Matter: Nernst equation (reversal potential), V = IR (Ohm’s law), GHK flux equation (action potential propagation), Cable theory equations (action potential conduction). [Inset] Bradly Hackworth, the inspiration for ‘Fire Dol’, had experienced a bad house fire as a child.

My good friend Bradly Hackworth and his sister were in a bad house fire as children, which left long-lasting emotional and physical scars, and naturally a fear of fire. With ‘Fire Dol’, my goal was to illustrate the spinal cord’s response to thermal noxious stimuli so beautifully that even he, with his incredibly painful history, would find beauty and peace within it. The etching features the human spinal cord in transverse cross section over a field of hot flame drawn with an average temperature of a campfire. The scientific story is based on how nociceptors protect us, and how pain itself can preserve life by warning us against its source.

When Bradly first saw ‘Fire Dol’ he contacted me to say it was ‘the most beautiful finished piece yet’ and he was ‘in love with it’ (Fig. 2 - Inset). I’m ill equipped to describe how that moment felt. This rewarding connection through my work inspires me to create further pieces on trauma, recovery and the human mind. These will accompany ‘Psychic Tears’ (see Front Cover) which focusses on tears caused by emotional and physical triggers and is drawn with chemical formulas for cortisol and acetylcholine.

Science is hard

As someone who is self-taught, this can be overwhelming and potentially devastating to my education. I don’t have a professor to guide me, nor do I have classmates to commiserate with or compare notes. When I hit upon a wall and feel the full burden of my ignorance in these unexplored worlds, I must rely on my passion to get me through. I’m currently studying neuroscience with a focus on the visual system, so as you can imagine, I have hit upon many walls. As of yet, I have not faced a wall that could not be overcome by the inherent beauty of the subject, but I must first be able to find that beauty to be driven by it. It requires more than a sole reliance on textbooks and open-online courseware to see the beauty of the body and brain. I needed to experience it in the flesh.

This limitation led to an important change in my personal education and my artwork last year. Frustrated with my text-based education of a physical world, I launched a Kickstarter campaign to build a dissection lab in my art studio. My goal was to cover the basic costs by way of offering pre-orders of prints and originals from the planned series. In less than a day, it was 100% funded and by the end the campaign had collected an astounding $11,677 (583% of the initial funding goal). My ‘Art Lab’ now housed both a compound and stereo microscope, surgical tools, and a variety of specimens and histological dyes. I finally had the tools to delve deeper into the brain.

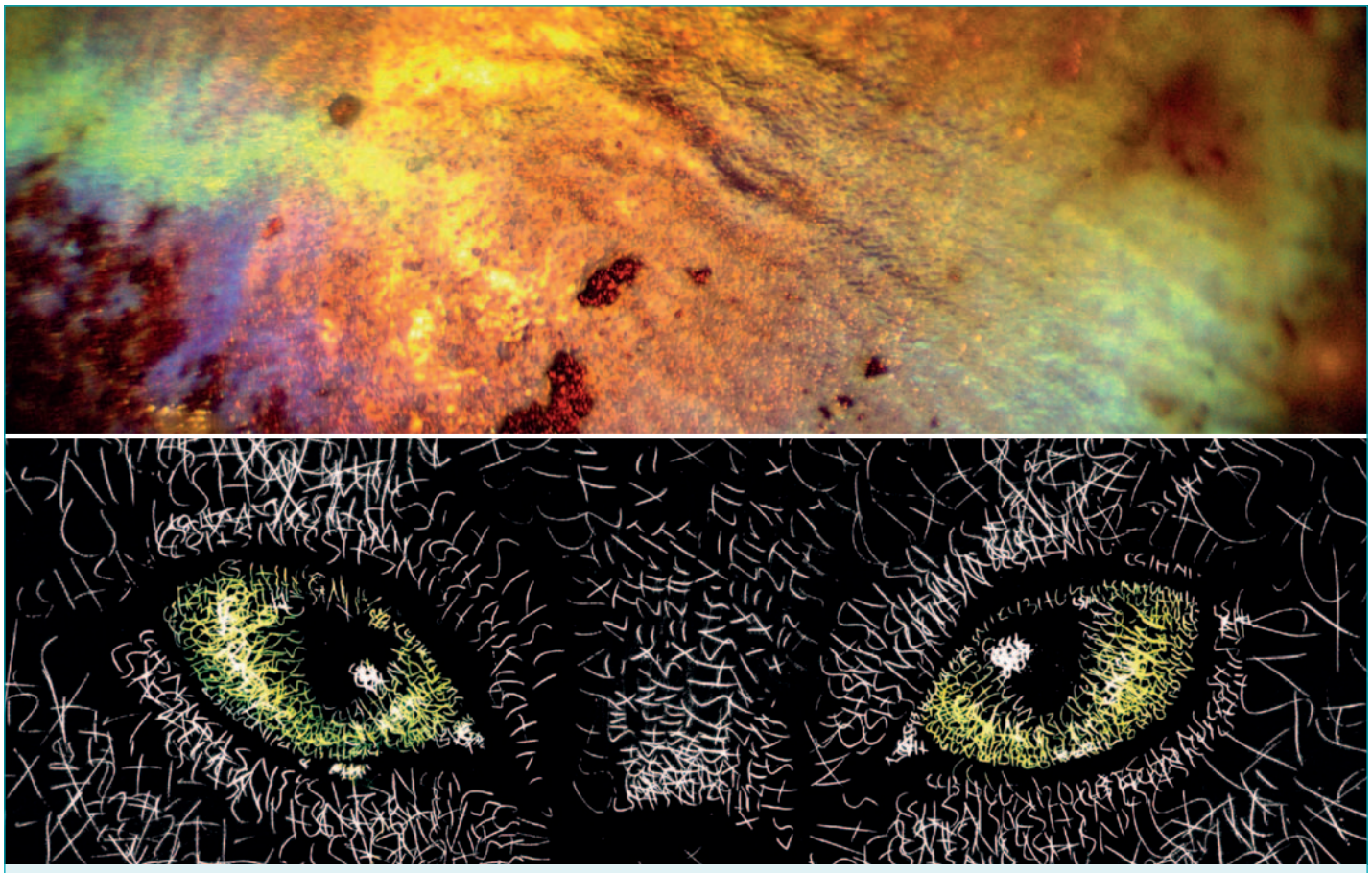


Figure 3. [Top Panel] 'Ovis Aries Nebula' - Brightfield image of sheep tapetum lucidum. [Bottom Panel] 'Felis Lucidum' explains how the tapetum lucidum at the back of a cat's eye enhances night vision and gives them eye shine, as well as the human to pet bond. 299,792,458 m/s (speed of light), $x = 2\pi r/\lambda$ (Rayleigh scattering equation), $C_5H_5N_5O$ (Guanine), $C_20H_{28}O$ (Retinal), $C_{43}H_{66}N_{12}O_{12}S_2$ (Oxytocin).

I made a mess of my first dissection, but found it truly fun and educational. In my first session, I dissected the eyeball of a sheep, cow and pig, dutifully separating the pieces onto Petri dishes to image later with my microscopes. I noted the difference between the viscous vitreous body and the fluid aqueous humour, tugged on the retina as it dangled from the optic disk, and twanged the clear zonular fibres suspending the lens. I felt like a child, enamoured and gloriously happy at the systematic mess I was making. I gathered up the rather foul smelling dishes and inspected them under my stereo microscope.

This is how I found the Universe at the back of a sheep's eye; one of the first images I took with my stereo microscope (Fig. 3 - Top). It features the crystalline structure of the tapetum lucidum at the back of a sheep eyeball, found beneath the retina. I had read about these in my research into the visual system, but none of my books had featured an image. Looking down into my microscope, I was suddenly gazing up into the infinity above. After much illuminating research, I created two Numberism etchings based on the tapetum; 'Felis Lucidum' (Fig. 3 - Bottom) and 'Lupus Lucidum', both of which are drawn with chemistry and physics that explain how it allows for night vision and produces eyeshine.

This is the foundation of my method. I am driven into my research by beauty and confusion. My education is a love affair with curiosity. My notebooks are full of sketches of beautiful systems that I am compelled to later illustrate, like the Ventricles of the brain, the purkinje tree, and the mesencephalon. Words like 'isoluminant', 'lacus lacrimalis' and 'arbor vitae' read like poetry to me and serve as calls to arms to know them better and share them through my illustrations. My path isn't very academic, although I embrace its virtues and methods. It is visceral and full of boundless admiration.

What I do does not come naturally to me, and without a mathematical background traversing these waters will never be easy, however that makes it all the more rewarding. I imagine that between us and the truth of the Universe is an infinite series of frosted panes of glass. Each new learning experience clears part of the frost of the nearest pane or removes it entirely. With an infinite set, we will likely never clear them all, but even reaching 100 panes closer to infinity is worth the effort. Being inspired by science means my palette can never go dry. Being self-taught means I understand my ignorance better than most and will therefore never be sated. As I will always be more unknowing than knowing, my journey will last a lifetime.

Further information

For more info on Numberism, Sienna can be found at the Portland Saturday Market (Oregon, USA) every Saturday and Sunday from March to Christmas Eve or online at the following:

www.fleetingstates.com

Etsy: siennamorris.etsy.com

Instagram: @SiennaMorris

Twitter: @MrsSiennaMorris

Facebook: facebook.com/numberism

Youtube: youtube.com/siennamorris

Why are the problems associated with the lack of international standards for Ca^{2+}/Mg^{2+} buffers still being ignored?

It is difficult to compare measurements from different laboratories with no agreed standard.

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Ca^{2+} and, to a lesser extent, Mg^{2+} play crucial roles in the regulation of intracellular processes. The intracellular ionised calcium concentration ($[Ca^{2+}]$) is in the nmolar range and the apparent constants (K') for Ca^{2+} and Mg^{2+} binding to intracellular ligands are in the nmolar and µmolar range respectively. These concentrations can be set by dilution but are bedevilled by contaminating concentrations of Ca^{2+}/Mg^{2+}, making buffers essential. The $[X^{2+}]$ in these buffers are either calculated or measured. Calculated values depend on the constants chosen and the method of computation and are so inconsistent, that until International Standards are available, the $[X^{2+}]$ in Ca^{2+}/Mg^{2+} buffers have to be measured not calculated. Lacking International Standards, means there can be no exact measurements of intracellular $[Ca^{2+}]$ and the K' values for Ca^{2+}/Mg^{2+} binding to intracellular ligands. This has repercussions for the modelling of intracellular Ca^{2+}/Mg^{2+} regulation. International Standards are long overdue.

Ca^{2+}/Mg^{2} Buffers

The easiest way to make up solutions of such buffers is to use the ratio method with the appropriate background solution. In this method, two solutions of identical pH are made up; 1) an equimolar solution of Ca^{2+}/Mg^{2+} and the ligand, and 2) a ligand solution. These are then mixed in various proportions ranging from 7:1 to 1:9 to give 10 buffer solutions, B1 to B10 (McGuigan *et al.*, 2006). Making your own buffers has the advantage that their composition mimics the experimental conditions, but is time consuming. Calcium buffers in which the $[Ca^{2+}]$ are calculated are available from either WPI or ThermoFisher. Buying such buffers is convenient, but has the disadvantage that their composition may differ widely from the experimental solutions.

Concentration, activity and activity coefficients

In physiological solutions due to the interaction between the positive and negative ions, elevation of the boiling point and depression of the freezing point are less than would be expected from the salt concentrations. The salts in such solutions have thus an 'effective concentration' or activity, which is less than the actual concentration. The ratio of activity/concentration is the mean activity coefficient ($\gamma\pm$), mean, because it depends on both the cation and anions in the solution. However, in calculations it is often not the $\gamma\pm$, but the single ion activity coefficients ($\gamma+$, $\gamma-$) that are used; while the $\gamma\pm$ can be measured, the activity coefficient of a single ion cannot, and a convention has to be used to calculate it.

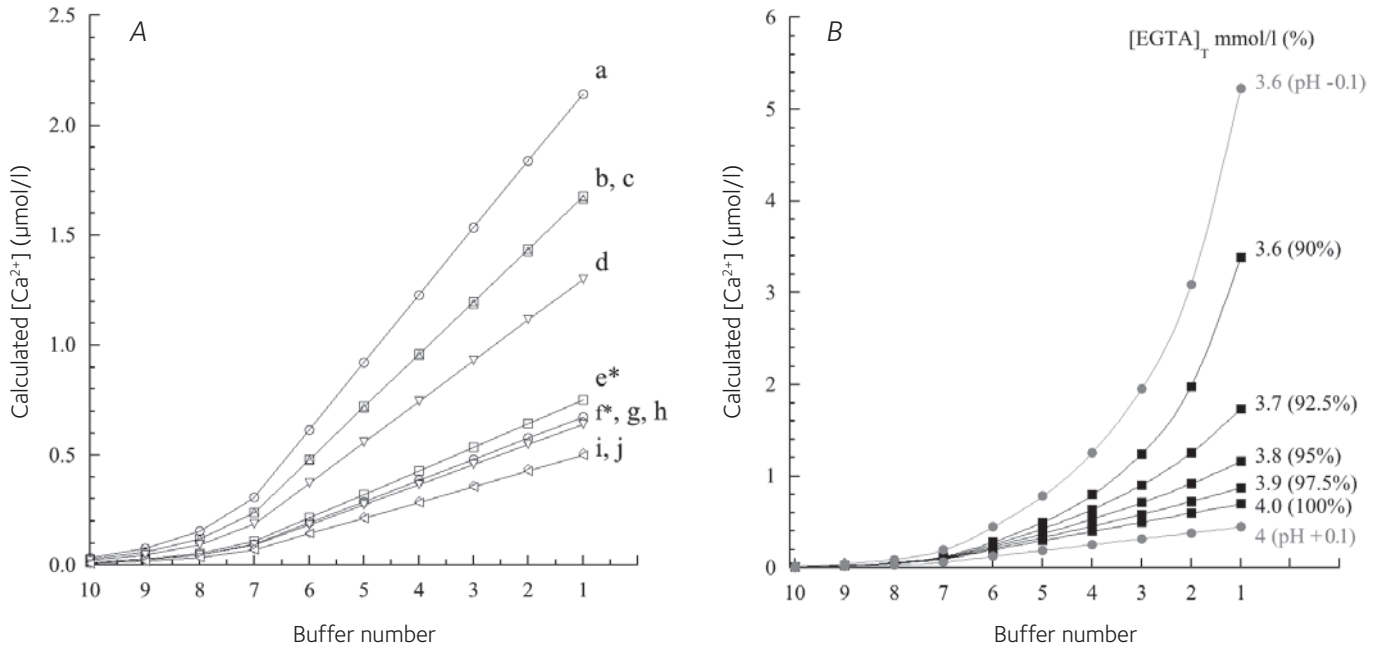

Figure 1. A. Calculated [Ca^{2+}] in the 10 Ca^{2+} EGTA buffer solutions. Summarised results are shown in Table 1. *B.* Influence of pH and $[EGTA]_T$ on the calculated [Ca^{2+}]. Details of calculation in McGuigan *et al.*, 2016.

Calculation of [X^{2+}] in the buffer solutions

Several papers describe how to calculate the [X^{2+}] in buffer solutions, but the inherent problems in these calculations are often glossed over. As shown in McGuigan *et al.*, (2016) there are four such problems.

1. Tabulated constants for Ca^{2+}/Mg^{2+} and H^+ binding to Ca/Mg-ligands vary, and the choice of constants influences the calculated [X^{2+}] values.

2. The constants have in many cases to be corrected for temperature and ionic strength. The data for temperature correction are not always available. The correction for ionic strength involves the calculation of the single ion activity coefficients for Ca^{2+}, Mg^{2+}, H^+ and the ionic forms of the ligand. A common method to do this is to use the Davies equation to calculate the γ± and the Debye-Hückel convention to calculate the single ion activity coefficient from this mean value. There are, however, other possibilities. The Debye-Hückel convention can be combined with the accurate equations of Pitzer & Mayorga, or the conventions of Bates *et al.* and MacInnes can be used; all give different results.

3. pH is defined in terms of hydrogen activity, but the tabulated constants for Ca^{2+}, Mg^{2+} and H^+ binding to ligands are in terms of concentration, so measured pH_a (activity, $[H^+]\gamma_{H^+}$) has to be converted to pH_c (concentration, $[H^+]$) by using a convention to calculate the ion activity coefficient for H^+-ions (γH^+) . There is no defined way of doing this. An accurate conversion from pH_a to pH_c assumes that the potential of the reference electrode is the same in both the calibration solutions and the sample solution. This is usually not the case, and such changes can lead to deviations of ±0.1 pH units in the measured pH_a, which influences the calculated [X^{2+}].

4. Due to absorbed water, ligands are not 100% pure, so purity has to be measured even if the [X^{2+}] are calculated.

Results of calculation for the ionised concentrations in buffer solutions

Ca^{2+} EGTA buffer solutions: These buffers are representative of the results of calculation for both Ca^{2+} /Mg^{2+} buffers.

Influence of constants and ionic strength corrections on the calculated [Ca^{2+}]. The [Ca^{2+}] in the 10 buffer solutions calculated with 4 sets of constants, corrected if necessary to an ionic strength of 0.15 mmol/l, a temperature of 25 °C and for a pH_a of 7.4, are illustrated in Figure 1A and Table 1. The most striking feature of Figure 1A is the variation in the calculated values for [Ca^{2+}]; Table 1 shows the influence of the method of correction for the ionic strength on the calculated values and lists the actual [Ca^{2+}] for buffer solution B1, and B10. The ratio maximum/minimum (curves a/j) for the calculated values was 4.3 for buffer solution B1 and 3.4 for buffer B10.

Software programmes for [Ca^{2+}] and [Mg^{2+}]

The [Ca^{2+}]/[Mg^{2+}] in buffer solutions can also be calculated using programs but these programs also suffer from exactly the same disadvantages as those of the calculations illustrated in Figure 1 (Figure 5B in McGuigan *et al.*, 2016 for [Ca^{2+}]).

Commercial Ca^{2+}-buffers

These commercial buffers are based on calculated values and as illustrated in Figure 1A, if different constants were chosen, different values for [Ca^{2+}] would be obtained. Moreover, these solutions are for an ionic strength for 0.1 mol/l, not the physiological ionic strength of 0.15 to 0.20 mol/l.

‘Over the past 40 years the need for International Standards for Ca^{2+}/Mg^{2+} buffers and the problems related to their lack, have simply been ignored’

Table 1. **The influence of the correction for ionic strength on $[Ca^{2+}]$**

Constants	Convention for correction for ionic strength	B1 (µmol/l)	B 10 (nmol/l)
Smith & Miller	(a) Debye-Hückel, Davies equation	2.14	26.5
	(b) Debye-Hückel, Pitzer & Mayorga equations	1.66	26.5
	(g) Bates *et al.*	0.65	10.3
	(h) MacInnes	0.64	10.1
Martell & Smith	(c) Debye-Hückel, Davies equation	1.67	26.7
	(d) Debye-Hückel, Pitzer & Mayorga equations	1.30	20.7
	(i) Bates *et al.*	0.51	8.1
	(j) MacInnes	0.50	7.9
Fabiato & Fabiato	(e)* not necessary	0.75	11.9
Pressler & Schindler	(f)* not necessary	0.67	10.7

Influence of $[Ligand]_T$ and pH on the calculated $[Ca^{2+}]$. The calculations are shown in Figure 1B. The constants of Pressler & Schindler were used (ionic strength 0.15 mol/l, temperature 25 °C, pHa 7.4) and the $[Ca^{2+}]$ calculated for $[EGTA]_T$ of 4 mmol/l to 3.6 mmol/l. The influence of pH on the calculated $[Ca^{2+}]$ is illustrated in red at 4 mmol/l for an increase of 0.1 pH unit, and at 3.6 mmol/l for a decrease of 0.1 pH unit. Figure 1B simply emphasises the difficulties with calculation.

Consequences of calculated values

To illustrate the consequences of calculation on published $[Ca^{2+}]$ values, the action of vasopressin on intracellular $[Ca^{2+}]$ in liver cells is illustrated in Figure 2, based on experiments by Woods *et al.*, (1987). In Figure 2A the $[Ca^{2+}]$ have been calculated using the values from Smith & Miller and the mean resting concentration for $[Ca^{2+}]$ was 220 nmol/l and the spikes reached a concentration of 650 nmol/l. However, as illustrated in Figure 2B, if the programs of Godt & Lindley (4 mmol/l EGTA) and Chelator are chosen the resting $[Ca^{2+}]$ varies from 150 nmol/l to 340 nmol/l and the spike amplitude from 400 nmol/l to 950 nmol/l.

Imagine such results in a clinical setting. The measured serum $[K^+]$ would be 3.4 mmol/l (hypokalaemia), 5.0 mmol/l (normal) or 7.7 mmol/l (hyperkalaemia) (Walker *et al.*, 2014). The patient either requires an immediate infusion of K^+, no treatment or is in danger of dying of K^+ excess! It is an absurd situation, but it accurately describes the current situation for Ca^{2+} and Mg^{2+} buffers.

Measurement of $[X^{2+}]$ in buffer solutions

Criteria for measurement. Because of the problems with calculation, attempts have been made to measure the $[X^{2+}]$ in the buffer solutions. McGuigan *et al.*, (2006) drew up a list of 6 criteria for the ideal method to measure $[X^{2+}]$ in Ca^{2+} and Mg^{2+} buffer solutions. Slightly modified and now including a 7th criterion for independent verification they are:

1. Be applicable at the composition, temperature, ionic strength and pHa of the buffers
2. Should estimate both $[Ligand]_T$ and the K'
3. Should be applicable to both Ca^{2+} and Mg^{2+} buffers
4. Should not involve using listed constants
5. Should not involve converting from pH_a to pH_c
6. Using simulated data, the method should accurately estimate both $[Ligand]_T$ and K'
7. Should be independently verifiable

McGuigan *et al.*, (2006) considered 7 different methods that have been used to measure the $[X^{2+}]$ but only one, the Ligand Optimisation Method (details in McGuigan *et al.*, 2006, 2014, 2016; calculation software: jimkay99@virginmedia.com) met all these 7 criteria. The method is based on the measurements of $[Ca^{2+}]/[Mg^{2+}]$ with a Ca^{2+} or

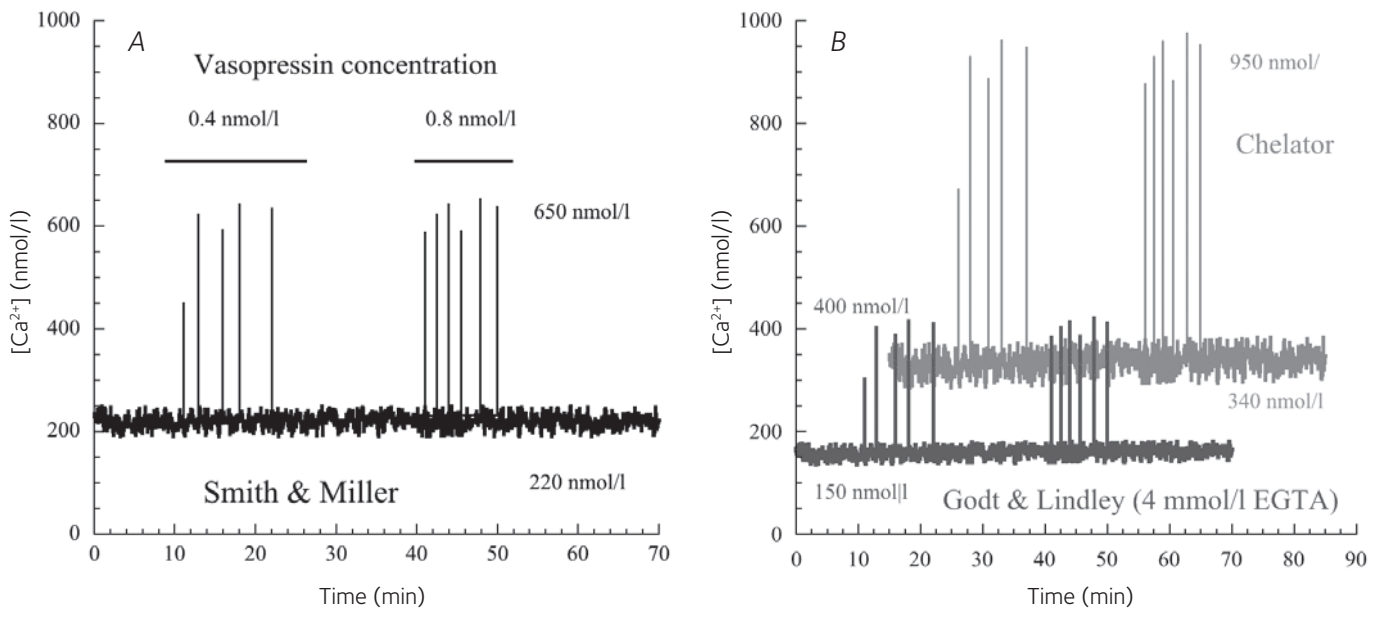

Figure 2. Action of vasopressin on rat hepatocytes. *A.* The $[Ca^{2+}]$ calculated using the constants of Smith & Miller. *B.* The same buffer solutions but $[Ca^{2+}]$ calculated with the programs, Chelator and Godt & Lindley, but with an $[EGTA]_T$ of 4.0 mmol/l instead of 3.8 mmol/l.

Mg^{2+} electrode. The electrode characteristics, electrode slope and the constant of the recording system are initially determined in calibration solutions ranging from 0.5 mmol/l to 10 mmol/l (pX 3.301 to 2.000). Using these parameters, the pK' values and the $[Ligand]_T$ in the 10 buffer solutions are then estimated using an iterative procedure.

Why International Standards for Ca^{2+} and Mg^{2+} buffers are necessary

As shown in Figures 1, calculated values for $[Ca^{2+}]$ in the buffer solution vary widely and it is similar for Mg^{2+} buffers (Figure 5A, McGuigan *et al.*, 2016). The intracellular $[Mg^{2+}]$ is around 1 mmol/l, a concentration at which buffers are not required. However, estimations of intracellular $[Mg^{2+}]$ with ^{31}P-NMR depends on the K' values for Mg^{2+} binding to ATP and related ligands whose estimation does require Mg^{2+} buffers. Since Intentional Standards do not exist, there is no way to determine which of the calculated values is correct, be it with spreadsheet, software programmes or commercial buffers. It is the classical 'Catch 22' situation.

Composition of International Standards for Ca^{2+} and Mg^{2+} buffers

That standards are necessary is beyond doubt, but the main question, and one that is still open to discussion, is the composition of such standards. Such buffers should have an ionic composition, ionic strength and pH similar to that of a physiological solution be it intracellular or extracellular, and be defined in terms of concentration not activity. To minimise the changes in potential at the reference electrode either a K^+ (intracellular buffers) or Na^+ (extracellular buffers) should be used instead of a 3 mol/l KCl reference.

Conclusions

Over the past 40 years the need for International Standards for Ca^{2+}/Mg^{2+} buffers and the problems related to their lack, have simply been ignored. If there are no International Standards, there can be no exact determinations of intracellular $[Ca^{2+}]$, ^{31}P-NMR estimations of $[Mg^{2+}]$ and of the K' values for intracellular binding of Ca^{2+}/Mg^{2+} to physiological relevant ligands. Lacking accurate measurements of these parameters means that the results of modelling of the intracellular regulation of Ca^{2+} and Mg^{2+} have to be regarded with a degree of caution.

Finally, we conclude, that until International Standards are available, the $[X^{2+}]$ in Ca^{2+}/Mg^{2+} buffers have to be measured not calculated. The only accurate way of doing this is to use the Ligand Optimisation Method (McGuigan *et al.*, 2016).

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Figure 1. An advanced bi-level positive airway pressure system integrated in a whole-body armoured suit for the treatment of acute and chronic respiratory failure in a Sith Lord. © LucasArts

Breath of the Sith: a case study on respiratory failure in a galaxy far, far away

Spoiler alert!

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While the eagerly awaited seventh instalment in the Star Wars saga has thrilled physiologists and non-physiologists alike, it may be worthwhile to take a look back at what we as respiratory physiologists have learned from the venerated space opera so far. It remains indisputable – at least between the authors of this paper – that the first six episodes' protagonist-turned-villain-turned-saviour Anakin Skywalker/ Darth Vader is the most fascinating case study on respiratory failure in the history of cinema. The enigmatic breathing sounds produced by his iconic whole-body armoured suit, as well as his mysterious underlying respiratory condition, have been source of bewilderment and fascination (and fright) to at least two aspiring respiratory physiologists that grew up in the outskirts of Denmark during the 1980s, a time when every child dreamt of becoming either a Jedi Knight or a Stormtrooper.

Health hazards of volcanic fumes

In the Star Wars saga, the highly talented Jedi knight, Anakin Skywalker, choses to abandon the monastic Jedi Order and instead join his father figure Sheev Palpatine in the more exclusive and politically involved Sith Order. As he does this, he assumes a new identity as Darth Vader, and earns the title Dark Lord of the Sith. For a number of reasons, this change of careers does not impress a former Jedi Master of his, and the two soon clash in a light sabre duel on the volcanic planet Mustafar. The confrontation results in a near-fatal outcome for Darth Vader who loses several limbs in the fight, and while he is incapacitated on the volcanic shore, he furthermore suffers inhalational injury and third degree burns. However, before he passes away, Palpatine comes to the rescue, and organises timely medical intervention.

Prior to the tragic events on Mustafar, Vader's health and fitness level are seemingly excellent. Even though the air on a volcanic planet is mostly composed of water vapour, carbonic and sulphuric gases, and nitrogen, with insignificant levels of oxygen (Cadle 1980), Darth Vader and his former Jedi Master readily engage themselves in the intense and extremely physically challenging light sabre duel in this climate (probably the equivalent of an hour-long high-intensity exercise bout at the summit of Mount Everest), without ever taking even a short break to catch their breath. After the incident, Darth Vader is, however, unable to breathe freely at all; outside his personal meditation chamber, which also appears to function as some kind of a fancy hyperbaric oxygen facility, he continually relies on a mobile life-support system, which is integrated in a whole-body armoured suit, in order to survive (Figure 1).

‘We deem it irrefutable that Darth Vader fulfils the diagnostic criteria for acute respiratory distress syndrome within a few hours after the incident on Mustafar’

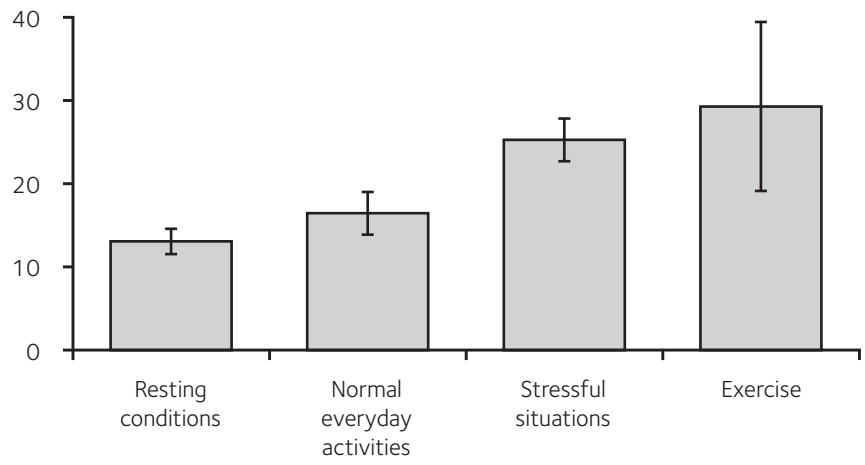

Figure 2. Respiratory rate according to activity level in a Sith Lord (n =1). Data are obtained from Plovsing & Berg (2014) and presented as mean (± standard deviation). ‘Rest’ includes recreational activities in a meditation chamber; ‘Normal everyday activities’ include various friendly encounters as well as torture of enemies, colleagues, and employees; ‘Stressful situations’ includes increased alertness and arousal; ‘Exercise’ includes running, combat and light sabre duels.

Darth Vader’s acute respiratory failure appears to be the consequence of a number of factors, including direct thermal injury to the airways, chemical damage to the lung parenchyma caused by inhalation of smoke and volcanic dust particles, carbon monoxide poisoning, as well as secondary effects to his severe third degree burns, which seems to cover ~100 % of his total body surface area.

Thermal injury caused by scalding volcanic fumes primarily affects the central parts of the lungs, because the dissipation of heat results in less damage to the peripheral areas (Eyal *et al.*, 1975). This causes oedema in the large airways, as well as peribronchial and perivascular haemorrhages, and acutely reduces pulmonary compliance, but without any marked effects on pulmonary gas exchange within the first few hours. In addition, so-called pyroclastic density currents, volcanic gases that move laterally near the ground at hurricane velocities, may induce immediate thermal injury beyond the central parts of the lungs (Hansell *et al.*, 2006).

Volcanic fumes furthermore contain numerous irritants that cause chemical damage to the airways (Nemery 2006). Gaseous irritants with high water solubility, such as ammonia and sulphuric dioxide, are mainly trapped in the aqueous surface of the upper respiratory tract, and give rise to immediate symptoms. They cause airway wall oedema, bronchospasm, ulcerations, and necrosis in the conductive airways. Volcanic gas irritants with a low water-solubility, such as nitrogen oxides, may pass the upper airways and eventually reach the alveolar compartment. These induce alveolar inflammation with oedema formation, and impair mucociliary function and surfactant production, but do not usually cause symptoms until after several hours. Many volcanic aerosols have an aerodynamic diameter of less than 5 µm, and are thus easily dispersed in the peripheral airways, where they may cause similar effects to gas irritants with low water solubility.

Inhalation-induced acute respiratory distress syndrome in a Sith Lord

Darth Vader’s immediate respiratory distress on the volcanic shore is probably caused by volcanic gaseous irritants with high water solubility in the volcanic fumes, which cause immediate symptoms of tracheobronchitis, and impair pulmonary gas exchange (Nemery 2006; Mlack *et al.*, 2007). Since Darth Vader may concurrently be exposed to high levels of carbon monoxide, which both impairs the red blood cell uptake of oxygen in the lungs due to its higher affinity for haemoglobin than oxygen, and furthermore shifts the oxygen-haemoglobin saturation curve to the left, so that the release of oxygen from the red blood cells to tissue mitochondria (and perhaps also the conceivably similar midi-chlorians) in various organs is impaired; severe tissue hypoxia therefore ensues. Due to his quite severe facial burns, it is difficult to determine whether Darth Vader exhibits ‘cherry-red cheeks’ at this stage, a typical clinical finding associated with carbon monoxide poisoning, but his rather agitated emotional state is characteristic of the cerebral dysfunction often encountered in this clinical condition.

Within a few hours, that is, after Darth Vader has been evacuated by Palpatine, the effects of direct thermal injury on the central parts of the lungs, as well as the effects of the volcanic water soluble gaseous irritants and aerosols set in. These give rise to acute chemical pneumonitis with non-cardiogenic pulmonary oedema and induce a reduction in ventilatory capacity with increased pulmonary ventilation-perfusion inequality, thus severely impairing pulmonary gas exchange (Nemery 2006). At this stage, the systemic inflammatory response to the severe skin burns may furthermore disseminate from the blood stream to the alveolar compartment, and thus exaggerate the pulmonary inflammatory response. Although appropriate diagnostic imaging would be required to establish the diagnosis here on Earth, we deem it irrefutable that Darth Vader fulfils the diagnostic criteria for acute respiratory distress syndrome within a few hours after the incident on Mustafar, which is a common complication both after inhalation injury and severe skin burns (Mlack *et al.*, 2007).

Following extensive robotic surgery, the medical droids choose to treat Darth Vader's respiratory condition by means of the iconic whole-body armoured suit. The suit contains a mobile life-support system, and from a careful analysis of *Episodes IV-VI*, we have concluded that it functions as an advanced bi-level positive airway pressure (BPAP) system that supports Darth Vader's intrinsic breathing both during in- and expiration, while preventing airway collapse, and continually supplying him with oxygen (Plovsing & Berg 2014). Accordingly, his respiratory rate varies with his activity level (Figure 2), and pressure equalisation with the surroundings can clearly be heard when his helmet is detached. Other scientists have noted that Darth Vader's whole-body armoured suit may furthermore function as a means of preventing infections, which is notably relevant in the immediate aftermath of the events on Mustafar, due to Darth Vader's extensive skin burns (Perrella *et al.*, 2015).

Dark Lord of the Sith: A blue bloater in disguise?

Studies have shown that patients with acute respiratory distress syndrome, including those that involve thermal and/or inhalational lung injury, suffer from permanent reductions in ventilatory capacity as well as impaired pulmonary gas exchange after discharge from hospital (Neff *et al.*, 2003). This also appears to be the case for Darth Vader, despite the timely intervention by Palpatine's medical droids. Hence, as we encounter Vader in *Episode IV*, two decades after the events on Mustafar in *Episode III*, it is clear that the treatment with the whole-body armoured suit has been maintained during all the intervening years.

Since Darth Vader continually relies on the whole-body armoured suit, the acute effects of the thermal and chemical injury must have led to lung fibrosis due to extensive scar tissue formation in the pulmonary parenchyma, which permanently reduces ventilatory capacity on a restrictive basis and impairs gas exchange by increasing ventilation-perfusion inequality (Plovsing & Berg, 2014). It is less clear whether he also suffers from chronic bronchitis, which could add a obstructive component to his lung disease. In contrast to General Grievous, the Supreme Commander of the Confederacy of Independent Systems during the Clone Wars, who is a clear-cut case of chronic bronchitis with a rattling cough, Darth Vader is never once observed to cough during the Star Wars saga. On the other hand, he clearly has the appearance of a 'blue bloater' with bluish colour of the skin and lips, and develops severe wheezing when Luke Skywalker detaches his mask in *Episode VI* (Figure 3). These are characteristic features of chronic bronchitis, and the lack of coughing from the Sith Lord thus rather reflects the efficacy of the treatment with the whole-body armoured suit than it reflects absence of obstructive pulmonary disease.

Conclusion

Our extensive analysis of the first six instalments of the Star Wars saga demonstrates that Darth Vader suffers from the chronic aftermath of acute respiratory distress syndrome caused by inhalation-injury and skin burns, which is treated by a whole-body armoured suit that features an advanced BPAP system. The findings of our study stress that volcano-associated pulmonary injury is far from trivial, and furthermore that acute respiratory distress syndrome and its complications are diagnostic entities that extend way beyond the traditional intensive care setting.

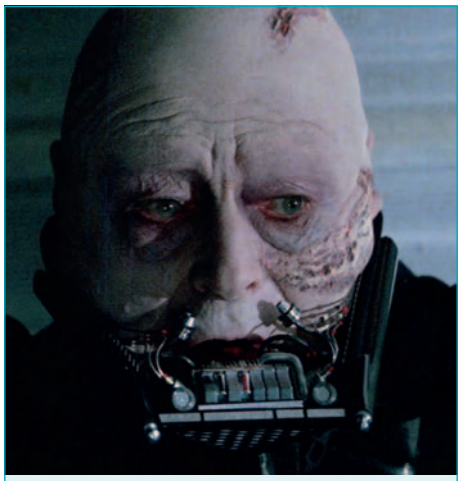

Figure 3. 'Blue bloater': beneath the mask, Darth Vader exhibits the characteristic physical symptoms of chronic bronchitis. © LucasArts

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The science of laughter

Laughter is a universal human emotional expression, but it is not confined to our species. Reports of cats laughing, however, are rare.

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Human vocal communication is primarily studied in the form of human speech – a remarkable talent and evolutionarily highly specialised motor act that involves high levels of precise motor control over the articulators and over breathing. However, we do not solely communicate vocally with speech: when we are in the grips of more extreme emotion, we frequently start to produce non-verbal vocalisations, often in a relatively involuntary fashion. This includes vocal behaviours such as screaming, sobbing and laughing.

I first started working with these kinds of vocal acts in the 1990s, when I was collaborating with colleagues who were studying neuropsychological patients who had specific deficits in the perception of emotions. They were looking at the perception and recognition of facial expressions of emotion, and wanted to extend this to other sensory modalities: my input was to investigate their perception of emotion from the voice. I first used emotionally inflected speech but quickly moved to non-verbal emotional expressions as they contained no lexical information and were therefore better analogues for the facial stimuli. This work was successful and the same patients who had difficulties recognising a frightened or an angry face, also struggled to identify a scream as frightened or a growl as an angry expression.

Although this started as a pragmatic solution to a problem posed by a population of subjects (how to test emotions in another modality), it soon became clear that there is very little work on these kinds of non-verbal emotional expressions. The majority of emotional vocalisation research focuses on emotional speech. However, non verbal emotional expressions such as laughter and screaming are more like animals calls than they are like speech: they require very little supralaryngeal articulation, are made using primarily laryngeal and breath control mechanisms, and are produced at the same time as the facial expressions which are more commonly studied.

Acoustically, we found particular profiles of acoustic properties that were associated with the perception of different kinds of non-verbal emotional expressions – the perception of laughter, for example, was strongly associated with the highly modulated amplitude envelope that results from the characteristic 'ha ha ha' sound.

This in turn is driven by the involvement of the intercostal muscles: normally used smoothly to pull air into and out of the lungs during metabolic breathing, and to produce a constant sub glottal pressure, to vibrate the vocal folds during speech and song, the intercostal muscles and diaphragm start to produce large contractions during laughter, each of which contributes to a single 'ha' burst, as air is forcibly exhaled (NB it is also possible for these contractions to be largely acoustically silent).

Sophie Scott having a laugh with conference attendees

If these contractions start to run into one another, then the laughter can start to sound more like silent wheezing. From this perspective, laughter is more like a different way of breathing than it is a different way of speaking. Another physiological change is a constricting of the pharynx, meaning that some sounds are made during laughter as a consequence of this constriction (e.g. glottal whistles). The intercostal contractions made during laughter are much greater than those used to control breathing during speech production, and this also affects the noises made during laughter, with very high pitched noises being produced, which would be difficult or unlikely to produce under voluntary control. My laugh can be very high pitched, and I can hit pitches when laughing that I would be unable to produce while singing.

Laughter is an interesting human behaviour to study, even in isolation: it appears to be a universal emotional expression, however claims that only humans laugh have transpired to be incorrect. Laughter has been reported in gorillas, chimpanzees and orangutans, where it can look and sound quite similar to human laughter. However, we are unable to hear many of the noises made by other animals, meaning that there may be many more examples out there: it's also probably true that no one is out there looking for laughter. Certainly a vocal behaviour which is contextually identical to laughter has been described in rats: rats make a distinctive chirping sound when they are playing together, and when they are being tickled, and when they are anticipating being tickled. Indeed, at its heart, Panksepp has argued, laughter can be considered an invitation to play.

As all mammals play when juveniles, and some continue to play through into adulthood (dogs, humans, otters), this argument would suggest that laughter is likely to be widely found across mammals. This role in play seems counterintuitive to humans adults, who strongly associate laughter with humour, jokes and comedy, however Robert Provine has shown that even in humans, laughter is primarily a social behaviour, which is strongly primed by other people – we are 30 times more likely to laugh with someone else than if we are on our own.

What this means in practice is that we are laughing mostly when we are in the company of others – and we are still not laughing at jokes. Indeed we laugh mostly at comments and statements and although we report laughing because we are amused, we are laughing to show that we like people, understand them, agree with them, are affiliated to them as much as if not more than because something is 'funny'. Within conversations, laughter is very tightly co-ordinated, with members of a conversation laughing together at the end of sentences, even if the conversation is in sign language rather than a vocal language, and in theory people could be laughing all the way through if they wished to. We also laugh much more often than we report: all studies that have compared actual to reported laughter find that people laugh more than they say they do. Indeed, laughter is probably the most commonly encountered non-verbal vocal emotional expression, occurring at around 7 times per 10 minutes of conversation. Provine has also noted that laughter is highly behaviourally contagious, and people will frequently laugh simply because others are laughing. Like other such contagious behaviours, such as yawning, contagious laughter is modified by social factors, and people are much more likely to catch a laugh (or a yawn) from someone they know than from a stranger.

‘Laughter is an interesting human behaviour to study, even in isolation: it appears to be a universal emotional expression’

We have found, at a cortical level, that laughter leads to a much larger amount of orofacial mirror system activation than a negative vocal expression emotion like disgust: we interpreted this as due to the social use of laughter, and there was an implication that this might relate to behavioural contagion: the perception of yawning leads to very similar patterns of orofacial mirror actuvation, and activation within this network correlates with the rated contagiousness of the yawns.

We investigated this further using two different kinds of laugh - spontaneous laughter, and more controlled, posed laughter. This was inspired by a literature showing facial differences between spontaneous and controlled smiling, and by findings that chimpanzees laugh differently if they are being tickled, or are trying to make play last longer. We recorded people laughing helplessly, and also laughing in a pleasant but not spontaneous fashion. Acoustically, these laughs are quite distinct, with the spontaneous laughter being longer and higher in pitch than the posed laughter, and the posed laughter frequently being nasalised in a way that the spontaneous laughter was not. In an fMRI study, we found significant differences in the cortical responses, with the spontaneous laughter leading to greater activation in auditory cortices, and the posed laughter leading to greater activation in medial prefrontal cortex and the anterior thalamus. We interpret this as showing a greater response in auditory fields to the genuinely novel sounds of authentic laughter, while the posed laughter was associated with more extensive processing for meaning, and was associated with activity seen in explicit mentalising tasks (although no overt response was required). This likely reflects the importance of laughter, as even when people are listening to sounds passively in in MRI scanner, they are trying to understand the laughter that they hear.

We did not find the greater activation in orofacial mirror regions that we had expected to see to the spontaneous laughter: we assumed that as it is rated as more contagious than the posed laughter, these laughs would be associated with greater activation reflecting such priming, following our earlier study. What we found instead was considerable orofacial mirror responses to both spontaneous and posed laughter, and that this was associated across participants, with their post-scan scores on a test of laughter perception. There was a positive correlation, with higher post-scan test accuracy in distinguishing spontaneous from posed laughter correlating with greater activation within peak orofacial mirror responses. This suggests that the orofacial mirror responses may not be solely linked to contagion, but that being primed to respond to any laughter might improve understanding of what the laughter means.

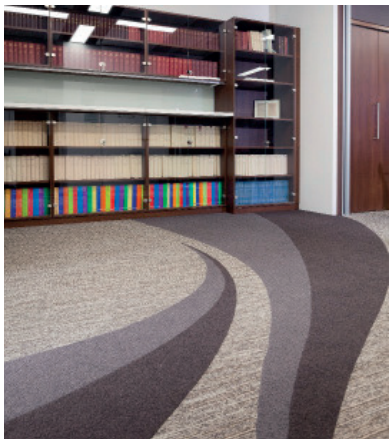
Sophie Scott giving the Annual Public Lecture at Physiology 2015, Cardiff

We do not currently know what the behavioural and affective consequences of accuracy in laughter perception might be: we are currently exploring this in studies with people who are experiencing depression, and in young adults who have conduct disorders. However, in addition to being an important social emotion, research is now showing that people in close emotional relationships use positive affective expressions, commonly laughter, to regulate their emotional states, together. Couples who manage stressful situations with laughter not only start to feel less stressed (according to physiological measures) but over a longer time scale, are the couples who are more satisfied in their relationships, and stay together for longer.

These are still relatively early days for laughter science: a search on Web of Science using the terms ‘emotion expression fear’ returns 6863 papers, while the term ‘emotion expression laughter’ returns 188. Much more needs to be done, and an important step is to see the value in laughter research for the wider community. Rather than being a necessarily trivial or silly thing to study, laughter is a very commonly encountered emotional expression, which can let us map between emotional processing and social interactions. I would argue that is time to start taking the science of laughter seriously.





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Oh the places you'll go: my postdoc in the USA

Mary Morrell

National Heart and Lung Institute, Imperial College London, and NIHR Respiratory Disease Biomedical Research Unit at the Royal Brompton and Harefield NHS Foundation Trust and Imperial College London

This year The Physiological Society and the American Physiological Society are hosting Physiology 2016 in Dublin on the 29–31 July 2016. By coincidence, this year also happens to mark 20 years since I did my Post Doc at the University of Wisconsin-Madison, USA. I have been asked how spending time in the USA has influenced my academic career; here are some of my thoughts...

Got your PhD? Do you need a BTA?

My PhD studies were focused on the control of breathing during sleep, and in particular the mechanisms that led to respiratory instability. My supervisor was Professor Abe Guz, a physician and great man (Morrell, 2014). He believed that clinical observation and careful data collection were the key to good physiology research. It is hard to think now that this was before the days of computers with vast storage capacity, MRI was not readily available, and there was no internet. Maybe this was why my colleagues and I found ourselves visiting hospital wards in the middle of the night to study patients with Lateral Medullary Syndrome. These patients had localised unilateral brain stem lesions, and we wanted to understand how breathing was controlled by the bulbar spinal pathway (asleep), compared to the cortical spinal pathway (awake). These were my first research studies and they felt very difficult. What I learned in those early painstaking hours is that 'it's all about the data'.

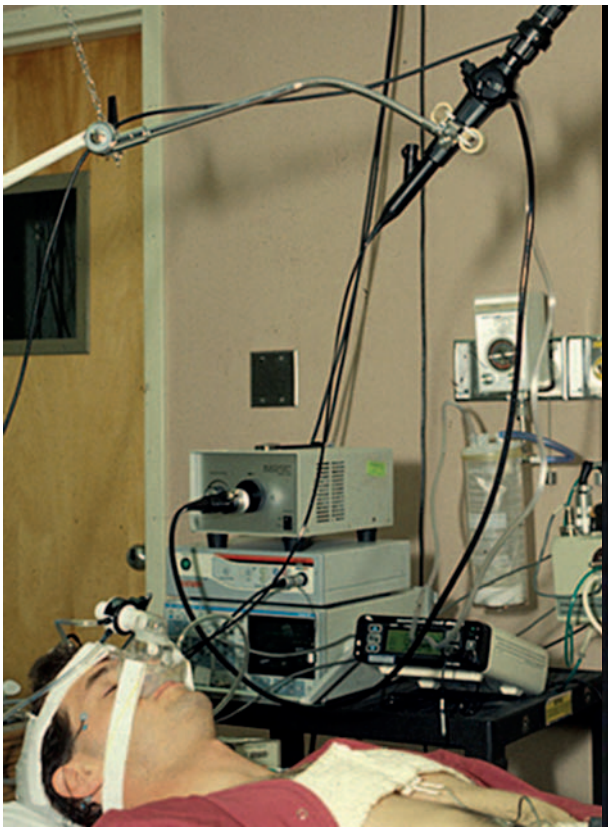
Later, when I moved to America, the ability to set-up physiological studies and collect high quality data was a huge advantage. We found that the overseas Fellows often had a greater ability to set-up the equipment needed for their studies. This may have been because North America PhD students typically spend the first two years of their PhD programme studying, rather than in the lab. My experimental skills were not something I had appreciated before I went to the USA, and they are something I now try to pass on to the Fellows that train in my lab.

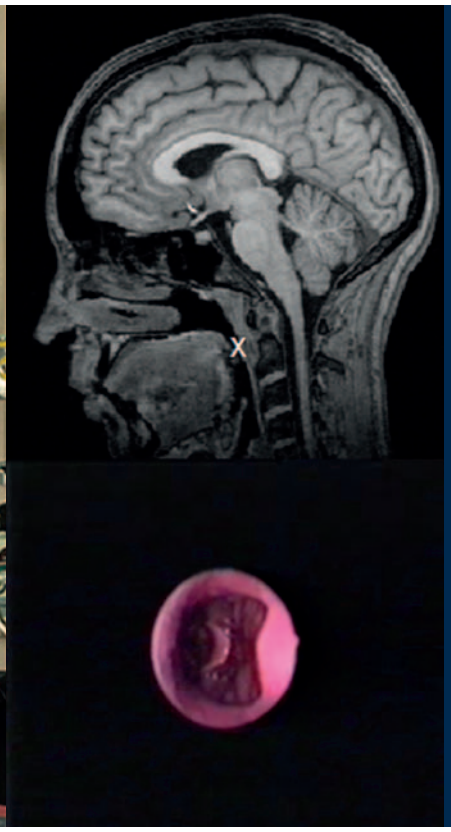
My early PhD studies brought me into contact with a concept named the Hypocapnic Apnoeic Threshold. This notion was first tested by Professor Dempsey and his team at the University of Wisconsin-Madison, and refers to a critical threshold above which $PaCO_2$ must rise to maintain stable breathing during sleep. So imagine my nerves and excitement when discussions of where I should Post Doc focussed on Madison.

I went to Madison Wisconsin in 1994, with great thanks to Professor Dempsey who offered me a Post Doctoral Fellowship, and The Wellcome Trust who awarded me an International Prize Travelling Fellowship. This was a three year grant, with two years in the USA, and one year back in the UK. The importance of this funding strategy is highlighted by the fact that the two previous PhD students from our sleep laboratory both went to North America, because back then in our group we got our PhD, and then we got our BTA (Been To America); however, neither came back. The Wellcome were, in my view, very wise to offer the year funding upon return to the UK; it gave me time to develop my career in London, and without it I know I would have gone back to the USA.

What did I get out of doing a Post Doc in the States?

The main thing I got from the USA was the confidence to debate my science. Looking back, I think this was especially important for me. I was immersed in my field of respiratory-sleep disorders, working with world leaders. I formed my own ideas, defended hypotheses, discussed protocols and explained my data interpretation. Lab meetings started at 3:00pm on a Friday afternoon and frequently went on for hours – so many times I was told to 'speak–up' and eventually, slowly I did. I lost my British reserve; I embraced the American can-do attitude, and grasped new opportunities. My scientific vision became international. I was right at the edge of what was known in my field, working with those who were shaping what we know today. In particular, my project was focused on the effects of sleep on the pharyngeal airway.





The experimental equipment used to measure breathing in a healthy subject during sleep. Breathing was monitored via airflow and respiratory chest wall/abdominal movements, and changes in upper airway by fiberoptic scope. The scope was placed through the nares to the level retro-glossal level. In the top right panel the MRI is marked with a white cross at the level of the scope tip. In the bottom right panel, the image is taken with the scope of the retro-glossal airway cross sectional area during (Figure modifed from Morrell & Badr, 1998).

We developed the technology to monitor the upper airway in real time during sleep using a fibre-optic scope (Fig 1). These studies revealed airway collapsed during both inspiration and expiration (Morrell *et al.*, 1998; Morrell & Badr, 1998) and the findings were later used to build the algorithms in machines that support the breathing of patients with sleep-related breathing disorders (autotitrating positive airway pressure).

My USA experience changed my career. It was an amazing in so many ways, and it was also a very productive; the lab was literally a research factory and I wrote many papers. However, more than this I developed an international network of colleagues and friends that have remained close ever since; we still meet up at meetings. It maybe that the impact of my time in the USA was greater back then because email had only just become available, and information was not as freely available as it is now. However, all I can say is that for me doing a Post Doc in the USA was life changing. I cannot say what would have happened if I had not gone, that's an experiment I cannot do.

Why did I come back to the UK?

I came back for both personal and professional reasons. I am English and I missed the quirky English culture that is very different to the Mid-West. I also wanted to (rather naively) set-up a comparable sleep lab in London. By the time I returned my supervisor had retired, and I thought that in a city as big as London it was important that someone should promote sleep health.

On my return, I based my research at the Royal Brompton Hospital; I was awarded a Wellcome Trust Career Development Fellowship, and I started another journey. My clinical colleagues and I initially carried out physiological studies that highlighted the age-related changes in breathing during sleep, and their cardiovascular and neural impact. This research has now translated into to Randomised Controlled Treatment Trials in people with respiratory sleep disorders (McMillan *et al.*, 2014; Quinnell *et al.*, 2014) and the formation of a network of respiratory-sleep labs across the UK that collaborate together to carry out sleep research.

Spending time in North American does not mean that it has all been highs, there have been some dips. However, when these have occurred my links with the USA have enabled me to seek advice and support. When I returned to the UK, I chose to maintain my USA connections by serving on the Board of Trustees of the American Thoracic Society, and I was the first non-North American to be Chair of the ATS Sleep and Neurobiology Assembly. I have found that my international network invaluable, in so many ways at all stages of my career – maybe because the sleep field is small we all know each other and (mostly) get on very well (Fig 2).

And would you go back?

This is the question I have been asked many times – and I have had two very serious amazing offers. Both times I almost went; such is the draw for me of working in a system that is (still) better funded for physiology than the UK (despite recent cuts to NIH funding).

However, in the end, my science is about making a difference, and for me that is with people in the UK. There are many things do well in the UK, and one is education and another is innovation. Education in the UK is, relatively speaking, widely available and I have benefited so much from this in my life. Working in the UK allows me to give some of this education and freedom back to others.

The UK is a country full of people with imagination and new ideas – it is exciting and energising to live and work in this environment. I am lucky enough to work at an excellent university in one of the most amazing cities in the world. America's gene pool is one of pioneers, and the courage to discover new lands, and this is great...but London is one of the most culturally diverse cities in the world. You can choose to eat food from every nationality, and on the bus hear people speaking many different languages. We have a health care that is still free at the point of delivery, and our gun laws are safer – so here I am 20 years later. My aim has always been to make a difference, and I will always be grateful for my time in the USA and the difference it made to me and my science.

Acknowledgements

This article is dedicated to all my colleagues and friends on both sides of the Atlantic with whom I have shared my research journey. To those at Imperial College London, Royal Brompton Hospital, and the University of Wisconsin-Madison it has been a privilege to work with you.

My post-college year in the UK, 1949-50

Victor Wilson

The Rockefeller University,
New York, USA

During my final year 1947-48 as a pre-med student at Tufts, I had to decide what to do next. As the time approached to apply to medical school, I was pretty impressed with how good I was, and decided that only the best would do. I applied to several medical schools none of which accepted me. As a result, I spent another year at Tufts getting a Master' degree. While doing this I applied once again to three medical schools that had previously rejected me, but not to Tufts where I had been promised admission. This is a clear indication that I was beginning to consider a career in research. I have often felt that in the field I ended up in (spinal cord, then vestibular neurophysiology), a medical degree and a residency in neurology would have broadened my outlook and made possible a career combining research and the clinic. Had I gone to medical school in 1949, however, it is likely that I would have ended up on a purely medical path. One can't tell how things would have worked out, but I have no regret about pursuing research.

In due time the medical schools rejected me again. Why? I suppose there were several reasons, not necessarily in order of importance. I was very young (19) the first time I applied, and was competing with returning veterans; I don't think that I did well in interviews; at Harvard I was asked how I felt about being Jewish, a question you couldn't ask today. My reply was that I was proud of it. This last item leads into the fact that in those days the schools I was applying to had an admission quota for Jewish students, which was not large.

A key influence on me at Tufts was Professor Kenneth Roeder, a youngish English neurophysiologist (today he would be called a behavioral neuroscientist). He was an excellent lecturer and inspiring teacher, who even managed to make comparative anatomy interesting. His own work was on the behavior and nervous system of insects. He helped me apply for further research training in England as an alternative to medical school. Roeder was a Cambridge (England) man, and at that University there was an insect physiologist, JWS Pringle, who had published some very good papers in 1939. During the war, he, like many other scientists, had been involved in war-related research, in his case, I believe, on radar. Roeder wrote him and the appropriate papers must have been sent for application for admission to the University. Pringle agreed to have me as a student at Peterhouse, the College of which he was a Fellow, and the University accepted me as a Research Student.

I received a pre-doctoral fellowship from the National Science Foundation, which would support me during my stay in England. In the late summer of 1949, I sailed for England on the Washington, a liner that had been used as a troopship and was not completely converted back for civilian use. I was lucky and had a cabin of my own, Accompanying me was a special amplifier, needed for experiments, which Pringle was unable to get in England. The trip, which must have lasted about a week, was pleasant. There were other students on board, including an English girl who I became friendly with, and we all had a good time. I was not seasick during the journey. However, when I woke up in Southampton after the ship had docked I felt queasy when I got up: I had adapted to the ship's motion.

England and Cambridge

For some reason, perhaps because of their solitary stand against the Germans in the early years of the war, I have been something of an Anglophile, and although my stay in England lasted only about 11 months, I had a wonderful time. It was made even better when, just before I left the US, the UK devalued the pound. As my fellowship paid me in dollars, this immediately increased my income.

On arrival in England, I spent a couple of days in London, and then went on to Cambridge. Unlike most Universities, Cambridge and Oxford are made up of self-governing Colleges. I had to be accepted not only by the University but also by one of the Colleges, where you live and usually eat. In 1949, England was still recovering from the war, and

food was rationed. I was issued a ration book, which I turned over to the College where I ate most of my meals. No coupons were needed in restaurants. Each College consisted - and still does - of a number of old and newer buildings. Many have their backs, typically gardens, on the river Cam. The various University departments are scattered among other buildings in the town. I would spend my time in the Zoology department, which was within easy walking distance of the College. Because many other things of interest were not, my first purchase on arrival was a bicycle.

I moved into rooms in Peterhouse, the oldest College in the University; one of the buildings dates back to 1284 or thereabout. Housing was spacious, but spartan. I had a large living room, and a small bedroom. The problem was that the only source of heat was a gas fire in the living room. Even though it was only September the bedroom was cold, and when I first arrived, tired from the trip, I started asking myself what I was doing there. The bathing or shower facilities were in another building two courtyards away. In many ways, it was like suddenly being immersed in a medieval world. College gates were locked at night, and undergraduates staying out late without permission, faced trouble (climbing over the wall was not unknown).

When I arrived in the Department, I was pretty soon assigned a laboratory with some equipment so that I could do whatever I had in mind. That was when I realized that at Tufts I had been a big frog in a rather small puddle, and wasn't ready for this environment. Apparently, research students coming from English Universities, certainly from Cambridge and Oxford, were much better prepared than I was. Expecting to work with Pringle and learn from him, I had no particular project in mind. Although, as it turned out, I had relatively little contact with him. Pringle was the kind of person who, if he met you on the street, would be likely to look right through you without any acknowledgement - he was busy thinking.

I did play around with some experiments, but nothing memorable came of this. Finally, rather late in my stay, Pringle came into the lab one day to say that he had come up with an idea for mathematical analysis of biological systems. What was needed were data to test his idea. A good place to collect such data was from a large spine on the cockroach leg, which was to be stimulated (displaced) by a sinusoidal stimulus. The only other thing that had to be done was to record the activity of the nerve innervating this spine. Would I follow some suggestions and collect the data? He was going away for a while, but if I would leave him the data, he would take care of the rest. I spent some time doing experiments, and on my departure from England left him what he had asked for.

When I was back in the US doing my PhD work, probably in 1951, I received a manuscript that described the data collection and the analysis of the results. Except for the general approach, the analysis was incomprehensible to me, but I went over the manuscript as best I could and returned it to Pringle. The paper, with me as an undeserving co-author, came out in the summer of 1952. Shortly afterwards I received a letter from someone whose name at the time meant nothing to me, congratulating me on this pioneering work, which is what it turned out to be. Many years later, in the 1970's, I was doing experiments which, with the help of my mathematically and computer-knowledgeable colleagues, were using related approaches.

Besides doing my work in the Zoology department, I attended some lectures in Physiology across the street. They were given by Adrian (who had won the Nobel Prize in the 1930s). Unknown to me, there was other Nobel Prize work under way in that department by Hodgkin and Huxley on the conduction of the nerve impulse, and famous studies on protein structure were ongoing in the Cavendish (Physics) laboratories. The closest I came to this was when John Kendrew, eventually a winner of the Nobel Prize for elucidating the structure of the muscle protein myoglobin, had me in his office to persuade me that IBM punch cards were an excellent way of storing references. He convinced me, and I used the system for a long time. Many years later software was developed for storing and finding references to the literature, but by that time I felt that I had too many to start transferring them into one of these systems. I stored the information in folders, and in my head. Not very efficient, but it usually worked.

From the personal point of view, the stay in England was a great success. I enjoyed College life, made friends, and did sports. In the winter I played squash. In the spring and summer I played quite a lot of tennis, including matches for Peterhouse's second team.

Peterhouse had extensive sports grounds with beautiful grass tennis courts (here I am, in the picture above, ready to go). Playing on those spoiled me: when I came back to the US and to cement courts at Illinois I couldn't (or wouldn't) get used to them. I wasn't any good at cricket, but I enjoyed going to matches and keeping score for the Peterhouse team. We also had (sometimes vicious) croquet games on the College lawn. In the spring there were boat races on the Cam, and it was great fun racing down the towpath on my bicycle, keeping up with the College boat. I also played a fair amount of bridge, often with a College Fellow who later became a well-known expert in Italian history, and with the owner of an antique store down the street.

Game, set, match: Ace Wilson

Finally, some of us would occasionally go to London. I recall one trip to the then Saddlers Wells Opera where we heard Simone Boccanegra sung in English; I have had a fondness for that opera ever since. I also must have had a social life of sorts. I had a date for the May Balls, a couple of days of parties held simultaneously in many Colleges: we dined at Peterhouse, then spent the night wandering from one College to another dancing and drinking. I was always a barely adequate dancer, but must have managed.

During vacations I traveled. For the Christmas holidays I went to France. In the summer, I traveled to Italy with a friend, and ended up on the Italian Riviera with friends of my parents.

After this interlude, it was back on the long train, and boat, trip to England. After a pretty short stay in Cambridge I was off to London, in early August, for some brief sight-seeing, then on to the airport and home.

What was the benefit of my year in England, besides the facts that I enjoyed it immensely, broadened my horizons, and co-authored a pioneering paper? It showed me that, my high college grades notwithstanding, I didn't know as much as I thought I did, and needed some serious training if I was to make science my career.

Memories of a postdoctoral fellowship with Otto Hutter

Thomas and Carolyn DeCoursey in 1980

Thomas DeCoursey

Molecular Biophysics and Physiology, Rush Medical College, Chicago, USA

My first interactions with Professor Otto F. Hutter were by conventional airmail. As I neared completion of my Ph.D. with Professor Shirley H. Bryant at the University of Cincinnati College of Medicine, Cincinnati, Ohio, USA, I sent unsolicited letters to a half dozen labs that I considered to be scientifically exciting. The respondents suggested that I could join their lab provided I could generate my own funding.

Of these options, my wife Carolyn and I chose Glasgow because we could speak English more fluently than German and it was not so far away as Australia, yet was in an exotic location (i.e., not the U.S.). The subject of my dissertation project was a hereditary disease, myotonia congenita, which Adrian & Bryant (1974) [R. H. Adrian of Cambridge] had shown elegantly to be caused by a lack of Cl^- conductance in skeletal muscles.

I was of course familiar with the pioneering studies by Otto Hutter and Anne Warner on the pH dependence of the Cl^- conductance in skeletal muscle. I applied to the Muscular Dystrophy Association for a Postdoctoral Fellowship to study Cl^- channels in skeletal muscle with Professor Hutter in Glasgow.

We proposed to determine single Cl^- channel conductance in mammalian muscle using current fluctuation (noise) analysis. The start date for the Fellowship was to be January 1, 1980. I received the letter awarding the Fellowship in early December, 1979. This gave my wife Carolyn and me three weeks to sell our house (a tiny structure purchased for ~$10,000 in a dubious neighborhood near the medical center), pack or store all our earthly possessions, and move to Scotland. Those were exciting times! But we were young and crazy!

We arrived in the U.K. via Leiden in the Netherlands, where my older sister has lived most of her life. We took a boat from Den Haag, watched *Blazing Saddles* before retiring to our below-the-water-line berth, and proceeded to vomit the night away. To this day, my wife refuses to see any Mel Brooks film. We later learned that my sister had inadvertently poisoned us via a tasty sauce kept too long. We took the train north to Glasgow. My instructions were to identify Otto, whom I had never met, at the train station by his carrying a copy of *The Journal of Physiology*, of which he was an Editor.

Carolyn DeCoursey and Otto Hutter on the Isle of Bute

The inner sanctum of Otto Hutter's lab. Anne Warner's storage oscilloscope is in the centre. The high-speed chart recorder just to the right provided a complete history of each cell. Baseline drifts, etc. become obvious on a slower time scale. One day there was a thunderstorm; each bolt of lightning left a dramatic impression on the current noise records!

Perhaps because I had seen only bound volumes and he was carrying a paperback single issue, I managed to walk right past him. Still feeling peaked and disheveled, we related our miserable tale of travels, to which Otto commented that we evidently were not good sailors! After this inauspicious beginning, things improved spectacularly.

On several occasions, Otto and his wife Yvonne took us to their vacation home in the village of Kilchattan Bay on the Isle of Bute. This was a fine house in a small community facing the bay, where we could fish for cod or dig mussels. Hiking was excellent, with bright yellow gorse blooming and nearby a nice example of columnar basalt (the hexagon-shaped columns that are also seen in the Devil's Tower in Wyoming). Otto explained that one of the virtues of Scotland was that landowners could not prohibit hiking across their land – provided that you respect the property and leave it as you found it.

Otto once related a story of when he moved to the UK from Austria in 1938, escaping the German occupation. During his first day at school (at age 14), the teacher introduced him to the class as a new student. She pronounced his surname Hutter (as we say it now, rhyming with 'butter'). He immediately corrected her pronunciation, 'It is pronounced Hutter' ('hooter' – the German pronunciation, rhyming with scooter; or worse, did it have an umlaut?). Later, on the playground, the other children made fun of his name 'Hooter' (i.e. big nose). From this experience, Otto concluded that when one lives in a country where the inhabitants are not able to pronounce your name correctly, you should simply allow them to pronounce it the way they are able.

The first lesson Otto impressed upon me was that when one receives a letter that demands a response, it is essential to reply immediately. Even if all you can say is that you have not yet made a decision, it is important to keep the correspondent aware of the situation. The occasion for this admonition was that I had written to Professor Hutter to enquire about a position, he had responded favorably, and I had communicated nothing for about 6 months. Then suddenly I appeared on his doorstep! Although I still err on this point occasionally, I do so far less often.

Another important lesson was how to give a scientific talk. Otto suggested that I present my Ph.D. dissertation results at The Physiological Society meeting in June 1980 in Oxford. If I had known that the likes of Andrew Huxley and Bernard Frankenhaeuser would be in the audience, I would have never had the courage to proceed. Otto had me practice beforehand, and I learned a great deal. When you use a pointer, especially a laser pointer (which did not exist at that time), do NOT wave it around wildly. Point directly at the part of the image you are discussing, and hold the pointer still. To this day, when I see a lecturer waving the pointer randomly or continuously in circles, I can envision Otto shaking his head in dismay. When you show a graph, tell the audience what is plotted. Do not expect them to read the axis labels themselves – it is your job to explain to them what they are seeing, and more importantly, what you want them to see. You say, 'Here we plot…' and at the same time point at the graph. It seems obvious, but it is amazing how often this is not done.

In those days, papers were written by hand (with a pen or pencil on actual paper), then typed by a secretary (if one were so fortunate), and then edited by means of cutting and pasting (or more literally, taping). Manuscripts gradually turned in to scrolls. Here are some of the rules that Otto taught me during this period, about writing and about reviewing manuscripts and grants:

- A manuscript reviewer may make all kinds of criticisms on the first round of reviewing, but on the second round, it is not acceptable to introduce a new complaint. One may address only the resolution of those complaints that were duly noted in the first round. I wish the referees for *Nature* and their offshoot journals would learn this rule!

- Otto stressed the importance of writing a thorough and accurate Methods section, which I found quite tedious to write. Its purpose is not so much for readers of the paper, but rather to remind the authors precisely what they did a few years later.

- Otto felt that one should write down everything one would like to say, and then take away all superfluous words. The resulting sentence will be concise, yet easier to understand, and less ambiguous. The adverb 'very' is empty and should never be used – there is always a more descriptive word that can replace it.

- A very (oops!) important point is that a manuscript should include one or several sentences that tell the reader clearly what s/he is supposed to learn from the study. However obvious the conclusions appear to the writer, the reader is less intimately acquainted with the work, and needs to be told what to think. This is perhaps even more important when writing a grant application. The reviewers do not want to have to think for themselves (and might not arrive at the correct conclusions) – your job is to provide them with all the summary phrases and conclusions they will need to understand the paper or write their review.

- When a lucid thought came into being during a discussion, if it did not fit into the section of the manuscript we were working on, we wrote it down on a scrap of paper, and put it into a small box. When the writing was nearly finished, we would look through the box and retrieve any lost gems.

- Precise wording was of the utmost importance. One day we worked from 9-11am, when everyone was required to go to the Tea Room and have tea and biscuits. By tea time, we had managed to complete one solitary sentence. Just before we left for tea, we crossed it out.

- While doing experiments, it is helpful to make a note of any cell that has particularly beautiful currents. One is always searching for the 'typical' experiment to use in figures. A cell that behaves normally, produces complete measurements without odd features, and which is aesthetically pleasing may occur just once, if ever, and is to be cherished!

- Otto felt that the best work is done by at least two scientists – one to work the controls or the computer and change solutions, the other to take thorough notes in the lab notebook and help think what the next measurement should be. This approach remains valid for electrophysiology, in which each cell has a finite and often brief lifespan, and it is important to get all the information from each cell that is humanly possible.

- Otto advised that it is better to make positive contributions than to attack prevailing ideas. The latter must be done sometimes, but this should not be the basis for one's reputation.

Otto showed me the lab, the set-up I would use, and introduced me to John Dempster, who worked on the project too. He was a very clever native Scotsman, whose lowland accent I eventually learned to understand, almost. Our attempts to extract Lorenztian power spectra from Cl^- current fluctuations failed. We induced fluctuations by changing the pH, which Hutter & Warner (1967; 1972) had shown introduced time-dependence into the nearly time-independent Cl^- conductance at neutral pH. Unfortunately, these fluctuations were too slow, with time constants of hundreds of milliseconds. After this situation became clear, Otto suggested that we change course and study inwardly rectifying K^+ channels, which have the virtue of much faster kinetics (in the range 1-5 ms). These channels proved to be amenable to our approach, and we eventually published two papers in *The Journal of Physiology* (DeCoursey & Hutter, 1984; DeCoursey *et al.*, 1984), my first high-quality publications.

Then approaching age 60 and Department Chair, Otto still visited the lab and occasionally did actual experiments. One day he dissected a turtle to obtain the heart, which entailed his wearing wonderful aviator-style goggles and using a hand-held power saw to cut through the shell.

The final two months of my precisely 2-year fellowship (the US-UK tax treaty allowed us to pay US tax only, provided we did not stay one day longer than two years – an extra day would mean paying two years of tax retroactively to the UK) were among the most memorable. I spent most of each day sitting next to Otto in his gorgeous sunny office overlooking Kelvingrove Park, writing papers. This was when I learned most of what I know about writing scientific papers. I had to sit on Otto's right side, because he was practically deaf on his left side. Even so, and despite his hearing aid, I still had to shout at a considerable volume to be heard. The two secretaries sitting in the next room were aghast at the impudent American shouting at the distinguished Chairman of the Physiology Department. In general, I got away with a lot in Scotland, being excused as being just an American who did not know any better. In fact, there was some truth to this, because I was an American, and I really did *not* know any better!

Toward the end of my postdoctoral stint, we felt we had enough good 'normal' data, but that it would help validate the results if we could obtain data at a different temperature, to confirm that the results varied as might be expected. The experimental chamber lacked temperature control, but it was winter so I opened all the windows in the lab and did measurements at ~10°C. True to the Rule of Science, these final experiments, done with limited time available in order to 'clinch' the story, produced no useable data.

When I left Glasgow near the final day of December 1981, I thought that we had finished our manuscript and were ready to submit. Otto's perspective was, however, quite different. He decided that we should correct certain systematic errors that crept into the results due to the geometry of skeletal muscle. The voltage clamp can control the surface membrane potential, but the membrane extends into tiny topologically continuous 't-tubules' and as they descend into the interior of the fibre, their membrane voltage deviates progressively from the 'command potential'. John Dempster attacked this mathematical problem and produced quantitative corrections. Meanwhile, I had moved on to a postdoctoral position in Michael D. Cahalan's lab at the University of California at Irvine. Serendipitously, Otto's daughter lived in Pasadena (50 miles north across all of Los Angeles) so he came to visit on two occasions. Besides seeing his daughter, he spent some time with me working on the manuscripts. By now, the paper had been divided into two. Eventually, the papers were submitted and appeared in 1984 (DeCoursey & Hutter, 1984; DeCoursey *et al.*, 1984), more than two years after the last experiment had been done.

The value of a foreign postdoc

I credit Otto with dramatically advancing my career in many ways. He once told me that to succeed as a scientist one must be willing to do whatever was necessary. The example he gave was traveling to a foreign country to take advantage of unique opportunities. Having a foreign postdoctoral experience elevates you to a different level. Americans are secretly in awe of British science, with a tradition of excellence that produced Hodgkin and Huxley, to name obvious examples. Europeans (including Brits) recognize that the United States remains at the forefront of modern science, in part by sheer volume, but they also value the disappearing American tradition of pushing relentlessly forward and getting things done, surmounting or ignoring all obstacles. Otto is correct on both counts – the experience has intrinsic value, but more importantly, it reflects your dedication to do what is necessary to advance your career. On a practical note, the postdoctoral era is one time when you can explore life anywhere in the world, with no commitment or expectation to stay. I would not trade those two fabulous years in Glasgow for anything.

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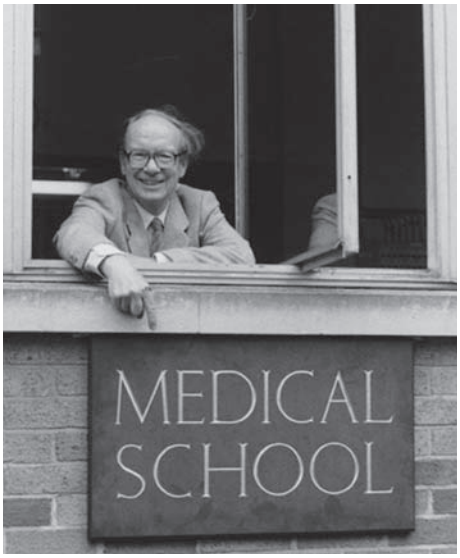
Obituary:

Declan John Anderson 1920 – 2016



Bruce Matthews

Declan Anderson was a dentist and physiologist; but foremost, a scientist. He died at the age of 95 on Easter Day, 27 March 2016. He was educated at Christ's Hospital School and Guy's Hospital. After graduating in dentistry in 1942, he went on to obtain a B.Sc. in Physiology in 1946, and a Ph.D. in 1955. During these latter studies, he held clinical posts and a lectureship in Physiology at Guy's.

He published widely and his first paper, on the temperature changes in teeth produced by drilling, was on research done as an undergraduate. He was the first person to record masticatory forces in humans during natural chewing. He did this with a miniature transducer that he skilfully engineered and incorporated into a gold inlay in a molar. This was featured in a live broadcast from his laboratory in one of the early programmes in the BBC's *Tomorrow's World* series. But he is best known for his work on the sensory mechanisms responsible for pain from human dentine, a field to which he and his students have contributed extensively. His early work on this topic, together with that of Martin Brännström in Stockholm, provided evidence that the sensitivity of dentine was not due to stimulation of bare nerve endings when dentine was exposed, but to the displacement of the contents of the dentinal tubules to which the stimuli had been applied. It was postulated that this displacement then activated sensory receptors sensitive to movement or pressure changes deeper in the dentine or in the underlying dental pulp. The extent to which dentine was innervated was hotly disputed at the time: the histological evidence was inconclusive because of problems with fixing, sectioning and staining the calcified, non-vascular tissue, even after decalcification.

Declan showed that the topical application of local anaesthetic solutions to dentine did not desensitise it, and the application of isotonic solutions of KCl and other substances that cause pain when applied to exposed nerve endings in skin, do not cause pain when applied to exposed dentine. He also showed that the solutions that do cause pain from exposed dentine, such as sugar solutions, act by the osmotic effects they produce.

He found that the outer half of the dentine in the crown of a tooth, although sensitive to stimulation, is devoid of any vital cellular material, and that nerve terminals penetrate no further than 150 µm from the dental pulp into the dentinal tubules, which are 2 to 3 mm long. And not all tubules contain such nerve terminals.

Other experiments in his laboratory showed that many nerves in teeth are capable of responding to any form of stimulus that causes movement of the contents of the dentinal tubules, which was further evidence to support a hydrodynamic mechanism.

He also made important contributions to dental education. He believed strongly that staff involved in teaching or research in dental sciences should not be based in small, isolated departments in dental schools; but in larger departments in medical schools or the science faculties of universities. This emphasis on the integration of dental and medical sciences was reflected in his 'Textbook of Physiology for Dental Students', published in 1952.

He found support for this view in the 1960s from Arthur Darling, who was dean of the Faculty of Medicine in Bristol at the time, and also a dentist. As a result, Bristol created lectureship posts for dentists in the departments of Anatomy, Biochemistry, Physiology and Pharmacology in the Medical School, and a chair in Oral Biology for someone to oversee these posts and integrate basic science and clinical teaching in the Dental School. Declan was appointed to that chair in 1966, and remained in the post until he retired in 1985.

The group that he formed in Bristol was very successful, and representatives from dental schools around the world came to see how the system worked. Dental students were encouraged to intercalate a B.Sc. in a basic science during their course and continue to a Ph.D.; and many did so. As a result, a large number of senior posts in dental research in this country and abroad have been filled by Declan's students. At the last count, 12 of his Ph.D. students are professors and amongst these are past or present heads of department and deans, and the editor of an international research journal.

Declan was great fun; he had a wonderful sense of humour and sharp wit. He always included amusing anecdotes relevant to the subject under discussion in his lectures, and they were very popular with students. He was very fond of practical jokes, which he often devised with his friend James Mansie, an oral surgeon at Guy's.

Declan was an accomplished silversmith, and was commissioned to make many pieces as gifts or presentations for individuals and organisations; all with his DJA hallmark, of which he was very proud. He wrote a book on silversmithing.

His wife, Joy, predeceased him, as did two of their seven children.

The Journal of Physiology

Special issues

Hypoxia, fetal and neonatal physiology: 100 years on from Sir Joseph Barcroft

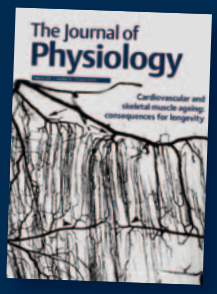
Volume 594, issue 5, 2016

Barcroft's research has interested scientists for decades and many accounts of his works are available today. In this issue of *The Journal of Physiology*, there are additional biographical articles. Lawrence Longo describes this 'Victorian physiologist's contributions to a half century of discovery' with authority as a physiologist and a medical historian. John West writes a controversial piece highlighting 'Barcroft's bold assertion' that all dwellers at high altitudes are persons of impaired physical and mental powers), a statement that understandably continues to trigger much ongoing discussion today! Finally, Peter Nathanielsz adds a personal touch, reporting on the 1972 symposium on Fetal and Neonatal Physiology that he helped organise for The Physiological Society to celebrate the centenary of Joseph Bancroft's birth.

In addition to the biographical pieces, this issue contains reviews and research papers that cover the full breadth of the work originally pioneered by Sir Joseph Barcroft.

Cardiovascular and skeletal muscle ageing: consequences for longevity

Volume 594, issue 8, 2016



The invited Topical Reviews, symposia articles and selected research papers in this Special Issue of *The Journal of Physiology* focus on the effects of ageing on cardiovascular and skeletal muscle function, including cardiac and muscle performance in exercise. The articles provide an up-to-date overview of the molecular mechanisms underlying cardiovascular and skeletal muscle ageing and further highlight the therapeutic potential of targeting function to enhance healthspan and longevity.

The special issue was guest edited.

A note from the *The Journal*'s new Editor-in-Chief, Kim Barrett

It is an honour to be writing as the incoming Editor-in-Chief for *The Journal of Physiology*. The opportunity to lead this journal, with its storied history, is certainly one of the most important professional highlights of my career. I am also making history. I am the first woman to serve as Editor-in-Chief in the 138 years since *The Journal* was founded, which seems fitting because my appointment was announced in the year that The Physiological Society celebrated the centenary of admitting women to The Society's membership,

I feel especially well-prepared to take on my new editorial role, having served on *The Journal*'s editorial board for almost 10 years at this point. , This background has given me great insights into the current status of *The Journal* and its accomplishments, as well as new opportunities on the horizon.

It will be my goal to maintain *The Journal*'s exceptional reputation for fair, detailed, constructive and timely peer review, while also maintaining the current rigor of the process.

Another vital goal will be to rationalize the overall Editorial Board, making it more nimble and aligning the expertise of its constituent Reviewing Editors with our content, while ensuring diverse representation in terms of gender, geography and career stage.

Traditionally, we have had great strength in muscle, exercise and integrative physiology, cardiovascular physiology, and several aspects of neuroscience. Nevertheless, while their volume has been less, we have also published highly influential papers in other areas, and we will actively seek to expand submissions in these subdisciplines and thereby broaden our appeal.

We will also ensure that *The Journal* upholds the highest standards for data reproducibility and ethical use of animals in research, ensuring that *The Journal of Physiology* will stand the test of time and represent a solid foundation for subsequent work.

It is my firm belief that the most important role for any journal editor is to serve as the advocate for her authors. I hope you will look to *The Journal* for its ability to illuminate all areas of our diverse discipline, and that you will consider us first when deciding where to submit your very best work. In accepting my new role, I aim to be fully deserving of the trust placed in me by the physiological community.

The full Editorial can be found in Volume 594, issue 7, 2016.

Physiological Reports

Author guidelines and data-sharing

The final strand in the journal's data-sharing policy is now in place. When submitting their articles to *Physiological Reports*, authors can also upload the underlying data files (datasets, video, audio, traces) to the manuscript submission/review system ScholarOne. The data files can be peer reviewed alongside the article. If the article is accepted for publication, they are then automatically deposited in figshare, which allows public access to the files with direct links from the published article online.

The *Physiological Reports* author guidelines are being revised to explain the process. Initially the journal will 'encourage' rather than 'expect' or 'require' authors to deposit data. The importance of sharing data is explained in this editorial by Gareth Leng (although it pre-dates the new figshare scheme): **http://onlinelibrary.wiley.com/doi/10.14814/phy2.12186/full**

Experimental Physiology

Virtual issues

EP has two new virtual issues published online – **Editor's pick 2016** – a selection of the most highly read articles published in 2015, and **Highlighting key themes in the life sciences** – a collaborative issue containing selected content from different biomedical society journals.

Symposium issues

From Experimental Biology 2015:

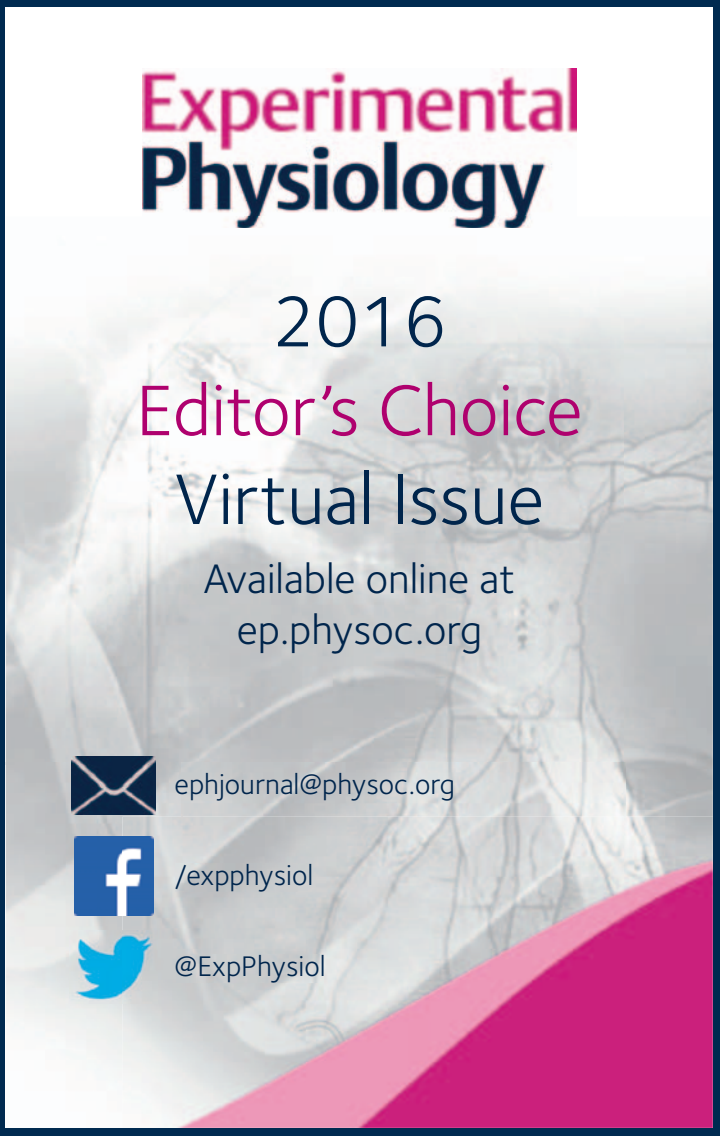
- **Sex hormone effects on autonomic and endothelial function** – organised by Nina Stachenfeld
- **Gastro-Renal Communication** – organised by Pedro Jose
- **Sex differences in the physiology of exercise: an integrative perspective** – organised by A William Sheel

Sponsorship

EP is sponsoring the forthcoming symposia at Physiology 2016: **Circadian regulation of cardiovascular and kidney function –** organised by David Pollock. , and subject to review will publish selected Symposium reports immediately following the meeting.

ICPS (Beijing) September 2016

Role of ion channels in pulmonary arterial hypertension – organised by *EP* Editor Jian Wang



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W Jon Lederer
University of Maryland, USA

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