PN
Physiology News
Issue 106 / Spring 2017

Immersed echocardiography

Mindfulness and maternal epigenetics

The Physiological Society

Future Physiology

December 2017

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Physiology News

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Welcome to the Spring 2017 edition of *Physiology News*

Introduction

News in brief

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Cover image: 'Immersed Echocardiography' by Richard Moon, winner of our photography competition 'Physiology in our time'. The experimental subject is performing exercise on a cycle ergometer while immersed to the neck in 20°C water. Systolic and diastolic properties of the left and right ventricles are being examined to provide insight into the mechanism of immersion pulmonary oedema. The echocardiographer is performing the exam using a sheathed probe. The echocardiographer and research technician are both wearing wet suits to protect from the cold water.
Back cover: A collection of photographs entitled KIND Scientist by Anne McArdle from The University of Liverpool (top). Sleepy Muscles by James Betts from the University from Bath (bottom). Second and third place winners of the competition, respectively.

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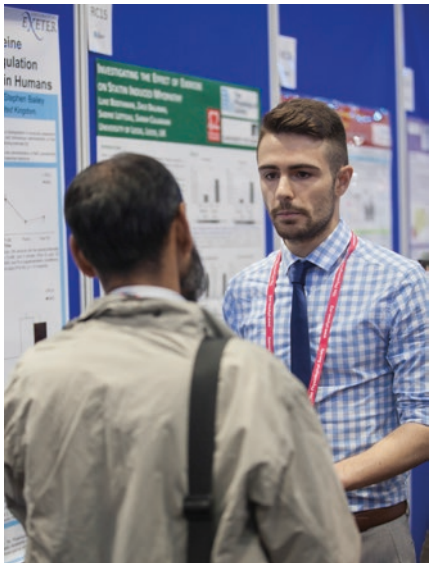
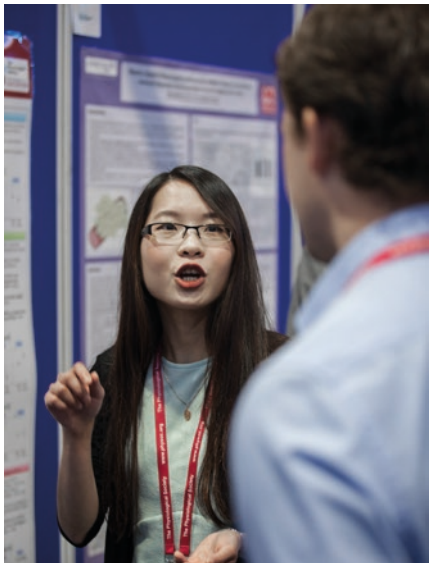




Roger Thomas
Editor

This issue is the eighth since my appointment as editor, but this is only my sixth editorial. I am really still unsure what sort of essay I am supposed to write. Is there really any point in my mentioning some of the selected contents? You the reader can see the list of contents on page 3, and indeed may well have gone straight to an article that you hope is interesting. I suspect that my editorials are quite often not read at all. Indeed, when friends mention that they enjoyed the magazine and are later surprised to learn of my stair downfall a year ago, I know they did not read the editorial in *PN* 102 even though my photo sported a black eye. One article in this issue I particularly enjoyed for its revelation of a new aspect of Andrew Huxley's research is that by Jonathan Coles. The long article on mindfulness was also intriguing. Ken O'Halloran has given full rein to his sense of irony in his article on meetings. We also include a new item – a page of answers to questions that the authors remember being asked quite often. New questions welcomed!

I have recently attended several research talks given by people aspiring to a lectureship, and have been again saddened by the poor quality and style of some of the presentations. The most fundamental mistake is to have too much information on each slide. Often there are as many as six different graphs or diagrams, usually pasted from manuscript figures. The font is often too small to be readable from anywhere except the front row, and the different bars or lines are not explained clearly. Are the presenters only used to talking to very small groups? Do they think that slides still cost money? I was trained during my PhD to have only one experimental result per slide, and to check that all details were legible from the back of a medium-sized lecture theatre. I later learned to speak as clearly as possible, by giving talks to non-native English speakers. Ideally, slides should be understandable by people who can understand written English much more easily than spoken. Labels on slides should be as detailed as possible, and avoid acronyms.

Are PhD students still trained to make clear presentations? A senior Member tells me that he gives the PhD students in his department a talk entitled, 'How to give a really bad talk '. He shows some of the most common mistakes. These include bizarre colour schemes so the text can't be seen against the background; multi-panel figures, especially when only one of the ten panels is relevant to the talk, etc, etc. Sadly, he has come to the conclusion that many people don't want to communicate but, rather like dogs urinating on lamp posts, they only want to mark out their (scientific) territory. Most PhD students are required by their funders to give annual talks of some sort, so all departments do something, but the format varies.

Sometimes there is an away-day event at which all students are required to talk, other places have student talks in weekly slots mixed with other speakers. Postdocs, however, are often not well catered for. One of The Society's representatives mentioned that she was involved in organising a UK conference and wanted to invite several postdocs as it was good for their careers. But she was asked by co-organisers to invite only PIs as postdocs tended to give poor talks. Her co-organsisers didn't seem to see that unless postdocs are given the opportunities to give talks, they won't learn the necessary skills! Another rep reports that in Scotland, several researchers were worried about the lack of speaking opportunities for young researchers so set up the Scottish Neuroscience Group, which has an annual meeting on the last Friday of August each year. It has now been running for about 13 years, and about 180-200 people attend each year. Each of the six participating universities proposes two speakers – one PhD student or postdoc and one other.

Another correspondent remembers that, 'When I came to the UK just over 20 years ago, it was the opportunity at PhySoc meetings for PhD students and young postdocs to give oral presentations at a real 'tough' scientific meeting that set it apart from our situation in Germany, and I thought it was brilliant'. Such opportunities are now rare. But there are moves to have more 'Early Career' meetings sponsored by the Meetings Committee. So far I believe there is only one such meeting a year, but surely there could be more. Last year's was in Dublin, and Otto Hutter was the keynote speaker. Oddly, I can find no mention of this meeting in the main meeting programme book, but we did publish a photo of the organisers in *PN* 104, page 21.

The Society could alternatively simply publicise the many departmental one- or two-day events already occurring up and down the country, and perhaps take steps to encourage better-quality presentations by agreeing to publish on a website the abstracts of the best talks. They could also stop supporting visiting speakers and switch the money to support postdoc talks.

Until the 1990s, The Society met annually in Cambridge, and key organisers behind the scenes were Alan Cattell and Paul Frost, who are both retiring this year after 47 years in the department of first Physiology then PDN. The many members who remember them will wish them a long and happy retirement.

Responding to Zaineb Henderson's Letter to the Editor in *PN* 105

Judy R Harris FRSB
School of Physiology, Pharmacology & Neuroscience
Faculty of Biomedical Sciences
University of Bristol

Chrissy Stokes
Head of Education & Outreach
The Physiological Society

As co-editors of The Physiological Society's publication 'Recognising Teachers in the Life Sciences', we are pleased that Zaineb Henderson enjoyed reading it (Letter to the Editor, *PN* 105) and its review by Katharine Hubbard (*PN* 104). We would like to respond to Dr Henderson's interesting point about the importance of teachers maintaining currency and scholarship in the subjects they teach. It is of course important to keep up with developments in the field as appropriate for the nature, degree programme and level (first, second, third year undergraduate, etc) of the teaching being delivered. However, the current reality is that academics pursuing career paths that focus on teaching, rather than 'bench' research, are usually required to deliver teaching across a very wide range of topics within their discipline. It would not be realistic for them to keep up with the primary literature across all those topics.

By contrast, the fruits of researching, implementing and sharing innovative ways of delivering teaching and supporting learning can be applied across any number of taught subjects. Indeed, there are many examples of fruitful collaborations between teachers in biomedical, biological and physical sciences that enable such 'educational cross-fertilisation' to occur, to the benefit of both staff and students. Good teaching requires not only subject knowledge on the part of the teacher but also willingness and skill to engage with their (often very diverse) students in imparting their own understanding and enthusiasm for the topic.

Many university promotion panels are becoming more aware of the value of staff engaging with educational scholarship to support their teaching, particularly given the strength of the student voice through the new fees structure and the forthcoming Teaching Excellence Framework, with its reputational and financial implications for universities.

Such educational scholarship does not, of course, preclude teaching-focused staff from carrying out additional extensive reading at the cutting edge of the material being delivered, as suggested by Dr Henderson, as appropriate to the level of students being taught (and time and energy permitting!). Effective application of such discipline-specific scholarship to teaching should also, of course, be rewarded through the promotion process.

Remembering Tam Dalyell

Tim Biscoe
University of Bristol

Ann Silver
University of Cambridge

We write to remind Members of the great help given to the Society by Tam Dalyell MP who died on 26 January 2017. He was the Labour Party shadow spokesman on science during the progress through parliament of the Animal (Scientific Procedures) Act, which replaced the Act of 1876 under which we all did experiments. At the same time there was a long debate at the Council of Europe on the issues. So the times were very lively. The Physiological Society, having roots in 1876 in the arguments about animal experiments, was concerned to be involved in decisions that would affect the activities of the members. So also were other biologists, especially perhaps the Pharmacologists. For many years since then he has been involved representing us in discussions with the Home Office and with the EU.

Those of us involved in the Palace of Westminster with the arguments about the potential legislation became known to Tam, and he was a wonderful guide to the procedures. We were all naïve and learned from him. The Society members chiefly involved were Denis Noble (initially), Ann Silver, Cecil Kidd, Jim Pascoe, Bernard Ginsborg, Tim Biscoe, Tony Angel and several others. Our role was to write draft speeches especially for Tam, but also for the MPs; to attend briefing meetings in one of the small rooms off Westminster Hall; to attend the Parliamentary sessions where the issues were discussed, in particular during the Committee stage; to respond to issues arising in those meetings, and so on. At every step Tam Dalyell was there advising, arguing and presenting the case for us. We could not have had a better advocate. At one point he demonstrated the difference between a rabbit and a mouse, an issue that had arisen out of the ignorance of our opponents.

One of our opponents wrote to Jim Callaghan, leader of the party, and requested that Tam Dalyell be disciplined and removed from the debates. Naturally we responded to point out how ludicrous was such a suggestion coming from someone with no argument to support himself. So Tam remained within the argument and on our side. He was for us a fearless advocate and stood up to be counted about the importance of science over decades when others quailed. The world is a lesser place without him, for he was a good man.

Please send your correspondence to **magazine@physoc.org**

Ask a physiologist: Your physiological questions answered

How to survive extremes?

'In the news recently a couple of mountain walkers and their dog were forced to spend the freezing night on top of a Scottish mountain. They luckily had bivvy bags. Even one for their dog. What is such a bag, and should all walkers carry one?'

Answer by MJT. The major routes of heat loss in a survival situation are evaporation and convection, and conduction/convection if it is very wet or you are laying down on cold ground. A bivvy bag (or bivouac sack) significantly reduces heat loss by providing a wind- and waterproof shelter thereby helping to maintain the insulation of the clothing/sleeping bag of the occupant. A mat helps reduce heat loss to the ground. The consequent reduction in heat loss can significantly extend survival time from hypothermia. Modern bivvy bags are 'higher tech' and include vapour-permeable membranes to keep the occupant dry (increases comfort and further reduces heat loss); but the big step forward comes from getting inside something that is wind- and waterproof. The advantage of a bivvy bag over a tent is that a bag is lighter, easier to pack (more likely to be carried) and can be used in situations where a tent cannot be pitched (limited space) or in severe weather conditions where it would be too difficult to pitch a tent. As such, bivvy bags are life-savers – don't leave home without one! More info: http://bit.ly/2jmlpRp

Why should physiological media be bubbled with carbon dioxide gas mixtures?

Answer by RCT. A stable intracellular pH is essential for normal function. Nearly all the ionic mechanisms regulating intracellular pH require at least several mM of bicarbonate in the extracellular fluid. Human plasma normally has 24mM. At normal extracellular pH levels (around 7.4), a solution's pH level is only stable if equilibrated with a gas mixture containing 5% carbon dioxide, depending slightly on the temperature. If the CO_2 in the solution is allowed to equilibrate with room air the solution pH will slowly increase, calcium salts will precipitate and intracellular pH will also increase. This will happen in any kind of open dish, and even high levels of a buffer such as Hepes will only slow the pH increase. If your experiments require stable intracellular and extracellular pH you must include bicarbonate and CO_2 in your solutions. For recent media recipes for culturing mammal neurons from the leading pH lab see Salameh, Hubner & Boron (2017) *J Physiol* **595.1** 93–124.

After a long training run, should I have an ice bath or a sauna?

Answer by CJS. This is a hot topic. Post-exercise ice baths – or more generally cold water immersion (CWI) – is used to aid recovery and reduce pain and has been studied extensively. Radcliffe, Phelps and Murray have endorsed CWI: football teams, rugby players, weight-lifters and even dancers use it despite limited evidence that it is beneficial and suggestions that it may be counter-productive. We know that CWI is associated with ill-effects including arrhythmias and potentially heart attacks, and given how unpleasant it is, there seems little reason to recommend it even for high performance athletes.

Saunas are, however, the antithesis of CWI: few famous athletes recommend them but there is much evidence that they – or generally heat acclimation – provide aerobic benefits, are enjoyable, safe and offer other health benefits. Whilst there has been debate on whether heat acclimation always improves aerobic performance there are good physiological reasons to recommend it. Heat acclimation makes sweat glands bigger and reduces sodium loss. This is important during prolonged exercise, like marathon running, since it enables water to flow from the large intracellular fluid compartment into the plasma. This reduces the decline in blood volume that would otherwise limit marathon performance. An individual heat acclimation session or exercise bout causes a temporary (~24 hours) expansion of blood volume. By repeatedly exercising or heat acclimating slower adaptations can occur such as an increase in the pumping capacity of the heart (eccentric hypertrophy) required for fast endurance running. But, saunas or hot weather training are not the only way to heat acclimate – simply 'over-dressing' on your training runs will have the same effects. Now, where are my coats – I am off for a run to pump-up my blood volume amongst other things!

Bringing you snippets of the latest intriguing research

Do You Speak Virus?

Viruses sense chemical signals left behind by their forebears so they can decide whether to kill or just to infect their hosts. This is the first time that any type of viral communication system has ever been found, and it may exist in other viruses and provide a new way to disrupt viral attacks.

DOI: 10.1038/nature21049

6-Letter Genetic Code Semisynthetic Organisms

A newly created unnatural base pair consisting of synthesised DNA bases, X and Y, has been successfully stably incorporated into *E. coli* bacteria. Although the additional base pair is non-functional at present, this represents a new form of life with the virtually unrestricted ability to maintain increased information.

DOI: 10.1073/pnas.1616443114

Initial Results from Astronaut Twin Study

After spending nearly one year in space, NASA astronaut Scott Kelly was compared with his earthbound identical twin, Mark. He was found to have longer telomeres, decreased DNA methylation, different gene expression and gut microbiota.

DOI: 10.1038/nature.2017.21380

A Psychological 'Vaccine' Against Fake News

In the context of climate change, an inoculating warning statement, 'Some politically-motivated groups use misleading tactics to try and convince the public that there is a lot of disagreement among scientists' – and picking apart misinformation to show how it was fraudulent – helped stop misinformation spreading by up to 13% by giving people the tools to accurately identify the science.

DOI: 10.1002/gch2.201600008

US Scientists Support Heritable Human Germline Editing

The US National Academies of Sciences, Engineering, and Medicine published a report outlining human genome editing criteria and governing principles: Promote well-being, Transparency, Due care, Responsible science, Respect for Persons, Fairness, Transnational cooperation.

DOI: 10.17226/24623

PhySoc convenes sectoral input to the Teaching Excellence Framework (TEF)

Henry Lovett

Policy and Public Affairs Officer,
The Physiological Society

The Society is continuing its work on Higher Education, working on the introduction and further development of the Teaching Excellence Framework (TEF). This follows on from our meetings at last summer's party conferences discussing the interplay between TEF and the Research Excellence Framework (REF). To this end, Policy and Education & Outreach committees hosted a meeting on 26 January between a number of learned societies from the STEM sector and Universities UK (UUK), the representative body for Vice Chancellors of UK higher education institutions (HEIs), who have been working closely with the Department for Education (DfE) on the design and implementation of the successive iterations of the TEF.

Representatives from The Physiological Society, the Royal Society of Chemistry, the Royal Society of Biology, the Academy of Medical Sciences, the Royal Academy of Engineering, the Royal Statistical Society and the Institute of Physics were around the table. This gave the opportunity for a wide range of views to be aired and ideas for the future TEF rounds to be discussed in detail.

The first phase of discussion covered the current operation of TEF2, the deadline for submissions to which was the day of our meeting. This is the first version of TEF to base its awards on metrics, covering the general areas of teaching quality, learning environment and student outcomes. There is general acceptance that these high-level themes are appropriate, but much less satisfaction with the specific metrics chosen within them. The benchmarking process to set institutional targets is also contentious. The metrics are supplemented by a written submission, but it is acknowledged that the main element of the result is the metric scores. Exceed enough benchmarks and a gold award is given; fall below enough and you rate bronze. Given this is the case, there is a disturbing lack of trust in the National Student Survey and its reporting on student satisfaction. Similarly, the Destination of Leavers from HE (DLHE) survey only gives a snapshot 6 months after graduation, at which point many graduates have not yet entered their careers or made significant decisions. The focus in recent years on widening participation has been welcomed, but these students often require more support and are less likely to complete their course. The metric focus on continuation may reverse the widening participation agenda if the effect of students dropping out begins to bite.

The Society has long focused on the reward and recognition of teaching in HE. All participants agreed that the TEF as it stands does not touch on the status of teaching within universities, even though a good way to increase teaching quality would be to encourage and reward those staff members who focus on teaching. The trend in reality is towards increasing casualisation of teaching, including the use of zero-hours contracts and other non-permanent arrangements for teaching. While this will likely not be recognised in the TEF metrics or submissions as they stand, it is likely to be detrimental to teaching quality. A better appreciation of teaching staff by the TEF would be likely to help it achieve its original goals.

The conversation then moved on to proposals to increase the specificity of the TEF, moving to subject-level assessment. Current plans envision a blend of subject- and institution-level factors being combined to produce an overall score. Awards may potentially be given to institutions and departments separately. It is proving difficult to define the correct scale to identify a 'subject'. Differentiation down to the level of individual courses leads to cohorts so small they do not produce statistically significant data. Broader categories such as high-level JACS codes group subjects which are not at all closely related and could have greatly differing levels of quality. Proposals exist for a TEF which combines certain schools and courses into units of assessment, but these may not be universally accepted. An alternative under consideration is an assessment of how much departments deviate (above or below) from the overall quality rating of the entire institution. The model used by Athena SWAN for department and institutional awards was discussed and is being evaluated.

The participants considered the meeting to be very successful, and the UUK representatives were pleased to receive a different viewpoint to that from the heads of institutions. The Policy and Education & Outreach committees hope to convene this group again and continue working to make the TEF as effective as possible.

Will Hammonds of Universities UK explains the current state of Teaching Excellence Framework (TEF) development at the workshop held at H[3]

Biobakes 2016 – the winners!

Anisha Taylor

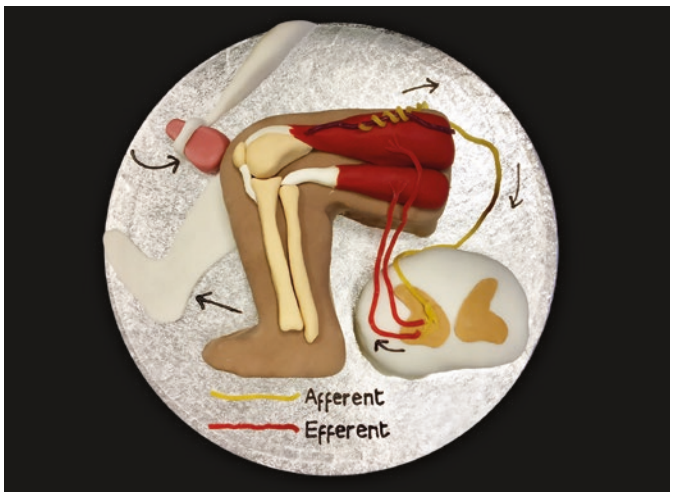
Outreach Officer, The Physiological Society

Back in October we celebrated our fourth Physiology Friday as part of the Biology Week's annual festivities. Our Members carried out activities all over the country and beyond; some visited local schools or had physiology fun days on campus, while others took activities into their local communities with pop-ups in shopping centres and at science festivals. We, once again, held our annual physiology baking competition, BioBakes!

Our physiologist judge Charlotte Haigh, Associated Professor of Human Physiology at the University of Leeds, and cake judge Richard Burr, Great British Bake-Off Finalist 2014 and author of Bake it Yourself, whittled down the 86 entries to a shortlist of 10 put to a public vote held during Biology Week. They also each got a chance to choose their favourite cake for the Physiologist's Choice and Baker's Choice prize. Many congratulations to all the winners!

Physiologist's Choice Award

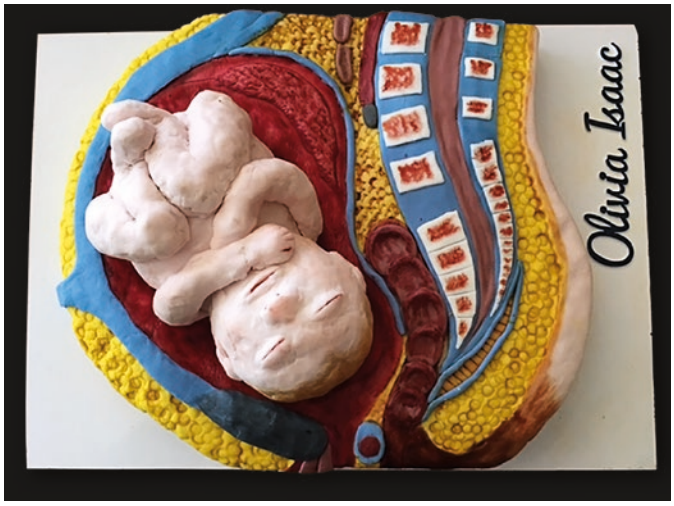
Knee Jerk Reaction – Sports Therapy Unit, University of Bedfordshire



Charlotte had the tough decision of choosing the Physiologist's Choice award. Her favourite, and the cake she felt best represented physiology, was *Knee Jerk Reaction*. Congratulations to the Sports Therapy Unit at The University of Bedfordshire for their cake illustrating the patellar tendon reflex test.

Public Choice Award

In Utero – Olivia Isaac



The cakes shortlisted for our coveted Public Choice Award were pitted against each other to find the ultimate winner. After casting thousands of votes, the public chose Olivia Isaac's beautifully crafted *In Utero*. Richard added that this cake was 'obviously a true labour of love'.

Baker's Choice Award

Romance and Reality – David Howells

With a keen interest in science and baking, Richard was back for a second year of judging. He was taken aback by all the entries but ended up awarding the Baker's Choice prize to David Howells for his cake *Romance and Reality*, commenting that it was 'Beautifully piped and a very thoughtful and clever design'.

Physiological Society archive update

Georgina Lever

Cataloguing Archivist,
The Physiological Society

The archives of the Physiological Society have been deposited at the Wellcome Library since 1991, with additional deposits made by the History and Archives Committee (HAC) every few years. In July I was hired to catalogue the latest accrual of material, as well as the papers of Professor Maureen Young (1915-2013), donated to the Wellcome by her nephew Michael. I qualified as an Archivist from UCL's Department of Information Studies in 2011, and have worked in a variety of archives including those of Kew Gardens, the Royal College of General Practitioners and the architect Richard Rogers.

I had 6 months to work my way through the 25 boxes of PhySoc material, mostly on paper but also CDs, cassette tapes and VHS videos; Professor Young's papers were contained in 27 boxes.

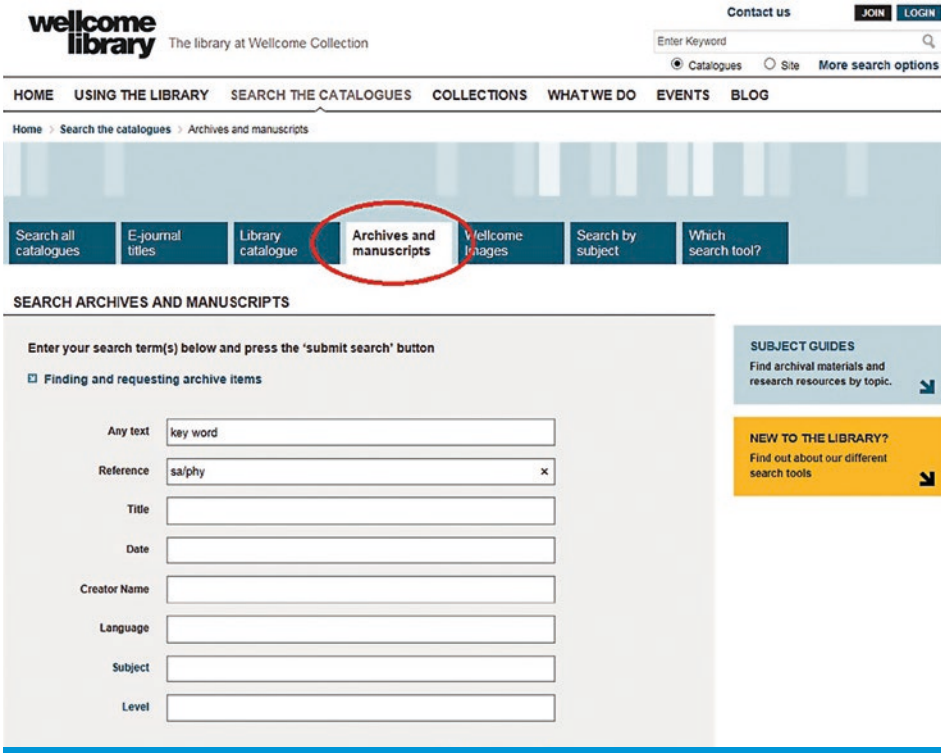
Professor Maureen Young

A big challenge of the job was getting to grips with the existing catalogue and finding appropriate locations in the collection for the new additions. On its arrival at the Wellcome Library, the decision was made to create an arrangement for the collection which would reflect the activities of the Society and its officers.

The present arrangement is as follows:

A. The Grey Book, 1888-2013
B. The Committee, 1895-2002
C. Scientific meetings, 1876-2004
D. Prize lectures, symposia and events, 1955-2009
E. Membership, 1882-2005
F. Publications, 1877-2012
G. Animal welfare and research: issues, policy, and legislation, 1941-2007
H. Education, 1941-2010
I. Films and photographs sub-committees, 1951-1972
J. The Secretary's correspondence and files, 1937-1997
K. Finance, 1951-2005
L. The Foreign Secretary's files, 1955-2005
M. Grants and awards, 1968-2004
N. Archives and history, 1954-2016
O. Relationship with other societies including IUPS, 1923-2013
P. Histories, catalogues and publications commissioned by The Society, 1927-2007
Q. Governance (from 2001): Council and Executive Committee, 2001-2015
R. The Physiological Society's Audiovisual Collection, 1948-2011
Z. The Physiological Society's Photographic Collection, 1860s-2010

The majority of the papers I worked on could be slotted in neatly to these existing sections. Happily, many gaps were filled in the Council, Executive Committee and Editorial Board minutes, as well as substantial enhancement of the photographic collection. The oral history collection is a key new asset to the catalogue (reference: SA/PHY/T/1). Other highlights include a series of correspondence with heads of university physiology departments (reference: SA/PHY/H/6/9)



Using the Wellcome Library online catalogue

surveying entrants and graduates to university courses, 1983-1992, and prize lecture VHS recordings, 1987-1997 (SA/PHY/T/2/1)

The oral history project was started by Tilli Tansey and Martin Rosenberg of The Society's History and Archives Committee (HAC). It aims to interview physiologists and members of The Society about their backgrounds and work in the field of Physiology. Recordings have been made on cassette tape and more recently digitally, with transferral onto CD. Typed transcripts are also produced, many of which are available on the Society's website at **http://www.physoc.org/oral-history-transcripts**

Professor Maureen Young's papers

Professor Maureen Young (1915-2013) studied physiology at Bedford College for Women, graduating in 1938. She spent much of her career at St Thomas's Hospital Medical School in London, specialising in advancing understanding of placental transport, fetal growth and nutrition.

The papers have been arranged into three main sections:

A. Correspondence (1953-2008)
   This includes letters filed alphabetically by the author, letters relating to grant applications, societies and journals, conferences and events, and teaching roles.

B. Writing (1940-c.2011)
   Manuscripts, drafts, research notes and correspondence with researchers relating to specific published and unpublished papers and chapters.

C. Research (1930s-1982)
   The files generally consist of laboratory notes, including graphs and data tables, and some correspondence with collaborators on particular experiments.

For more information on Maureen Young's papers see the Wellcome Library blog: **http://blog.wellcomelibrary.org/**

Accessing the Wellcome Library

The catalogue for The Physiological Society's archive can be searched and browsed on the Wellcome Library website – **archives.wellcome.ac.uk** – by searching for the reference 'SA/PHY' and the relevant key word(s) for the material you're interested in. Professor Maureen Young's papers can be found by searching 'PP/MYG'.

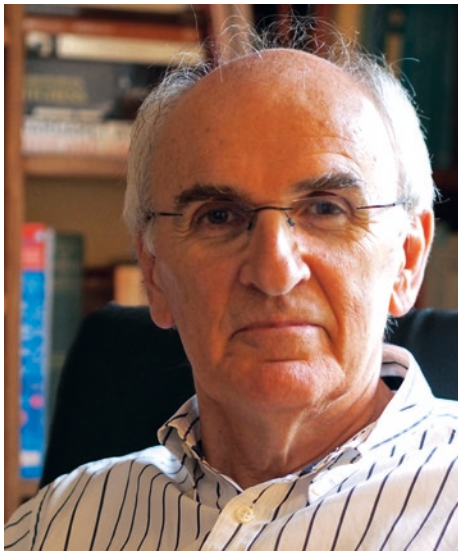
Registering for the Library is straight forward via **http://wellcomelibrary.org/using-the-library/joining-the-library/** Fill in and email the registration form, and an account will be created. This will allow you to access the archives by ordering items from the catalogue to view in the rare materials room. On your first visit bring in two forms of identification to complete the registration process.

'I had 6 months to work my way through the 25 boxes of PhySoc material, mostly on paper but also CDs, cassette tapes and VHS videos'

Acknowledgements

For the support provided on this project I would like to thank Amanda Engineer at the Wellcome Library and Chrissy Stokes, Anisha Tailor, Tilli Tansey and Jennie Wallace at the Physiological Society.

The Society's winter party & AV Hill's Nobel Prize



David Miller

Former Chair, History & Archives Committee
& Honorary Research Fellow,
University of Glasgow, UK

The Society's informal Winter Reception was held at Hodgkin Huxley House (H^3) on 1 December 2016. This was an opportunity to meet members of AV Hill's family as his Nobel Prize Diploma was formally received as a gift from them to The Society. We were delighted to welcome several of AV's grandchildren (Julia Riley, Nicholas Humphrey and his wife, Ayla, Charlotte Humphrey, Alison Hill, James Hill and Griselda Hill attended) plus a great granddaughter (Jenny Hill). The President, David Eisner, spoke to welcome the many Society members who attended as well as to thank the Hill family for their generous gift. Dr Julia Riley (Girton College and the Cavendish Laboratory, Cambridge) gave a charming and entertaining speech with anecdotes of dinghy capsizes and multiple pet tortoises amongst cherished memories of her and the other grandchildren's frequent visits to AV's Hampstead home and of shared holidays.

At the age of just 36, AV Hill (1886-1977) was awarded the Nobel Prize 'for Physiology or Medicine' for 1922, shared with Otto Meyerhoff. An unusual twist is that the prize had not been awarded in 1922 and thus two prizes were awarded in 1923. (Banting and Macleod shared the '1923' Prize 'for the discovery of insulin'). Hill's Nobel citation was for 'his discovery relating to the production of heat in muscle'. This and his subsequent work relating to electrically excitable cells and to muscle function are foundations of the discipline now termed biophysics. In parallel with his research, AV's life-long humanitarian, science-administrative and collegiate work is also of unprecedented quality. Members unfamiliar with the great man will be richly rewarded if they read any of the biographical reports on AV (e.g. Katz, 1978, Vrbová, 2013).

The ornate and unique Nobel Diploma is held in a beautifully crafted leather folder. The artwork for all the Physiology or Medicine Prize diplomas from 1919 to 1927 was by Anna Berglund. These valuable items will be securely housed in The Society's archive at the Wellcome Library. A high-quality facsimile will be prominently displayed at H^3, where one of the meeting rooms is already named after AV. The Nobel Medal is held by AV's former school, Blundell's, in Devon. A final charming artefact that The Society keeps at H^3 comprises AV's dissection spectacles, together with those of his student, fellow Nobel Prize winner and one-time lodger, Bernard Katz.

Face and obverse of the 1922 Nobel Prize Medal – 66mm in diameter (Image courtesy of Blundell's School, Tiverton)

The following talks were given on the occasion of the presentation to the Society of AV Hill's Nobel Prize certificate :

The Physiological Society's President, David Eisner, on accepting the Nobel certificate

It is nice to see many of our members here, in particular those from our very active History and Archives Committee for whom today is a special day. I would also like to greet the representatives of our sister societies and those other groups we interact with. There is no doubt that, particularly in these challenging times, those of us who wish to see science flourish need to stick together.

The Physiological Society was founded in 1876. We are therefore very pleased to be celebrating our 140th birthday this year. During this time several members have been awarded a Nobel Prize. We are here to celebrate one of these, Archibald Vivian Hill (always known as AV) who was born in 1886 when The Society was just 10 years old. The guests of honour here are therefore the members of the Hill family who have generously donated AV Hill's Nobel Certificate to The Society. We have the pleasure of welcoming several of his grandchildren and one great granddaughter. I won't embarrass them by listing all their achievements but they include astrophysics, psychology, sociology, medicine and pottery. In a few minutes the family will hand over the certificate. Before that, I would like to spend a couple of minutes reminding you about the debt we owe to AV Hill and why we are so excited to have received this certificate.

AV Hill made massive scientific contributions. The eponymous Hill Equation is still used to report on interactions and cooperativity of binding. This work was published in 1910 as a communication to our Society. A year earlier he had analysed the time-course of muscle contraction produced by nicotine and concluded that this reflected 'a gradual combination of the drug with some constituent of the muscle'. This must be one of the earliest mentions of what we now call a receptor for a drug. His Nobel Prize was awarded for his elegant studies on the relationship between muscle heat and contraction and work. He developed incredibly precise methods to measure the heat generation and showed that the initial contraction did not require oxidative metabolism. He demonstrated that oxygen is required during recovery from contraction. This oxygen debt is noticed on recovery after sprinting, for example.

AV Hill's Nobel Diploma (actual size c. 39 x 29cm)

His scientific achievements alone would be sufficient to celebrate him but he is equally well known as a humanitarian. He was awarded the Nobel prize in 1923 together with the German, Otto Fritz Meyerhof. This was only 4 years after the end of the very bloody First World War. In his Nobel speech he said, 'The War tore asunder two parts of the world as essential to one another as man and wife. Physiology, I am glad to know, was the first science to forget the hatreds and follies of the War and to revive a truly international Congress: my own country, I am proud to boast, was happy to be its meeting ground. For a while, my friend Meyerhof was an enemy: today he is again a colleague and a friend'. The mention of a 'truly international Congress' is significant. The previous international meeting had been held in Paris in 1920 but was restricted to scientists from allied and neutral countries. AV Hill had objected to this and was delighted when the 1923 meeting, held in Edinburgh, was open to all. One might note that he was ahead of his time as the invitation to German scientists to participate meant that many French scientists declined.

Much later, during the Second World War, he said, 'It may be then that through this by-product of international cooperation science may do as great a service to society (just as learning did in the Middle ages) as by any direct results in improving knowledge and controlling natural forces: not – as I would emphasise again – from any special virtue which we scientists have, but because in science world society can see a model of international cooperation carried on not merely for idealistic reasons but because it is the obvious and necessary basis of any system that is to work'.

‘Hill, the humanitarian, is best known for his work in helping the scientist victims of Nazi persecution’

Although, it would be an exaggeration to compare Brexit with the situation that Hill was commenting on, the idea that science both requires international cooperation and can bind people together should not be forgotten.

Hill, the humanitarian, is best known for his work in helping the scientific victims of Nazi persecution. Together with Ernest Rutherford and William Beveridge, in 1933 he established the Academic Assistance Council, which was set up to meet this need. It is worth noting that, this was at a time when the events in Germany were not known to the majority of people in the UK. This organisation helped 1000 scientists escape including many members of The Physiological Society. Not only did his foresight saved these individuals but it energised British Science with some wonderful individuals. One thinks of Bernard Katz, Hans Krebs, and Edith Bulbring to name but three.

I could go on at greater length but I hope I have said enough to remind you that AV Hill was one of the towering figures of the 20th Century. I will end simply by welcoming the Hill Family again and thanking them, on behalf of The Physiological Society, for this most generous donation of AV’s Nobel certificate.

Katz B (1978). *Biog Memoirs Fellows Roy Soc* **24**, 71-149

Vrbová G (2013). *Eur J Trans Myology* **23** (3), 73-76

My grandfather, AV Hill: by Julia Riley (née Hill)

Our grandfather AV, known to us all as Grandpa, was much loved by his grandchildren. There were 14 of us – and also one step-grandchild and two honorary grandchildren. From an early age we appreciated him as someone who was able to do things for us and with us that really intrigued us. He always had time for us, and we will all have regarded him as very approachable and very understanding of the way children operated. Obviously as we grew older we all came to know that Grandpa was a hugely distinguished man, and I am sure I can speak for us all in saying we are very proud to be his grandchildren. In return we knew he was very proud of us in all our varying ways and greatly enjoyed and valued our company.

Our family visited our grandparents at their house, Hurstbourne in Highgate, maybe every couple of months, staying for lunch and tea and usually meeting up with the London cousins for one or other of the meals. One of my brother Mark’s memories of him there is that he had an enormous love of mechanical calculating machines, encouraging the young to make daring calculations such as an approximation to the square root of 2. Mark also recalls our fascination with the fact that he took snuff – this was for the simple reason that in his time as an MP it had been available free and he thought he should take advantage of this facility! We all remember the wonderful garden at Hurstbourne – among other things there was an aviary with parakeets (which escaped) and at least four tortoises. To stop the tortoises from escaping into the neighbouring gardens, Grandpa’s solution was to link a pair together with a long piece of string, each end of which was tied through the back edge of the shells of the tortoises so that they did not get very far.

There were the family holidays as well. Grandpa had a great love of Devon (from his schooldays at Blundells School near Tiverton); he and my grandmother (who we all called Gran) had a family holiday house near Ivybridge called Three Corners. We stayed there on occasion, enjoying lovely walks through the wood called Hawns and Dendles with its tumbling stream running down through a beautiful oak-beech wood, and exciting walks on Dartmoor. We visited the beach at Mothecombe where we collected winkles which we cooked and ate with a pin; I recall the journey home in which at some point at the top of a hill some distance away the driver of the car would switch off the engine and aim to get back to Three Corners by free-wheeling the whole way.

When we reached a certain age, the older ones amongst us were taken one or two at a time by Grandpa for a special visit to Plymouth – Grandpa had many colleagues in the Marine Biological Association Laboratory and loved visiting them to talk about science but also wanted to show his grandchildren the things he loved about Plymouth. My sister Alison and I remember being driven down to Plymouth by him – singing ‘Are we downhearted noooo!’ (a famous First World War song) at the tops of our voices as we went along; Alison recalls visiting Stonehenge on the way and walking round the stones. We stayed with Grandpa in the Strathmore Hotel on Plymouth Hoe, and amongst other things, visited Eric Denton and his wife (who were great friends of his) and went out in one of the research ships, Sarsia. Both Alison and my brother James ended up working in Plymouth because of the connection with Grandpa – and James has worked in Devon as a GP since he completed his training (I am very pleased that James’s daughter Jenny is here tonight – particularly as she wrote a dissertation on AV and his work with the academic refugee council when she was doing her undergraduate degree in History).

(R-L) David Eisner and Julia Riley (plus David Colquhoun's sleeve)

Later on, Gran and Grandpa bought The Hall at Sea Palling in Norfolk as a holiday house; this was a rambling house divided into two halves so that two of the four families could stay there at once, or Gran and Grandpa could stay in one half with one family in the other half. One of the attractions was sailing on Hickling Broads, and our grandparents bought a small sailing dinghy which they kept there. I don't think sailing was one of Grandpa's great strengths and I was completely convinced the entire time I was in the boat with him that he would capsize it. In fact he did capsize quite regularly – Alison remembers doing so – and they had to be rescued as they couldn't right the boat, and she recalls watching her bobble hat sailing away across the Broad; there was another occasion on which he capsized when he decided he needed to save his watch from the water and, in his practical way, took it off and put it in his mouth whilst attempting to right the boat.

Grandpa was a very practical person though he was not himself very dextrous and he greatly admired people who could build things and make things. He was not too much bothered by what things looked like so long as they functioned in the right way – his books were numbered indelibly on the spines as this meant he could find them easily and if they fell apart through use were mended with bright blue tape (several otherwise priceless first editions were treated in this way). He did not collect things and only valued things which were of use to him; if something got broken he would mend it so that it functioned afterwards – but its appearance didn't matter. I have a large blue and white jug which I got from him which has to spend its time with one side facing the wall because it is covered in a thick and very unbeautiful layer of araldite (but the jug is watertight).

He and our grandmother moved to Cambridge to a large 'flat' in our family house in Chaucer Road in 1967 - when Gran who had Parkinson's could not negotiate the steps at Hurstbourne anymore. He had a large study upstairs which used to be the bedroom I shared with Alison. In Cambridge he and Gran were looked after by the redoubtable Susan Rendell who had, years before, looked after Gran's parents. We all remember Susan with great affection too, and she was an integral part of our grandparents' old age. She was particularly good at making immensely sweet puddings. However, as in almost everything, Grandpa had very simple tastes in food and there was nothing he liked more than rice pudding – I think he could have lived on it. Susan baked one almost every day, and he particularly loved the thick burnt skin on the top. When Alison stayed with him and Susan one holiday, Susan baked two puddings every lunch and asked him which one he wanted – he invariably said rice pudding, so Alison had to eat the other one!

Finally, a word about AV's Nobel Diploma. I am not quite sure how I came to have it, but I think he must have given it to me at some point when he was living in Cambridge. For the past 40 years it has lived in a cupboard in our attic, and to be honest I had completely forgotten we had it until my husband reminded me of it when we were thinking about AV after the celebration of 100 years of the Cambridge Physiological Laboratory. Through meeting David Miller at the Blue Plaque event at Hurstbourne and hearing from him that there was an AV Hill Room at the Physiological Society we realised that this would be an excellent home for the diploma – not tied to any of the universities AV was associated with but obviously associated with his work as a physiologist. We are delighted that it is now in your archive – much more safely looked after than in our damp attic!

What is the hatter with me? We're all mad here!

Ken O'Halloran

Meetings Secretary,
The Physiological Society

I received correspondence from a Member recently, enquiring if The Society (and by extension the Meetings Committee, I suppose) had gone bonkers in its approach to the organisation and hosting of scientific meetings. Always open-minded to considered critique and deliberate diagnosis, I mused on the idea, for perhaps there is merit in it. Moreover, if we are 'barking' it would require someone, not-so-mad, to politely point it out.

The centrepiece of the criticism is concern with the structure, style and settings of our meetings portfolio. In short, everything is wrong: The Society has lost the plot! Two years into my tenure as Meetings Secretary, high time for a therapeutic trot down memory lane, to ponder recent history and perhaps find factors driving this apparent manic malaise. Indeed, analysis reveals that The Society's Meetings Committee has for some time now, effected change of unprecedented measure in style and substance of our scientific meetings.

What are the features of this frenzied folly? The Society's calendar of scientific events now offers first-class meetings in portions suited to all tastes and appetites – small, medium and large. The now firmly established H^3 meetings provide for focussed one-day themed gatherings arising from open calls for ideas proffered by members, or occasional solicited events originating from the Meetings Committee, with counsel from The Society's theme leads who ably represent their constituents. Typically hosted at The Society's headquarters in London, there have and will continue to be H^3 meetings outside of London too. Topic meetings, a legacy from David Wyllie's stint as Secretary, have delivered on the lofty ambition set by The Society to better engage in cross-disciplinary topical issues of wide societal interest. These 2- to 3-day meetings for up to 200 retain intimacy but open new doors and opportunities for physiology in the life sciences and medicine. At least one each year aligns with The Society's annual theme providing a fulcrum to year-long exciting initiatives driven by Society staff and members engaged in education and outreach activities, bringing physiology to the masses. The move to the annual bonanza, feast of physiology, that is the main meeting of The Society, can be traced back to Prem Kumar's insightful innovation, recognising the cross-themed development of our discipline, understanding that we are much more than the mere sum of our parts. The annual meeting showcases the discipline in the round, providing ample attendant opportunity for members to engage, beyond symposia and prize lectures, in career-focussed workshops that seek to support members and guests whatever their stage. The yearly gala has become a hub for a broad range of activities centred on The Society's charitable objects, including the AGM with record attendance noted at the Dublin meeting.

Thus it is evident the desire for change took hold of The Society's senses some time ago. What's more, it is pervasive. The current Committee, with yours truly in the Chair, have demonstrably been keen to revel in revolution. Building on the predilections of our predecessors, we have established new partnerships and alliances endeavouring to place physiology front and centre at home and on the international stage. In the light of a full moon, we determined that topic meetings afforded opportunity to develop cross-disciplinary events of public interest with opportunity too for The Society to seek new venues, the crazed circus thus far visiting Newcastle, Nottingham and Warwick, with plans for Leeds, Exeter and Portsmouth in the offing complemented by visits to old haunts of Edinburgh and Birmingham. Our blossoming relationship with the American Physiological Society culminated in the wild successes of *Physiology 2016* in Dublin, where we really lost the run of ourselves, celebrating novices to Nobel laureates, broadcasting our advances to the world.

However, the exemplar of our chaotic collaborative efforts internationally is the symbolic show of support for the Brazilian Physiological Society and International Union of Physiological Sciences (IUPS), ahead of the Congress later this year. One wonders what physiologists from around the globe will make of The Society's midsummer madness? Imagine: The Society's President, David Eisner, will deliver the annual lecture of The Society in Rio de Janeiro, the beating heart of Brazil, emblematic of our common mission with IUPS for the advancement of the physiological sciences, and their central tenet of physiology without borders. Future plans extend to adventure with the Scandanavian Physiological Society, Deutsche Physiologische Gesellschaft and the Federation of European Physiological Sciences with the introduction of the *Europhysiology* series (2018-2022). Further folly can be found in friendships forged with the British Neuroscience Association (Festival of Neuroscience 2017), and soon it is hoped with the Biochemical Society and British Pharmacological Society on one or more initiatives. All of this in addition to continued support for physiology in Africa, China and South-East Asia. These promising plays appear to be drawing more members than ever before, a risk that this silliness might yet be further perpetuated. It beggars belief!

Of course, all lingering criticisms carry some inconvenient truths echoing our own ideals. To be fair, my learned colleague's principal gripe in correspondence to me was well-intentioned concern at the apparent erosion of a revered cornerstone of PhySoc meetings – oral communications of the classic 10+5 minute style. The value of that time-honoured tradition has not escaped our fragile faculties. Indeed, our ambition to better celebrate and promote early career members by way of a topic meeting towards the tail of 2017 will see an abundance of this favoured format, a platform for the future of physiology with an eye on the past. It is recognised too that this platform for all members ought to be a visible mainstay and centrepiece of all Society events, whatever their mad ambition!

From the Archives: reports by the Meetings Secretary JS Gillespie of the Guys, Kings and UCL meetings of 1967

Transcribed by Roger Thomas

Until a few years ago it was the custom at each meeting (of which there were up to ten a year) dinner for the Meetings Secretary to read out his written account, described as 'minutes', of the preceding meeting, typically about 500 words and including some mildly humorous remarks. The head of the host department then asked the diners if the account was correct, and signed the minutes. Next, one of the pre-chosen diners thanked the host for a splendid meeting, and the host replied passing his thanks on to the relevant staff.

Guys Hopspital Meeting, 14 January 1967

On the invitation of J.N. Hunt, a meeting of the Society was held in the Department of Physiology, Guy's Hospital Medical School, on Saturday 14 January 1967. Pressure by authors to read papers at this meeting was particularly heavy and was met by the local chairman very kindly agreeing to split the meeting. As a result, starting at 10 a.m. the first pair of thirty communications was taken in two theatres under the Chairmanship of J.N. Hunt and R.T. Grant, FRS. The opening paper in Theatre I was somewhat prolonged by an inexplicable inability of the lantern to focus the slides unless carried by the projectionists several feet in front of its stand. The discovery by the chairman of an additional focussing device allowed it to be returned to a more conventional position where, other than the failure of a bulb and the blowing of a fuse, it performed satisfactorily for the remaining four papers before the demonstrations at 11.15.

Sherry preceding lunch and beer at lunch were very kindly provided by Smith & Nephew Research, Ltd. After lunch J.E. Cotes drew members' attention to the activities of a nomenclature sub-committee of the I.U.P.S. which was considering the definitions of some terms used in physiology. Copies of these with the proposed definitions were available, and J.E. Cotes asked members for their comments and also suggestion of additional terms which might be included. A.A. Harper, speaking on behalf of The Society, thanked the local chairman for an excellently organised meeting and, as was to be expected in a department so devoted to gastric physiology, for a splendid lunch.

In his reply J.N. Hunt welcomed members and guests to what was the first meeting of the society since he had taken over from W.R. Spurrell, and paid tribute to the work of his staff and his secretaries, Miss R. Lambert and Miss C. Jarratt, in arranging the meeting.

Beginning at 2 pm, with J.M. Robson and J.N. Hunt as chairmen in Theatre I and I.M. Macdonald in Theatre II, the remaining 20 papers were taken in perfect timing to allow the meeting to end at 4.30 with tea.

Signed by: John L. D'Silva

King's College London Meeting 17-18 February 1967

At the invitation of J.L. D'Silva a Meeting of the Society was held in the Department of Physiology, King's College, London, on 17 and 18 February, 1967.

Beginning at 2.00 p.m., with J.L. D'Silva in the chair, the time for explanation of demonstrations was used to such good effect by nine of the thirteen authors that communications did not begin until 2.30. The first paper passed without incident, but paper 2, which concerned the role of acetylcholine in adrenergic transmissions, was followed by a most animated, discussion, led by J.H. Burn, which was very much in the traditions of The Society. Eight papers were taken before tea at 4.25, followed by demonstrations in the new laboratories of the Physiology Department and in the Department of Pharmacology. Sherry at 6.45 preceded an excellent dinner in the Senior Staff Common Room. After dinner A.J. Buller, returned for the day to his old haunts, proposed The Society's thanks to their hosts. In his reply, J.L. D'Silva welcomed members and guests; and hoped that everyone was enjoying the meeting and that it would not be too long before the Society returned to King's College.

On Saturday beginning at 10.15 a.m. with J.L. D'Silva in the chair, nine papers were heard before lunch, and with D. Mendel as chairman the remaining papers were taken after lunch. The meeting ended at 3.30 p.m.

Signed by: Andrew Huxley

University College London Meeting 7-18 March 1967

At the invitation of A.F. Huxley, a meeting of The Society was held in the Department of Physiology, University College London, on 17 and 18 March 1967. Beginning at 2.00 p.m. on Friday, with A.F. Huxley in the chair, ten papers were quickly disposed of, leaving ample time for tea and demonstrations, the latter distributed over three departments. This was followed by an excursion to the Middlesex Hospital Medical School, where sherry and an excellent dinner were waiting. After dinner R.V. Coxon, proposing The Society's thanks to its hosts, drew attention to the difficulties of Easter as a moveable feast - difficulties which had made it impossible for University College to make the usual arrangements for accommodation and dinner. This dinner would have been the 21st anniversary of the return of the A.G.M. to University College after the disorganisation of the last war. In his reply, A.F. Huxley welcomed The Society and its guests, particularly Professor Schaeffer, from Germany. Most of the work of arranging the meeting had fallen, as usual, on Miss Mollie Kirk and Mr. Charlie Evans, and the arrangements for dinner on the staff of the Middlesex Hospital, to all of whom he was most grateful. Professor Huxley then read a most cordial letter from F. Peyton Rous in reply to the congratulations sent to him on behalf of The Society on the award of the Nobel Prize in Medicine in 1966. In a short speech, C. Keele recalled this was not the first time the Middlesex had come to the rescue of University College, as the Hospital had provided clinical training from 1830 to 1835 for the then new medical school in Gower Street. After dinner, H.E. Lewis entertained members and guests in the lecture theatre with a selection of recent portraits of physiologists, and with some short historical films, including the 1932 International Congress in Rome and one taken in Oxford in 1936 which included shots of A. Krogh, J.S. Haldane, C.S. Sherrington and others.

The meeting resumed at 10.05 on Saturday morning, with A.F. Huxley in the chair. Twelve papers were heard before lunch and remaining four after lunch. The scientific meeting ended at 3,15 and was followed by the Annual General Meeting, and, at 5,30 p.m., by tea.

Signed by: A. Hemingway

2017 Forthcoming events

11-12 April
The Neurobiology of Stress Topic Meeting as part of BNA 2017
The ICC, Birmingham, UK
www.bna.org.uk/meetings/bna2017/stress/

27-28 April
Practical innovations in life science education
H³, London, UK
www.http://www.physoc.org/practicalinnovations

12 May
H³ Symposium: Glio-vascular coupling
H³, London, UK
http://www.physoc.org/glio-vascular-coupling/

1 August
IUPS 2017 – The Rhythms of Life
RIOCENTRO Exhibition & Convention Centre
www.physoc.org/iups2017/

Meeting Notes

H³ Symposium: Gene Editing and Gene Regulation with CRISPR

15 November 2016,
Hodgkin Huxley House,
London, UK

Nisha De Souza

Kings College London

The H³ Symposium about CRISPR was the first one of its kind I have attended, and I am really glad I took this opportunity. As a third-year undergraduate student of Medical Physiology at King's College London, I had the chance to take a module in Medical Genetics. I thought the symposium would be a great opportunity to explore the forefront of research in the overlap in the fields (between physiology and genetics).

We were given name badges as soon as we got in, offered tea and coffee, and took our seats.

The symposium opened with the Chair of the Symposium, Patrick Harrison, giving a brief introduction to CRISPR. My knowledge of the subject was scarce, having only fleetingly touched on the topic in a Stem Cells module from the previous year. Thus, this opening was particularly helpful to give us a basis to start on.

Dr Julia Reichlet's talk, including a special animation, also deserves special mention, as it clarified my understanding of the technique. I talked to her at the end and told her how grateful we were that she had taken the time to go through it, even though it wasn't necessary for the rest of the attendees.

There was a wide variety of talks on the application of CRISPR to many diseases, calcium-dependent calcium release, cardiovascular applications and the treatment of Epidermolysis Bullosa. Interspersed throughout were talks from current PhD students about their ongoing work. We definitely took full advantage of the tea breaks throughout, and the lovely lunch.

Particularly interesting were the talks that overlapped with our course material. These included 'Gene Editing for Muscular Dystrophies' by Dr Linda Popplewell, 'Gene Editing in Skin Diseases' by Julia Reichlet, and the discussion of Amyotrophic Lateral Sclerosis in 'Gene Editing of iPS Cells to Study Neurological Disease' by Dr Rowan Flynn.

Following each talk, there was an opportunity for discussion and questions. We thoroughly enjoyed this part as a majority of the participants, who were more knowledgeable than us, were able to question the rationale behind certain methods.

At the closing drinks and a networking session, I took the opportunity to approach particular speakers with questions, which I was not confident enough to ask as a member of the audience.

The speakers were all very friendly and took the time to explain some basic concepts to me. Overall, attending the symposium was an enlightening and interesting experience, and I hope to be able to use some of this extra information to enhance my answers come final exams. It was exciting to hear about real-world application of these techniques and how many different diseases can benefit from the use of CRISPR.

I am extremely grateful to the physiology department for funding my attendance to the symposium, in particular Professor Peter Jones and Dr Rachel Tribe, who relay many physiology society events to us.

Meeting Notes

Bile Acids in the Small Intestine and Colon

17-18 November 2016,
Hodgkin Huxley House,
London, UK

Stephen Keely

Royal College of Surgeons, Ireland

Cormac Gahan

Alimentary Pharmabiotic Institute, Cork, Ireland

Julian Walters

Imperial College London, UK

The Bile Acids in the Small Intestine and Colon Meeting, or BASIC for short, was held at the Physiological Society Headquarters, Hodgkin Huxley House, on 17-18 November 2016. Over 40 'bilophiles' were in attendance, coming from the UK, Ireland, Europe and the USA, to discuss this rapidly evolving and highly dynamic field of study.

Classically known as facilitators of fat digestion, we now appreciate the importance of bile acids as a family of hormones in their own right that control many diverse aspects of human physiology. With their biological activity being inextricably linked to the shifting populations of bugs in our guts, it is a daunting challenge for researchers to figure out how such interactions impact our physiology, let alone how they can be targeted to treat disease. This was a unique meeting, funded by a Catalyst Award from Science Foundation Ireland, that aimed to bring together many of the leading academic researchers, clinicians and industry partners in the field to discuss the state of the art, identify areas of research priority and to seed new collaborative links.

Topics of discussion covered such diverse subjects as how bile acid biosynthesis is regulated, how they contribute to the pathogenesis of diseases both within and beyond the gut, how they can be used as biomarkers, new experimental models to study their physiological functions and how they can be therapeutically exploited for the benefit of patients. With our fast-growing knowledge of how bile acids and the intestinal microbiota interact with each other to contribute to the development of cancer, chronic bowel disorders, diabetes, obesity and psychological disorders, along with the emergence of potent new drugs to target bile acid receptors in the therapeutic setting, there was much ground to cover over the 2 days of the meeting.

A definite highlight was the meeting dinner, which was held at The Easton, not far from H^3. This cosy Gastropub was the perfect venue to continue the lively discussions and debates, while relaxing and enjoying some delicious Great British gastronomical fayre. Early career investigators mingled with their more experienced counterparts, and as the night wore on, new connections were made, new ideas sown and new collaborations formed. When the participants parted ways at the meetings end, there was a consensus that even though great progress is being made, there are still many more questions than answers. We are only beginning to understand how 'microbial fingerprints' create 'bile acid signatures' and how the molecular messages encoded by these interactions are critical to the maintenance of our health and the development of chronic diseases. As we continue to work towards understanding the science involved, all agreed that the first BASIC Meeting should not be the last.

The Organisers would like to extend sincere gratitude to Science Foundation Ireland for funding the BASIC meeting. We also thank our Industry colleagues, from Falk Pharma, Intercept Pharma, the Johnson and Johnson Innovation Centre, and GE Healthcare for attending and contributing so greatly to the discussions. Finally, we also give thanks to the Physiological Society staff for providing us with such a fantastic venue at H^3, with an extra-special thanks to Christine Carr for her warm welcome and making sure that the BASIC meeting was such a success.

40 'bilophiles' from UK, Ireland, Europe and the USA outside H^3

Meeting Preview

The Neurobiology of Stress A Physiological Society Topic Meeting in association with the 2017 BNA Festival of Neuroscience

10-13 April 2017,
ICC Birmingham, UK

Sue Deuchars

University of Leeds
(Meetings Committee)

Nick Boross-Toby

The Physiological Society

The Society is delighted to be partnering with the British Neuroscience Association's Festival of Neuroscience, being held in Birmingham this year. Readers will be aware that The Society is running a series of cross-departmental activities throughout 2017. Our aim: Making Sense of Stress!

As Professor Stafford Lightman (Bristol), President-elect of the BNA writes, 'Our ability to survive depends on our ability to respond to a changing environment. We have developed coordinated nervous system, hormonal, immunological and social mechanisms to maintain the healthy state of our bodies. Unfortunately these are not always adequate, and when external stressors – either mental or physical – exceed our ability to cope, this results in physical or psychological disorder.' This topic meeting, running alongside the BNA meeting, has brought together some of the world's leading researchers in the field to speak on various aspects of the neurobiology of stress at the four Society sponsored symposia. We are delighted that over 30 abstracts have also been submitted within this theme, covering subjects as varied as the role of particular receptors or neurones in specific stress responses, the analysis of stress responses, the effects of stress on neurogenesis and the upregulation of protective mechanisms in response to stress. We are sure that many Society members will find these sessions fascinating, regardless of their particular research focus. In particular, the joy of attending a meeting such as this is the chance to connect with new faces and consider how you may adapt techniques or interpret your research findings in the light of new data from the meeting.

Our Society has always had a thriving and extremely active cohort of members who consider neuroscience as their main topic of interest. Indeed, their input to the main meetings of The Society is invariably considerable, lively and often controversial! We aim to provide this neuroscience cohort – and all cohorts within The Society – with opportunities to present their research by a variety of means, including our Topic Meetings. Since The Society has such a diverse number of subjects on which Topic Meetings could be focussed and limited resources for each year, these are carefully allocated to cater for all the needs of our members. With this in mind, one way to enhance the experience of Society members when the time comes round for a Topic Meeting is to hold joint meetings with like-minded researchers to boost the numbers of delegates and activities available, without extra cost. The Society is always aware of the importance of strong links with other learned societies, such as the BNA, and many of our members are also members of the BNA.

Stafford Lightman

The introduction of joint meetings such as this with the BNA provides an opportunity for Society members to interact with 1500 delegates from around the world and enjoy 40 symposia on a variety of other neuroscience themes, not just those sponsored by the Society. Thus, the links were forged with the BNA some time ago, with a thought to holding a joint meeting. As a trustee of The Society, Sue Deuchars was invited onto the programme committee to work with Professor Lightman on developing the topic meeting symposia. It is interesting to see that many of the programme committee for this joint meeting are indeed members of our Society, proving beyond doubt our bond and belief in collaborative ventures to further one of our main charitable objects, which is to promote physiology to all. Members of our Society were asked to suggest symposia with the four themes listed below, and we received some brilliant proposals from which the final four were chosen. These, together with posters and lightning talks given by many of the younger presenters, ensure that Society members will be immersed in stress for a couple of days!

The Society's Neurobiology of Stress Topic Meeting explores how current research is gaining an understanding of the stress-responsive systems that protect us from the forces that threaten our bodily balance and stability. Our programme runs on 11 and 12 April and includes four symposia covering the broad topics of 'Stress and cardiovascular control', 'Behavioural and emotional aspects of stress', 'Influences of stress on neurodegeneration/neurogenesis' and 'The neuroendocrinology of stress'.

Stress and cardiovascular control

Stress disorders are associated with an elevated risk of a range of different cardiovascular events, including stroke, coronary heart disease, heart failure,

and cardiovascular death. There is a need for animal research to understand the mechanisms involved in these events and to increase therapeutic approaches. In this context, the symposium will give an example of acute stress-induced cardiovascular alteration, with a focus of corticotropin-releasing factor implication in the bed nucleus. Cardiorespiratory function in stress states, such as epilepsy, hypertension and sleep apnoea seems also to be linked to PACAP and microglia in the brainstem and spinal cord; will also be addressed, as will chronic stress-induced anxiety and how alteration of the autonomic system is associated with a neural circuit involving serotonin in the brainstem. Finally, the symposium will talk about potential cardioprotective effects of a pharmacological approach that targets the endocannabinoid system in rats with high-anxiety behaviour.

Behavioural and emotional aspects of stress

Stress is a major risk factor for mood disorders which are accompanied by altered emotional functioning. Until the establishment of functional magnetic resonance imaging (fMRI), first in humans and more recently in rodents, it was extremely difficult to determine the nature of the altered processing within brain networks that underpins dysfunctional emotional behaviour. This symposium will describe the neural correlates of emotion and the consequences of stress upon the emotional circuitry. The advancement of animal imaging techniques described in this symposium allows assessment of 'biomarkers of network functionality' using directly translatable paradigms, hence facilitating translation of potential novel therapies from preclinical rodent studies to man.

Sue Deuchars

Influences of stress on neurodegeneration / neurogenesis

Environmental stressors have very potent effects both on synaptic function and on cognitive processes. Recently we have been able to recognise how both stressful events and glucocorticoid hormones can modify glutamate receptor function and synaptic plasticity, while novel molecular studies have begun to show how both genomic and non-genomic responses can modify synaptic chemistry and structure. This symposium goes from the most basic dynamic control of glucocorticoid-responsive genes through glutamate receptor trafficking and into mental illness and finally into aspects of brain ageing.

The neuroendocrinology of stress

Even before it is born, the conditions an animal experiences can have a significant impact on later life. Several studies have shown that detrimental developmental conditions can have long-lasting effects on a range of important phenotypic traits, and the main candidate mechanism is activation of the HPA axis and increased exposure to glucocorticoid hormones. This neuroendocrine response to stress has the power to programme a wide range of traits, from behavioural to neural, and there is now a consensus of just how important proper regulation of the HPA axis is in mediating health and well-being in humans and other animals. The symposium will showcase the cutting edge of the research currently underway in this field of glucocorticoid programming, focussing on integrating information from behavioural data (cognitive abilities), neuroendocrine responses (HPA axis regulation and the effects on behaviour), epigenetic mechanisms underlying gene expression changes in the brain (specifically changes to DNA methylation of specific genes involved in stress responses) and the potential for programming of resilience to stress. It will present data from a range of animal models and will take a comparative approach to understanding the pervasive effects of early life adversity.

Plenary lecture

We are also pleased to be supporting a plenary lecture by Professor Alon Chen (Max Planck Institute of Psychiatry) on Wednesday, 12 April. Professor Chen's research focuses on the Neurobiology of Stress, particularly the mechanisms by which the brain is regulating the response to stressful challenges and how this response is linked to psychiatric disorders. His lab has made discoveries linking the action of specific stress-related genes with anxiety, depression, weight regulation and diabetes. His research team uses both mouse genetic models and human patients to ultimately create the scientific groundwork

Nick Boross-Toby with Robert Winston

for therapeutic interventions to treat stress-related emotional disorders such as anxiety, post-traumatic stress, eating disorders, and depression.

His lecture entitled 'Genetic and optogenetic dissection of the central stress response and stress-linked psychiatric disorders' will be one of the highlights of the festival and should not be missed!

The Physiological Society will be exhibiting at the festival. If you are attending the meeting please do come and say hello and grab your very own copy of 'An eclectic A-Z guide of Birmingham – for when you don't quite know what you want!' written in 2013 by YO Blacola!

'Stress is life and life is stress'

Hans Selye

Mindfulness matters to physiologists

Mindfulness: helping people to understand themselves, and helping neuroscientists to understand the plasticity of the adult brain

Lee de-Wit

Institute of Continuing Education, University of Cambridge, UK
& Psychology and Language Sciences, University College London, UK

Our minds are often busy planning the future or thinking about the past. Mindfulness involves becoming more aware of what is happening right now. That might involve becoming more aware of feelings in your body. It might involve becoming aware of the sensations of your breath. It might simply involve becoming more conscious of the fact one's mind is thinking about the future or the past. This practise of mindfulness has proved effective in treating certain clinical conditions, and can influence behaviour on a range of tasks. In parallel to this, there is also a large body of evidence showing that mindfulness has a range of measurable outcomes on both neural activity and even neural structures. Research on mindfulness not only helps us to understand this practise per se, but has also increased our understanding of plasticity and localization of functions within the adult human brain.

The recent upsurge in interest in mindfulness is reflected in a recent All-Party Parliamentary Report from 2015, which highlighted the potentially beneficial role of Mindfulness in Health, Education, Prisons and Companies. In the current political climate, this cross-party agreement certainly stands out. The report (Mindful Nation, UK) also makes for surprisingly pleasant reading (for a scientist reading a policy paper), because despite the heavy use of anecdotes and obvious advocacy, there is also a substantial body of evidence cited in the report. Indeed, the report also highlights some key limitations in our knowledge in areas where large-scale trials are needed to test whether mindfulness really will benefit certain patient groups or help improve the learning in our classrooms. Before exploring the existing findings, let's take a step back to ask, what exactly do I mean by mindfulness?

Secular mindfulness without Buddhism

Mindfulness is a relatively recent approach that extracts some of the core teachings from Buddhism and reformulates them as a secular practise to help patients recovering from chronic pain or to deal with stress. This approach was first pioneered by Jon-Kabat Zinn at the Massachusetts University Hospital. Jon-Kabat Zinn had been inspired by his experience of Buddhism and wanted to use it in a clinical setting. It seems however that Buddhism's broader cultural, philosophical and moral implications proved difficult to bring to the hospital ward!

Jon-Kabat Zinn therefore developed a secular program of mindfulness training that focused on developing some of the key skills involved in Buddhist meditation and awareness training, but left out some of the broader philosophical ideas and values expressed in Buddhism. He formalised this

approach as an 8-week Mindfulness-Based Stress Reduction (MBSR) course. This model was then further developed by Mark Williams and colleagues at Oxford, who developed the 8-week Mindfulness-Based Cognitive Therapy (MBCT) course. This 8-week MBCT course was developed over 10 years ago, as a treatment to prevent the relapse of patients who have suffered multiple episodes of depression. Two recent meta-analyses have provided evidence that MBCT offers an effective treatment in preventing relapse for patients who have had depression (Kuyken *et al.,* 2016), and in the treatment of mood and anxiety problems in clinical populations (Hofmann *et al.,* 2010)

At its most simple, mindfulness is about becoming more aware of one's experience of feelings, emotions, thoughts and mental and bodily state in the present moment. As we will see below however, going into this 'experiential mode' requires the recruitment of certain areas of the brain that you may struggle to recruit unless you have already had some mindfulness training. Thus, unless you've practised becoming aware of your experience of the present moment it can be hard to understand from a verbal description what exactly that means. Perhaps one of the best ways to get a sense of this is to close your eyes (once you've got to the end of this sentence...) and to turn your attention to the feeling of your feet making contact with the floor, and to just try and focus on that for 10 seconds. You might have noticed a sensation of contact with the floor that you simply were not aware of, prior to paying attention to it. You might have also noticed that simply paying attention to nothing but your feet for 10 seconds is actually quite a challenge. All kinds of ideas are likely to jump into consciousness when you try to focus on something as simple as the present moment experience of sensations in your foot. Mindfulness is a training in allowing oneself to focus on such simple aspects of one's present moment experience. That certainly doesn't mean that as soon as you start practising, those wandering thoughts will go away, more likely when you first start you'll realise just how much the mind wanders off when you try and focus on a simple aspect of your present moment experience. Critically however, mindfulness doesn't mean one starts judging oneself for having a mind that wanders off, rather one seeks to acknowledge one's wandering mind and patiently learn the skill of bringing it back to the present moment.

To really develop this practise, it can be useful to have extended periods of meditation where you focus on areas of your body, or the sensation of your breathing in a formal meditation posture. Mindfulness isn't just something you do sitting on a mat on the floor however. You can mindfully eat your dinner, mindfully draw a picture, mindfully read an article about mindfulness.

You don't have to drive a taxi to change your brain

Except perhaps for Einstein's oversized parietal lobe, neuroscience has (in the past) tended to ignore individual differences between people's brains. In fact, it is probably a very reasonable approximation to say all of our brains are very similar. By and large we all have an area dedicated to face perception in the temporal lobes, we all have a hippocampus that plays a key role in memory and spatial navigation, we all have an amygdala that is important in detecting threatening stimuli. I sometimes think that one of the most important and under-communicated (to the general public) findings of the last 50 years is just how remarkably similar our brains are. Not necessarily similar in terms of their exact anatomical structure, but in terms of the way different cognitive or perceptual functions are predictably localised to particular parts of the brain in different individuals.

More recently however, there has been an increasing recognition that our brains sometimes differ in ways that have interesting functional and theoretical consequences. This focus within neuroscience gained particular prominence with an ingeniously simple observation: London taxi drivers have a larger than average hippocampus. This finding highlighted that individual differences in brain anatomy can have functional implications and suggested that even the adult brain has a degree of neuroplasticity that can influence quite large-scale neuroanatomy. The finding that taxi drivers had a larger hippocampus was quickly followed by other similar observations. Violin players have an enlarged area in their motor cortex, and experimental demonstrations showed that a number of weeks' experience in learning to juggle increased the size of an area of the brain associated with the perception of complex motion.

In 2004, meditation joined the list of factors that were associated with changes in the brain's structure. Building on work from the previous year, showing that the brains of experienced meditators had higher levels of coherent activity (Lutz *et al.,* 2004), researchers at Harvard, Yale, MIT and Massachusetts General Hospital found that there were also large-scale differences in the structure of certain areas of the brains of experienced meditators (Lazar *et al.,* 2005). These changes were not random, they were found in areas of the brain that could be logically interpreted given the skills practised in meditation. In particular, one of the areas that was larger in experienced meditators was the insula. This is an area of the brain that we know is important in interoception, the perception (visceral, not visual) of our own body. Given that mindfulness often involves the development of a greater awareness of one's present moment bodily experience, it seems logical that the area of the brain that seems to be involved in that would be one of the areas to be influenced by long-term mindfulness practise.

However, whilst this might seem logical, it isn't the only plausible interpretation of these findings. Firstly these studies were performed on Buddhist monks, who not only practise mindfulness, but who also live very different lives, providing all manner of potential confounding influences on their brain's development. Secondly this was a cross-sectional observation (like the first study with taxi drivers and violin players), so it's possible that those individuals with a larger insula area were more likely to become Buddhist monks in the first place.

The other big limitation to these findings was that these monks had tens of thousands of hours of meditation experience. If mindfulness only brings about changes after thousands of hours of experience, then it is unlikely to be of any practical benefit in the contexts (Health, Education, Prisons and Companies) outlined in the All-Party Report (Mindful Nation, UK).

7 years in Tibet vs 8 weeks of mindfulness

Science thrives on being able to systematically manipulate something and then measure what happens following that manipulation. Typical experimental manipulations in psychology and cognitive neuroscience tend to be rather limited. They involve momentary changes in the task participants are performing or stimuli they are presented with, and then measuring changes in behaviour (often reaction time) or measures of brain activity. The 8-week mindfulness courses developed by Jon Kabat-Zinn and Mark Williams have offered neuroscience a chance to implement a much more substantial manipulation, and measure its effects.

A recent review (Gotink *et al.,* 2016) of over 20 studies argues that the changes observed after a relatively short period of practising mindfulness are closely comparable to those observed following long-term meditative practise. Thus, just as the insula appears to be larger than average following long-term meditative experience, it also appears to be more active, and sometimes larger, after only 8 weeks of mindfulness. For example, one early study found that when asked to go into a more experiential (rather than narrative) mode, novices didn't show more activity in their insula. After 8 weeks of (a particular form of) mindfulness training, participants showed significantly more activity in their insula when asked to go into an 'experiential mode'.

This finding highlights again that whether you are able to enter into a more experiential mode of being isn't simply a matter of having a perfect verbal definition of what mindfulness is. Rather like riding a bike, mindfulness is a skill that has to be practised.

One might wonder what are the benefits of a larger or more active insula? Especially given the broader benefits of mindfulness as a treatment for relapse from depression and to deal with anxiety and stress. The answer to this isn't totally clear, but one potentially important theoretical perspective that could help explain this is Antonio Damasio's concept of 'somatic markers'. Somatic markers are visceral (bodily) manifestations of emotions that seem to be able to influence our reasoning and decision making. Thus, whilst we might think of decision making as a purely rational process that only occurs in our head, it seems that the manner in which our brain makes decisions is shaped by the way we experience emotions in our body. It could be that by developing a better awareness of what is going on in our body (a critical role of the insula) we are more conscious of this influence, and potentially have more control over it. One area where this body awareness might prove particularly significant is in the domain of addictions, often maintained by very visceral urges, which might be easier to control if one is more aware of them. Indeed, there is already some promising evidence that mindfulness might offer a useful treatment in reducing certain forms of addiction such as smoking (Tang *et al.,* 2016).

No fear: brain training worth paying for...

One of the other brain areas consistently implicated in the practise of mindfulness is the amygdala. The amygdala is a brain structure that is important in interpreting fear and detecting threat. Indeed, recent research has confirmed that the amygdala can respond differently to threatening stimuli before we are even conscious of the existence of that stimulus. It's a brain structure that also exists in much simpler mammals, and seems to play a very basic role in signalling threat.

Long-term meditation experience seems to cause a reduction in the size of the amygdala, and even shorter periods of mindfulness training can result in reduced levels of activity in the amygdala in response to threatening stimuli. We have also already seen that mindfulness can influence the insula. There are however numerous other areas of the brain that are influenced by mindfulness training. For example as little as 11 hours of mindfulness can increase the connectivity between the anterior cingulate cortex (ACC) and other areas of the brain (Tang *et al.,* 2010). These changes in the brain are also accompanied by a wide range of behavioural implications, from improved attentional performance in well-controlled experiments, to reduced symptoms in a number of clinical conditions.

This 'generalisation' from the practising of a particular skill to a wide range of implications is perhaps one of the most significant findings regarding the cognitive neuroscience of mindfulness. Typically when we train a particular skill, such as riding a bike, we get better at that skill, and that learning will inevitably depend on changes to the neural circuits required to perform that particular skill. With mindfulness however, the practise of bringing one's focus back to one's experience of the present moment seems to have much broader implications.

This generalisable effect sits in clear juxtaposition to recent findings with 'brain training' games, which have recently attracted some controversy for claiming that they can elicit broader changes in cognition. This claim has proved controversial, because the evidence suggests that whilst one can certainly improve one's performance on particular brain training games, the impact of that doesn't always generalise to other aspects of cognition. With mindfulness training however, training one's attention to return to the present moment seems to have wide-ranging implications.

Mindfulness over matter or mindfulness via matter

Given that mindfulness has a range of measurable impacts on certain forms of behaviour, and improves the outcomes in a number of clinical conditions, we should not be surprised that there are also changes in the brain. In a recent review of Educational Neuroscience, Jeff Bowers concisely reminds us: 'unless one is a dualist, the brain necessarily changes whenever learning takes place'. Nevertheless, the idea that mindfulness can actually change the physical structure of our brain is probably intuitively surprising to a lot of people.

Indeed, the science of mindfulness brings to life the complexity of some of these causal relationships between the way in which our behaviour is shaped by our brain and our brain is shaped by our behaviour. Even if one isn't interested in mindfulness, the extended periods of practise required in mindfulness programs provide scientists with an excellent opportunity to understand the nature and extent of neural plasticity, and provides an additional source of evidence regarding the functional role of the areas influenced by mindfulness practise. From the increased recruitment of the insula and the ACC, to the reduced recruitment of the amygdala, mindfulness can help us to understand what particular parts of the brain do. Moreover, mindfulness can also help us understand the way in which different areas of the brain are connected, and can change their connectivity, and the potential broader implications that can have for the recruitment of networks of brain areas. Understanding exactly how these neural changes are implemented (with an increased density of synapses, or increases in the myelination of white pattern pathways) offers an excellent challenge and opportunity for neuroscientists to understand how the brain learns more generally.

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You are what your mother ate

The effects of maternal obesity during pregnancy on offspring obesity and cardiovascular diseases

Laura Dearden

Susan E Ozanne

University of Cambridge Metabolic Research Laboratories & MRC Metabolic Diseases Unit, Wellcome Trust-MRC Institute of Metabolic Science, Cambridge, UK

The obesity epidemic in the developed world is hard to escape. Media coverage and observations from everyday life emphasise the rise in obesity in the UK across all ages and socio-economic classes. By 2050, obesity is expected to affect 60% of adult men and 50% of women. The rapid increase in obesity is shortening average lifespan and has enormous financial implications for society. Much of the latter comes from treatment of type 2 diabetes, which is largely associated with an increased body mass index (BMI).

Obesity-generated type 2 diabetes now accounts for nearly 90% of the total diabetes diagnoses in the UK. It was revealed recently that the cost of treating diabetes in England accounts for 10% of annual NHS prescribing costs, or about £2.2 million on average every day in 2013-14. One in seven hospital beds are occupied by someone with diabetes. The rapid rise in obesity has occurred – in evolutionary terms – over a very short period of time. Whilst several genetic polymorphisms associated with obesity have been identified, these only account for small increases in body weight and explain a small amount of the heritability of the condition. Therefore the changing environment is thought to be a major driver of the obesity epidemic. We are living increasingly sedentary lifestyles. Recent surveys show that over one in four females and one in five males in the UK are classified as 'inactive' because they undertake less than thirty minutes of physical exercise a week. This combined with the widespread availability of highly palatable calorie-dense fast food is inevitably fueling a rise in body weight. In addition to these genetic and lifestyle factors, it has recently become clear that the early life environment is also important in shaping the risk of obesity in later life.

Environment and metabolic disease

An interaction between the early life environment and later life metabolic disease risk was first proposed in the seminal papers by Hales and Barker in the early 90s, who reported an association with low birth weight (used as an indicator of reduced fetal growth) and cardio-metabolic disease in adulthood in a Hertfordshire UK Birth Cohort. Further studies examining individuals who were *in utero* during the Dutch Hunger Winter, a six-month famine in the Netherlands during the Second World War, confirmed the association between *in utero* under-nutrition and the development of cardio-metabolic disease. Due to the rapid onset and abrupt end of the famine, studies of individuals who were *in utero* during the famine have provided an invaluable insight into the effects of exposure to under-nutrition exclusively during the *in utero* period. Individuals who were *in utero* during the famine display a range of disease phenotypes as adults, with many of the phenotypes varying depending on sex and the time of exposure to the famine (i.e. early or late gestation). As well as the detrimental effects of exposure to **under**-nutrition *in utero*, there is now a wealth of evidence that demonstrates early life exposure to **over**-

nutrition – for instance in cases of maternal obesity or diabetes during pregnancy – is also associated with increased risk of the same cardio-metabolic diseases. This is particularly concerning as it is estimated that about half of women of childbearing age in England are either overweight or obese. The prevalence of obesity in women of this age bracket increased from around 12% in 1993 to over 19% in 2013 and is predicted to rise further.

The consequences of maternal obesity on health of the offspring

It is hard to distinguish between obesity due to inheritance and obesity resulting from the uterine environment. Therefore, studies comparing siblings with different maternal exposures (be it maternal obesity or diabetes) are imperative. Studies of siblings born before and after the mother underwent gastric bypass surgery have revealed that the children born after the mother had lost weight have reduced adiposity and improvements in insulin sensitivity compared to their siblings born prior to surgery (Guenard *et al.,* 2013). Similarly, with siblings of diabetic mothers, the sibling who was *in utero* when the mother was diabetic has an increased risk of developing type 2 diabetes later in life. Of course as well as sharing a similar genetic make-up, children within the same household will often have similar current lifestyles (i.e. diet and exercise habits) and therefore any differences in their body weight and diabetes risk are likely to be a result of their different *in utero* environments. To fully control these extra variables that can impact on obesity risk, researchers have used animal models of maternal obesity in which the genetic background and diet of the mother and offspring can be tightly controlled.

Animal models

Increased weight gain in offspring exposed to maternal obesity *in utero* is often preceded by increased food intake. This suggests altered neural regulation of energy homeostasis as an underlying cause of metabolic phenotypes. Central control of food intake can be broadly divided into two areas: homeostatic control originating in the hypothalamus, and reward-related feeding behaviour orchestrated through the mesolimbic pathways. The main regulators of feeding behaviour in the hypothalamus are orexigenic (appetite stimulating) neurons expressing Neuropeptide-Y (NPY) and Agouti-Related Peptide (AgRP) and anorexigenic neurons expressing Pro-opio Melanocortin (POMC). Rodent studies have shown that exposure to maternal obesity and diabetes *in utero* causes changes not only to the numbers of these neurons but also to their axonal projections. Changes in these vital neuronal circuits are associated with hyperphagia in the offspring. The feeding circuits in the hypothalamus may be particularly vulnerable to disruption by maternal obesity as their embryonic development is orchestrated by the precise levels of metabolic hormones, in particular leptin and ghrelin (Dearden & Ozanne, 2015). This is significant considering that the levels of these hormones are altered by obesity – and therefore also during an obese pregnancy – providing a potential mechanism by which maternal obesity can directly impact on hypothalamic development in the fetus.

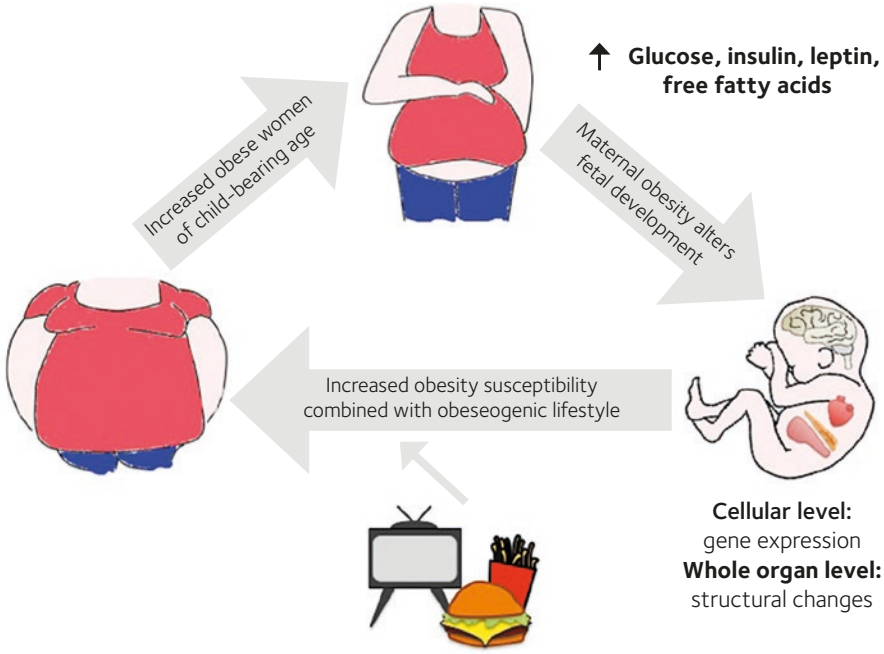

Figure 1. During pregnancy in an obese mother, increased circulating levels of hormones and nutrients in the mother can impact on fetal development. These changes occur via either gene expression changes at a cellular level, or structural changes at a whole organ level. The end result of both processes is a change in function of the cell or tissue that can result in an increased susceptibility to develop cardio-metabolic disease later in life. This, combined with the current obesogenic environment, results in an increase of women of child-bearing age who are overweight and obese, thus perpetuating the cycle of maternal programming of cardio-metabolic disease.

Maternal obesity can also alter offspring dietary preferences. A recent study in non-human primates has shown that maternal obesity greatly increases the preference for fatty and sugary – rather than low-calorie food – in offspring, leading to obesity (Rivera *et al.,* 2015). This is particularly relevant when considering the ease of availability of highly palatable fat- and sugar- rich foods in modern society, and explains why animal models repeatedly report that the offspring of obese mothers are quicker to develop diet-induced obesity when fed a high-calorie diet compared to control animals. The effect of the early life environment on susceptibility to diet-induced obesity may explain why there is variation in risk of obesity in two individuals living in the same obesogenic environment.

Dysfunction in the hypothalamus could also be a cause of disrupted glucose homeostasis in individuals exposed to maternal obesity, as changes to the levels of metabolic hormones such as leptin and insulin during fetal life result in abnormal development of the circuits linking the brain to the pancreas and liver, which are important for maintaining glucose homeostasis. Due to the importance of the hypothalamus – pituitary – adrenal axis in regulating stress responses, changes in the hypothalamus may also underlie the anxiety phenotypes often reported in offspring in rodent and NHP models of maternal obesity.

The offspring of obese mothers do not only have an increased risk of becoming obese, but also of other related disorders such as cardiovascular disease. Evidence from the Helsinki birth cohort has demonstrated a positive association between maternal obesity and offspring cardiovascular disease and type 2 diabetes. Similarly in the sibling pair studies mentioned earlier, the sibling exposed to maternal obesity has a higher blood pressure compared to their un-exposed sibling (Guenard *et al.,* 2013). Causative associations between maternal nutrition and offspring cardiovascular function have been demonstrated in animal models, which have shown striking evidence of cardiac structural and functional changes.

'Obesity-generated metabolic phenotypes can be transmitted intergenerationally'

Such changes are often reported prior to changes in offspring body weight, demonstrating that cardiovascular dysfunction is programmed independently of body weight phenotypes. The consequences of maternal-obesity-induced alterations in cardiac structure (and thus function) are clear: a study of a human cohort by Reynolds *et al.* showed that offspring of obese mothers have a decreased life expectancy due primarily to cardiac dysfunction (Reynolds *et al.,* 2013).

Molecular mechanisms underlying phenotypes in the offspring of obese mothers

Whist the phenotypes associated with exposure to maternal obesity are relatively well described, the underlying mechanisms and the factors related to an obese pregnancy that transmit the effects from mother to fetus remain unclear. It has recently been reported that some metabolic phenotypes arising as a result of maternal obesity in animal models can be transmitted trans-generationally to the grand- and even great-grand- offspring of obese mothers. This, combined with the stable nature of cardio and metabolic phenotypes throughout the lifetime of the exposed individual, suggests permanent changes in gene expression. Epigenetic regulation represents a stable but modifiable level of genomic regulation; the term epigenetics literally means 'on top of genetics' and refers to a system of processes that induce heritable changes in gene expression without altering the genomic sequence. Significantly, *in vitro* experiments have shown that the activity of much of the epigenetic machinery is dependent on energy availability, and could therefore be altered in situations of nutrient excess. There is emerging evidence from human studies of the impact of maternal obesity on the offspring epigenome. A study of siblings with different exposures to maternal obesity *in utero* showed significant differences in the methylation and expression of gluco-regulatory genes (Guenard *et al.,* 2013). Many studies in animal models are now aiming to establish whether the disease phenotypes previously reported are caused by – rather than associated with – epigenetic changes.

A role for accelerated ageing?

As humans undergo the natural ageing process they display increased body weight, a shift in adipose distribution, and deteriorating function of organs such as the heart, kidney and reproductive system. Many of these natural ageing processes are the same phenotypes observed in offspring exposed to maternal obesity *in utero*. This has led researchers to consider whether accelerated ageing is one of the mechanisms underpinning the phenotypes related to exposure to an adverse early life environment. Indeed, several animal studies have shown that under-nutrition *in utero* causes accelerated cellular ageing in organs including the pancreas, liver and skeletal muscle.

Telomeres are guanine-rich nucleotide sequences present at the ends of chromosomes that prevent chromosomal deterioration. An essential part of the ageing process in telomerase-negative somatic cells is telomere shortening that occurs after each cell division. When telomeres become critically short in length, they undergo a conformational change which results in them representing double-stranded breaks, causing the cell to enter growth arrest and senesce or become apoptotic. Differences in telomere length have been implicated in developmental programming in response to maternal body weight. A recent study has shown that maternal pre-pregnancy BMI is negatively associated with telomere length in both the placenta and cord blood at birth (Martens *et al.,* 2016). If similar changes are present in other tissues they could explain the organ dysfunction that ultimately develops in the offspring of obese mothers, and suggest this phenotype is caused by an accelerated ageing process.

Breaking the cycle of obesity transmission

The current research from animal models suggests that the majority of phenotypes in offspring exposed to maternal obesity are caused by either structural changes in whole organs or gene expression changes at a cellular level. In both instances, these changes are likely mediated by altered hormone and nutrient levels resulting from the maternal obesity (acting directly or via intermediary mechanisms such as oxidative stress). Some of the current trials underway in the UK include studies aiming to normalise metabolic hormone levels in obese mothers via lifestyle intervention (in the form of increased exercise), or pharmacological intervention with insulin-sensitising drugs. In some instances, if the intervention is found to correct a defined aspect of the maternal physiology the study can also be used to investigate the importance of this specific factor in mediating the detrimental effects on offspring health. This is particularly true when an intervention can be modelled in animal as well as human studies, as animal studies allow us to examine at a molecular level what effect the intervention is having on the mother. These investigations will be instrumental in allowing us to discover the 'programming factor(s)' in the mother that are responsible for causing the offspring phenotypes. This is vital in achieving the ultimate aim of developing future clinical advice and treatment for obese mothers during pregnancy that will stop the transmission of obesity risk to the offspring.

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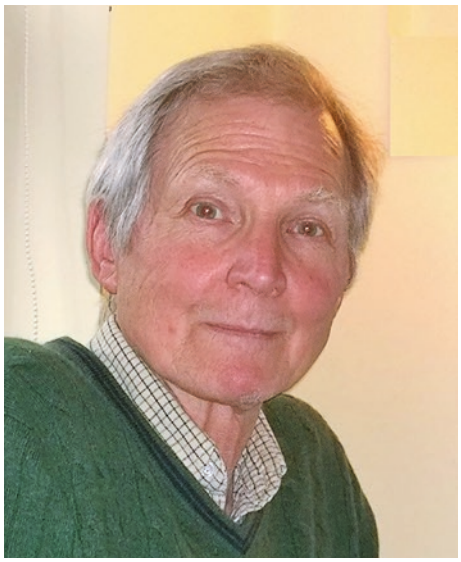
Memories of Andrew Huxley at UCL and his contribution to the science of photonic crystals



Jonathan A Coles

Visiting Researcher
Institute of Infection, Immunity & Inflammation,
University of Glasgow, UK

The author was a postgraduate at UCL in the late 1960s, and here recalls an aspect of Andrew Huxley's work which is relatively unknown compared to his famous experiments on the nerve impulse and muscle contraction , to honour the centenary of Huxley's birth.

Andrew Huxley at UCL in the 1960s

Huxley had taken the chair of physiology at UCL in 1960, and applied himself conscientiously to his duties. He was very present, punctiliously attending morning coffee and afternoon tea in the common room. At the Christmas party, he would dance the valeta with the technicians and win the drinking-a-yard-of-ale contest. His intellectual presence is illustrated by the advice given to students preparing their first talks: 'Andrew will probably ask a question, and if he does, there is only one possible answer: Yes, you're quite right, I should have thought of that.' The three most closely related departmental heads included Huxley himself, JZ Young in Anatomy, and Bernard Katz in Biophysics, all three outstanding scientists who did experimental work with their own hands, and the atmosphere trickled down. Doug Wilkie and Barbara Banks could be seen crossing by chance in the corridor and haranguing each other with great passion about the thermodynamics of ATP.

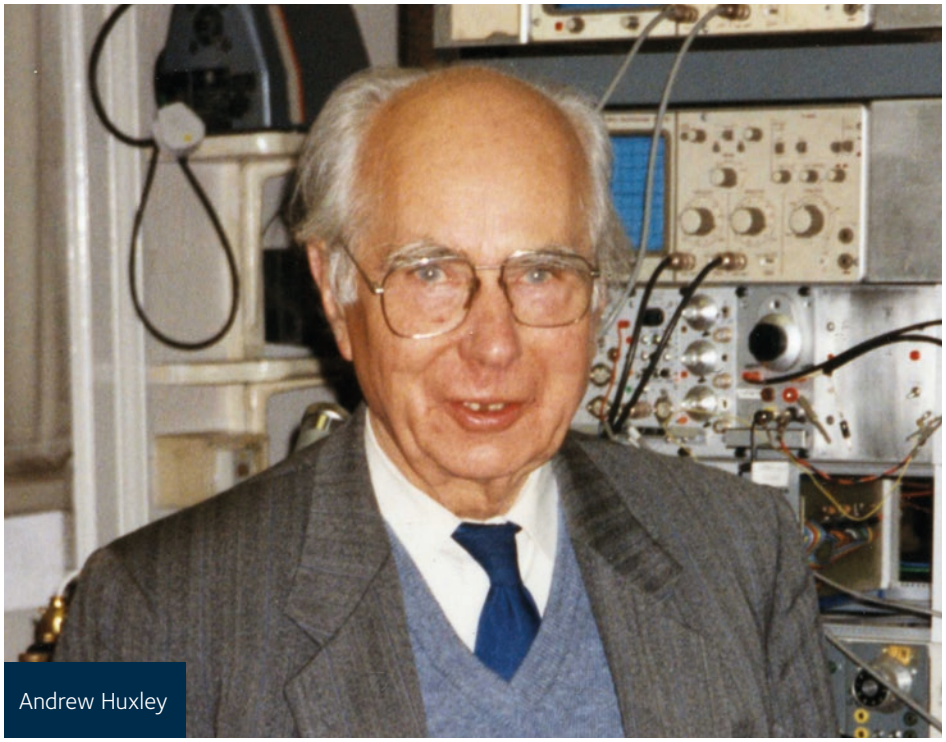
It is hard to say how much was due to Huxley's direct influence, but in addition to subjects like cybernetics and thermodynamics being applied to physiology, many technical aspects of modern electrophysiology were gestating in UCL during his time. He himself motorised the focus on his dissecting microscope, controlling it with his knee. To aim a microelectrode at a selected cell, you need a microscope that can move independently of the micromanipulator, and one early solution was to slide the microscope on a glass plate above a stationary preparation. An early computer, which could just be lifted by a strong person, was acquired for averaging cortical evoked potentials, and people built simple transistor circuits. However, micropipettes were still filled laboriously overnight, as Murakami's invention in Tokyo of capillaries containing a fused filament had not reached the West. In 1967, Chris Smith and I asked some lecturers what had been the department's greatest achievement of the year, and the answer was: 'Kept Huxley'.

The appreciation was not total. People complained about interminable staff meetings, and his lectures were not widely popular. He would demonstrate the compound action potential in frog sciatic nerve in front of about two 200 medical students, and do the calculations, first mentally, then checking on the slide rule he always carried. The medical students asked for him to be taken off, the gist of their argument being that intellectually demanding lectures were an invasion of their safe space, and hearing about the nerve impulse from the person who first quantified it did not make up for this. It was not surprising that Huxley was overjoyed when, in 1969, he was appointed to a Royal Society Research Professorship, and could devote himself to his research.

Biological reflectors

Although Huxley's main research at UCL was on the mechanism of muscle contraction, he published on a range of subjects. In addition to 'Proposed mechanism of force generation in striated muscle' (with Bob Simmons [Huxley & Simmons, 1971]; 1,722 citations), he contributed to a lively exchange in *Nature* on 'Sexual activity and beard growth' (Huxley, 1970: 1 citation), and, prompted by Jack Diamond, did maths on electrotonic potentials. He was also interested in the work of Eric Denton (in Plymouth) and Mike Land (at UCL) on biological reflectors, which work by interference of light in a stack of layers of alternating high and low refractive index. One example is the reflecting scales that camouflage the sides of silvery fish. (If you hold a mirror vertically in the sea, it is hard to see from below because of the way it reflects the sky.) To pass the time on the train home to Grantchester on Wednesday and Friday evenings, Huxley did a mathematical analysis of such one-dimensional multilayer reflectors (Huxley, 1968). The equations for a number of biologically relevant cases were then helpfully plotted by Mike Land (Land, 1972).

‘A beetle cuticle on a bench top will iridesce, beautifully and odourlessly, for decades, while a herring, say, will not’



Andrew Huxley

Materials that modulate the passage of light by having structure at optical wavelengths are now called ‘photonic crystals’, and multilayer reflectors are a relatively simple, but by no means trivial, case. The first use of ‘photonic crystal’ in an article title seems to have been in 1991 but a search for the term now brings up 46,589 hits, and this does not include spin-offs such as invisibility cloaks. Opticists have been very interested in the diverse kinds of biological reflectors, particularly those in insects. I suspect that one reason for this choice is that a beetle cuticle on a bench top will iridesce, beautifully and odourlessly, for decades, while a herring, say, will not.

Eyeshine in cats

Virtually all nocturnal mammals have a reflecting layer, the tapetum lucidum, behind the retina so that light that escapes absorption on the first passage is not wasted. In Carnivora, the structure is not alternating strata, as in fish scales, but layers of cells each containing arrays of rodlets, as shown for the cat in a 1963 e.m. study by Chris Pedler at the Judd Street Eye Institute (Fig. 1A). For my little MSc project I was told to ‘do something’ with the cat tapetum and to begin by showing Pedler’s images to Huxley. Huxley’s immediate response was that it would give Bragg-type lattice diffraction at optical wavelengths (much as far shorter X-rays are diffracted by atoms in mineral crystals) and that this was interesting and worthwhile demonstrating.

I was provided with a rather nice little brass microscope, and I borrowed Prior manipulators from the teaching lab and reassembled them with various chiralities. It was always a rush restoring them to normal the evening before a practical class.

Huxley was tremendously helpful, generous and supportive, but never interfering. He would advise me, for example, to ignore the numbers written on the lamp bulb and to run it at the highest voltage that did not blow it up. He let me use the lathe he kept in his lab, and a Cooke microscope objective that he had had specially modified for water immersion. Of course, we needed cats’ eyes. To get these, I would hang around while people finished cat experiments, which meant working late at night. Bruce Lynn was one of the worst: he rarely finished an experiment before about 3 am, and only then could I start myself. I learnt that Huxley was often still in his lab at 1 am, and that there was a Czech postdoc who sang magnificently when he thought that everyone else had left.

It was quickly apparent that each domain of rodlets in the tapetum reflected a different colour (Fig. 1B), and Huxley joked of ‘spots before the eyes’. This was one of only two jokes I ever heard him make, but he made the best of it, and repeated it for some weeks. I eventually managed to show the key point, that there could be reflexions from more than one lattice plane, but this took more time, and the project continued well beyond the official 6-month period. When I came back from summer holidays, the nice little brass microscope had disappeared. After some enquiry, I learned that it had belonged to Bayliss and had been taken to be exhibited in the Wellcome Trust museum. With remarkable generosity, Huxley let me use the Zeiss microscope he had bought with some of his Nobel prize money. Huxley was very patriotic about optics, and it was painful for him to concede that German microscopes were better than the British-made ones.

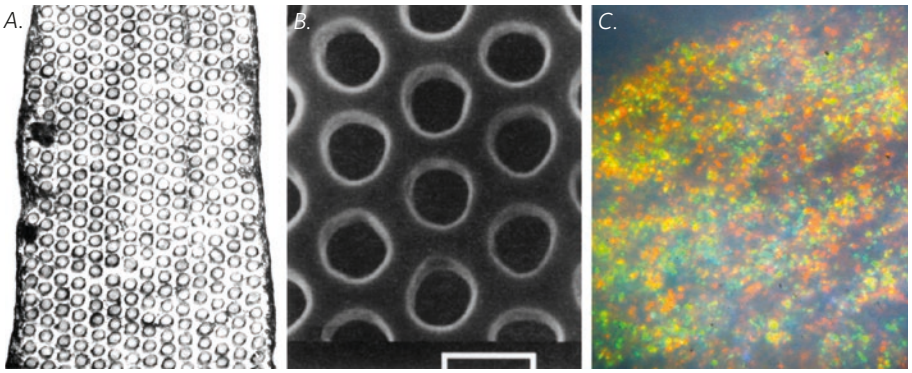


Figure 1. Natural and man-made photonic crystals.

A. An e.m. cross-section of a domain of rodlets in the tapetum lucidum of the cat. The distance between centres is about 0.45 µm. From Pedler, 1963 (Pedler, 1963).

B. A photonic crystal made in Glasgow in 1996 (Krauss *et al.,* 1996). The scale bar is 0.2 µm. Adapted by permission from Macmillan Publishers Ltd: Krauss *et al.,* (1996). *Nature* **383**, 699-672, copyright.

C. 'Spots before the eyes'. An area of tapetum illuminated with a narrow cone of light. Each domain, about 5 µm across, reflects a particular colour. Seen in car headlights, the spots fuse to give a general yellowish-green colour. See Coles, 1971, for more details.

'When I came back from summer holidays, the nice little brass microscope had disappeared'

The story was, that when his Zeiss arrived, he took it completely apart and reassembled it properly. He was constantly interested in the latest developments. Halogen bulbs had just been introduced, for motor cars and slide projectors, and he quickly suggested I use one. If he had been working in say, 2000, he might well have controlled his experiment with an app on his smart phone; obviously, if he were working now, most of us would have no idea what he might do.

Problems with photocopiers

The time I annoyed Huxley most was when I had gradually tracked literature on the cat tapetum back in time to a paper by Schultze in the Sitzberichtung der niederrheinische Gesellschaft für Natur-und Heilkunde, 1872, which I went to read in the British Museum. To get entry, in 1970, a uniformed curator let you into a long corridor. About halfway down, another uniformed curator opened a door into a side corridor, narrow and long, but well-appointed in light wood with an olive green carpet. At the end was a small office with a light oak counter behind which another curator was bent over a ledger. When it seemed that he would never look up, I coughed and asked if I could see the Sitzberichtung der niederrheinische Gesellschaft für Natur-und Heilkunde, 1872. He harumphed and said I could see it in Edinburgh. But I pleaded poverty and he grudgingly gave me an appointment to use the Reading Room. What Schultze and I had in common was that we did not do things properly. The professional approaches were either to fix the tissue, to measure transmission spectra or to try to work *in vivo* (looking through the pupil). But if you just expose the tapetum of a freshly dead cat and use a little bit of optics, you can see the 'spots before the eyes' that pleased Huxley (Fig.1C). I made some notes on Schultze's article, which correctly ascribed the reflexion to interference phenomena, noticed that the next one was Kekule's description of the benzene ring, and went back to the lab. Huxley generally expressed his annoyance by the length of his silences: in this case it was a very long one. I had not photocopied the article. At that time, as far as I knew, there were two photocopiers in the whole of UCL. UCL was a modern and student-friendly institution: my small imagination had not considered that it might be possible for a student to get a photocopy in a place like the British Museum

To the naked eye, an isolated cat tapetum looks like a bit of wet rag. This is perhaps one of the reasons why optical engineers have neglected what may be the first two-dimensional reflecting photonic crystal to be described, even though they have proudly manufactured similar structures (Fig. 1B). And it probably explains why biologists (apart from Schultze) had been reluctant to affirm that the reflexion was due to interference. Indeed, immediately after the tapetum optics article (Coles, 1971) was published, an angry reader telephoned to demand a retraction. I was relieved that Huxley was almost rude in his assessment of the angry reader.

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SHAPE: Shaping Healthy Attitudes and Protecting the Environment

Hephzi Angela Tagoe

PhD candidate at UCL Great Ormond Street Institute of Child Health

SHAPE, an acronym that stands for Shaping Healthy Attitudes and Protecting the Environment, connects high school pupils in Ghana with tertiary level students and STEM professionals to work together on a 12-month challenge. GhScientific, a Ghanaian-based organisation with a focus on science communication and public engagement, organised the project. The Wellcome Trust has provided funding for the SHAPE project.

For the pilot, we recruited 104 junior high school pupils from 16 private and public schools and placed them in eight teams. Teams were tasked with identifying health conditions with environmental triggers and crafting innovative solutions to reduce these environmental triggers. Each team was then paired with two students to serve as project ambassadors to support the development of their solutions. A professional served as their designated mentor to advise on the scientific content of the project.

We launched in December 2015 at the annual meeting of the Ghana Science Association with representatives from the various schools, invited guests, and selected media houses. The meeting's theme was 'National Development Through Scientific Innovation', and the SHAPE project served as a showcase of how the scientific community can engage with the public to promote an interest in research.

Science education in Ghana has historically been challenged with a lack of creativity in lessons and minimal translation of theory into practise. Many public schools are without laboratories, and pupils are often left to their imagination. Engaging pupils with projects such as SHAPE gives them an opportunity to better appreciate a future with science. Bearing this in mind, it was important to train the teams in several capacity-building workshops to better prepare them for the task.

Students at a capacity-building workshop with volunteers from Google

Partnerships

We formed a partnership with the Grameen Foundation to provide volunteers from a Google international reach program to run these workshops. They taught the teams the scientific method of conducting research, including data collection and analysis, and communication and presentation skills, including presenting with PowerPoint and preparing posters, and general skills, including time management, idea generation and teamwork. The last week of each workshop was held with the ambassadors and teachers on effective project management.

Through partnership with the Ghana Science Association, we had a network of professionals to support the project. The teams had the chance to visit a number of research departments. The Multimedia Group, one of the largest media houses in Ghana, also supported the project by providing a media platform to publicise the project. They interviewed the individual teams and aired the interviews on a weekly basis and also showcased the SHAPE project in a segment about the need for public engagement with science on their morning breakfast show.

The teams

With teams formed and workshops completed, the pupils were ready to take on the challenge. They met regularly over the course of the project to research their selected topics and compile their findings, which were showcased at the closing ceremony.

The project from the 8 teams were:

- The Effect of Carbon Cycle Disruptions (The Sparkling Stars of Science)
- Impact of Poor Human Waste Disposal (The Blessed Blue Kings)
- You Are What You Breathe (Scholars of Nativity)
- Alternative Solid Waste Management (The Eco-Warriors)
- A Story of Water, Waste and Marketplaces (Agents of Change)
- Creating Sustainable Environment Clubs (Brainstormers)
- Alternative Approaches to Reducing the Impact of Mosquitoes on Health (Youth Environment Activists)
- Air Pollution In Urban Communities (St Maurice Champions)

The closing ceremony

In a room full of students, teachers, parents, invited guests and professionals from the scientific community, the teams took turns showcasing their various projects to the audience and a panel of judges. They also put together poster presentations. The impact of the capacity-building workshops and success of the project was evident in the final presentations. Their growth over the course of the project came through as they confidently shared and answered questions on their chosen health condition, identified environmental triggers and explained their innovative solutions to reducing the impact of these environmental triggers on health. The Most Practical Project, the Most Innovative Project and the Best Poster Presentation each received awards. A final award went to the Best Teacher.

Students conveying their project in a sketch

Judges deliberating on the final scores

Conclusions

The SHAPE project set out to show that by equipping pupils with the right tools and resources they could excel regardless of their background. The pupils indeed showed this to be true. It also set out to encourage more higher-education students and STEM professionals to take up public engagement with science and to promote collaborations on STEM educational projects for maximum impact. Based on the success of the pilot, GhScientific intends to run the project annually to give the opportunity to as many pupils as possible. The project diary is available online at shape.ghscientific.com.

Personal reflections on the process of obtaining a PhD

Ole H Petersen

School of Biosciences,
Cardiff University, Wales, UK

A former president of The Society explains how he himself never obtained a PhD (he has an MD instead) but had a major role in initiating the lengthening of the period for which grants are available.

I may not be fully qualified to write about the PhD, as I don't myself have one, but shall nevertheless attempt to do so! In fact, I never even had a supervisor! I started my research in 1965, when still an undergraduate (clinical) student in the Faculty of Medicine at the University of Copenhagen. Having received good grades in my basic science examinations, I – like many others – was hired as an Instructor in Physiology to teach students just a few years younger than myself. The University had to operate in this way because there was insufficient staff to deal with the large numbers of students 'invading' the University at that time. This was also a somewhat chaotic period for the Department of Physiology with an old Chairman, who barely recognised even the senior members of staff!

Figure 1. Drawing included in an article about my public thesis defence published in 'Politiken' (one of the two most important Copenhagen newspapers) on 10 November 1972 (the day after the thesis defence). Translation of the Danish text under the drawing: 'The candidate physician Ole Holger Petersen (left) and the first official opponent Professor Anders Lundberg from Gothenburg. (Drawing by Holger Worm).'

My own doctoral research

It was therefore relatively easy for me to take over an empty laboratory, find unused equipment and start experimental work on the electrophysiology of salivary glands. During my years as a clinical student, I actually spent much more of my time in the Department of Physiology than in the hospital and published quite a few papers in what was then *Acta Physiol Scand*. After my final clinical examinations, I was immediately appointed as a Lecturer in the Physiology Department and started thinking about my doctoral thesis.

At that time, in the Faculty of Medicine at the University of Copenhagen, there was only one 'doctoral option', namely Dr. Med. (Doctor of Medicine). This was an unsupervised degree that could be taken at any time. Most people wrote a substantial review article (book) based on a series of their own original papers. These were then submitted to the Faculty and after a very long period (typically about one year!), one would be told whether the thesis had been accepted (or rejected) for public defence. If successful, a date would be set for the public defence, where the candidate would have to answer questions from two official opponents who would criticise the thesis (typically in front of a substantial audience including all departmental staff and often staff from adjacent departments as well as family and friends). The Dean of the Faculty would preside. The Review Article had to be published as a book and had to be available for purchase in the University bookshop a couple of weeks before the defences and anyone could act as an unofficial opponent in addition to the two official ones.

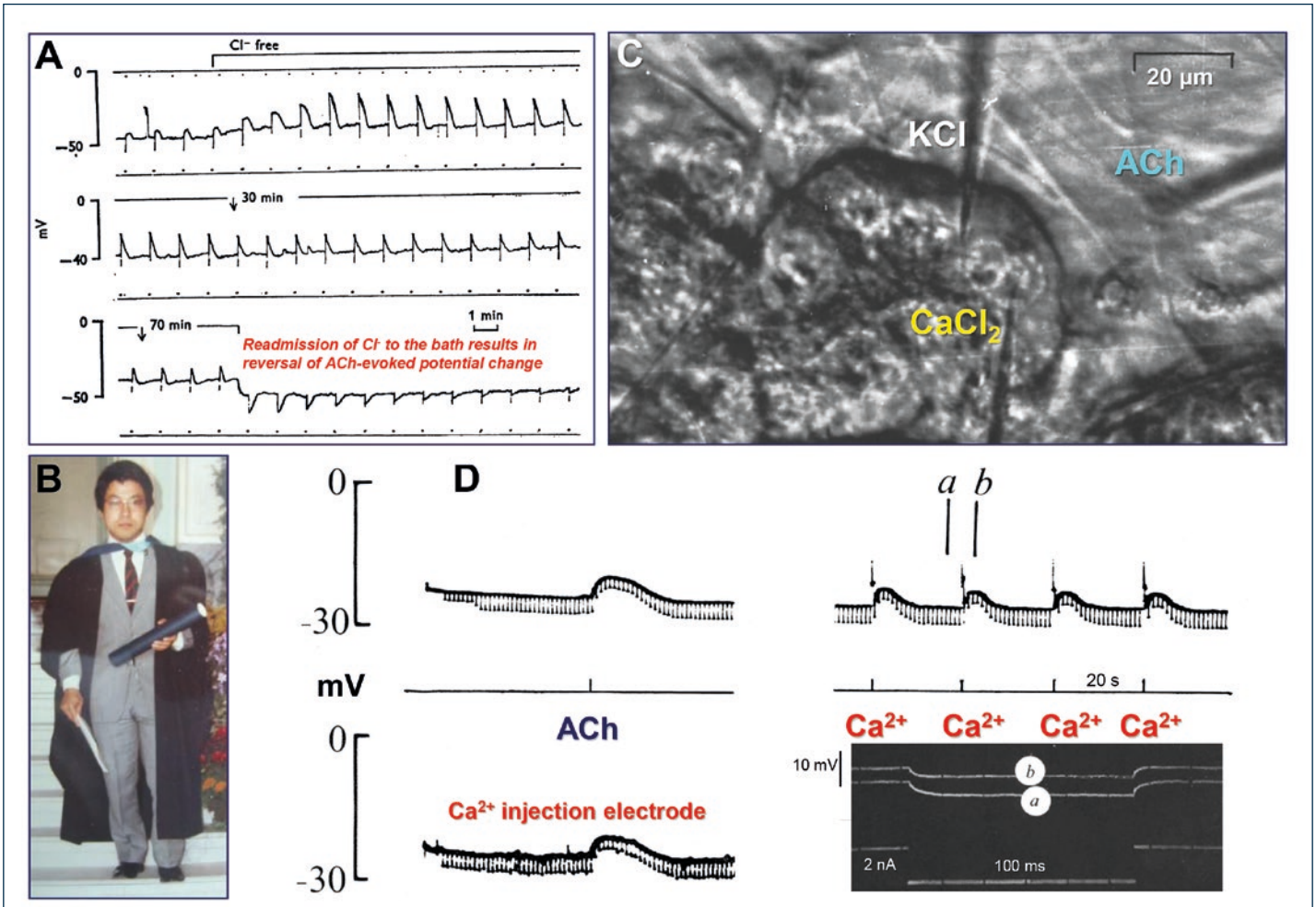

Figure 2. My first PhD student (Noriyuki Iwatsuki - NI) and some of his most important findings. *A*. Continuous trace of membrane potential recording (sharp intracellular micro-electrode) from mouse pancreatic acinar cell. At regular intervals, short ionophoretic acetylcholine (ACh) applications are made from an extracellular pipette resulting in short-lasting depolarisations. After removal of extracellular Cl^-, there is a transient increase in the amplitude of the ACh-evoked depolarisations but, most strikingly, after re-introduction of external Cl^- the ACh-evoked depolarisations are reversed into hyperpolarisations. *B*. NI after the graduation ceremony at the University of Dundee (1979). *C*. The experimental set-up favoured by NI: Two micro-electrodes have been inserted into neighbouring acinar cells, one filled with the conventional KCl solution and the other with $CaCl_2$. The extracellular electrode is filled with an ACh-containing solution. *D*. Result from an experiment in which the effect of extracellular ACh application is compared to the effect of intracellular Ca^{2+} injection. Both extracellular ACh application and intracellular Ca^{2+} injection cause depolarisation and reduction in input resistance. The experiment relies on the complete (gap junctional) coupling between acinar cells within an individual acinar unit (and the complete isolation between different acinar units). This was also shown by NI (in other papers).

After the public occasion the Dean and the two official opponents would meet to decide whether the defence had been acceptable.

Thesis defence

For me the public defence was a particularly 'dangerous' occasion, because the key element of my thesis (based on three single-author original articles published in *J Physiol* in 1970 and 1971) demolished the conclusions from a series of papers by my first official opponent (Fig. 1), Anders Lundberg (Professor of Physiology at the University of Gothenburg), on the electrophysiology of salivary glands, which had been published in *Nature*, *Acta Physiol Scand* and *Physiol Rev* in the late 1950s. To my surprise and relief, the defence went reasonably well, and Anders Lundberg gracefully acknowledged that he had been wrong. I was 29 when my Dr. Med. degree was awarded, which may seem late from a UK perspective, but was actually seen as very early at that time in Denmark (most colleagues obtained the degree in their late 30s or 40s). The public defence of a Dr. Med. thesis was, in those days, regarded as sufficiently interesting for the general public to merit a quite detailed description in the major Copenhagen newspapers, including drawings of the candidate and the most important official opponent (Fig. 1). Whatever the merits or demerits of this system, it certainly gave prominence to the scientific doctorate.

My experience as a PhD supervisor

My first experience of supervising a PhD student happened after I had, just a few years later, been appointed Symers Professor and Head of Physiology at the University of Dundee. My first PhD student, Noriyuki Iwatsuki (Fig. 2), was truly exceptional. As acknowledged in the preface to my Physiological Society Monograph, The Electrophysiology of Gland Cells, published in 1980, Noriyuki's data dominated the book. His PhD output of original papers (1976-1980) was astonishing, consisting of no less than six full papers in *J Physiol*, three in *Nature*, three in *Pflügers Arch* and one each in *J Cell Biol* and *J Clin Invest*. More importantly, he made some key discoveries. Fig. 2 shows results from what I consider to be his two most significant papers (Iwatsuki & Petersen, 1977a,b) in which he demonstrated that acetylcholine evokes a marked increase in the Cl^- conductance of the pancreatic acinar plasma membrane and further showed that this was mediated by intracellular Ca^{2+}.

‘Too often it seemed that PhD students were just used as highly specialised technicians’

Figure 3. The four Liverpool investigators responsible for the UK’s first Wellcome Trust-funded 4-year PhD programme at the celebration 20 years after its start. From left to right: Ole Petersen, David Eisner, Graham Dockray and Bob Burgoyne.

These results have stood the test of time, but of course with more detail emerging in the better-known papers based on the patch clamp experiments conducted in the 1980s and 1990s. Noriyuki was an immensely confident experimentalist, so it was no surprise to me that his live demonstration, at the 1978 PhySoc meeting in Dundee (Iwatsuki, 1978), of gap junctional communication between neighbouring pancreatic acinar cells was completely successful, as testified in the Meeting Secretary’s minutes. It may not be particularly useful to be nostalgic about the ‘good old days’, but it is undeniable that the loss of regular opportunities to make live demonstrations of new techniques and to give short talks at PhySoc meetings has removed a very valuable element of PhD education for physiologists. It was an extraordinary piece of luck for me to have had such an able and enthusiastic person as Noriyuki as my first PhD student, and it certainly set the bar very high, possibly too high, for his successors.

Move to Liverpool and the introduction of 4-year PhD support

I became Rod Gregory’s successor as George Holt Professor of Physiology at the University of Liverpool in 1981 and held this chair for 28 years until I succeeded Sir Martin Evans as Director of the School of Biosciences at Cardiff University early in 2010. In my Liverpool period, I had many PhD students but, in spite of significant research successes, it was in general not easy, in the 1980s, to attract the best PhD students to Liverpool, although there were of course some outstanding exceptions. In my almost daily conversations about departmental matters with Graham Dockray in this period, we often returned to the PhD theme. We were not convinced that the standard 3-year PhD training was optimal. Too often it seemed that PhD students were just used as highly specialised technicians who were simply told each day exactly what they should do, without having much intellectual ownership of their own project. We felt that a 4-year course, in which the first year would mainly consist of lab rotations, might be a better option. In this way, the students could become acquainted with what was on offer in the department and would be able to make informed decisions about their choice of host lab and supervisor. Hopefully, this would also enable them to have a more creative role in structuring their own PhD project.

At that time the Wellcome Trust (WT) only funded individual 3-year PhD studentships, as did the Research Councils, so we approached the WT and had several discussions with the Trust, which led to a proposal for a 4-year PhD programme along the lines just described. However, the WT did not appear to take much notice of our proposal, and we had the impression that it had been shelved for good. Nevertheless, several years later and, I believe, mainly thanks to the efforts of Julian Jack, our proposal was somehow re-discovered and Bob Burgoyne, Graham Dockray, David Eisner and I were asked to provide an up-dated proposal, which was eventually approved and funded. In 2015, we could celebrate the 20th anniversary of the actual start of the programme (Fig. 3). The Liverpool WT 4-year PhD programme in Cellular and Molecular Physiology became the very first such PhD programme supported by the WT, but was soon followed by many other similar programmes throughout the UK.

Within a surprisingly short time this approach to PhD training became popular, and there are currently 32 WT programmes of this type operating throughout the UK in various branches of the Life Sciences.

As soon as the WT programme started in Liverpool, we noticed the high quality of the students and the particularly high level of motivation for their project work. Having selected their own projects and supervisors, based on direct experience and interactions with potential labs and their PIs, the students had a great start to their PhD work and, generally, a stronger feeling of intellectual co-ownership than had been the case for their predecessors on 3-year programmes. We also noticed that the students often imported techniques from one lab into another because they, during the initial rotation year, had made valuable contacts with labs they had not finally selected for their main PhD project. In some outstanding cases, students generated entirely new projects based on combining expertise from two different labs.

International aspects

Science is international, and the UK University System has always welcomed PhD students from other countries. We can only hope that this will continue in an era where immigration control seems to have become the most important policy goal! After my arrival at Cardiff University, I was keen to expand our international PhD programme, and sometime after a visit to Guangzhou in 2011 (Fig. 4) the first PhD student from Jinan University arrived. One uncomfortable, but apparently widespread, 'rule' in China is that a successful PhD thesis must be based on publications in journals with an Impact Factor (IF) above 5. This is of course nonsensical as there is no relationship between the quality of an individual article published in a particular journal and the average number of citations, even within a ridiculously short time frame, to papers in that journal. In fact, the number of citations, even to an individual article, cannot be regarded as a measure of quality, but just indicates interest in the work and, to a large extent, depends on the size of the particular research field. Nevertheless, one cannot jeopardise the future career of an individual for the sake of a general principle, and we did solve this 'problem' in the case of our first student from Jinan University (Peng *et al.*, 2016). However, it is undoubtedly necessary – again and again – to explain (even in our own Universities!) the general damage to the reliability and reproducibility of our science which is caused by relying on the IF as a measure of quality. In this respect, I think the unreasonably maligned REF actually gives a good example by explicitly forbidding the use of IF as a method of evaluation.

Conclusions

Overall, I believe that the now popular 4-year PhD courses present an improvement on the previous 3-year model, although there will always be students who know exactly what they want to do immediately after their BSc Hons degree without having to go through an initial lab rotation year and, therefore, we need a degree of flexibility. The principal problem we face in today's increasingly over-audited and over-regimented University World, with massive teaching loads, is lack of time to guide our PhD students. No amount of auditing and tick-boxing can compensate for intensive in-depth discussions! We may also want to rethink the rather low-key way in which we are now able to acknowledge the accomplishments of our PhD students, which has become exacerbated by the loss of opportunities for demonstrating and speaking at PhySoc meetings. The final PhD examination in the UK, which is really a rather private discussion with PhD examiners, is in stark contrast to the rather more festive conclusion to doctoral studies (Fig. 1), which can still be experienced in some other countries, as I found out recently when acting as official opponent at a public thesis defence at the Karolinska Institute in Stockholm.

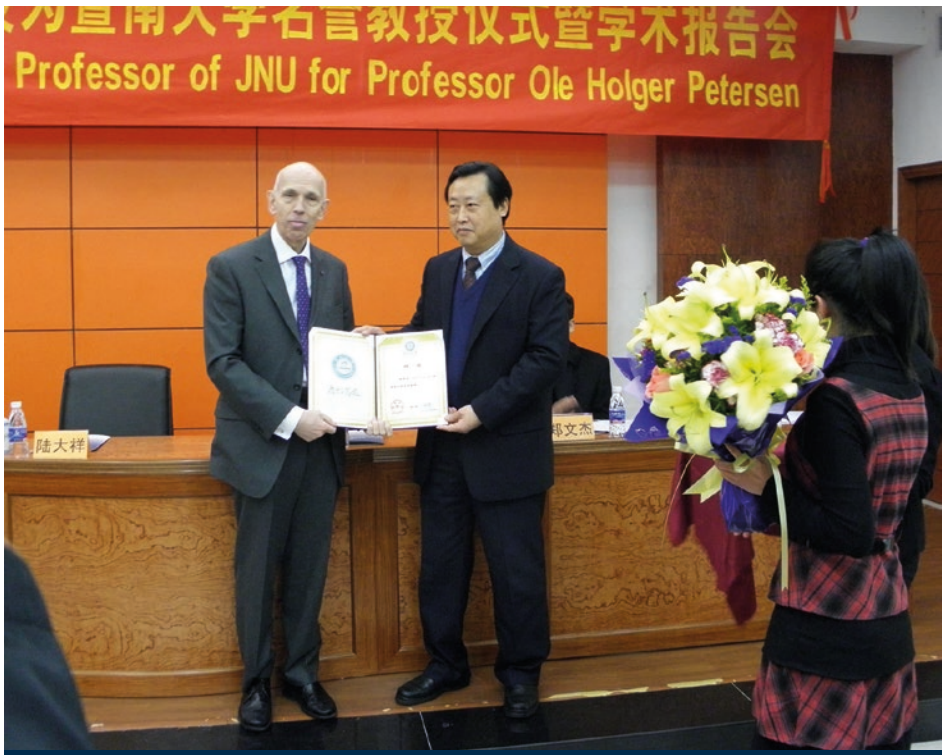

Figure 4. Ole Petersen at Jinan University in Guangzhou, China, in 2011 after negotiations with the Dean of the Medical College about PhD collaboration between Cardiff and Jinan Universities.

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Leon Popielski and his discovery that histamine stimulates gastric acid secretion

Oksana Zayachkivska

Department of Physiology,
Lviv National Medical Physiology,
Lviv, Ukraine

11 April 2016 marks the 150th anniversary of the birth of Leon Popielski (1/03/1866 – 8/10/1920) (Image 1), Professor of Lviv National Medical University (formerly known as Jan Kazimierz Lviv University), Ukraine. Popielski was the first to recognise that histamine stimulated gastric acid secretion (Modlin & Sachs, 2004). He produced over 100 publications and founded Lviv's strong pharmacology tradition. He is less well known today than he deserves to be.

Popielski began his scientific career at the Military Medical Academy in St Petersburg, then dominated by Pavlov (Image 2). In 1901, he published work indicating the existence of a peripheral 'reflex center' controlling gastric secretion (Popielski, 1901). His findings contradicted the prevailing 'nervism' theory of Pavlov, who had supervised Popielski's PhD thesis. Perhaps not surprisingly this caused friction between them. Pavlov then started a process to verify Popielski's results which was later described in Boris Babkin's memoirs. The results were confirmed thereby establishing the idea that processes other than conditional-reflexes, and in particular peripheral mechanisms, also controlled gastric secretion.

Popielski's work on histamine was carried out in Lviv during the World War I period, although published only later (Image 3). He clearly showed that histamine was a strong stimulant of gastric acid secretion. His PhD student W Koskowski subsequently introduced the histamine test for gastric secretion in patients, which in a somewhat modified form was used clinically for many decades (Polland, 1930). In the 1960's and early 1970's, Professor Sir James Black, at what was then Smith, Kline and French, brilliantly extended Popielski's model of the role of histamine in gastric secretion through the development and use of a new class of antisecretory drug – the H_2 receptor antagonists (Black *et al.*, 1972).

Image 1. Leon Popielski

These studies proved the essential role of histamine in stimulating acid secretion. An early example, cimetidine, became the first truly blockbuster drug, and revolutionised the treatment of peptic ulcer disease. Popielski's work provides a clear example of how basic physiological research can, with time, be translated into the clinic for patient benefit.

Based on presentations earlier this year at the 4th Global GI Club meeting 'Brain-gut axis', Experimental Biology/FASEB San Diego 2016, and 9th International Symposium of Cell/Tissue Injury and Cytoprotection/Organoprotection in Cracow.

All photos from family collections with permission kindly provided by L. Popielski & W. Greblicki. The author of this article is supported by a Paton Bursary of The Physiological Society.

Image 2. St Petersburg Military Mediacal Academy, *Circa* 1901

'An early example, cimetidine, became the first truly blockbuster drug, and revolutionised the treatment of peptic ulcer disease'

Image 3. Popielski's department in Lviv. Poielski pictured centre. *Circa* 1910

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Triathlon danger: causes and risks of Immersion Pulmonary Oedema

Richard Moon

Duke University,
Durham, NC, USA

Taking inspiration from our archived images, the 2016 'Physiology in our time' photography competition sought to record present day physiologists in their working environment. Richard Moon, first prize winner, tells us about the research captured in his photo.

Investigator Anne Cherry supervising an experimental subject underwater in the cold water submersion pool

A physically fit woman in her 30's was training for a triathlon. After several minutes she was short of breath, began coughing up blood, and had to stop swimming. She was rescued and taken to hospital, where she was admitted to the intensive care unit with a diagnosis of pulmonary oedema. After she recovered, investigation of her heart and lungs revealed no abnormalities.

This scenario has been experienced by numerous healthy individuals, most notably naval combat swimmer trainees. The condition has been named immersion pulmonary oedema ('IPO', also called swimming-induced pulmonary oedema, 'SIPO'). SIPO was first reported in the 1980's by Dr Peter Wilmshurst, who described it in 11 swimmers and scuba divers (**https://www.ncbi.nlm.nih.gov/pubmed/2562880**). SIPO usually resolves spontaneously but it may require oxygen therapy and hospitalisation, and can even be fatal.

Pulmonary oedema is most commonly seen in patients with heart disease or who are otherwise critically ill. What could be the cause of pulmonary oedema in such physically fit individuals? Peter Wilmshurst had observed that susceptible individuals had an exaggerated vasoconstrictive response to cold, perhaps triggering heart failure due to excessive cardiac afterload when immersed in cold water. Whether this was the explanation for all SIPO-susceptible individuals was unknown.

We initially studied the cardiopulmonary response to cold by submersing volunteers in 20°C water and using radial and pulmonary artery catheters to study them during exercise. We then studied 10 SIPO-susceptible volunteers in the same way. During submersed exercise, susceptible individuals had higher pressures in their pulmonary arteries than those who had not experienced SIPO. The combination of exercise and water submersion, which causes redistribution of blood from the periphery to the thorax, precipitated high pulmonary vascular pressures that were sufficiently high to induce haemodynamic pulmonary oedema. Pulmonary vascular pressures decreased after administration of Sildenafil, suggesting that this drug might prevent SIPO (**https://www.ncbi.nlm.nih.gov/pubmed/26882910**).

High pulmonary capillary pressure provided an explanation for pulmonary oedema. However, systemic arterial pressures were similar in both groups. We still did not know why these pressures were higher than normal. In order to investigate further, we performed 2-D echocardiography during head-out immersed exercise in cold water in both SIPO-susceptible and control groups. We are currently analysing our data analysis, but preliminary results suggest that the left ventricle of SIPO-susceptible individuals is stiffer than in non-susceptibles, thus requiring higher pressure to fill the heart, which in turn exerts a back pressure on the pulmonary blood vessels.

Although all of the volunteers in our study had normal hearts, some SIPO victims do have obvious predisposing factors such as hypertension, left ventricular hypertrophy or cardiomyopathy. These conditions can cause high pulmonary vascular pressure due to abnormal systolic or diastolic left ventricular function. Indeed, we have proposed that SIPO could be a cause of otherwise unexplained death during triathlons, particularly in individuals with such conditions (**https://www.ncbi.nlm.nih.gov/pubmed/27900191**).

We hope that our work will make people more aware of immersion pulmonary oedema, its predisposing factors and the risks that it poses.

Europhysiology 2018

A partnership between The Physiological Society, the Scandinavian Physiological Society, Deutsche Physiologische Gesellschaft and the Federation of European Physiological Societies

14–16 September 2018
The QEII Centre, London, UK

Call for symposia closes 30 April

www.europhysiology2018.org

Experimental Physiology

EP to accept Case Studies

Experimental Physiology is pleased to announce that we will now be accepting Case Studies. Case Studies are articles that provide a perspective on one-off cases and unique presentations in both humans and animals. As these presentations are generally studies of n=1 they provide compelling and revealing insights that other papers do not.

Mike Tipton to attend HbiM

Human body in motion

The EIC of *Experimental Physiology*, Mike Tipton, will be attending the Human Body in Motion (HbiM) Conference (Brussels 28-29 April) **http://www.hbim.be/congress/**

On the first day he will be presenting a plenary session: Physiology in Extreme Conditions to Clinic. This will be an excellent opportunity to meet Mike and find out more about *Experimental Physiology*.

Editorial board update

We welcome Mark Frey from the University of Southern California to the *Experimental Physiology* Editorial Board as Senior Editor in the area of GI & Epithelial physiology.

Reviewing Editors

Experimental Physiology has expanded its Editorial Board to include carefully selected Reviewing Editors in each of *The Journal*'s key subject areas:


Marcus Amann


Matthew Bailey


Jill Barnes


Tracy Baynard


R Matthew Brothers


Rebecca Campbell


Jason Carter


James Clark


Silvia Conde


Joseph Costello


Davi José de Almeida Moraes


Mary Diaz


David G Edwards


Dominique Eladari


Andrea Fellet


Yumei Feng


James Fisher


Federico Formenti


Brian Gulbransen


Caroline Jolley


Matthew W Kay


Carsten Lundby


Fiona McBryde


Louise Naylor


Julien Ochala


Jaume Padilla


Jason Peart


Gary Pierce


R Scott Rector


Raymond Reynolds


Harry Rossiter


Fadi Salloum


Bill Sheel


Reetu Singh


Nina Stachenfeld


Dick Thijssen


Gail Thomas


Richard Wainford


Matthew Whim

Daniel Wilkinson

Song Yao

Qiujun Yu

The Journal of Physiology

Review of the past year

Read all about our achievements in 2016! Kim Barrett (Editor-in-Chief) and Sally Howells (Managing Editor) have recently published an editorial covering the exciting developments we made in 2016. The article appears in the 15 April 2017 issue and can be found using the following DOI 10.1113/JP274162.

New Editorial Board members

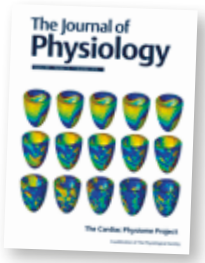
We are delighted to announce that Dennis Brown (Harvard, USA), Fiona Gribble (Cambridge, UK) and Weifang Rong (Shanghai, China) will be joining *The Journal* Board from July 2017. With these appointments, we hope to encourage more high-quality submissions from renal, endocrine and gastrointestinal physiologists.


Dennis Brown


Weifang Rong

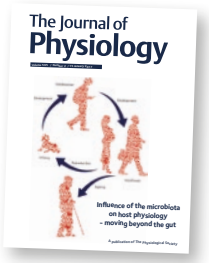

Fiona Gribble

Our recently published special issues



The Cardiac Physiome Project

Volume 594, issue 23 December 2016



Influence of the microbiota on host physiology – moving beyond the gut

Volume 595, issue 2, February 2017

Attending Experimental Biology?

The Society will have a stand in the exhibition hall during this year's meeting. If you have any questions about publishing in The Society's journals, please come to Booth 541 and talk to Managing Editors Sally Howells and Emma Ward. We will also be having 'Meet the Editor' sessions for each of our journals.

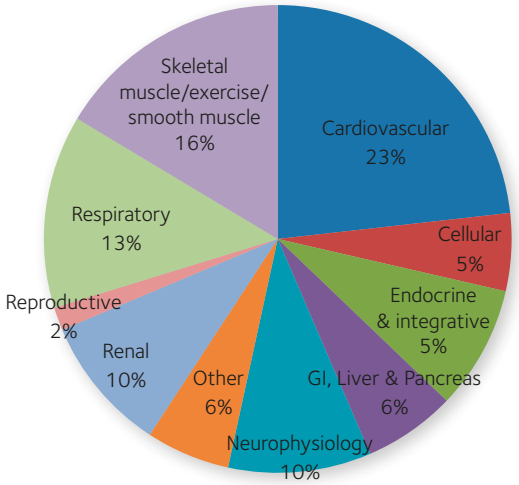
Experimental Physiology are pleased to be sponsoring the Symposium 'Sexual Dimorphism, Plasticity and Genomic Diversity of the Paraventricular Nucleus' chaired by Willis Samson on 26 April, 10.30 am, and look forward to publishing Reviews from the symposium in *The Journal* following the meeting.

The Journal of Physiology is sponsoring the symposium 'The Modulation of Aging through Altered Proteostasis' chaired by Benjamin Miller on 26 April, 8.00 am, and will also be publishing Reviews from each of the authors in a future issue.

Physiological Reports

Encouragingly, 2016 saw submissions to *Physiological Reports* resume their strong upward trajectory after some flattening out in 2015. Submissions totalled 540 (versus 431 last year and 399 in 2014), broken down as 416 transferred from the APS and Physiological Society subscription journals and 124 direct. The maturing publication we described in the last issue of *PN* is going through a late-teen growth spurt.

An interesting feature of *Physiological Reports* is its broad and even coverage of the subdisciplines of physiology, perhaps reflecting that the APS has specialist journals publishing in renal, respiratory and GI/liver physiology and in endocrinology/metabolism, all transferring papers through the cascade mechanism. Note that the pie chart below shows articles submitted rather than articles published.



Submission Discipline Distribution, 2016 YTD

At an editorial meeting in December, much of the discussion was devoted to how this coverage could be expanded still further, perhaps into the areas where physiology overlaps with other sciences. Sounds exciting, doesn't it?

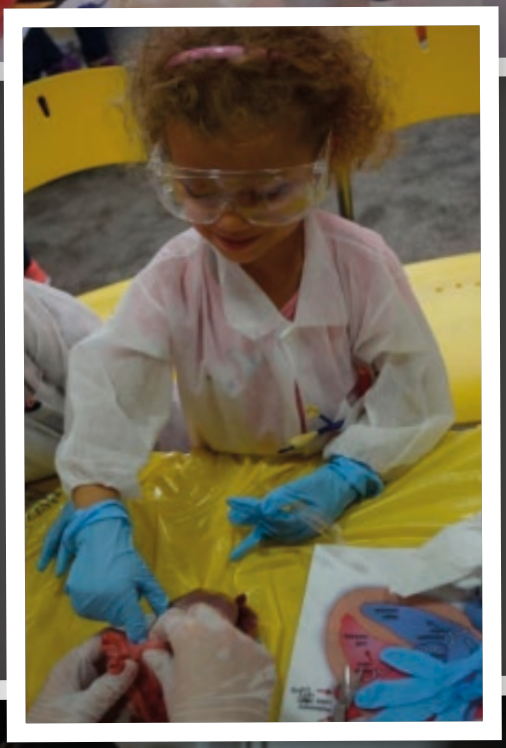
When you've got a few minutes to spare, do listen to some of the *Physiological Reports* author podcasts on the journal's website on Wiley Online Library.

Message to Peer Reviewers

Are you aware of Publons? A free service to Peer Reviewers enabling you to effortlessly track, verify and showcase your contributions. It also has information resources for Peer Reviewers. **http://prw.publons.com/**

WILEY Wiley Online Library also have an excellent resource for Peer Reviewers: **olabout.wiley.com/WileyCDA/Section/id-828000.html**

The Society journals are extremely grateful to all those who act as Peer reviewers.



The Physiological Society

'Physiology in our time' 2017 Photography competition