PN
Physiology News
Issue 105 / Winter 2016

Changes at the top

Valedictory and prospective thoughts

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Cover image: Detail of an untitled fantasy of experimental physiology painted by Tony Hillier, late lecturer in Physiology, University of Cambridge






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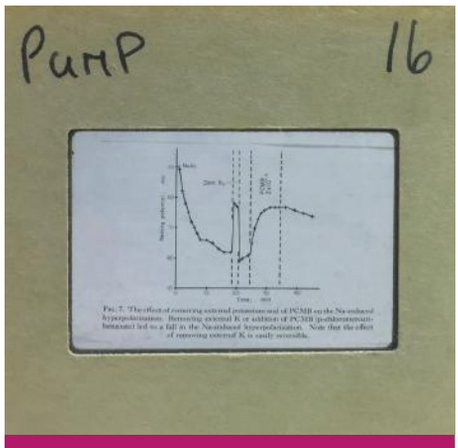
Roger Thomas
Editor

This issue offers *Physiology News* its first opportunity since the Dublin AGM to include a variety of valedictory and prospective thoughts by old and new members retiring from or elected to Trusteeships and Executive posts. Although not yet retiring, the Honorary Treasurer has written, after some persuasion, a fascinating article about her role. The new President David Eisner has described his pleasure at his election, his gratitude for the work of his predecessor Richard Vaughan-Jones and our acting CEO Casey Early. He also welcomes our new CEO Dariel Burdass. She comes from the Microbiology Society. Is there a research area called microbial physiology, I wonder? (Yes of course, and there seem to be many related journals). I would myself like to welcome Julia Turan, the magazine's new Managing Editor. She seems very helpful and efficient, much needed qualities in her new job.

This issue of *Physiology News* has no overall theme, and may well strike the reader as rather cobbled together, as indeed is this editorial. Actually all issues tend to be like that, in part because planning and being topical are rather mutually exclusive. Most authors do write their articles in good time, but not all do. Writing grant proposals has a much higher priority. Teaching too. As I write this editorial I am also planning a first-year lecture on ion transport. As it is about 51 years since I first lectured to students (on the sodium pump), this stimulates thoughts about changes that have occurred in the process of lecturing since 1965. My lectures of 51 years ago were to graduate students, and I myself hastily prepared 5 x 5 cm photographic slides (reverse-processing black and white 35mm film, a then cutting-edge technique) of key published figures. I still have some of them, as shown in the illustration! I probably devoted a whole lecture to the sodium pump; now my 50 min has to include several other ATPases, 49 ATP-binding cassette transporters and at least 390 members of the Solute-Linked Transporter superfamily.



Slide first used in 1965 showing the effect of sodium injection on the resting potential of a snail neurone

When I started lecturing to undergraduates in 1970 it was all chalk and blackboard. Only histologists were expected to use slides. At first students had to make their own notes during the lecture, but later they were given quite detailed printed paper hand-outs. Meanwhile blackboards were replaced by overhead and then by PowerPoint projection. Students now expect the PowerPoints and the lecturer's own notes to be on a web site. Just recently my department has stopped giving any paper handouts. We tell the students that note-taking is a valuable skill for use in real life if you are a medical practitioner. Many students do print out the website notes, though we discourage them. Throughout the last half-century, in spite of all the technological changes, the actual live lecture remains at the heart of the process of University education. Perhaps I have led too sheltered a life, and this is no longer true. Attendance at lectures here is voluntary, but at laboratory-based classes is compulsory.

I did wonder if I should write more about Brexit, but Karen covered this very well in her editorial in *PN* 104. If anything, the gloom has deepened in the last 3 months. What does Brexit really mean? Doom for those of you who get grants from Europe I suppose. Several recent Nobel laureates have expressed disquiet about the likely effect on British science. It is not just the likely loss of European-wide research projects, but the general chauvinism revealed since the referendum, and the denigration of experts by Michael Gove. How can such a view encourage support for research?

I was pleased to learn that the next Annual General Meeting of the Physiological Society is to be held in London rather than in Brazil, as originally contemplated in Dublin. When I went to my first AGM in the early 70s I was disappointed by how boring it was. I suspected this was part of a cunning plan to minimise attendance. As I rose in power in academia, I began to see that the views of people who had often not even read the agenda for important meetings could be a great nuisance. At the AGMs in the 60s there was no election result to announce, as in those days the committee nominated for election only the number of new members to replace the retirees. After several more dull AGMs I and four others set out in 1974 to nominate one more candidate as permitted by the rules, thereby forcing a real election. Our nominee was duly elected. The rest, as they say, is history. Eventually the committee even decided to nominate me! I was elected in 1977, and served for two years. When I nominated myself as a trustee about three years ago I was (apparently narrowly) rejected. Hah!

Letters to the Editor

Respiratory control in a fallen Jedi

Ken O' Halloran
Department of Physiology,
University College Cork, Ireland

How wonderful to learn of the considerable advances for the treatment of respiratory failure made by physiologists and bioengineers in a distant galaxy (*PN* 103; pages 31-33). Berg & Plovsing colourfully cover many aspects of combating respiratory malaise in the ill-fated Darth Vader. Beyond the benefits proposed by the authors, I suggest that Lord Vader's iconic whole-body suit offers additional life-preserving qualities. I suspect that the suit functions as a proportional assist ventilator with the capacity to dramatically reduce the work of breathing, which is typically raised, even at rest in respiratory patients to the detriment of exercise performance (an otherwise significant set-back for one such as Vader with ambitious plans for inter-galactic domination). The suit likely alleviates debilitating dyspnoea, common in respiratory disease, providing comfort and much relief. More importantly, however, in the context of deadly duels, assisted ventilation is capable of reducing the cost of exercise hyperpnoea, where ordinarily respiratory muscle oxygen uptake increases considerably during intense effort, 'stealing' locomotor muscle blood flow with implications for performance. As such, assisted ventilation likely proves very handy for Vader when sorting out disputes with former friends. Moreover, since such ventilators can be programmed to operate when triggered by inspiratory activity, respiratory muscle weakness secondary to chronic unloading is likely limited, though admittedly this may be much less relevant compared with patients on Earth, owing to intrinsic properties of Jedi muscles wherein 'the force' is presumably strong.

In short, respiratory assisted support for Vader appears to provide considerable benefit, minimising the work of breathing, improving exercise performance without deleterious effects on the diaphragm such as proteolysis, atrophy and weakness.

I also wonder if Vader's mask provides added positive end-expiratory pressure, which might aid distressed alveoli, thereby improving ventilation-perfusion matching, limiting oxygen usage, the cost of which must surely add up when one considers delivery and rental to Death Stars in galaxies far, far away. But that's a story for a different day...

Engaging with the educational literature

Zaineb Henderson
University of Leeds
School of Biomedical Sciences

I read the article in *PN* 104 'A celebration of education focused careers...' by Katharine Hubbard with great interest, and downloaded and read the Physiological Society's publication *Recognising teachers in the life sciences*. I noticed that on the publication's last page 'Top Tips', the 'Scholarship and Pedagogy' section recommends only 'Engaging with the educational literature'. Surely, to be an excellent teacher you should also be able to include in your portfolio an expert understanding of the subject you are teaching, acquired not necessarily through running a lab or getting research grants, but from extensive reading, keeping up with the current literature and writing learned textbooks on the subject being taught. The icing on the cake would be to include forays into the physical sciences or other biological disciplines to add novel insights into the chosen field, which could enliven the teaching and make the subject more relevant to students.

Mistakes in minutes

Tilli Tansey
QMUL, Honorary Archivist
The Physiological Society

I write in some dismay concerning the 'From the Archives' section of *Physiology News* 104. There are several typos in the transcriptions, the most noticeable of which are the mis-spellings of the names of a number of Society members - RC Garry, E Denton and M de Burgh Daly all appear in more than one guise. However, what gave me especial pause for thought was the list of Nobel Laureates appended to the Minutes of the meeting held at Bart's in December 1966 – and incidentally John Gillespie from Glasgow was the Meetings Secretary at the time, not Eric Denton. At the dinner in the Great Hall (also appearing as the mysterious great hail), HP Gilding noted the recent award of the Nobel Prize to an Honorary Member, F Peyton Rous. Rous, an American pathologist then aged 87, was finally awarded the Prize for work on sarcoma virus done 40 years earlier, and three years after his son-in-law Sir Alan Hodgkin had shared the same prize. Gilding remarked that it 'brought the number of present members of The Society who were Prize winners to *14', an asterisked list naming all 14. That list, as reproduced in *PN*, is however inaccurate, and intrigued as to whether the mistakes are of contemporary or more recent vintage, I consulted the original Minutes Book in the Society Archives.

One mistake is clearly of recent origin – 'Lord Plorey' is correctly recorded in the Minutes as Lord Florey, the Oxford biochemist and pathologist, who shared the 1945 Nobel Prize for Physiology or Medicine with Ernst Chain and Alexander Fleming for their work on the discovery, isolation and production of penicillin.

The second mistake is more glaring and is in the original. The first name on the list is that of Professor Charles (always known as Charley) Best. As a young medical student Best worked with Frederick Banting in Toronto on the isolation and therapeutic use of insulin for diabetes mellitus. But he did not share the 1922 Prize in Physiology or Medicine with Banting – that honour went to their boss, the Professor of Physiology John Macleod, an expert in carbohydrate metabolism, who had supported the work with space, resources and advice. The exclusion of Best created an uproar at the time, and somewhat ostentatiously, Banting shared his half of the Prize with the younger man. Macleod responded by sharing his half with James Collip, the biochemist who had undertaken the extensive purification work necessary to turn Banting and Best's crude canine pancreatic extracts into therapeutic samples. Hostility towards Macleod in Toronto, much of it fuelled by Banting, continued to such an extent that when he finally left in 1928 to return to his native Aberdeen he is reported to have very publicly wiped his boots so as to 'wipe away the dirt of this city' (Bliss, M 1982 The discovery of insulin. University of Chicago Press). Macleod, elected to the Physiological Society in 1900, died just a few years after his arrival in Scotland.

So the total number of Physiological Society members holding a Nobel Prize in 1966 was 13, rather than 14. However, amongst the living Laureates in 1966 was a former member of the Society. Elected a Member in 1918, John Boyd Orr was a nutritionist and politician, who resigned from the Society in 1949 when he moved into business activities upon his retirement as Director of the United Nations Food and Agriculture Organization (FAO). That same year however he was awarded the Nobel Prize, but not for Physiology or Medicine, but for Peace for his work at the FAO. He rarely, if ever, appears on lists of Physiological Society members who became Nobel Laureates. Note that one of this year's winners in Physics is the son of Hans Kosterlitz (elected 1939; Honorary Member 1984).

Editor's Note: My apologies. Future transcripts will be sent to Tilli before publication!

Affiliate Working Group formed to support Early Career Researchers

The group, made up of the current Affiliate Representatives to Council and Affiliate members, was formed to ensure the needs of early career researchers are met.

As an Early Career Researcher, you are at a point in your career where networking and opportunities to present your work are key to your development. This is why we want to make sure we are supporting you.

Current ideas in development include regional networking events, an Affiliate focused meeting with ample opportunities for oral presentations, and the introduction of Affiliate Society Representatives to work alongside Full Member Reps and support you in your institutions.

The group needs your support to succeed; whether that's inputting ideas for new initiatives or raising awareness of the issues you are facing in the workplace.

To get involved, provide ideas or feedback email membership@physoc.org

Making the most of your Society membership benefits

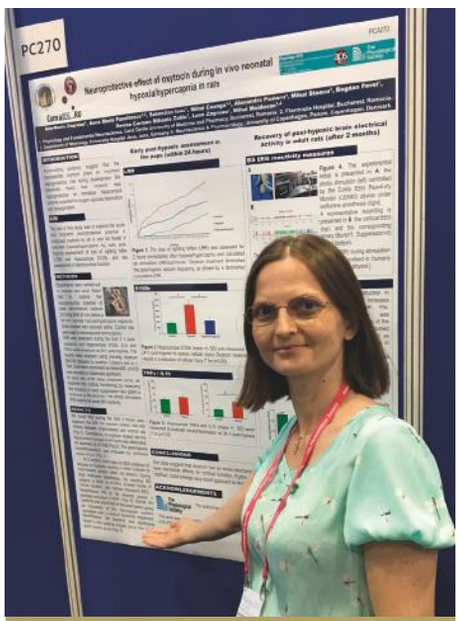
Did you know that we offer our support to members to present your work, visit another laboratory or attend a workshop or training course?

Travel Grants recipients are required to acknowledge the support provided by The Society as part of their attendance. This can be done by including The Society logo and a note of thanks on your poster or as part of your oral communication.

Submitting content for our news channels is a great way to help us raise awareness of your attendance at meetings, your work and the support from The Society. Your write up could feature in a future edition of *Physiology News*, in the monthly newsletter or on our blog.

For all the details and how to submit your content visit www.physoc.org/travel-grant-recipients

Full details of travel grants, including deadlines and Terms and Conditions can be found at www.physoc.org/travel-grants



See more photos of members with their posters at Physiology 2016 – storify.com/ThePhySoc/physiology-2016-travel-grant-recipients

Spotted some interesting research? Send it to us at magazine@physoc.org

Bringing you snippets of the latest intriguing research

The limits of the human lifespan

Analysis of global demographic data has shown that improvements in survival with age tend to decline after age 100, and that the age at death of the world's oldest person has not increased since the 1990s. The authors suggest the chances of someone living past 125 years in any given year are less than 1 in 10,000.

DOI: 10.1038/nature19793

Fighting drug-resistant superbugs without antibiotics

Shu Lam, a 25-year-old PhD student has developed a star-shaped polymer that can kill six different superbug strains without antibiotics, simply by ripping apart their cell walls.

DOI: 10.1038/nmicrobiol.2016.162

Knowingly taking placebos pills eases pain

Lower back pain patients who knowingly took open-label placebos reported 30 percent less pain and 29 percent reduction in disability compared to control group.

DOI: 10.1097/j.pain.0000000000000700

2016 Nobel Prize in Physiology or Medicine

Yoshinori Ohsumi was awarded the prize for his discovery of the mechanisms for autophagy and their role in cell recycling.

bit.ly/2fp18hv

2016 Ig Nobel Winners

The famous prize which honours research that makes people laugh and then think, awarded the medicine prize for discovering you can use a mirror to relieve an itch on the opposite side of your body, and the reproductive prize for studying the effects of different clothing materials on sex life.

bit.ly/2d94t3i

CRISPR in healthy human embryos

For the first time Swedish scientists have used CRISPR-Cas9 to edit DNA in viable healthy human embryos. By knocking out a series of genes they hope to learn about their roles in embryonic development and which ones cause infertility.

n.pr/2d3pw4e

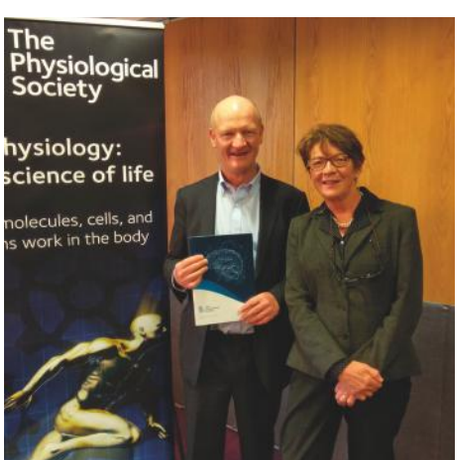
Party Conference Fringe Meetings

Building on the success of our 2015 events at the political party conferences, The Society held roundtable discussions entitled **TEF vs. REF: Are Teaching and Research now Adversaries?** as part of the Labour, Conservative and SNP conference Fringes.

The political situation has changed somewhat since 2015's conference events. While the Teaching Excellence Framework (TEF) was a rumour in 2015 it is now in a draft Bill going through Parliament, and significant changes are planned in how the research structures of the UK will be arranged. The Society has utilised its experience of working in the area of reward and recognition of Higher Education teaching to be a strong voice feeding in to the creation of the TEF. As part of this, the fringe meetings were an excellent way to bring politicians together with academics and policy experts in order to put forward suggestions on how best to implement this new system.

At our Conservative conference event we were joined by Lord David Willetts, former Science Minister; at Labour by Roberta Blackman-Woods MP, the Chair of the APPG on Universities; and the SNP conference by Shirley-Anne Somerville MSP, the Minister for Higher Education and Science, along with Roger Mullin MP and Carol Monaghan MP, who are on the committee examining the Higher Education and Research Bill. At each event a Trustee of The Society set out our involvement in the area and made our case for changes to the TEF structure.

We were very pleased with the levels of attendance and participation, and a fruitful conversation developed at each meeting.



Conservative Party Conference: Lord David Willets with Professor Bridget Lumb

There were a number of similar strands of argument across each event, and analysing the points made has allowed us to make recommendations to government. We have produced a report summarising the discussions and making recommendations to those drafting the structure of the TEF. These are:

- **Say what you mean** The TEF as planned is measuring the whole student environment, not just teaching. Greater clarity is required on the range of expected inputs and the institutional changes required to score highly.
- **Include details from the student voice** The National Student Survey (NSS) is a very broad tool which makes it hard to distinguish between institutions as almost all universities cluster around 80-90% satisfaction. More direct input - e.g. from Students' Unions/Course Reps - will address the information requirements of the TEF.
- **Compare learning gain** Student satisfaction doesn't correlate to course strength and teaching ability. Utilise the external examining system where peers judge the learning gain across the sector and consider transferable skills as well as subject learning.
- **Recognise the good teachers and educational researchers** The TEF as currently planned is impersonal. Instead, it should create a structure where demonstrating good teaching and teaching innovation reflects positively and has tangible career rewards.
- **Celebrate course diversity** Teaching should be linked to local research. Researched-focused academics are pushed to think differently when they are teaching, and students engage more with their subject if they are exposed to real life research. Without this, courses around the country could become homogenised.
- **Beware of perception** Students must be aware that education is more than a transaction. They should know that good teaching isn't spoon-feeding, and their education and development comes down to more than simply contact hours.

The Bill is currently going through Parliament and has a number of chances to be amended. It is hoped that with the combination of further scrutiny and sectoral involvement the TEF can emerge looking more considered and effective.

SNP Conference: Shirley-Anne Somerville MSP with Professor Blair Grubb

Engagement with devolved administrations

The Society has been increasing its efforts to interact with the devolved administrations in Scotland, Northern Ireland and Wales, by taking part in events at Holyrood, Stormont and the Senedd. We have recently joined the Welsh Cross-Party Group on Science, Technology, Engineering and Mathematics (STEM), as well as the Scottish Cross-Party Group on Science and Technology. We are in the process of joining the Northern Irish All-Party Group on STEM.

These groups bring together politicians and government officials from the devolved areas and are a powerful platform to influence science policy right across the UK.

We have also attended **Science in Stormont in Belfast** and **Science in the Parliament** in Edinburgh. In recent years these conferences have become high profile events in the political calendar and involve the party leaders, chief scientific advisors and senior policy makers. By developing our relationship with policymakers in the devolved administrations, we are able to raise the profile of physiology in Scotland, Wales and Northern Ireland, as well as using this network to further influence UK legislation at Westminster.

Interested in these or any other policy related issues?

Please contact us via policy@physoc.org

New President and CEO

Dariel Burdass and David Eisner

David Eisner

President, The Physiological Society

It is a real pleasure to begin my term as President of The Physiological Society. Not only was it the first Society that I ever joined (in 1980) but it was where I gave my first scientific talk. This was no minor undertaking. As well as the usual fear of speaking in public, there was the added trepidation of the then custom of the Members voting on whether or not the abstract should be published (it was). Since those early days, I have enjoyed serving as both Chair of the Editorial Board of *The Journal of Physiology* and International Secretary.

We owe my predecessor, Richard Vaughan-Jones, a great debt for the way he has led it in the last two years. He has set a very high standard which will not be easy to match. What would I like to achieve in my own term? I see no need for revolution. Rather, I would like to consolidate all the excellent activities which the Society is carrying out. One exciting development is the creation of the *Europhysiology* series of meetings. This is a partnership between The Society and the two other large European Physiological Societies: the Scandinavian and the German Societies, in partnership with FEPS (the Federation of European Physiological Societies). Starting in 2018 with a meeting in London, there will be a meeting every two years, in 2020 in Germany and in 2022 in Scandinavia. These meetings will replace the usual annual meetings of the partner societies.

While I am sure that members will be well aware of our meetings and journals, many may not realise how much else we do. We have an active Policy Committee. This Committee engages with politicians and others to try to influence them on behalf, not only of our subject but of science in general. This area is a particularly busy one in the post Brexit era. Another important and related Committee is Education and Outreach which is charged with spreading the influence of physiology to students both in schools and universities. It appears to me that, although The Society does excellent work in these areas, we could do much more to involve our members and the public. My major goal is therefore to improve communications. In this context, it is frustrating that so few people seem to know what the word *physiology* means. It may be over-ambitious, but I would like to change this such that everyone from schoolchildren to politicians and captains of industry, not only recognises the word but has some idea of what the subject involves.

I am sure that all of our activities will benefit from closer links with other Societies. The science at our meetings has many overlaps and synergies with that of our sister societies in different areas of biology. More shared symposia and involvement in each other's meetings can only be a good idea. While we quite properly have our own identity, many of the threats we face are also similar to those of our sisters and, again, joint work seems to be the way forward. A few months ago, The Society became an enhanced member of the Royal Society of Biology, an organisation which can speak to government as a single, unified voice for the biological community. Other links are also valuable. Further afield, we should work hard to persuade non-scientists of the importance, not only of physiology, but of science in general. This will require making common purpose with our colleagues in Physics and Chemistry as was done a generation ago by Joe Lamb and Denis Noble when they established *Save British Science*.

I am delighted to welcome our new Chief Executive Officer (CEO), Dariel Burdass who will take up her post this month. Dariel has a degree in Microbiology and, after spending time teaching, moved to the Microbiology Society. She began as Education Manager before becoming Head of Communications. In these roles she has developed the Society's communications strategy in both traditional and digital media. Most recently, Dariel has served as Deputy CEO as well as Director of Strategy and Communications.

As well as the activities I mentioned above which are visible to all, much occurs behind the scenes. Our building (Hodgkin Huxley House) is a valuable financial resource and, as well as occupying it ourselves, we let it to tenants. As a charity and a business with an annual turnover of >£3M, we are subject to an ever increasing raft of regulations. The 30 or so staff employed by The Society carry out all this work in partnership with the Trustees and other members. The role of the CEO is of course to lead and coordinate these activities while helping the Trustees develop strategy. I am sure that Dariel will relish the challenge!

This is an appropriate moment to thank our interim CEO, Casey Early for the outstanding service he has provided since November 2015. Casey, Director of Finance, has been with The Society since 2003 as Director of Finance. Last year he was persuaded to put his beloved spreadsheets to one side and, while continuing his financial responsibilities, assume the mantle of CEO. In this position he led The Society's staff with great aplomb. I have been particularly impressed by the way he has spearheaded our interactions with sister Societies. His workload has been enormous and we owe him a great debt.

As a charity and a business with an annual turnover of around £4m, we are subject to an ever increasing raft of regulations. Our 26 staff carry out all this work in partnership with the Trustees and other members.

Meet our new Trustees

We welcome four new Trustees who were appointed in July 2016

Professor Bridget Lumb

University of Bristol

Proposed by Frank Sengpiel, Judy Harris, Sue Wray, Lucy Donaldson, Clive Orchard

My life would have been very different (and poorer!) if I hadn't taken a gap year before taking up my intended BSc place to read Geography & Sociology at Manchester University. It was during that formative year in the late 1970s that I had my first exposure to Physiology; working as a research technician in the then Department of Physiology at the University of Nottingham. I was hooked, changed my degree course to Biological Sciences at the University of Birmingham where, after the first year, I specialised in Physiology and Neuroscience. I have never looked back.

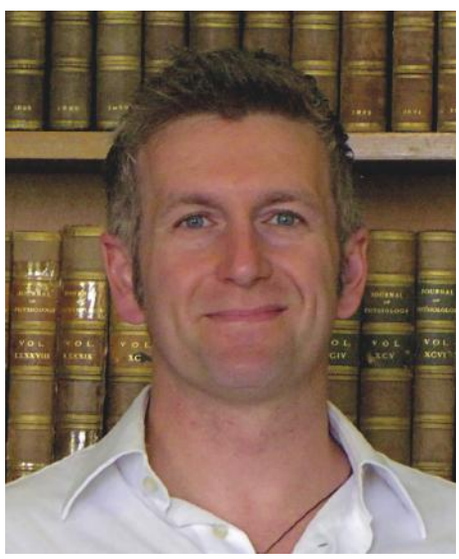
My final year undergraduate research project was when I discovered my enthusiasm for science and the excitement of working at the cutting edge; of being able to ask, and hopefully answer, questions for the first time. There are many others who can say the same and I'm a huge supporter of student projects. Since that first exposure my research has focused on central nervous system mechanisms of pain, anxiety and fear.

My career is not what I expected at the start of the journey – I thought it was about being at the laboratory bench, I'm a scientist after all! An academic career is what you make it, it is multifaceted and if you are lucky you can explore all sorts of avenues that are intellectually stimulating and make best use of your skills. Along the way I've taken on diverse management and scientific roles.

A BSc and a PhD from the University of Birmingham were followed by eight years of research positions in Birmingham, Leeds and Bristol, before securing a Lectureship in Physiology at the University of Bristol in 1990 where, since 2008, I have held a Chair in Systems Neuroscience. I was Head of the School of Physiology, Pharmacology & Neuroscience from 2008-2015 and am currently an academic member of the University's Board of Trustees.

Like most academics my day job encompasses teaching and research. The research has been funded since 1990 by RCUK and The Wellcome Trust and I've taught Physiology and Neuroscience for the best part of 40 years. One of the most enjoyable and satisfying aspects of the job is training students at an early stage in their careers and then watching them fly once they leave the nest.

I have a long association with The Physiological Society; presenting my first communication in 1983 and becoming a Member of the Society in 1990, the year I secured a lectureship and my first research grant – good things come in threes! I have held a number of significant positions within The Society which will equip me well for my new role as President Elect. These include, Meetings Secretary (2002-2006), Chair of the IUPS Organising Committee (2009-2013), Editor then Deputy Chairman of Experimental Physiology (1996-2003). In 2015 I was delighted to be elected as an Honorary Member of The Society. In the role of Deputy President of The Physiological Society I will endeavour to execute my remit of guarding the long term future of the Society, championing the discipline of Physiology and ensuring the highest possible standards of governance. I also hope to have some fun along the way.



Federico Formenti

King's College London, Guy's Campus

Proposed by Jeremy Ward, Keith Dorrington, Peter Robbins, Prem Kumar, Steve Harridge

I am arguably one of the most grateful members of the Physiological Society, through which I have met my wife. Beware any unmarried physiologist who is planning to attend the annual meeting! Jess and I met at the International Union of Physiological Sciences in 2013, in a potentially romantic city with more canals than Venice: Birmingham. We were joined this summer by a little baby, Joy Nella, who bravely gave me my first practical class on the positive feedback mechanism of childbirth.

I attended my first human physiology course at the university in Verona, Italy, my hometown. The lectures were taught by the late Giampaolo Fantin, who made physiology simple and fascinating for the few curious students attending his Friday afternoon lectures. I then worked in a few rather different areas, starting with human locomotion biomechanics and energetics with Alberto Minetti at Manchester Metropolitan University. An adventurous scientific expedition on the Himalayas linked me to the world that lives with little oxygen, hypoxia.

The enlightening Peter Robbins and Keith Dorrington stimulated my interest in exploring the role of the hypoxia-inducible factor in the regulation of human metabolism and respiratory physiology. Most experiments were performed in their laboratory in Oxford, in the less adventurous environment of a hypoxic chamber, from which one can see Mount Everest, but only in a picture on the wall. I was one of the Society's Affiliate representatives during this time. After some time in Greg Anson's department in Auckland, and a postdoctoral fellowship developing a rapid intravascular oxygen sensor with Andrew Farmery and Clive Hahn in Oxford, I joined King's College London in January 2016. Here, I hope to continue a multidisciplinary research programme, and to be for many students as good a teacher and supervisor as those who guided my studies.

I am delighted and excited to join our colleague Trustees on Council. It is a great privilege and responsibility to guide the Society in achieving its charitable aims; I am interested to hear constructive criticisms from members who would like to suggest changes to the way the Society is run. I will support in particular the development of research and educational ideas. Meanwhile, I may start with something small, such as suggesting that we change the name of the 'Unconscious bias' courses to 'Subconscious bias'. And I apologise in advance if I am ever found unconscious, and appear to behave in a very biased fashion.

Professor Graham McGeown

Queen's University of Belfast

Proposed by Susan Wray, Ken O'Halloran, David Eisner, Stewart Sage, Prem Kumar

You never can tell how life is going to turn out! One's professional life may look like it was all part of some strategic plan when laid out in a CV, but often the pattern is only clear looking back, like an already-completed puzzle.

That has certainly been my experience, at least. At secondary school, I so disliked biology I gave it up after 3 years to concentrate on maths and the other sciences. By sixth form I was set on a career in physics, when a forceful relative persuaded me to apply for medicine, as that was a 'proper subject'. I now recognise that this was a dubious proposition but I was easily swayed back then. In those early years of study, however, physiology struck me as a subject which combined serious science with a desire to understand the body, something which attracted me then and still attracts me today. So, after a couple of years as a junior clinician and a PhD in physiology to go with my intercalated BSc, I settled down to an academic career that has kept me engaged and largely out of mischief ever since. I have been a full member of the Society since 1990 and have previously served on Council and Executive Committee, acting as Honorary Treasurer.

The widespread re-organization of British universities around research themes has, I believe, been a largely sensible strategy, but it does pose its own challenges, generating considerable existential angst as to what it means to be a physiologist. However, emphasising broad definitions that focus on the importance of function and control, rather than specific experimental approaches, reveals how central our interests are to all biology. Any biomedical science that does not embrace these ideas is a rather limited construct. From the explosion of molecular information through to rapid developments of functional imaging techniques, physiology is all around us in research and clinical practice. And many of the great challenges in biology, particularly those inherent to the study of complex integrated systems such as the brain or the whole body, take us back to the roots of physiology as a science that looks at the connectedness of things. If physiologists don't put Humpty together again, who will?

That said, the concept of physiology as a body of knowledge and way of thinking is under threat. My sense is that relatively few young scientists identify themselves as part of the community of physiologists and the level of 'name recognition' among the general public for 'physiology' is possibly lower than that for subjects such as anatomy or microbiology. Of course, much of this is speculation and perhaps we need to do some research to find out just what the world thinks of us, if anything.

I believe The Physiological Society should play an important role in all of this, providing a virtual 'home' for those engaged in teaching and researching how life works, as well as promoting the excitement of it all to the public at large. For me, it will be both a pleasure and an honour to contribute to this as a Trustee and member of Council. Who knows how this 'piece' will affect the 'puzzle' that is my life but it will be fun finding out.

Dr Sarah Hall

Cardiff University

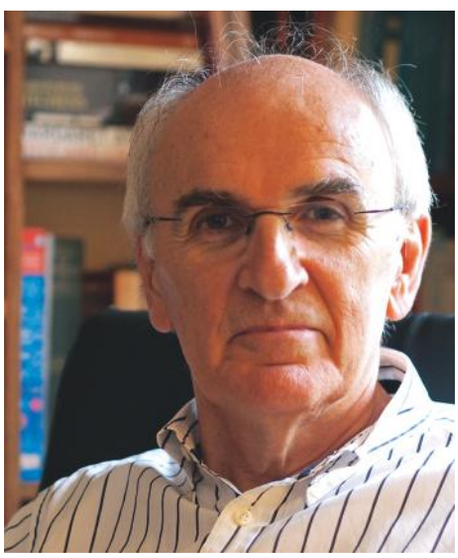
Proposed by David Miller, Daniela Riccardi, Rachel Tribe , Susan Jones, Judy Harris

I am a Senior Lecturer in Physiology at Cardiff University and am involved in physiology teaching and learning at all levels and across all biomedical science degree schemes, as well as the Medical and Dental courses.' My research career was built on a foundation of electrophysiology, but more recently I have developed a primary focus on education. I remain connected to current research activity through my role as coordinator of the research placement 'sandwich' year degree schemes; I have a particular interest in evaluating the academic, professional and personal benefits of undergraduate research placements, and have established scholarship activity in this area. I also contribute to a range of education and outreach activities and am committed to engaging school pupils and the general public with the discipline of physiology and the activities of the Physiological Society.

I have been a member of the Society since 1996; I have served on Council once before and also on a range of committees. As a Trustee and Chair of the Education and Outreach Committee, I will work to uphold and foster all the aims of our Society, particularly those supporting teaching and learning of physiology and raising the general awareness of and appreciation for our discipline.

Editor's Note: Sarah was for very many years a valuable member of the Editorial Board of Physiology News. (We had no term limit until recently.) I found her always very helpful and diligent, and would like to thank her for her particularly rapid writing of an article about Cardiff for the 2015 main meeting. I am sure she will be a brilliant Trustee.

Valedictory thoughts on the History & Archives Committee



David Miller

Former Chair, History & Archives Committee

In August, I finished a four-year stint as Chairman of The Society's History & Archives Committee (HAC) and the Editor asked me to offer some thoughts on my time.

I first joined HAC in 2006. It had recently been revived by Dafydd Walters. DW, the Committee Secretary from 2002 to 2004, was keen to re-establish a wider appreciation of the people and ideas that characterise both The Society and the discipline we serve. In 2012 I succeeded Dafydd as HAC Chair. The main planks of HAC's work have continued to be: promoting interest in all aspects of the history of physiology, managing the Paton Fund for Historical Studies (physoc.org/paton-prize-bursary) and overseeing The Society's archival collection (see: archives.wellcome.ac.uk [use the Reference SA/PHY under the 'Archives & Manuscripts' tab for a comprehensive listing]). HAC also administers the Paton Lecture (jointly with the *Experimental Physiology* Board – see **www.physoc.org/sites/default/files/page/Lectures%20and%20Prizes%20to%202015_3.pdf**) and runs an Oral History programme where senior members are interviewed in an informal manner (physoc.org/oral-history-transcripts). HAC encourages the submission of short articles, notes and pictures for *Physiology News*. In a more sombre role, we try to ensure that death notices and, where possible, obituaries of deceased members are made available in *Physiology News* and/or on the website (**physoc.org/obituary-notices and via physoc.org/obituary-notices/members-obituaries-h for full alphabetical listings**).

In an earlier article in *Physiology News* (*PN* 90, Spring 2013, p13), I tried to encapsulate our role thus: 'From the earliest days, the Society has sustained an interest in its own history. This includes how and why the Society was founded, the background to our owning *The Journal of Physiology* and *Experimental Physiology*, how we ran and run our scientific meetings, the forging of our international membership and collaborations. These aspects often entwine with the careers and collaborations of prominent personalities amongst the membership. Furthermore, as with any organisation, there are more formal elements to the archiving of paperwork and records. An abiding interest is to clarify how the intellectual discipline of physiology can be understood better through knowledge of these historical strands.'

At The Society's annual meeting, the HAC stand affords an excellent way to meet members and to increase awareness of, and contributions to, HAC's work. It has proved a valuable opportunity to meet members and gain new insights from them. I have also used the chance to photograph quite a number of you – my vain attempt to add to the work of the late Martin Rosenberg who, for many years and with great distinction, was photographer to The Society.

In 2014, I launched the free-access, web-based Physiology Family Tree (hosted at **academictree.org/physiology**). This provides a dynamic, user friendly way that each of us can locate ourselves in the tangle of roots and branches that helps to describe our science. A strict genealogy based on the near-parental, supervisor-research student relationship is not reliably adhered to in the entries. However, the intellectual and practical links between physiologists and to cognate disciplines becomes very evident. (I have been amazed how relatively few colleagues are aware of, never mind familiar with, their own scientific 'grandparents' and thus the thinking and technologies that will have helped to inform their own supervisors). I encourage you to add or enhance your own 'presence' on this family tree with whatever information you can provide.

I helped to instigate HAC's current planning to enhance the representation of physiology and physiologists in Wikipedia. We will commission input from a professional Wikimedian both to facilitate enhancing the quota and the quality of entries on Wiki, as well as to broaden the generic skill-base in Wiki editing amongst the membership and Society staff at Hodgkin Huxley House.

HAC stands (clockwise from top left) at Edinburgh Physiology 2012 (P12), London P14, Birmingham P13 & IUPS, Cardiff P15

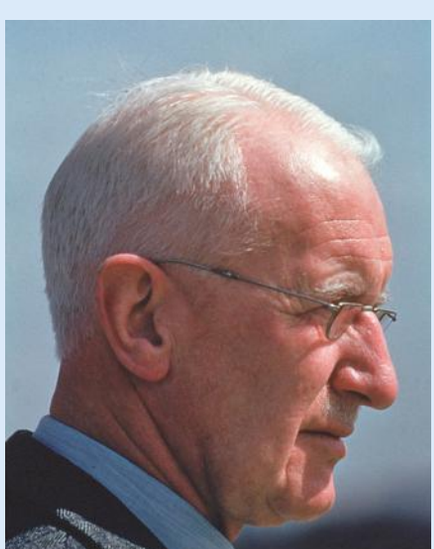
As ever with committee work, one is greatly dependent on the support and advice of colleagues. I have been fortunate to share my enthusiasm and interest with some exceptional Society members. I especially acknowledge Tilli Tansey, the Society's Honorary Archivist whose professional expertise in biomedical science history and intimate knowledge of The Society's long story have been a constant reassurance. Staff at Hodgkin Huxley House have provided excellent support and advice to HAC, and to me personally, in helping fulfil our tasks: Jonathan Goodchild and, more recently, Chrissy Stokes and Anisha Tailor have made my work possible and enjoyable.

Future plans for HAC include a greatly enhanced 'presence' for our work and resources on the Society website as its planned overhaul unfolds.

I hand on these responsibilities now to my successor, Graham Dockray. I wish him every success, as well as the pleasure I have found in experiencing The Society's workings close-up and especially the chance to interact with so many of you, the members.

The Society receives AV Hill's Nobel Prize Certificate

As reported previously (see *PN* 101, pp16-17, Winter 2015) a Blue Plaque was unveiled at AV's former home in Highgate last year. Dr Julia Riley (of Cambridge University and Girton College), one of AV's grandchildren, was attending the event where she met me. She generously offered AV's Nobel Prize Certificate to The Society on behalf of the family, several more of whom were also at that event. (The Nobel Prize Medal is held at AV's old school, Blundell's, in Devon.) AV's grandchildren attended the Society's 'Winter Party' at Hodgkin Huxley House (HHH) for the formal hand-over of the magnificent Certificate. A facsimile will be on permanent display at HHH with the valuable original suitably archived. A charming personal detail is that HHH already has AV's dissection spectacles on permanent display, together with those of AV's pupil, Bernard Katz.



AV Hill pictured in 1955 (Photograph by Harold Lewis)

Chair of the Policy Committee 2012–2016: From start to finish

Mary Morrell

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

In the 1960-70's Harold Wilson championed the phrase 'a week is a long time in politics', and as we have recently found the political landscape can change very quickly. The impact of these changes is not always immediately apparent; nevertheless, the actions of policy makers within Government (and beyond) do matter. It was this belief that led me to apply to be Chair of The Physiological Society Policy Committee back in 2012.

Four years ago I knew that the Policy Committee was active in responding to government legislation that affected physiologists, in particular supporting the need for essential animal research. I proposed that by expanding these activities it may be possible to raise awareness inside and outside government of the importance of physiology; ultimately leading to an increase funding and career opportunities for physiologists. To achieve this there was a need to increase awareness of the Society's policy work, and to expand the number of people involved.

Since 2012 much has changed within The Physiological Society. It has entered a new phase, buying its own headquarters (at Hodgkin Huxley House) and appointing a new CEO. The Policy Committee has also changed significantly; it has become a vibrant, influential team of people, working hard to make a difference. This article outlines many of our activities past and present and I would encourage you to read on, and as you do so, ask yourself: *is there something you can get involved with?*

Health of Physiology

When starting a journey it is necessary to know where you are, before you can move forward. The Policy Committee was therefore pleased at the adoption of an early suggestion to investigate the 'health of the discipline of physiology'. A steering group of Society Members and external stakeholders, chaired by the Society's (then) Deputy President, Professor Richard Vaughan-Jones, was formed. The group was the first of its kind to review the amount and scope of physiology research, plus the number students being trained and the location of courses. Data was collected from approximately thirty universities. The legislation affecting physiology was also reviewed. The intention was to use this information to inform the work of the Society, to decide how to support the future of the discipline, and to select areas of priority.

It is fair to say that it was harder than anticipated to produce the Health of Physiology report, not least because it needed to be fitted into all the other activities of The Society. That said, the report was released at the annual conference in July 2016. The overall conclusion was optimistic, with physiology remaining a key discipline and a healthy number of students being trained. The report can be downloaded from the website, and its recommendations are stated here in Figure 1. Please see: **www.physoc.org/health-physiology-0**

Engaging with MPs

A critical part of the Policy Committee's work is to engage with policy-makers. sometimes this has resulted in a call to our members to contact their local MP about specific issues. In 2014, the Policy Committee organized a workshop to provide members with more information on engaging with policymakers. The Policy Committee also often works in collaboration with other organizations to widen its network, and strengthen its voice. In particular, unifying the voice for biosciences has helped in our responses to many consultations (Figure 2).

Moreover, the Policy Committee was delighted when in March 2016 The Physiological Society became an enhanced supporter of the Royal Society of Biology. It is hoped that this link will facilitate closer working in key areas throughout our remit.

Animal Research

The *In Vivo* Sub-Committee exists in part to respond to consultations on regulation and legislation around animals in research. The Society position statement on the use of animals in research, which the committee have developed, can be found on our website. The Society is also actively involved with the Animals in Science Regulatory Unit of the Home Office and I would personally like to thank Professor Max Headley for all his work in this area. His knowledge and skills have been a great help to the Policy Committee. To find out more about our important work on issues such as the 2015 European Citizens' Initiative 'Stop Vivisection', and the Transposition of EU Directive 2010/63 please visit (**www.physoc.org/animals-research**).

Supporting Women in Physiology

The Society is committed to increasing equality and diversity in Physiology, and the Policy Committee has supported many initiatives, including responding to the House of Commons Science and Technology Committee inquiry on 'Women in STEM careers'. In 2013 the Society produced a 'Women in Physiology' booklet. Launched at IUPS in 2013, interest in the booklet exceeded all expectations and we ran out almost immediately!

On the 23 January 2015, The Physiological Society marked 100 years since its first women members. To celebrate the achievements and contributions of 20th and 21st century women physiologists, The Society has produced a second book. I am also delighted that in the not too distant future, Professor Bridget Lumb will become The Society's first female President.

The skills pipeline

- Physiology teaching at all levels should include effective practical content, and assessment of practical skills
- Universities and learned societies should ensure that career advice and development is available to those pursuing physiology (or to physiology students taking their skills elsewhere)
- Schools and universities should promote physiology so it is something that students are aware of, can identify with and want to study

The value of research

- The value of animal research should be consistently and openly communicated, with support for the 3Rs (reduction, replacement, and refinement of animals in research)
- Government should commit to a long-term increase in the science budget. Further, it should ensure the formation of UK Research and Innovation and reorganisation of the Research Councils allows flexibility of funding for fundamental, applied and interdisciplinary research covering all branches of physiology and associated subjects

Diversity

- Diversity should be promoted in the STEM subjects, and learned societies must increase diversity within their leadership and membership

Visibility

- Physiology research and teaching should be identified and defined as such in order to retain the academic community of physiologists
- Organisations representing physiology should strengthen national and international collaborations to communicate a united vision for the future of physiology

Figure 1. Recommendations made by the Policy Committee's Health of Physiology report

Education Policy

Hardly a week appears to go by without an announcement from the Government on education policy. For many years, The Policy Committee has linked with the Education and Outreach Committee to actively support physiology education at all levels. Within higher education, The Society has led work on the reward and recognition of higher education teaching, chaired by Professor Judy Harris, who has had a huge impact on the field.

In 2014 The Society, in collaboration with the Academy of Medical Sciences, Heads of University Biosciences, and the Royal Society of Biology, conducted a survey of over 250 academics across UK bioscience departments. The resulting report called for an urgent change in the teaching/research culture. In 2015, The Society also published a booklet to raise awareness of the status and valuation of teaching in careers in Higher Education. In addition, teaming up with the think tank Demos, we held fringe meetings at the 2015 Labour and Conservative Party conferences. The meetings aimed to raise awareness of the issues associated with Higher Education teaching. They were well attended, and this engagement route has been used again this year. Then came the Department for Business, Innovation and Skills' Green and White Papers, with changes that include the introduction of a Teaching Excellence Framework (TEF) to assess the quality of undergraduate teaching at all higher education institutions in the UK. The impact of the TEF is yet to be determined but we are working to positively influence it.

Imagine where it will end...

It has been a privilege to Chair the Physiological Society Policy Committee. The Committee has dealt with a wide variety of issues that are of importance to physiology, and I have learned a huge amount from our members and staff. My particular thanks go to the past and present Policy Staff: Michelle Brook, Ed Hayes, Saranjit Sihota and Henry Lovett, plus the Education Team led by Chrissy Stokes and chaired by Professor Blair Grubb. We could not have done any of this without the support of past Presidents Professors Jonathan Ashmore and Richard Vaughan-Jones, as well as CEOs Philip Wright and Casey Early, and of course all the members of the Policy Committee. I am delighted that the Committee will be continuing its important work in the capable hands of Dr Lucy Donaldson and the Physiological Society Policy Staff.

Above all, I hope I have said something that will prompt, inspire or irritate you enough to take action. The recent vote to leave the European Union will have significant effects on the science sector, some of which are already being felt – I personally have been asked to step aside from a (European/EU) Horizon 2020 application that I helped to develop. The future policy work of The Society will aim to protect physiology research in the new regulatory regime, ensuring access to funding and the success of international collaboration. Sometimes when you start a journey you can never imagine where it will end, but I will continue to believe that if we act together, we can make a difference, although sometimes we have to play the long game.

February 2016

Contributions to Innovate UK's integration with Research UK

December 2015

Independent Commission on Freedom of Information

November 2015

BIS Green Paper on Higher Education and Research

June 2014

Section 24 of the Animals (Scientific Procedures) Act – Home Office consultation

September 2013

Women in STEM careers – Commons Science and Technology Committee inquiry

May 2013

Research funding – The Department for Business, Innovation and Skills call for views

March 2013

Open access – HEFCE call for views

February 2013

Open access – Select Committee inquiry

September 2012

Institute for Public Policy Research call for evidence on the future of higher education

June 2012

Sport and exercise science and medicine: building on the Olympic legacy

Figure 2. Policy Committee consultation responses 2012-2016

2017 – 2018

10 February

Fulfilling your obligations as an A(SP)A Project Licence Holder
Hodgkin Huxley House, London, UK

www.physoc.org/fulfilling/

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/

1 August

IUPS 2017 – The Rhythms of Life
RIOCENTRO Exhibition & Convention Centre

www.physoc.org/iups2017/

14-16 Sept

Europhysiology 2018
The QEII Centre, London, UK

www.europhysiology2018.org

Meeting Notes

Limits of Perception: Advances in Bio-imaging

8-11 August 2016,
University of Warwick, Warwick, UK

Daniel Stuckey, Tim Witney & Mark Lythgoe

Centre for Advanced Biomedical Imaging, University College London, UK

Nearly two years ago the Physiological Society approached us at University College London's Centre for Advanced Biomedical Imaging (CABI) to help them plan and organise a Topic Meeting. Our goal was to explore the interface of biomedical imaging science and physiology, emphasising the next generation of imaging tools that may not be visible to those in the field of physiology. We were excited by the challenge of bringing together many of the world's leading imaging researchers in order to bridge that gap in understanding. Our primary aim was to kindle discussion and future collaboration across all scales of physiology and imaging, from the microscopic, through to the whole organism and into the clinic. In order to facilitate discussion we decided to make the conference residential, so there was nowhere to escape! Thankfully Warwick University provided the perfect venue, with good food and a well-stocked bar!

We were delighted to have been able to attract such a broad range of truly leading international scientists to speak about the next generation of imaging tools, including the current President of the World Molecular Imaging Society, Prof Christopher Contag. Notable highlights included Clare Elwell's use of Near Infrared Spectroscopy to image autism in babies in rural Africa, Chris Contag's next-generation fluorescent endoscope and Dara Kraitchman's use of MRI to image large animals (including a tiger at one point!), to name but a few. We were also fortunate to hear a wide range of exceptional proffered talks from young investigators. The success of the meeting however was not built around the speakers or the programme, but relied on the audience. What stood out for us was the quality of the discussions after every talk, sometimes lasting 30 minutes or more. The fear of being called upon for a question by our random number generator, made sure everyone from the audience had a contribution for each speaker!

This Topic Meeting provided the platform for us to learn, challenge and interact with scientists from different disciplines, whilst building relationships that hopefully can change imaging science in physiology. But most importantly we had lots of fun, enjoyed the exciting science and made some new friends.

Mark Lythgoe presenting the coveted Prize for best Oral Presentation to Natalie Andrews from Imperial College London

Meeting Notes

History & Archives Committee seminar

13 September 2016,
The Wellcome Library, London, UK

David Miller

Former Chair, History & Archives Committee

The Society's History & Archives Committee (HAC) hosted a seminar at the Wellcome Library on 13 September with over 30 members attending. Our aim was to link up with members who had expressed an interest in aspects of the history of the discipline and of those who have contributed to our science.

The session was introduced by Graham Dockray, the new Chair of HAC. Tilli Tansey, the Honorary Archivist, gave a *Brief History of The Society*, touching on several strands of the mid-Victorian scene that led to the inaugural meeting in 1876 called by John Burdon Sanderson. The early stages of the transition from dining society to science-based meetings with an associated dinner were delightfully related. Anisha Tailor from Hodgkin Huxley House outlined the broad strands of HAC's work and its place within The Society's organisation. I gave a presentation on aspects of my biographical work on Sydney Ringer, emphasising how I have actually gone about researching his life and times. Amanda Engineer, an archives project manager at the Wellcome Library and long-time member of HAC, then provided an overview of the collections at the Library and explained how the online catalogue covers The Society's archive that is housed there. The group then split into two with one half forming small break-out sessions to consider a few pre-set questions. These were designed to encourage feedback to HAC on aspects of how we can best further our aims to record our history and that of physiologists of note. The other half enjoyed a conducted tour of the Library and a wonderful 'hands-on' encounter with a range of photos, letters and other items chosen by Amanda Engineer from our archive. Examining some Grey Books from the first decades of The Society, riffling through Edwardian photos of the great and the good, their labs and colleagues and similar fascinating items was a true novelty for many attending. The two half groups then changed places.

The final session of the meeting was a Plenary Lecture by Vanessa Heggie (University of Birmingham) entitled '*The History of Elite Performance*'. Vanessa revealed that historians have been rather slow to examine the history of sports physiology and sports science. She considered why that might be the case, and discussed the challenges and rewards of writing about this sort of history. Going beyond the usual stories of drugs and training, she outlined the interactions between Western sport and science over the past two centuries, and explained how and why physiologists' ideas about human performance have evolved. She also showed how sports people have helped to change the way we research, and how we think about our bodies, as well as contributing to the development of space travel, premature infant care, and even public health interventions. It proved a fascinating excursion from the Victorian enthusiasm for 'Pedestrianism', extreme long-distance track walking as a public spectacle, right through to the evolution of physiological testing at the Olympics and the present-day preoccupations with drug testing.

The seminar proved a lively and stimulating event. HAC has made an excellent connection to a number of Society members through this first-time seminar under our auspices. We intend to use the feedback from the breakout sessions and individual participants to inform our work and to foster links with a network of those enthusiasts for this route to insight into physiology and physiologists.

Meeting Notes

The inaugural H³ Bayliss Starling Symposium: Novel Approaches to Hormone Sensing

14 September 2016,
Hodgkin-Huxley House, London, UK

Timothy Wells

Cardiff University

Since Bayliss and Starling's initial discovery of secretin more than a century ago, the number of hormones identified in humans has risen to more than seventy. This success has been achieved by quantifying hormones using antibody-based approaches in plasma or serum, but processing blood samples in this way limits our understanding of the more dynamic processes of hormone secretion. To address the challenge of developing the device on every endocrinologists' wish list – a sensor to measure hormones *in vivo* – the Physiological Society held the Inaugural H³ Bayliss Starling Symposium on Novel Approaches to Hormone Sensing at Hodgkin Huxley House on 14 September.

Organised by Drs Tim Wells (Cardiff University) and Paul Le Tissier (Edinburgh University), this symposium brought together endocrinologists, protein chemists, physicists and engineers and representatives from the UK-based funding bodies to explore novel approaches to real-time hormone sensing. Delegates from a range of academic and commercial backgrounds were treated to presentations on the significance of hormone dynamics, hormone-receptor interactions, light-based biosensing and electrochemical biosensing.

With such a wide range of expertise on show, the day proved to be mind-stretching and the discussion sessions lively and incisive. Among the experts to address the meeting, Frank Vollmer (Max Plank Institute for Light, Germany) commented that 'The H³ symposium was a great success. The discussions opened my eyes to the powerful applications that will be enabled by emerging optical biosensor technology. I left London with a notebook full of exciting new ideas and contacts for collaborations. I hope there will be more meetings just like this!' Similarly, John Kopchick (Edison Biotechnology Institute, Ohio, USA) commented that the variety of views presented and expressed 'will ultimately help define this novel area'.

Fiona Marshall (Heptares Ltd, Welwyn Garden City, UK) concluded that 'If only we could easily measure hormone levels in real time in precise locations without having to take lots of blood and tissue samples, it would revolutionise our understanding of disease and responses to drugs. This symposium brought together experts in endocrinology, hormone receptors, physics, engineering and material sciences to begin to make this a reality.' It will be gratifying to witness the development of functional hormone sensors from such blue-sky events.

Three cheers to the Physiological Society for hosting such a forward-thinking cross-disciplinary event.

This symposium was supported by funds made available as a consequence of the merger in 2014 of the Bayliss and Starling Society with the Physiological Society. The Bayliss and Starling Society had originally been formed in 1979 to promote research on central and peripheral regulatory peptides. The same funds also support the Bayliss and Starling Lectures of the Physiological Society.

Meeting Notes

International Conference of Physiological Sciences (ICPS) in China

25-28 September 2016,
Chinese International Congress Centre,
Beijing, China

Fiona Gribble

Professor of Endocrine Physiology,
Institute of Metabolic Science,
University of Cambridge, UK

Chuanyong Liu, David Grundy, Kim Barrett, Fiona Gribble, Tor Savidge, Weifang Rong, Speakers and chair at the *JP*-sponsored symposium at ICPS

Having to divide my time between research, teaching, clinical responsibilities and my family, it was with some caution that I agreed to speak at the ICPS jointly organised by the Chinese Association for Physiological Sciences (CAPS) in Beijing, to be held from 25-28 September 2016. Even then, I admit, I was only moved to accept because the invitation was from our new editor of *The Journal of Physiology*, Kim Barrett, who submitted a proposal to hold a symposium on Enteric Neurobiology and Sensory Signalling, jointly sponsored by The Physiological Society and *The Journal of Physiology*.

I have been to Beijing twice before. The first was in 1994 when China was still relatively closed. We were accompanied around the clock by an official escort who took us only to approved tourist destinations. We spoke to local people whom our Chinese official had organised in advance, and we saw what we were meant to see. I visited again briefly in 2011, although didn't then have the opportunity to see much more than my hotel room, an official souvenir shop and the conference venue.

My impressions of Beijing in 2016 are of a city transformed over the past 20 years. We travelled freely around the city – or at least as freely as it is possible to travel without any knowledge of the language. Our hotel was in a less than salubrious side street – not a problem except when trying to find a taxi driver who would admit to knowing its location. On one occasion it took me 5 attempts to find a taxi willing to take me the 10 minute ride back from the conference centre, even though I showed them my hotel card containing a map with the directions in Chinese. One taxi driver even threw me out after a circuit round the block, waving his hands to indicate that he really didn't know where to go.

What of the meeting itself, though? It was centred around the 90th anniversary of the Chinese Association of Physiological Sciences, and jointly supported by physiological societies from around the world who had partnered together to sponsor individual symposia. Apart from physiologists within China, CAPS made efforts to secure the participation of the many Chinese physiologists who have established laboratories in other parts of the world. The conference location was the Chinese International Congress Centre, just across the road from the Olympic Park. To say that we 'populated' the Congress Centre would be to stretch the imagination, as like other Chinese enterprises, the International Congress Centre is vast. With approximately 1000 delegates, however, ICPS did manage to occupy one small section, centred around a poster/exhibit area and with a number of halls variously capable of seating 50 to 500 people. The overall atmosphere was much like many other national and international conferences, and the meeting structure was based around a few selected plenary sessions, followed by series of parallel specialised symposia.

As I sat down, slightly late, to watch my first plenary talk (on lipid droplet fusion and growth), delivered by Peng Li, a Chinese physiologist who trained abroad, I was feeling after the first 5 minutes that I was wasting my time as the lecture was covering some very basic introductory concepts that I'd heard many times before. Almost in an instant, however, the gear then changed and I was treated to some outstanding science, images and mathematical modelling, that I suspect are world-leading in the field. Of course I should have guessed that plenary speakers are selected for a reason!

The symposium at which I was invited to speak consisted of 5 speakers, mixed international and Chinese. The room had a seating capacity of about 60 but was full. All talks at the meeting were conducted in English, and I suspect that the majority of the audience could follow most of the dialogue because we were neither requested to speak particularly slowly, nor was there an attempt at simultaneous translation. I was relieved at the latter, because my 2011 experience of speaking with simultaneous translation taught me that this slows a talk down to a snail's pace and requires the omission of all interesting minutiae! Our symposium was chaired by Kim Barrett and brought together speakers on enteric neurology (David Grundy, Sheffield, UK), entero-endocrinology (myself, Cambridge, UK), gut microbiota (Tor Savidge, Houston, US), enteric oxytocin (Chuan-Yong Liu, Shandong, China) and afferent dysfunction (Wei-Fang Rong, Shanghai, China). Our audience was mostly made up of young Chinese physiologists who were shy in asking questions (who wouldn't be in a foreign language?) but had all the appearances of being engaged. Certainly there was less discussion and debate after each talk than you might find at a UK meeting, but I don't believe that reflected a lack of interest from the audience.

Later in the day, I slipped into the back of a session for young physiologists. True to the spirit of the meeting, they were all speaking in English even though I was probably the only native English speaker in the room. I only once saw a speaker talk in Chinese, and I think she was added late to the programme to replace someone who couldn't attend. Her switch from English to Chinese was not met with approving looks from some of the more senior Chinese scientists in the audience.

Although I only stayed for one day (I generally prefer to arrive home before my body has even considered adapting to a change in time zone), the meeting was scheduled over 3 days and consisted of 7 plenary lectures, 38 symposia, 4 young physiologists' symposia and over 300 posters. Like other Physiological Society meetings, the symposia and poster sessions covered topics ranging from cardiovascular and respiratory physiology to cellular physiology and neuroscience. A poster session you might not routinely find at a UK Phys Soc meeting was one on Traditional Medicine, but this was relatively small, comprising only 12 presentations. From the levels of attendance I saw, I'd be surprised if most of the young Chinese physiologists didn't spend the majority of the meeting attending one session or another.

An outstanding feature of the meeting was the friendliness and generosity of our Chinese hosts. We met together for dinner the evening before our symposium and were treated to a feast that was accompanied by a large number of toasts with rice wine, and culminated in a generous serving of Peking duck. Our souvenir postcards informed us that we had been served something in the region of the restaurant's 1.96 millionth Peking duck! From there we took a taxi to an area of the city that translates as 'Back Sea' – a small lake surrounded by restaurants and bars. Our pavement table, on which was soon arrayed a multitude of beer bottles (the Chinese prefer German beer to their own brew), gave us views both over the lake and to the bar interior where we were treated alternately to a young band playing western-style music, and pole dancing, Chinese style. Witness some bad heads the following morning!

My take-home feelings are of a country much modernised since I last visited, and of the spirit and enthusiasm of the next generation of Chinese physiologists. Not for them will be careers of publishing in low impact journals or testing yet another traditional Chinese herbal extract. Many are gaining practical training abroad, and others who have spent time in the UK and US are returning to generous job offers in China. I suspect we are witnessing the tip of a future iceberg of Chinese excellence in physiology and other sciences – fuelled by increasing local scientific standards, the enormous and highly driven population, and the economic weight of the Chinese powerhouse.

Recognising then that we will likely be overtaken in the next decades by a tsunami of Chinese scientific excellence, I think it should be our pleasure and duty to arm the next generation with the tools of the trade, and with our ideals of collaboration and scientific integrity. Although a joint meeting of ICPS and the Chinese Association for Physiological Sciences is not one to which I would currently send my PhD students and post-docs – the benefit versus financial outlay does not yet stack up in its favour, except for researchers proactively seeking to develop Chinese contacts for career purposes – I strongly support its concepts and ideals. I would certainly encourage colleagues to accept any invitation to speak at a similar future meeting. It is an excellent forum to showcase state-of-the-art science to a growing cohort of young receptive physiologists who probably don't yet have many opportunities to travel to meetings in the west but are likely to include some of our future international scientific leaders.

Sally Howells at the ICPS conference site

Two other members who attended the Chinese meeting have also written about their impressions. We print these comments here to amplify Fiona's view.

David Eisner

President, The Physiological Society

My impressions of the Beijing meeting were very similar to those expressed by Fiona. I too heard some excellent science It was also a delight to have two days with blue skies when I could see the hills in the distance as opposed to the, all too frequent, smog. Our Chinese colleagues were wonderful hosts although I did have to invent a coping strategy to deal with the large number of toasts at dinner. It was worth getting ridiculed as I sipped the 50% spirits rather than downing in a single gulp. The success of this meeting augurs very well for the 2021 IUPS meeting to be held in the same conference centre. It would also be good if the links between our Society and the Chinese could be developed further by the Chinese attending our Annual Meetings.

Jeremy Ward

Faculty of Life Sciences & Medicine, King's College London, UK

I was delighted to be invited to the ICPS and speak in the Experimental Physiology symposium 'Role of ion channels in pulmonary arterial hypertension'. This was my second trip to Beijing, one of the world's great cities, and it was fantastic to hear some of the really world-class science being performed by our Chinese colleagues. Our symposium was organised by Jian Wang of Guangzhou Medical University and Arizona University, whose delightful students made us welcome and looked after us throughout the whole visit. Even though our session took place on the last morning of the conference and after the (highly enjoyable) banquet the night before, our lecture hall was completely packed (I even saw the CEO of the American Physiological Society in the audience). The presentations were novel and interesting (apart from mine of course), and elicited some excellent discussions.

All in in all it was a highly successful symposium in a highly successful conference. I look forward to the IUPS in Beijing a few years' time!

Meeting Preview

A cascade of falling dogmas? Brazil 2017 beckons with the theme The Rhythms of Life

1–5 August 2017, RIOCENTRO Exhibition & Convention Centre, Rio de janeiro, Brazil

Denis Noble

Department of Physiology, Anatomy & Genetics, University of Oxford, UK

Denis pictured in front of the Iguacu river waterfalls

On the border between Argentina and Brazil the Iguacu River (*I-guacu* is literally 'large river' in the local indigenous language) cascades down from a plateau in a series of spectacular waterfalls. Getting right up close to one of the largest drops I felt the thunderous noise and the fine spray as I watched it descend into the *The Devil's Throat*, where I was a few minutes previously, perched on the edge of the next big drop.

I had just lectured to a packed-out hall in a conference of the Brazilian equivalent of Experimental Biology, where, as in the USA, physiology plays a big role in these conferences. The theme of my lecture was the cascade of falling dogmas in biology as physiology moves back onto centre stage, so I naturally reflected on the metaphor of the waterfall cascade.

Two days earlier I was in Sao Paulo for the meeting of the International Scientific Program Committee for the 38th IUPS World Congress to be held in Rio de Janeiro on 1–5 August 2017. This meeting will also be the Annual Meeting of The Physiological Society, and of the Scandinavian Physiological Society. In fact, the world of Physiology is co-operating splendidly in the organization and financing of the Congress, with sponsorship of symposia and awarding of travel grants from many more of the IUPS national member societies. There is no doubt therefore that a first class program is being constructed. Five international experts, leaders in the field of Physiology, have been selected as Plenary Speakers. These include Ada Yonath from Israel talking on the hot topic of resistance to antibiotics with her thoughts about the future; Amira Klip from Canada on the way in which immune cells co-opt metabolism to cause insulin resistance; and Yasushi Miyashita from Japan talking on neural dynamics of cognitive memory system in the primate.

The list of plenary speakers also includes two from the UK: David Eisner on the ups and downs of calcium in the heart, and Daniel Martin on physiology at extreme altitude. Joining this prestigious group will be a stellar list of Keynote Speakers covering a wide range of physiological topics, which will include speakers from Brazil, Denmark, Argentina, USA, Belgium, South Africa, Italy, South Korea and France, illustrating just how worldwide the Congress will be. The Scientific Programming Committee is in the process of selecting 60 symposia from over 120 submissions to provide a broad and illuminating perspective of physiological science to this Congress.

The range of topics illustrates the growing strength of our discipline as it moves back onto centre stage in the biological sciences. This is therefore a good time to celebrate the 'Health of Physiology' to quote the important Report recently published by The Physiological Society (www.physoc.org/health-physiology-0). As IUPS President I have been lecturing all over the world on the ways in which the study of biological function, which is what physiology is about, has become relevant to core concepts in modern biology, including notably evolutionary biology. Many of the Conferences at which I have lectured have not been specifically billed as physiology, but that also illustrates a modern trend. Physiology permeates many cognate disciplines. The topics chosen for the lectures and symposia for Brazil 2017 also illustrate that trend. I find that these reactions worldwide fully bear out the general conclusions of the Health of Physiology Report.

I therefore strongly recommend readers of *Physiology News* to come to Brazil in August of next year to take part in this worldwide celebration of our discipline.

Rio itself is well-known as a spectacular city. It was the site of the recent Olympic Games, which were such a success for British athletes. The advantages of that success are that the Congress facilities in Rio have been greatly upgraded. Rio is more than ready to welcome the world of Physiology next year. And why not also take a family holiday while in Brazil? As my experience of the Iguacu Falls shows, Brazil, and South America generally, have many attractions to offer.

The Congress Website is already open to early registrations: **www.iups2017.com**

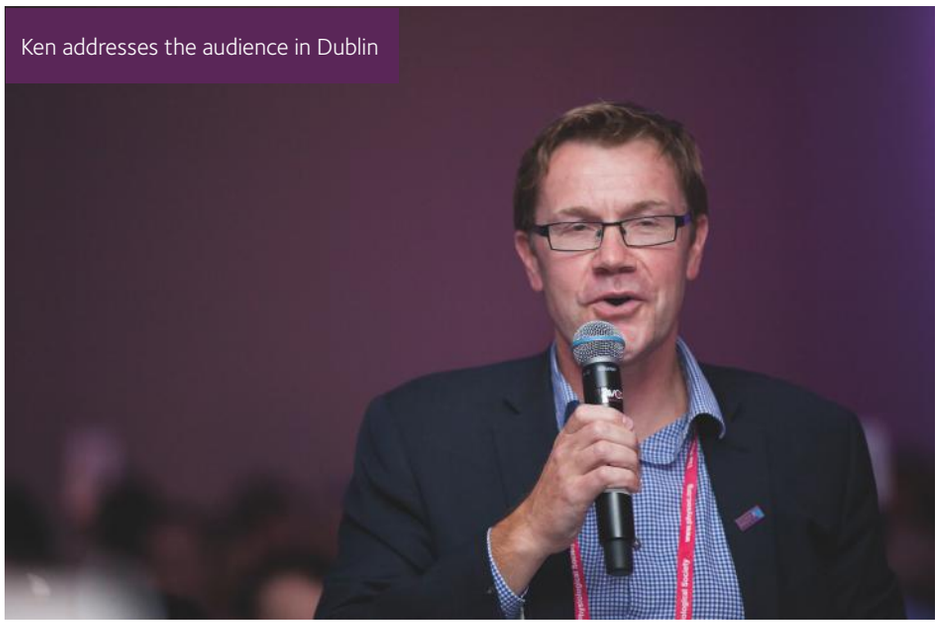
The statue of Christ the Redeemer overlooks the city of Rio

Meeting Preview

Celebrating the logic of life on the international stage in 2017 and beyond – a preview of our forthcoming programme of activities

Ken O'Halloran

Meetings Secretary,
The Physiological Society



Ken addresses the audience in Dublin

At the time of writing, the autumn meeting of The Society's Meetings Committee is fast approaching. It reminds me that I am mid-way through my four year tenure as Meetings Secretary. How time flies. Opportunity to reflect briefly on the year that's been, and more exciting than that, consider where The Society's meetings roadshow is next headed. World class topic meetings in Nottingham (April 2016) and Warwick (August 2016) and focussed H^3 meetings at Hodgkin Huxley House in London and at Oxford University throughout the year, complemented Physiology 2016, our collaboration with the American Physiological Society in late July, when Dublin played host to our annual meeting. Physiology 2016 set new benchmarks of grand scale success. More than 1,100 scientists from 69 countries – novices to Nobel laureates – enjoyed the four day fiesta of physiology, packed with plenary and keynote lectures, symposia and workshops, and more than 700 poster communications, celebrating the logic of life at a truly international affair. The rich portfolio on offer included sessions focussed on education and outreach, ethics, research careers, and publication. What a party; even before the local fare was sampled!

How do we follow that? Plans afoot for 2017 and beyond reveal continued ambition to celebrate physiology on the international stage. Our commitment in this vein dovetails with other activities within The Society, which reflect an increasingly outward-looking collaborative approach to the promotion of physiology, home and away. Council ratified the Meetings Committee recommendation that The Society should forego the annual meeting in 2017, in full and enthusiastic support of the IUPS Congress in Rio de Janeiro. Beyond financial support for symposia and Society prize lectures, and enhanced travel funds for members to facilitate attendance at the meeting, the gesture was warmly received internationally, and especially by the IUPS Council and the Brazilian Physiological Society, recognising the significance of the decision.

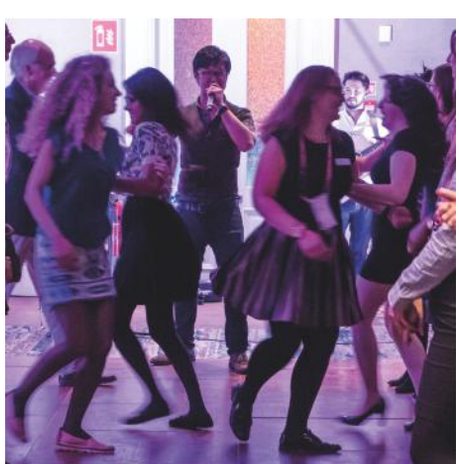
The change affords unique opportunity closer to home to develop an enhanced programme of activities in 2017, with 3 topic meetings and 7 H^3 focussed symposia in the offing. In April, we will embed the *Neurobiology of Stress* topic meeting within the British Neuroscience Association festival in Birmingham. Summer will see *Mitochondria: Form & Function*, with discussions at an advanced stage with sister societies for the topic meeting to function as a collaborative inter- and cross-disciplinary event. Meetings Committee is also keen to progress with a third topic meeting, the *Future of Physiology*, a cross-themed event centred on early career physiologists celebrating the broad reaches of the discipline, which should see a return to an abundance of the much revered traditional open communication sessions (without voting!), a move informed by feedback from the wider membership.

If that's not enough to whet appetites, we can peek ahead to the menu on offer in 2018. Two confirmed highlights are deep in the planning stage: *Sleep & Chronophysiology* will be one of two topic meetings, and Council has approved *Europhysiology 2018*, the inaugural meeting in London of a tripartite collaboration with the German Physiological Society and Scandinavian Physiological Society, that will see our annual meeting head to mainland Europe in 2020 and 2022.

The portfolio of collaborative events is a measure of the good health that physiology enjoys in the 21st century. The Society's commitment to the delivery of its charitable objects is assured. Your continued support of our activities and participation at meetings is much sought after and valued. Our ambition is to provide a platform for physiology and physiologists to shine. It is high time to return physiology to the lexicon of the biomedical community and to conversations in the corridors of our institutions. We do so with a strong sense of the proud and rich tradition of the past, and with a confident and optimistic understanding of our place and purpose into the future. Shine on!

Let's Dance!

The Meetings Secretary extends an invitation to the Science Ceilí after the banquet dinner in Dublin for just shy of 500 guests.



Lewis Hou, Affiliate member, and founder of Science Ceilidh, leads the attendees at Physiology 2016 conference dinner

Exercise like an Astronaut

How crew members stay healthy aboard the International Space Station

Alexander Ryan (centre) and colleagues, Alexander Rolph (left) and Nick Easton (right), at the Bluedot Festival

Alexander Ryan

University of Manchester, UK

On the 24 April this year, a man received a Guinness World Record for completing the London Marathon in 3 hours, 35 minutes and 21 seconds. This time may not sound all that impressive, but the record 'Fastest marathon in space' was achieved by Major Timothy Peake while aboard the International Space Station (Lynch, 2016). He did this harnessed to a treadmill via bungee cords, allowing an insight into the specialised exercise equipment aboard the ISS.

Under periods of low exercise, skeletal muscle begins to atrophy. This leads to muscle wastage, and potentially sarcopenia over a long time. Atrophied muscle is physically smaller, and weaker than healthy muscle. Individual muscle fibres are decreased in both size and number, there are less type I fibre and more type II fibre (Narici & Maffulli, 2010). Type II fibres are more prone to atrophy, leading to further deterioration. As skeletal muscle is a major site for glucose dispersal, there is an association between sarcopenia and Type 2 Diabetes.

Due to the low gravity, or microgravity, on the ISS crew members do not routinely carry out exercise. Therefore skeletal muscle begins to waste away, bone mass decreases and the volume of the heart gets smaller. A major problem with space exploration is how to combat these. Currently the longest running experiment aboard the ISS is the effect of microgravity on the skeletal system.

Crew members can lose up to 25% of the muscle mass within 6 months aboard the ISS, with muscle power and force also being significantly decreased. Furthermore, the muscle fibre type is similar to that in sarcopenic muscle. 'Spaceflight osteopenia' can cause crew members to lose more than 1% of their bone mass every month. This causes bones to weaken, and can increase the frequency of fractures (Malik, 2009). Due to the decreased workload on the heart, the heart muscle begins to atrophy (Lewis, 2014). This leads to a smaller amount of blood being pumped, and this decreased amount of blood flow can lead to low blood pressure when crew members return to earth.

In order to combat this specialised exercise equipment had to be developed. There are three pieces of equipment currently present on the ISS; COLBERT, CEVIS (NASA, 2015) and ARED (NASA, 2015). COLBERT stands for Combined Operational Load Bearing External Resistance Treadmill, and is the treadmill Timothy Peake used for the marathon. In essence COLBERT works in a similar manner to a standard treadmill, although crew members are connected via bungee cords. CEVIS is even simpler, in that crew members are strapped to an ergometer similar to a stationary bike. The clever part of both COLBERT and CEVIS is the mechanism in which they are connected to the station. A vibration isolation system is in place to prevent crew members from affecting other parts of the ISS.

Figure 1. Record breaker Tim Peake completes the 'Fastest marathon in space'

Figure 2. ISS Excercise equipment. *A.* COLBERT in use on the ISS, *B.* COLBERT treadmill unit in detail, *C.* CEVIS in use on the ISS. Images © NASA

‘Crew members can lose up to 25% of the muscle mass within 6 months aboard the ISS; spaceflight osteopenia can cause crew members to lose more than 1% of their bone mass every month, the heart muscle begins to atrophy’

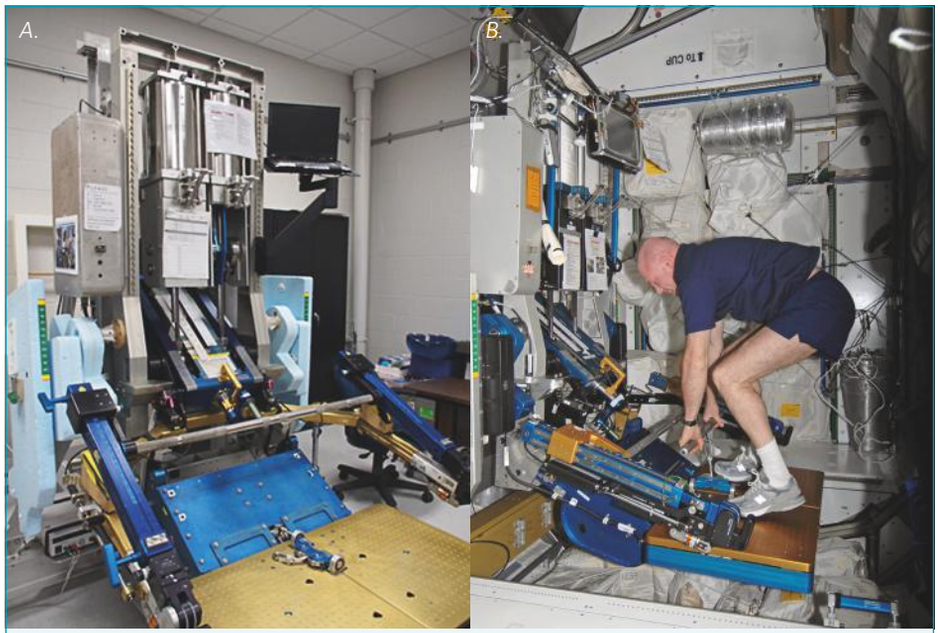


Figure 3. *A.* ARED unit in detail, *B.* Andre Kuipers uses ARED on the ISS.

Whilst COLBERT and CEVIS are good for aerobic exercise, they do not effectively build muscle. This is why ARED was developed, to stimulate resistance exercise. ARED is the ‘Advanced Resistive Exercise Device’ and uses piston-driven vacuum cylinders to mimic several weight-lifting exercises. Key to the function of ARED is its flexibility. By manipulating the apparatus 29 different methods of weight lifting can be mimicked; from squats to dead lifts to bench presses. This allows all the major muscle groups to be worked out. Moreover, the load is adjustable meaning that all crew members can use the equipment.

Together with my team of volunteers, and a generous outreach grant from the Physiological Society, I visited the Bluedot Festival to explain how to ‘Exercise Like An Astronaut’. Under the gaze of the Lovell telescope at Jodrell bank our tent described the mechanisms of exercise aboard the ISS. Whilst talking visitors through the problems inherent with a stay on the ISS, we explained the counter measures taken. We then used air pumps to show how effective pistons could be, setting off bottle rockets and blowing up balloons.

An interesting caveat involved explaining the sheer amount of exercise undertaken on the ISS. Our volunteers were tired after only a few minutes of pumping, whereas crew members are encouraged to carry out two hours of exercise a day. The feedback received was overwhelmingly positive, and we had a lot of repeat visitors. Younger visitors enjoyed the practical part, whereas older visitors were interested in the actual science of muscle wastage. In an age where the amount of sedentary lifestyles is increasing, it was interesting to draw direct comparisons, and demonstrate how important exercise is.

References

Lewis T (2014). How Zero Gravity Affects Astronauts’ Hearts in Space. www.space.com/25452-zero-gravity-affects-astronauts-hearts.html

Lynch K (2016). ESA astronaut Tim Peake achieves Guinness World Records title for the Fastest marathon in space. guinnessworldrecords.com

Malik T (2009). Space Station Astronauts Lose Bone Strength Fast. www.space.com/6354-space-station-astronauts-lose-bone-strength-fast.html

Narici MV & Maffulli N (2010). Sarcopenia: characteristics, mechanisms and functional significance. *Br Med Bull* **95**,139-159

NASA (2015). Advanced Resistive Exercise Device (ARED). www.nasa.gov/mission_pages/station/research/experiments/1001.html

NASA (2015). Cycle Ergometer with Vibration Isolation and Stabilization System (CEVIS). www.nasa.gov/mission_pages/station/research/experiments/841.html

Stable isotope tracers in muscle physiology research

The versatile tool in unravelling dynamic metabolism

Philip Atherton, Matthew Brook, Ken Smith, & Daniel Wilkinson

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For more than a century, stable isotope tracers (SIT) have been used in physiological research to investigate the regulation of mammalian biological and physiological functions in exquisite detail (for more detail readers are referred to Wilkinson, 2016; Wilkinson *et al.*, 2016). Indeed, much of what we understand of the control of amino acid, lipid and carbohydrate metabolism and the metabolic regulation of growth, development, and non-communicable diseases have been gleaned from SIT applications. The popularity of SIT extends from the fact that they can provide dynamic measures of the metabolism of a defined biological system (or combination of systems) *in vivo* (Wolfe & Chinkes, 2005). While still considered a niche technique, SIT remain as informative (if not even more so) to contemporary physiological researchers as they did to the early pioneers (e.g. Ussing, 1941).

Why SIT and not other approaches?

So why use tracers, when there are so many other more accessible and cost-effective analytical techniques available? The key to using tracers is that they provide true dynamic information relating to metabolism, something that few other techniques do. Measurement of the concentration of a metabolite within the blood or tissue provides only a 'snapshot' of the metabolic process; even making a measurement following an intervention or repeating this measure over a defined period of time provides limited information as to what is happening to the metabolite i.e. we have no way of knowing if more of the metabolite is being made or if less is being metabolised further or even if there is a combination of these two processes.

In most circumstances, concentrations of metabolites in biofluids such as blood are very tightly regulated and any perturbation from the norm is quickly rectified in order to re-establish homeostasis (e.g. Blood Glucose). However, with the inclusion of a tracer, not only can we measure the concentration, but we can also obtain the flux or rate of change of the metabolite/metabolic pathway of interest, and how other pathways may interact to regulate metabolism, providing a more accurate and complete picture of how an intervention is affecting metabolism. So what inherent properties allow stable isotopes to provide such diverse applications for investigating metabolism in physiological systems? To define this, we must first consider the chemical properties of a stable isotope.

‘Metabolism for the masses’

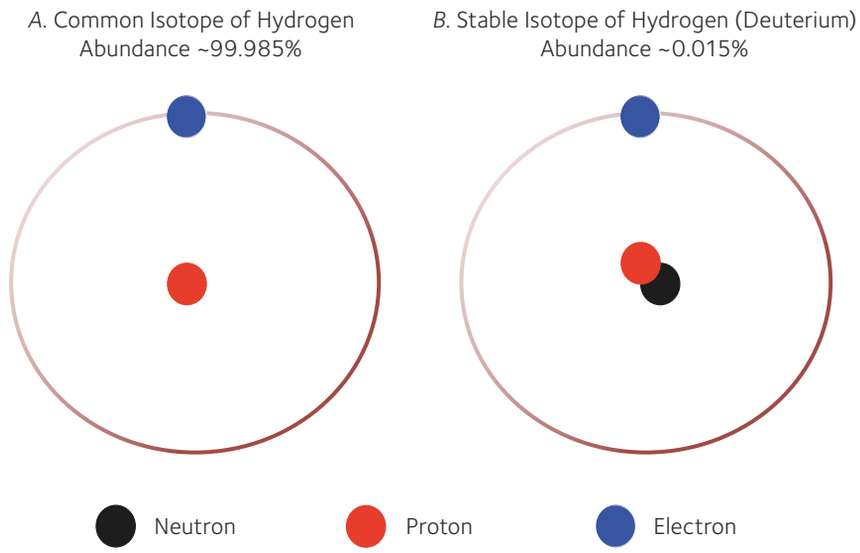

Figure 1. Diagrammatic representation of the stable isotope of hydrogen, highlighting the additional mass provided by the additional neutron in the atomic nucleus. The stable isotope of hydrogen has a single additional neutron in the atomic nucleus – this neutron influences mass, BUT due to its neutral charge it doesn’t influence its chemical behaviour. This important concept is key for the use of stable isotopes in physiological research.

An idiots guide to mass spectrometry and detection of SIT

A stable isotope is a species of an element (e.g. carbon, nitrogen, hydrogen or oxygen) that differs in mass due to the addition of one additional neutron within the atomic nucleus (see figure 1). Importantly stable isotopes, unlike their radio-active counterparts (i.e. $^{14}C/^{3}H$) are ‘stable’ (hence the name) and therefore unlike radioisotopes, are not subject to decay and release of damaging ionizing radiation. These stable isotopes can be substituted for their lighter counterparts in many biological substrates i.e sugars, amino acids, lipids, in either single or multiple positions to make a variety of SIT. Importantly, the extra neutron/s upon substitution into SIT adds mass allowing this to be safely ‘traced’ (hence the name) within the body. This difference in mass of SIT is measurable, using a variety of analytical techniques from mass spectrometry to magnetic resonance spectroscopy, meaning that these SIT (e.g. ^{13}C) are distinguishable from their lighter counterpart (^{12}C). Therefore oral or infused provision of a SIT leads to their incorporation into compounds and polymers of interest via chemical or enzymatic synthesis, e.g. carbohydrates, proteins or lipids. The incorporated ‘labeled’ compounds are biochemically identical to their endogenous ‘unlabeled’ counterparts within the biological system of interest, thereby permitting the ‘tracing’ of metabolic flux by monitoring the fate of the stable isotope throughout the various stages of the metabolic pathway.

But once we have got these compounds inside our pathways of interest how do we detect the presence of these SIT? The most common method for doing this is through the use of a mass spectrometer (MS). A mass spectrometer is essentially an expensive weighing machine, with many varieties available but maintaining the same essential principles. They are capable of separating and detecting whole molecules (typically using Gas Chromatography-MS) or atoms upon molecule combustion (using GC-IRMS)_based on their mass and/or charge after undergoing some form of ionization as they pass through either an electrical and/or magnetic field under vacuum. For more information about the types, configurations and history of mass spectrometers available please see Wilkinson (2016), this level of information is beyond the scope of this article. Mass spectrometers are traditionally combined with other separation techniques such as gas/liquid chromatography, to permit the separation of complex mixtures of organic compounds prior to ionization and detection in the mass spectrometer from biological samples such as blood, urine or tissues. For example if we were interested in the rate of skeletal muscle protein synthesis we might take sequential samples of muscle over a defined time period of a few hours whilst the subject is being infused with a SIT of an amino acid (i.e. 1,2,$^{13}C_2$ Leucine), we would then analyse each muscle sample for the presence of this SIT within the muscle protein. To do this, we would isolate the protein pool of interest (either mixed, myofibrillar, mitochondrial, sarcoplasmic or collagen) following a process of homogenization and differentiation centrifugation techniques.

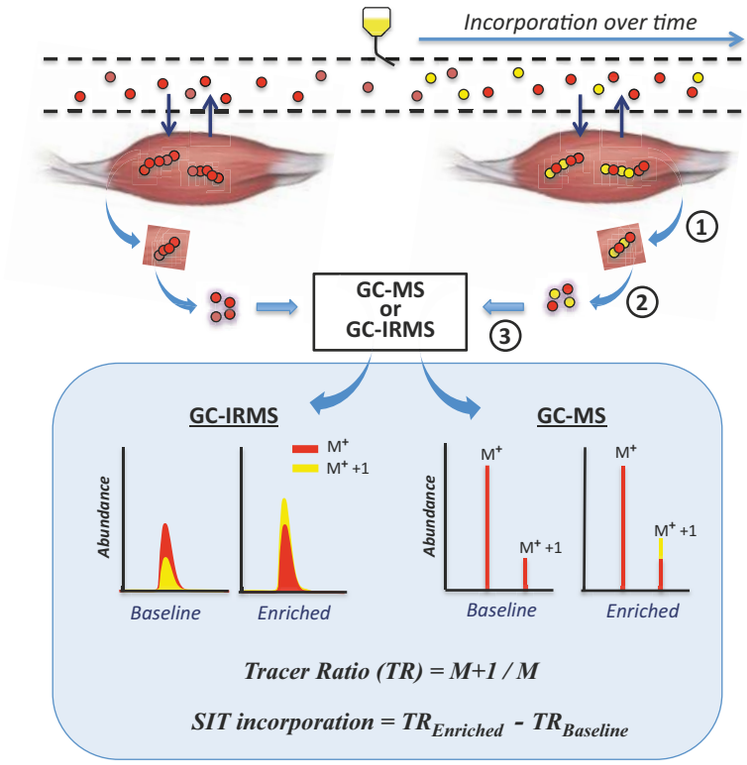

Figure 2. The rate of biosynthetic pathways can be calculated by acquiring a muscle biopsy both before (baseline) and after (enriched) the incorporation of a SIT (1). After hydrolysis, purification and derivatisation (2) substrates can be measured using GC-MS techniques (3). GC-MS measures the molecular mass (M) and the abundance of that molecule containing heavier isotopes (M+1). Comparatively IRMS combusts the whole molecule and measures the lighter and heavier isotope in the resulting gas produced e.g. $13CO_2$ vs. $12CO_2$. After SIT infusion, the 'heavier' isotope is increased more than what occurs naturally and the resulting difference represents the rate of SIT incorporation over that time.

These crude fractions can then be chemically hydrolysed (denaturing and breaking of the peptide bonds) by heating in acid overnight, to release the individual AAs. Following a number of purification and derivatization steps these AAs are ready to be separated and analysed for changes in the level of isotopic enrichment (due to the SIT) by mass spectrometry. The amount of the SIT incorporated over time into the muscle protein as detected by the mass spectrometer (Figure 2) provides information on the rate of muscle protein synthesis. For more information on the intricacies of these measurements and other SIT techniques the reader is guided towards Wolfe and Chinkes (2005).

Substrate specific SIT: what have they told us?

SITs are typically substrate specific. That is - stable isotopically labeled amino acids (AA) provide information on amino acid and protein metabolism, labeled fatty acids will inform on fat metabolism while glucose tracers will reflect carbohydrate (CHO) metabolism and storage. These types of tracers have been instrumental in yielding important information relating to the regulation of, flux through and perturbations to each of these pathways (Kim *et al.*, 2016).

In terms of CHO and lipid metabolism, SIT have been able to describe the relative contributions of hepatic and extrahepatic tissues to the regulation of gluconeogenesis, a key factor in understanding the regulation of hypo and hyperglycemia.

Moreover, we have been able to determine the rates of glucose uptake and utilization by these tissues under different stresses such as during exercise, as well as the role of disease, ageing and inactivity in development of insulin resistance. In addition, the use of stable isotope tracers has also been key to determining shifts in substrate utilization and fuel use during exercise e.g. highlighting reductions in lipid oxidation at increasing exercise intensities, and the important role of endurance training in increasing utilization of lipids to spare muscle glycogen.

However one of the areas where SITs have had some of their greatest impact over recent years has been in the study of protein metabolism. For example, SITs have helped to determine the key nutritional role of the EAAs, in particular the BCAAs, in driving muscle protein synthesis, alongside the important contribution made by insulin release (provided by CHO or protein ingestion) in suppressing muscle protein breakdown. Moreover, they have helped delineate the protein synthetic and breakdown responses to exercise, and the key interactions between exercise and nutrition for driving muscle adaptation (i.e. when performed in the absence of nutrition, exercise is in fact catabolic). Finally, these techniques have allowed us to start to unravel the intricacies of the major metabolic blunting associated with ageing, inactivity and disease, in an attempt to correct, delay or reverse these consequences through nutritional or lifestyle interventions.

While there are clear benefits to the use of these substrate specific SIT, there are also some significant limitations. To perform a SIT experiment requires preparation of sterile infusates, intravenous (I.V.) cannulation(s) and collection of tissue (usually muscle) biopsies. Such experimental design requires subjects to be studied in a controlled clinical or lab setting – restricting measures to < 24 h – and requires different SIT for each substrate to be 'traced' (e.g. $[^2H_2]$glucose for glucose metabolism, $[U\text{-}^{13}C]$palmitate for lipid metabolism and [1,2, $^{13}C_2$]leucine or $[^2H_5]$ phenylalanine for amino acid and protein metabolism) (Figure 3). The time limited and invasive nature of these types of studies narrows their application and as such, may not accurately reflect longer term metabolism in chronic free living situations common to everyday life. Moreover, the intensive and invasive nature may contraindicate their use within certain more vulnerable populations such as the very frail or adolescent.

Deuterium oxide: The renaissance of a non-substrate specific universally acting SIT

Recent developments involving the use of the novel stable isotope tracer: Deuterium Oxide, ($D_2O/^2H_2O$) or 'heavy water', have provided the opportunity to overcome some of these limitations. The use of D_2O features in some of the earliest SIT studies where it was apparent that deuterium is incorporated into many metabolic substrates. Soon after it was shown that by maintaining a constant level of D_2O in the body, the kinetics of various substrates could be obtained by measuring the amount of deuterium incorporated.

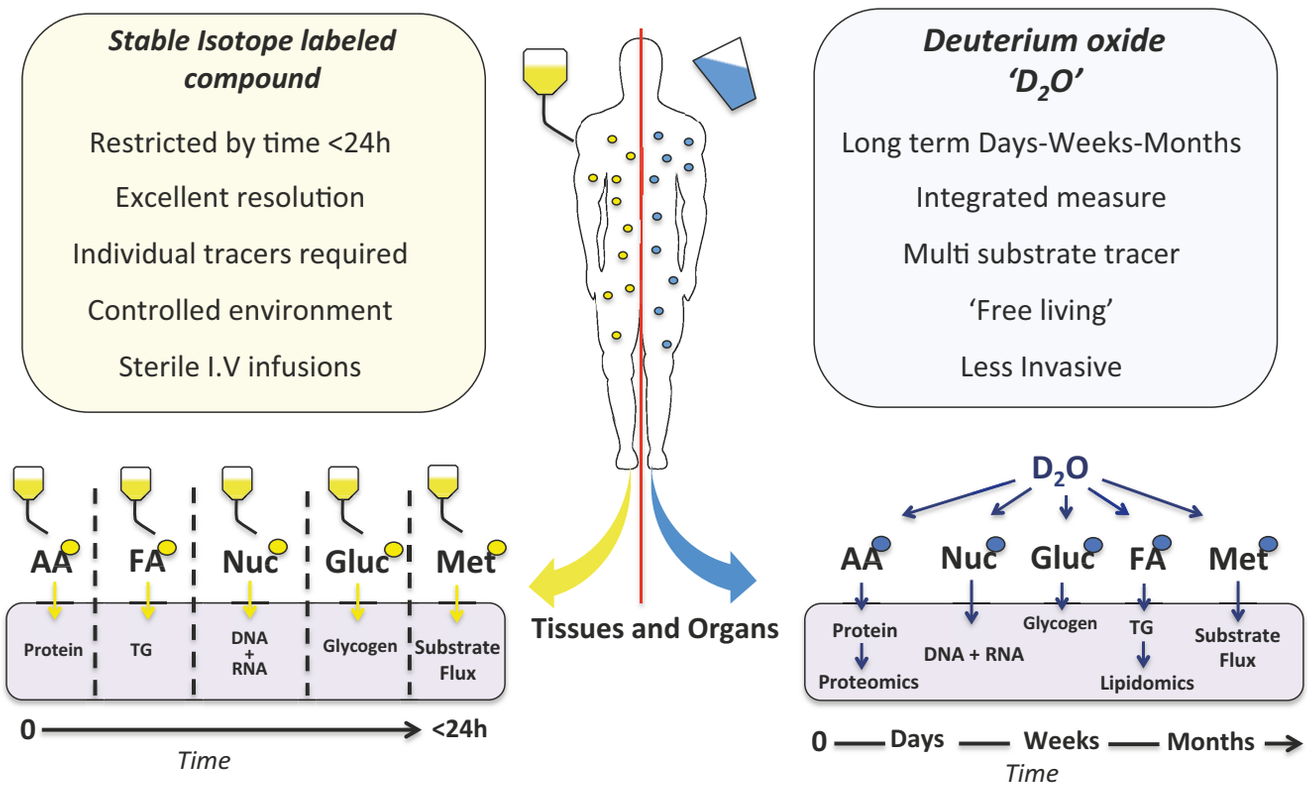

Figure 3. Representative diagram of the differences between the uses of substrate specific stable isotope labeled compounds and deuterium oxide 'D_2O'. **AA** – amino acid. **FA** – fatty acid. **Nuc** – nucleotide. **Gluc** – glucose. **Met** – metabolite. **TG** – triglyceride.

While the use of D_2O was sporadic until the end of the last century, subsequent advances in analytical instrumentation pioneered by Stephen Previs and Marc Hellerstein was key in re-establishing the application of D_2O in the measurement of protein, nucleic acid and lipid metabolism. D_2O is primarily administered by oral consumption with body water enrichment being monitored simply through collection of saliva samples. This avoids the need for preparation of sterile IV infusions, IV cannulation, and the need for constant subject monitoring in controlled environments. This greatly reduces the invasiveness of studies. D_2O rapidly equilibrates throughout the body water pool and is incorporated into any metabolic pathway that exchanges hydrogen with body water (ergo, most if not all!). Indeed, deuterium atoms incorporate into many substrates including amino acids, glucose, fatty acids and nucleotides, effectively enabling the body to create its own SIT labeled compounds (Figure 3). This engenders potential for determining simultaneous rates of turnover and flux in multiple substrate pools simultaneously. Crucially, relatively slow turnover of the body water pool permits measurement over longer periods i.e. days-weeks-months. This permits experiments to be extended beyond standard limits for traditional SIT studies of ~24h, thereby providing a vital mechanism for monitoring chronic, cumulative metabolic rates of greater translational and 'real life' relevance.

This key feature engenders it well to the study of muscle protein turnover in particular, which unlike many other metabolic pools turns over at a relatively slow rate (~1-1.5%/d), therefore through the provision of D_2O, MPS can be monitored over periods of several hours to several months in order to gain insight into muscle protein regulation on a long-term basis. Indeed, this technique has already shown its unique capabilities highlighting that increased MPS over the first three weeks of RET matched early, plateauing muscle hypertrophy, with these chronic D_2O MPS derived measures correlating well with long term muscle hypertrophy due to RET. This suggests that D_2O can provide a predictive real life representation of exercise adaptation, something which is not observed with traditional acute SIT.

Further to this, the ease of application and lack of invasiveness will have great utility in vulnerable and clinical populations, with measurements already being made in ageing, and renal and cancer patients.

Isotopomics – The next generation

Tissues are complex biological structures made up of thousands of individual components. Assessing changes in the dynamic flux/turnover of these tissues are generally (although not exclusively) made through their primary constituents i.e. mixed muscle or myofibrillar proteins for muscle.

However, these are crude fractions and represent the collective actions of many proteins and do not provide knowledge on how single proteins turnover and how they contribute to muscle homeostasis. To investigate the role of individual proteins stable isotopes have recently been combined with 'OMICS' methodologies. For instance, using D_2O ingestion in humans, Hellerstein *et al.*, devised a method to isolate peptides using nanoLC-MS/MS to quantify enrichment of deuterium within individual proteins to calculate rates of turnover (Price *et al.*, 2012).

Not unsurprisingly, these methods are rapidly being utilized to provide unique information regarding tissue and biofluid proteome dynamics in both health and disease. Rather intriguing, recently the same research group has reported development of the so called 'virtual biopsy'. Using D_2O derived dynamic proteomics, plasma proteins, such as the muscle specific creatine kinase M-type (CK-M) and carbonic anhydrase 3 (CA-3) have been shown to accurately represent rates of turnover of the same proteins (or crude fractions) sampled in muscle. Such novel techniques could prove useful in situations where muscle biopsies may be contraindicated, such as in young children or frail elderly, or where they are not easily obtainable such as *during* exercise or in ICU patients.

Alongside this novel proteomics application, the emerging application of SIT alongside metabolomics now enables 'fluxomics' (Figure 3), whereby flux through multiple metabolic pathways can be dynamically monitored. For example, using a [U-$^{13}C^{15}N$]-valine SIT, and monitoring the enrichment of ^{13}C labeling in downstream metabolites of valine and the ^{15}N labeling of transamination metabolites, it was shown that high aerobic capacity in a outbred rat model selected for high or low intrinsic or inborn aerobic capacity, was associated with increased flux through BCAA catabolic pathways combined with more efficient fatty acid utilization. Where these fluxomics techniques could become more powerful and informative is through the inclusion of D_2O rather than a substrate specific SIT, as this has the potential to provide flux data from a multitude of different pathways simultaneously, providing a more holistic picture of dynamic whole body metabolism and its regulation/dysregulation in health and disease.

Accessibility and costs

The issue of accessibility and costs for stable isotope tracers will always be somewhat of a limiting factor in setting up and running such experiments. Stable isotope tracers by their nature are expensive to purchase, this is due to the specialized way in which they are manufactured, and the limited number of companies that provide them worldwide. Moreover, there are additional costs incurred through the need to prepare sterile infusate, in addition to clinical consumables for placing of IV lines and collection of multiple biological samples, at least for traditional substrate specific tracers. As an example the average cost for an acute substrate specific SIT study to be performed within our laboratories is ~£450/study (inclusive of all consumables and pharmacy costs for IV tracer prep). This cost still doesn't take into account costs for the analysis of samples once collected, which usually means requiring access to the appropriate analytical platforms such as gas chromatography mass spectrometry, which dependent on lab and the type and number of compounds being analysed can range from £10 to >£100 per sample. Taking all this into account, the cost of performing a stable isotope tracer study can seem rather daunting, and some may consider that the initial cost outlay may outweigh the benefits provided by the outcomes of the study, we would argue this would not be the case in a well designed experiment. However, one should not be discouraged, there are ways of designing your studies to minimise some of these cost implications. D_2O, unlike substrate specific tracers is considerably cheaper (~£200/study) to produce and the cost of this tracer has been steadily decreasing over recent years, as its popularity as a technique has gradually increased.

Moreover, the need for sterile preparations, I.V. lines and other clinical consumables is greatly reduced due to the oral route of administration. In addition, as highlighted earlier this tracer is highly versatile, being applicable to measure changes in metabolism over periods as short as a few hours, acting as an alternative to many substrate specific tracers, whilst also being capable of measuring over more chronic free living periods of days, weeks or even months. Whilst this greatly saves on experimental cost, analytical costs remain. Isotope ratio mass spectrometry (the traditional workhorse for stable isotope tracers) can cost anything upwards of £150,000 and tends to only be available in specialist labs. However, improvements in design and sensitivity of (GC/LC based) tandem mass spectrometers (a more affordable and widely available piece of analytical equipment) increases accessibility to these analytical techniques whilst also reducing overall costs for analysis. Many university labs have some form of mass spectrometric equipment available to them, through core or central facilities, and there are even commercial providers available at certain prices. Moreover, we find scientific colleagues are always keen to collaborate on important and interesting projects and ideas. If you want to use tracers within your work, the scope and availability of these techniques is ever increasing.

Conclusion

SITs are unique and useful tools for use within the physiological sciences and have an application to a far wider range of disciplines beyond that of purely muscle physiology. If you can sample the tissue and model the metabolic pathways involved in its physiology, then SIT may provide benefit to your experiments. Moreover, its application can extend beyond human work and they are also routinely used within pre-clinical animal models, as well as in vitro cell culture. The availability of these techniques is increasing rapidly, and we highly recommend the follow reviews and books to the readers to provide them with more detailed insight into this fascinating field of research (Wolfe & Chinkes, 2005; Gasier *et al.*, Wilkinson, 2016; Kim *et al.*, 2016; Wilkinson *et al.*, 2016).

References

Gasier HG, Fluckey JD & Previs SF (2010). The application of 2H2O to measure skeletal muscle protein synthesis. *Nutr Metab* (Lond) **7**, 31

Holmes WE, Angel TE, Li KW & Hellerstein MK (2015). Dynamic Proteomics: In Vivo Proteome-Wide Measurement of Protein Kinetics Using Metabolic Labeling. *Methods Enzymol* **561**, 219–276.

Kim I-Y, Suh S-H, Lee I-K & Wolfe RR (2016). Applications of stable, nonradioactive isotope tracers in in vivo human metabolic research. *Exp Mol Med* **48**, e203.

Price JC, Holmes WE, Li KW, Floreani N a, Neese R a, Turner SM & Hellerstein MK (2012). Measurement of human plasma proteome dynamics with $^{(2)}H_{(2)}O$ and liquid chromatography tandem mass spectrometry. *Anal Biochem* **420**, 73–83.

Ussing H (1941). The rate of protein renewal in mice and rats studied by means of heavy hydrogen. *Acta Physiol Scand* **2**, 209–221.

Wilkinson DJ (2016). Historical and contemporary stable isotope tracer approaches to studying mammalian protein metabolism. *Mass Spectrom Rev* **47**, 987–992.

Wilkinson DJ, Brook MS, Smith K & Atherton PJ (2016). Stable isotope tracers and exercise physiology: Past, present and future. *J Physiol*; DOI: 10.1113/JP272277..

Wolfe RR & Chinkes DL (2005). Isotope Tracers in Metabolic Research: Principles and Practice of Kinetic Analysis, 2nd edn. John Wiley & Sons, Inc., Hoboken, NJ.

When will we classify a study as 'research'?

Thoughts about current research, its future, and the creation of the next generation of physiologists

Else Bartels

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As a senior researcher working for many years in both Copenhagen and Oxford, I have followed several generations of young researchers, working in both basic and clinical science. For the last couple of years I – and several of my colleagues – have become very concerned about the more and more predefined 'follow the framework' research. In basic science there is still a higher degree of freedom, although there are more set task PhD projects than previously, where we in my generation had to come up with an idea and a synopsis ourselves and had more 'play-time' in the lab.

In clinical research many of the PhD-students are directly told that they must not go away from their very set protocol, even if they get a new idea. The wonderful breakthrough with the Cochrane Collaboration in Medical research, demanding proper scientific setups, has also created a negative result. We now produce several 'researchers' who have never experimented or thought completely by themselves, but believe that there is a defined way 'how much do I have to do - and how do I do it - to get my PhD'. It is certainly not all, but it is not a negligible percent of the new researchers, who will deliver according to set rules, but forget to think Physiology into their findings in the discussion. It becomes more like a Physics or Biology report in a school setting. If we take away the need to think and use our special field knowledge when doing research, we could undermine development and progress.

The question is simple: *What can be considered as research and what characterizes a researcher?*

As an answer to some of this, I decided to consider my first known attempt to do science to start some discussion about 'what is (good) science'. This attempt could be given the title 'Do teddy bears with real fur grow their coat: A controlled case study' . The aim of this study was to test if a real-fur teddy bear would grow back her coat if trimmed, and alternating sides and body parts of this teddy bear was cut short. The growth of the fur was then checked over time, but sadly, more than 60 years later, no re-growth has appeared. It may therefore be concluded that 'Teddy bears with real fur coat cannot be expected to grow their coat, and should therefore not to be exposed to any removal of their fur'.

Although presenting this childhood research is to some extent written tongue-in-cheek, it is also a statement that this is a form of honest research, well thought through and with a finding of something unexplained. The experiment described was set up to be a real experiment right from the start by me at a very young age – but coming from a scientific family, I had some early knowledge about animal experiments.

‘We have to think carefully to make sure that systematic reviews are of a type that brings ideas and thoughts together and generate new hypotheses’

As a comparison I would suggest a systematic review and meta-analysis, I and some colleagues carried out as published recently: ‘EM Bartels, VN Folmer, H Bliddal, RD Altman, C Juhl, S Tarp, W Zhang & R Christensen (2015). Efficacy and safety of ginger in osteoarthritis patients: A meta-analysis of randomized placebo-controlled trials. *Osteoarthritis Cartilage* **23**, 13-21’.

While the Teddy bear study had got new ideas – in terms not previously scientifically studied – and an untried method for answering the problem, as well as an attempt to make the study controlled, the meta-analysis paper is answering something which has been studied and tried for several thousand years, and in a way with an expected outcome. It is highly cited, it is what I would call ‘bread and butter’ research, and it does differ from some studies of this type by suggesting some physiological explanation of the results. I am not speaking against a reasonable percentage of this ‘bread and butter’ in a PhD study, or in most researchers’ scientific life. I just want to point out that we have to think carefully to make sure that systematic reviews are of a type that brings ideas and thoughts together and generate new hypotheses, and that some study types are not just a mechanical way of generating a publication. In the laboratory setting I also wish us all to think about if repeating a set of, for instance, membrane transport experiments with another drug, and according to a defined setup, in itself is a valid project for a young person who wishes to become a researcher. If you are given a protocol which is that fixed, how much in terms of new thoughts and hypotheses do you have to come up with yourself to call it ‘your own science’.

I do believe we owe the next generation more free thoughts and less economy governed thinking, and I would like research to be for the part of a generation who does wonder and does ask questions. I do not believe it is a happy solution for anyone to continue in a school setting with no space for development. If you do not burn for your research and take charge of your project, you are in the wrong place.

Scientists and Social Media – can you tweet your way to impact?

In the era of social media, there are many ways a scientist can promote their work and engage with others

Priya Mistry

Editorial Administrator,
The Journal of Physiology

Twitter: @Pri_Mis

Twitter has over 313 million active monthly users and Facebook has over 1.71 billion. Research has shown that social media can increase the number of journal article downloads (Wang *et al.*, 2016 & Allen *et al.*, 2013). So why do some academics and research scientists avoid these platforms? Social media has become a global forum, allowing people to share ideas, make new connections and create new research paths at an international level. But can the reach of these platforms affect the impact of research? And if so, how can we measure it? As a scientist in your field, it's in your best interest to share your work and other related topics in your field. So how can social media help you?

What is social media?

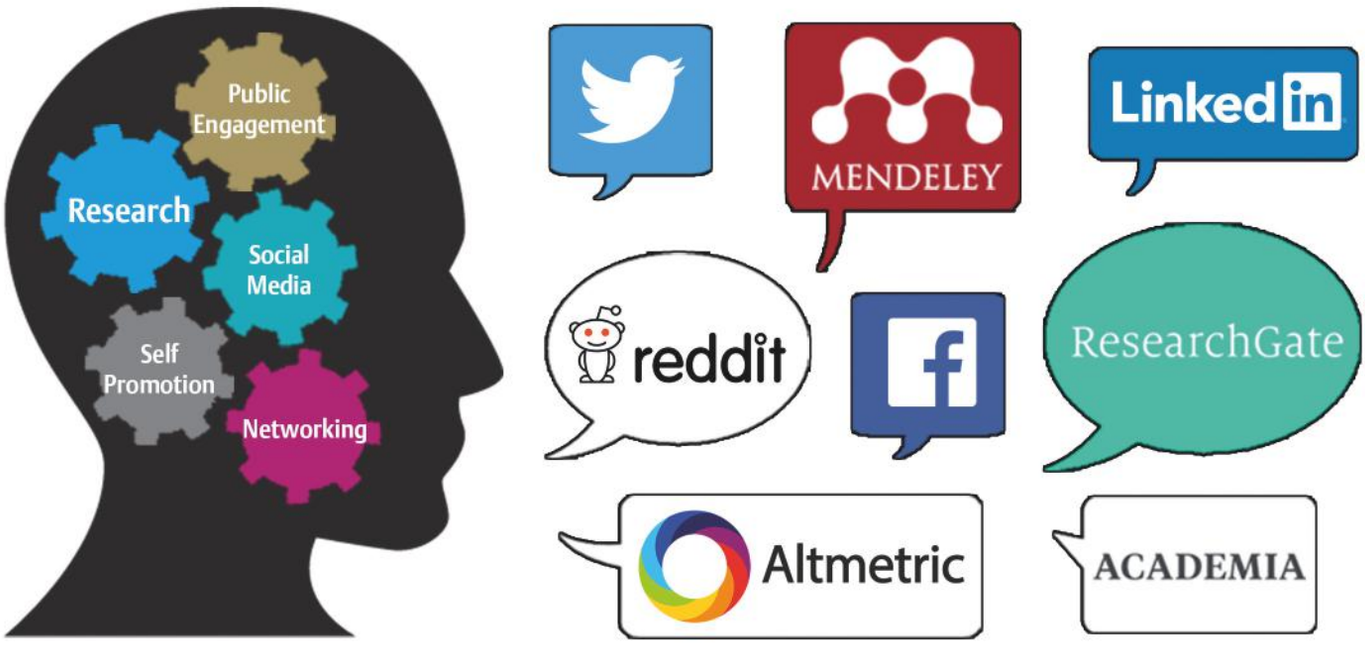
Social media consists of websites and apps which allow users to generate and share content while networking with other users. Social media platforms come in all shapes and sizes, but how do you know which ones are right for you and your target audience? The most popular platforms are Facebook and Twitter, however, there are many, many others covering different niche areas and demands. Online networking tools specifically for scientists include ResearchGate, Academia.edu and Mendeley, and these have millions of users. Reddit, a social news and discussion website, is so popular with scientists that Nature and PLOS have collaborated with them, allowing editors and authors from the journal to engage with verified accounts or 'flairs'. The 'subreddit' r/Science has over 13 million subscribers, so there is definitely a demand for a more informal platform of science discussion.

Why should I engage?

You're an academic, a professor, a PhD student, a science professional and you've been getting on fine without social media. So why should you engage online? There are so many ways that online networking can benefit you and others.

To network with peers

Social media can be used for peer to peer interaction and can help you collaborate with others at an international level. The community feel of online networking keeps you in touch with the latest scientific research and allows you to discuss and debate new ideas and developments. 'Hashtags' are a type of label used on social networks to categorize posts. Tweeting and following these during conferences helps you to follow the best parts of it, and others can be in virtual attendance – almost creating an online convention centre.



For Public Engagement
Scientific research is academically communicated through publishing, poster presenting and lectures. But this research can be disseminated to the general public through all forms of media, including social media. We should communicate science to the public as it allows them to make informed decisions - issues around global warming and vaccines are examples of where this communication is important. 79% of the British public said they trust scientists to tell the truth, in contrast to 25% saying they trust journalists (*Ipsos MORI*, 2016). This just goes to show that scientists have a responsibility themselves to not only communicate their own research, but also to represent the scientific community, to engage and to help the public understand and appreciate science. Knowledge about science can affect the public's attitude towards it and how they would vote in political ballots and elections, which can indirectly affect the support and funding for science research. Social media is an effective way to reach out to the general public and have a direct impact on them.

According to the Physiological Society's 'Health of Physiology' report, the visibility of 'physiology' as a whole is declining, as the science is becoming fragmented into other sub-disciplines. Now is as a good time as ever for physiologists to promote their work and the importance of the discipline, so physiology can be better represented with the public and scientific community. Engagement could also inspire the younger generation to follow the footsteps of a scientist and encourage them to study and pursue physiology.

For Self-Promotion
You have put your blood, sweat and tears into creating a research paper which has just been accepted. And now you want your paper to be easily found, read and ultimately, to be cited. Journals publish hundreds of papers every day so you can't rely on publishers to publicise your research. The best person to promote your article is you; you know the most about your research and the significance of it. ResearchGate and Academia.edu are excellent ways to share your research with other academics and sharing posts on Twitter and Facebook will further help with discoverability.

Academic networking profiles and LinkedIn are useful tools to use as a 'digital CV', however you must also think about your digital footprint. If you Googled yourself, what would you find? According to a recent survey by recruitment company Careerbuilder (Nikravan & Ladan, 2016), 60% of employers use social networking sites to research candidates in addition to looking at a CV or cover letter and 41% say they are less likely to interview job candidates if they are unable to find information about them online. If social media is used correctly, you can use it to create an effective digital profile, showcasing your work and knowledge and helping you with recruitment and self-promotion. The best part of this is that it's free!

The Editor's in Chief of both *The Journal of Physiology* and *Experimental Physiology* are keen Twitter users. Kim Barrett signed up for Twitter to engage with both authors and the readership. She says 'I am rapidly finding it useful in areas well beyond my Journal affiliation. More and more scientists are using Twitter to alert colleagues not only to their own work, but also that of other labs. By following colleagues whose work I admire, I am getting insights into exciting new areas of physiology.' Mike Tipton started using social media because of its immediacy. He mentions 'it is a quick and effective way to obtain and share information. The maths mean lots of people can hear what you have to say very quickly.'

How do I start?

Now that you've read all the reasons for engaging online, how do you start? As new publishing services emerge, there are more ways for authors to promote their own work. Specific tools are available for authors to help them improve the reach of their research articles. Kudos is a service which authors can use to explain their work in a lay summary and then share using the 'Kudos toolkit', which involves sharing by email, social media and through blogs. Other services available to communicate your research are blogging websites such as JSTOR daily and a more recent service of 'Cartoon Abstracts' offered by Taylor & Francis.

You are still the best person to share and discuss your work and social media platforms are a great way to get you and others talking. But the thought of all the profiles to create and platforms available can be overwhelming. Here are a few steps to help you get started:

- **Start off small**
  Michelle Lockett, Director of Social Media at John Wiley & Sons, suggests starting off small by creating a profile, looking at hashtags and browsing what's already available. Twitter is a good platform to start off with as you only need to think of 140 characters for a tweet.

- **Follow your interests**
  Once set up, you can 'follow' or 'add' other accounts depending on the platform you use. You can Follow your peers, follow your role models, follow companies and follow us (shameless plug)!

- **Engage**
  Michelle recommends to only engage on social media when you feel comfortable. Some may find this easier than others, but don't be discouraged if you find that your profile is looking a little bare or is slow to get attention. Practice makes perfect!

- **Post optimally and consistently**
  The lifespan of a tweet is about 18-24 minutes – this means that your tweet is 'pushed down' the feed and is less likely to be viewed after this time. So you should try to post at optimum times (in the mornings, lunch time and after work) and post consistently if you would like a bigger following. You can post about your own research, other papers in your field, your interests or anything that you want!

- **Download the apps**
  Having the social media apps on your phone means that you can have access to your profile at your fingertips and will make it easier for you to post wherever you are.

- **Be yourself**
  Don't be afraid to show your personality; giving your account a personal touch and sharing your interests distinguishes you from countless other social media accounts.

- **Have fun!**
  Once you get the hang of it, social media can be quite enjoyable and almost addictive. You'll find yourself constantly checking your profiles in no time!

How can I measure success?

As a scientist, you are hard-wired to want to track, analyse and evaluate anything you do. Luckily, tracking posts online can be easier than you think. Links created via the author service Kudos, can be easily tracked and analysed so you can see who's been clicking and sharing. Many publishers, including Wiley, have integrated Altmetrics onto their research papers. This service allows authors to track where the research paper has been mentioned. It gives articles a score based on popularity and the rank of the media on which it has been shared. This tool can also be used to check how well your paper is doing on social media and you can find the most trending research by looking at articles with high Altmetrics scores. Twitter and Facebook analytics are another easy way to track the number of views and clicks your posts have received.

A study from the *Journal of Medical Internet Research* (Eysenbach, 2011) showed that articles which were highly tweeted about were 11 times more likely to be highly cited than those with no tweets. In contrast, a study in *Scientometrics* (de Winter, 2015) has shown that the number of times an article is tweeted is weakly associated with the number of citations. So although tweeting may not be the cause of citations, Twitter can help to predict which articles will be successful and can give you an idea on how well your article will do. A paper from *PLOS ONE* (Allen *et al.*, 2013) has also shown that social media posts on a research article increase the number of people who view or download the paper, proving that social media can help to increase reach.

Finally, if you're looking for a more numerical value to measure the success of your Twitter profile, you can use the Kardashian Index; a metric proposed by genome scientist Neil Hall to measure the discrepancy between a scientist's social media profile and publication record (Hall, 2014). This index uses the relationship between the number of Twitter followers and the number of citations a scientist has to indicate over-blown or undervalued scientific fame - essentially a way to find out if you've become a 'Science Kardashian'!

Conclusion

Social media is a great add-on to your public profile, and although not essential to your career, it's a great tool which can be used to your advantage. In this day and age of the internet, it's difficult to keep your research distinctive, especially with around 2.5 million articles being published a year (STM, 2015). So why not give your paper, and yourself, a boost by engaging online?

Although Social Media is great for sharing, it's also important to note that it requires some responsibility. Opinions and discussion are welcome on these platforms, but posting provocative photos, discriminatory comments or negative remarks about a co-worker can affect your career, so be mindful about what you post and share.

It's difficult to know the relationship between reach and impact. Reach is something which is relatively easy to measure but impact is less straightforward. However, this doesn't mean that our efforts on reach are wasted. Sharing on social media can have many other hidden impacts, such as influencing the public, scientists, and readers. Citations are not always the end goal and you can extend your impact beyond the papers you've published. Knowledge is only useful if shared!

References

Allen HG, Stanton TR, Di Pietro F, Moseley GL (2013) Social Media Release Increases Dissemination of Original Articles in the Clinical Pain Sciences. *PLoS ONE* **8**(7): e68914

de Winter, JCF (2015). The relationship between tweets, citations, and article views for PLOS ONE articles. *Scientometrics* **102**, 1773

Eysenbach G (2011). Can Tweets Predict Citations? Metrics of Social Impact Based on Twitter and Correlation with Traditional Metrics of Scientific Impact. *J Med Internet Res* **13**(4):e123

Hall, N (2014). The Kardashian index: a measure of discrepant social media profile for scientists (PDF). *Genome Biology* **15** (7), 424

Nikravan & Ladan (2016). 'Number of Employers Using Social Media to Screen Candidates Has Increased 500 Percent over the Last Decade'. CareerBuilder, Accessed 07 Oct 2016. www.careerbuilder.com/share/aboutus/pressreleasesdetail.aspx?sd=4%2F28%2F2016&siteid=cbpr&sc_cmp1=cb_pr945_&id=pr945&ed=12%2F31%2F2016

'Politicians Are Still Trusted Less than Estate Agents, Journalists and Bankers' (2016). Ipsos MORI. Accessed 07 Oct. 2016. www.ipsos-mori.com/researchpublications/researcharchive/3685/Politicians-are-still-trusted-less-than-estate-agents-journalists-and-bankers.aspx#top

STM: The Global Voice of Scholarly Publishing (2015). The STM Report: An overview of scientific and scholarly journal publishing. Fourth Edition. www.stm-assoc.org/2015_02_20_STM_Report_2015.pdf

Wang X, Fang Z & Guo X (2016). Tracking the digital footprints to scholarly articles from social media. *Scientometrics*. doi:10.1007/s11192-016-2086-z

Our Research Grant scheme for early career physiologists

L-R: David Richards, Izzuddin Ahmad, Jonny Micklewright, Samuel Fountain, Janice Layhadi and Seema Ali.

The Society is particularly committed to supporting the progression of physiologists in the early stages of their careers. In 2012, the Education and Outreach Committee launched a new grant scheme to support those in their first permanent position. Research Grants provide £10k funding to members and non-members wishing to conduct pilot studies, develop a new technique or to finalise a project. Since then, the scheme has supported more than 50 physiologists and – as shown by a recent evaluation – has played a role in securing additional funding, publications and promotion for many of these individuals. The box on this page profiles the experience of one awardee, Dr Samuel Fountain of the University of East Anglia, who was awarded a grant in 2013 to study the role of purinergic receptor activation by chemokines.

In light of the success of the Research Grants scheme as highlighted by our evaluation, the Society has committed further funding to the scheme in 2017. Over the coming year, we will be looking to raise the profile of our grant holders and to develop a network of support for and amongst them. The next deadline for applications will be 28 February 2017. Applications can be made through the new portal. For more information please email **edufunding@physoc.org**

Case Study: Dr Samuel Fountain, University of East Anglia *– awarded Research Grant in 2013*

What attracted you to The Society's research grant scheme?

It represented a seed fund opportunity relevant to physiological research that would allow for investment in new research equipment to pursue a new line of research; the maximum amount that could be requested was significant.

How did you find the application process?

The guidelines associated with the application were very clear and the application process was straightforward. Publication of the marking criteria on The Society's website was also very useful when preparing the application.

What area of physiology do you study and can you briefly describe the project and its implications?

Our overarching research interest is to understand the physiological roles of purinergic receptors, a family of cell surface receptors activated by extracellular nucleotides under physiological and pathophysiology conditions. We are particularly interested in what functional roles P2X (ionotropic) and P2Y (metabotropic) play in the cardiovascular system. This project involved single cell calcium imaging of primary human monocytes. This was in an effort to understand the role purinergic receptor activation plays in supporting signaling from a family of peptides called chemokines. Chemokines are small molecular weight proteins that are involved in leukocyte tissue recruitment – this process is important physiologically (innate immunity) but also in human disease (atherosclerosis). We hypothesise that the purinergic signaling system supports the action of chemokines, and that antagonising P2 receptors may dampen monocyte responsiveness to chemokines.

What did you use the funding for?

The funds were used to purchase optics, filters, software and perfusion equipment to enable modification of an existing microscope for single cell calcium imaging. Funds were also used to purchase consumables associated with leukocyte isolation, purification and a small amount of animal costs.

How did the funding help you towards the next steps in your career/scientific endeavours?

Funding through the scheme facilitated the production of pilot data using the new microscope setup. These pilot data were used in a 3-year project grant application to the British Heart Foundation – which was successful!

What advice would you give to potential applicants?

Acquiring or modifying new equipment is key to expanding the research capacity of your laboratory. Think how a Physiological Society research grant could be used to bring adding value to your program of work. Small grant opportunities are limited in the physiological societies and this scheme could therefore be highly valuable when starting out as an independent researcher or enhancing your research capacity.

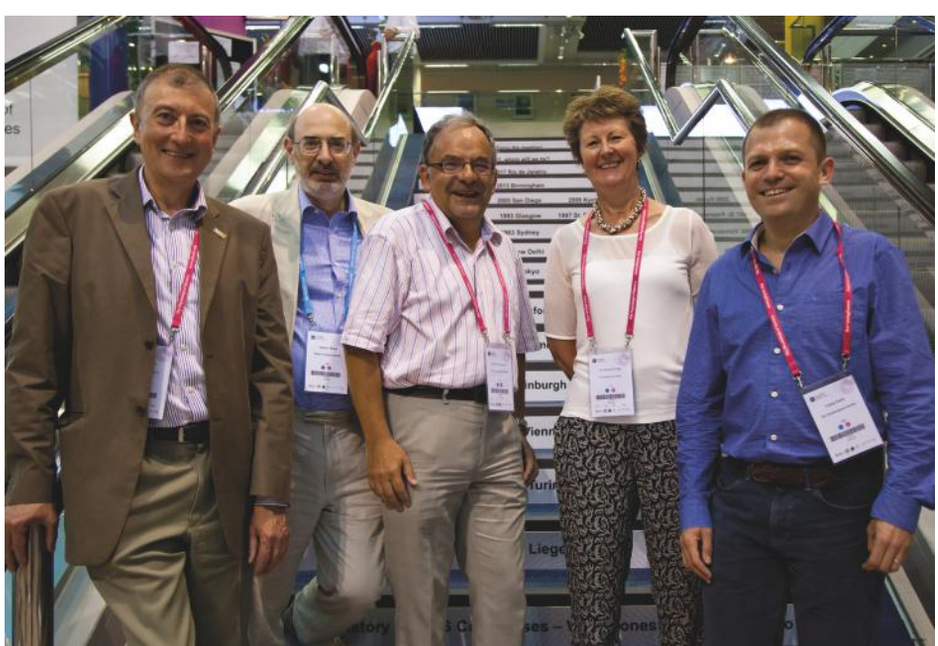
The face of finance: the Honorary Treasurer explains her role in keeping The Society solvent

Anne King

Honorary Treasurer,
The Physiological Society

I assumed the role of Honorary Treasurer in 2013, following in the footsteps of distinguished previous incumbents including Rod Dimaline, Graham McGeown and Jeremy Ward. In 2015, we celebrated 100 years of Women's Membership of The Society so it is a particular privilege to be the first female Honorary Treasurer at this time. In a list of previous Society Officers, I discovered that whilst I might be, to date, the only female Honorary Treasurer, I am not the first from Leeds University. That distinction goes to BA McSwiney FRS, erstwhile Professor of Physiology, who held this office for a heroic 11 years across 1934-1945. Considering the tumultuous historical world-changing events encompassed within these dates, my own hand-wringing over the potential impact of GREXIT and more recently BREXIT on our current and future finances seems a tad melodramatic – but more on that later.

On my first reading of the 'job description', the rather long list of roles and esponsibilities attributable to the Honorary Treasurer was quite daunting. Indeed you are right, perhaps I should have thought about this before I uttered 'yes' so fulsomely. Most scientists like me are used to manipulating data and numbers but rarely have a background in business or financial accounting. Consequently, the language of finance and accountancy that I was going to have to get used to seemed initially impenetrable. What does the acronym SORP stand for? What is a fiscal period (sounds painful?). What are 'tangible' assets and why are some assets but not others subject to annual depreciation? Would I ever be able to understand Ninja Casey's multi-layered Excel spreadsheets? The answer to that is no, actually. Would I be the first Honorary Treasurer to bankrupt The Society? These and many other unknowns suddenly presented themselves, necessitating a climb up a very steep learning curve in a short space of time. But setting these short-term challenges against the skills and experience I acquired, plus the fact that I gained an in-depth understanding of all aspects of The Society's business, then for me personally the equation is well-balanced.



Treasurers past and present: (L-R) Rod Dimaline, Jeremy Ward, Graham McGeown, Anne King, Casey Early

Meet the team (L-R) Bridget Lumb, Richard Fass, June Wang, Beverley Lyons, Anne King, Casey Early, Stuart Gray, Mike Russell

On assuming my new role, I rapidly appreciated the considerable support that came firstly, from our Finance Director, Casey Early and secondly, from all the members of the Finance Committee. Another route to my acquisition of requisite skills and knowledge was attendance at courses such as 'Charity Finance – the Essentials', 'The Role of the Honorary Treasurer' and 'Risk Management'. One of the most enjoyable aspects of attending these was the opportunity to meet with a multitude of enthusiastic delegates from a diversity of UK charities, including many I had never heard of. An Edinburgher by birth, I still have the contact details for the charity Royal Society for the Relief of Indigent Gentlewomen of Scotland – just in case! So let me take this opportunity to introduce you to the team who provide essential financial oversight and play an important part in strategy, planning and governance as it relates to finance. Many of you will know and have met our extremely knowledgeable Finance Director, Casey Early who recently completed a period as Interim CEO. Far fewer of you will have met our Finance Manager Gabina Alfonso who has the important job of, amongst other things, safely and securely moving our monies around and making sure all the bills get paid in a timely manner. Finance Committee membership is currently Bridget Lumb (our new Vice-President, Bristol University), Lucia Sivilotti (University College London), Frank Sengpiel (Cardiff University), Stuart Gray (Glasgow University) plus two independent members, Mike Russell (former Finance Director of the Zoological Society, surely not referring to our Finance Committee when he said 'proximity to animals had become a key part of his working life') and Richard Fass (a strong background in Charity Finance having been Treasurer and Trustee of several other health-related charities). The collective acumen and the sterling work of this team on behalf of The Society are herein acknowledged.

So what does the Honorary Treasurer actually do apart from act as Chair of the Finance Committee? The Society operates as a charity and so an important governance duty is to ensure that our accounting and auditing processes comply with statutory legal and regulatory requirements. The financial year follows a certain unvarying pattern that, in part, defines our activities – annual budgets and forecasts, income assumptions, investment reports and the audit exercise are all calendar firmaments. But for me personally, the most important job is to ensure that the trustees, the officers of The Society and Council understand the financial underpinning of The Society. This includes an appreciation of first, where The Society's money comes from and second, how it is being used to support its many charitable activities. All trustees have a duty and responsibility with respect to financial decision making and strategic planning but understandably look to the Honorary Treasurer and the Finance Committee for guidance. Few folks wish to spend several hours wading through detailed accounts and, in analogy with the delivery of a lecture to undergraduates, glazed eyes and befuddled expressions across the audience are a sure cue that you are missing your target in terms of communication. Our trustees and the membership are involved because they wish to interact with a network of like-minded individuals to support Physiology through activities driven by the various committees in areas such as publishing, meetings, education, outreach and science policy. So the essence of the role of the Honorary Treasurer is to distil and reduce financial facts into a format that can be grasped by anyone with a mind to think about it for a while. In other words, speak plain English. None of us should be beholden to self-appointed 'experts' who often have a less tenuous grasp of the facts than they would have us believe. Witness the recent catastrophic unravelling of the global banking sector and the systemic breakdown of totemic institutions managed and run by 'experts'. Sound financial strategy is reliant on an understanding of the actual rather than imagined wealth of any institution and the Finance Committee has been working towards provision of accessible quarterly management accounts to inform all of us about the status of The Society's financial health. We have also provided staff and trustees with workshops on aspects of charity finance such as investments or risk management which were well attended and informative.

I often hear members say 'The Physiological Society is wealthy' and indeed we are fortunate to have a strong and sustained income stream largely through the publication of our highly respected journals; *The Journal of Physiology*, *Experimental Physiology* and *Physiological Reports*. The first volume of our flagship publication *The Journal of Physiology* appeared in March of 1878 and included papers from Sydney Ringer, WH Gaskell and JN Langley. There is every prospect and expectation that The Society's prosperity will continue undiminished and that our charitable activities and scientific endeavours will endure and expand. But which one of these early authors could have conceived of how the scientific publishing landscape would look in the post-internet 21st century? Indeed I challenge any of you to predict how the issues faced now – open-access mandates, data (ir)reproducibility, validity of peer review, prodigious expansion of journals (~30,000) to name but a few – will be resolved. In addition to publications, which together generate ~90% of our income, The Society has a substantive investment portfolio which supplements our income and, as importantly to my mind, gives us another means to establish future security. Those of you who have attended the AGM or have perused The Annual Report will appreciate the pressures created by the current turbulence in the financial environment. Since becoming Honorary Treasurer, we have faced both Grexit and Brexit and I, along with many others, have found the rollercoaster ride rather unpleasant. There is a saying that '*a full purse is not as good as an empty one is bad*'. So how do we protect ourselves and build in resilience for the long-term? All trustees have a duty of prudence to safeguard the assets of the charity – these are not just for use as a piggybank by us the current membership, but are there to guarantee the future too. One strategy is through the reserves fund – well-managed charities should have sufficient reserves to cover known liabilities, absorb setbacks or capture opportunities. The topic of 'reserves' is a bit like 'governance' – only mildly interesting to most of us. But the sorry demise of high profile charities such as Kids Company,

‘Soon it will be necessary to identify someone interested to take this job on for the next four years. Might that be you? ’

“THANK YOU FOR THE TREASURER'S REPORT, MISS ELKINS”

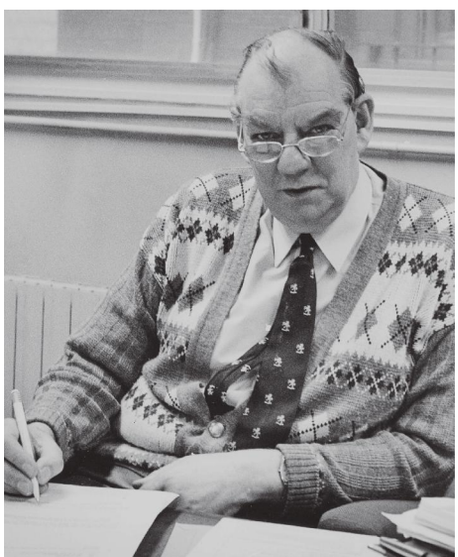
resulting at least partly from the lack of adequate reserves and poor governance, reminds us of their importance. Our recently established ‘perpetuity’ reserves model seeks to grow the reserves to a level that would allow The Society to exist indefinitely even with *zero income* from other sources. The investment-backed reserves are projected to reach the target level by 2024 on the not unreasonable proviso that The Society can move towards a break-even cash budget by 2020.

At the risk of triggering a flood of comments into the Editor’s in-box, I thought I would finish by saying something on the sometimes controversial topic of ethical investments. The reason for this is firstly, it is one of the most frequently asked questions I receive as Honorary Treasurer and secondly, this issue is raised without fail at The Society’s AGM, Dublin P16 being no exception. It was also one of the first questions I asked when I began to scrutinize our investments portfolio. Do we have investments in the payday lender Wonga? But what does the term ‘ethical investment’ actually mean? Divestment from sin stocks, typically pornography, gambling, tobacco and munitions, in my view does not instantly make you an ethical investor. Companies can misbehave on environmental, societal and governance (ESG) fronts. Egregious behavior and corruption within institutions with apparently gold-plated international reputations is well-documented. Some fund managers are unapologetic about investing in the US Barrier Fund, also known as the Vice Fund, which deliberately targets sin stocks and cite as justification the high returns even during recessions. But the primary driver for investment decisions has to be more than financial. The term ‘responsible investing’ is used in the industry and better reflects our own current strategy. To this end, there is an expectation of striking a balance between the aims and values of The Society, the return on our assets and where our money is invested. Cazenove Capital Management manages our funds in accordance with The Society’s agreed investment strategy which accepts a degree of risk in order to generate long term capital growth. As one of the biggest fund managers for the charity sector, they achieved the highest ESG score of A+ in the independent UN Principles of Responsible Investment annual assessment. I don’t doubt that many of our members have strong views on this topic – send them to the Editor, not me!

In conclusion, I can genuinely say that I am thoroughly enjoying my stint as Honorary Treasurer. It is a real pleasure to work with the Finance Committee, the Officers and Trustees of The Society, the membership and the dedicated professional staff at Hodgkin Huxley House. Looking ahead, my term as Honorary Treasurer will be complete in 2017 - how quickly the 4 years will have flown by. Soon it will be necessary to identify someone interested to take this job on for the next four years. Might that be you? If yes, then feel free to contact me as I would be happy to answer any questions you might have. So what, I hear you ask, are the key attributes you need to fulfil this role? I can start more easily with what you don’t need – you most certainly don’t need an MBA, a degree in Economics or an accountancy qualification, you don’t need to become the *Wolf of Wall Street* or compete with George Soros and you don’t have to take out a subscription to the *Financial Times*. What do you need? Mainly the desire and the time to commit to the role but as important is to be the sort of person who can keep a cool head when the world’s next financial meltdown hits... but that will not happen any time soon... right?!

Obituary:

Dr Frederick John Imms 1936 – 2016



Frederick John 'Fred' Imms

Dr Frederick John Imms died peacefully on 28 July 2016 aged 80.

Fred was educated at Maidstone Grammar School and University College London (UCL), where he completed his medical degree and PhD in Physiology before becoming a lecturer at St Thomas' Hospital Medical School. He then moved to the MRC Environmental Physiology Unit at the London School of Hygiene and Tropical Medicine, where his research included gait studies in the elderly and recovery after injury. In 1980, Fred joined the Department of Physiology at Guy's Hospital Medical School where he remained, as it merged with St Thomas' and King's College London, until his retirement. His main research interest was always applied human physiology; as well as papers and chapters in this area, he also wrote a textbook and an MCQ book on applied physiology aimed at trainee clinicians.

To his colleagues, Fred was a great team player, always cheerful, efficient and helpful. To students, he was an enthusiastic teacher and loyal supporter of many university sports clubs. He taught generations of BSc, MSc and PhD students the mysteries of venous occlusion plethysmography and lower body negative pressure.

Sport was Fred's passion, particularly rugby, hockey and cricket. He played hockey as a student and as a lecturer with the students at St Thomas. He played cricket for Dorking Cricket Club (DCC) and later for the Forty Club. He was very involved in the running of both clubs and regularly umpired. As a member of the MCC, he regularly attended matches at Lords. Fred was a referee for the London Society of Rugby Football Referees and later on a referee assessor, mentoring and assessing the next generation of rugby referees.

Fred had his share of health problems but his indomitably positive personality meant that many will not have realised this. In his early forties, he was diagnosed with cancer that had already metastasised. Fortunately, following surgery and chemotherapy, he made a full recovery.

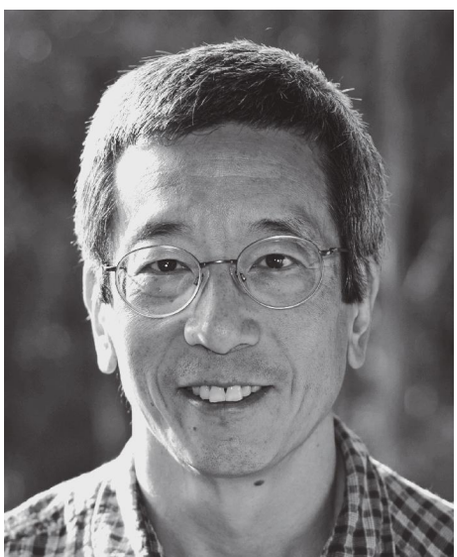
In more recent years, health problems reduced Fred's energy and mobility but, being a glass half-full person, he focused on what he could still do. Less than two weeks before pneumonia and his other health problems finally caught up with him, Fred attended an England v Pakistan match at Lords with Val and Andrew and had a great day.

Fred is survived by his wife Val, his sons Andrew and Jeremy and four grandchildren. He will be greatly missed by Val, the family and his many friends.

Jane Ward
Visiting lecturer, Dept. of Physiology,
King's College London, UK

Obituary:

Roger Yonchien Tsien MD, PhD 1952 – 2016



Roger Tsien

Roger Tsien died suddenly on 24 August 2016. He was a scientific and inventive genius who straddled traditional subject boundaries and shared the 2008 Nobel prize for chemistry for his work on the green fluorescent protein. Roger is best known for the extraordinarily diverse 'optical toolkit' of molecular probes that he created to study the physiology of intact living cells, many now used by thousands of scientists worldwide whose work they facilitated and transformed. His death at the age of 64 was a shock, not only to his family, but also to the scores of scientists who were trained by him and collaborated with him, and to the many who knew and used his work.

Childhood and early education

Roger Tsien was educated at Livingston High School, New Jersey and went up to Harvard aged 16, graduating at 20. He then moved to the Physiology Laboratory at the University of Cambridge for his PhD and postdoctoral research.

His parents were Chinese, his father an engineer who had done post-graduate studies at MIT before World War 2. He was later able to emigrate to the US in the aftermath of the war with his wife, a nurse, and their first son Richard. Roger developed a keen interest in chemistry from a very early age, and from the age of 8 performed increasingly complex, potentially hazardous, reactions in the home basement and garden with home-made glass apparatus and the then ubiquitous red rubber bungs. An amusing account of these activities is given in Roger's 'Nobel Biographical'. In 1967 he did an NSF sponsored summer internship at Ohio University on the ambident co-ordination of thiocyanate, which won him the $10,000 first prize in the prestigious nationwide Westinghouse Science Talent Search. In 1968 he entered Harvard and studied a wide range of subjects including art history, music, economics, relativistic quantum mechanics, astrophysics, molecular biology and neurobiology. Interestingly, he did not take chemistry because he considered those 'ironically, the worst courses'. His first published paper was written in his final undergraduate year, in theoretical physics!

Doctoral research at Cambridge

Roger's most abiding interest was neurobiology and the relationship between brain and mind. That led him to the Physiological Laboratory in Cambridge on a Marshall Scholarship. Strangely his assigned PhD advisor was Richard H Adrian, a distinguished muscle electrophysiologist who had no research expertise in neurobiology. But in those days PhD students were often left essentially to their own devices, with supervisors providing occasional 'adult supervision' and moral support. This allowed the student considerable freedom to operate in whatever area of research they chose. Roger did not even work in Adrian's laboratory, but was allocated a windowless store room in the biophysics sub-department headed by Dennis Haydn. Early experiences with microelectrodes had convinced him to design and synthesise new dyes for recording nervous activity. To pursue his plan, he needed to learn synthetic organic chemistry. He persuaded two faculty members in Chemistry to guide him informally, and Roger commenced working at the one spare place in the Chemistry Department's third year teaching laboratory. He related that once he was doing chemistry aimed at producing a probe he had designed to be useful, he enjoyed and became highly proficient in these syntheses.

His first attempt to make voltage sensing dyes by labelling tetrodotoxin was not successful. Roger then turned his attention to the design of dyes that could measure intracellular free Ca (Ca_i), and among other things report action potential activity indirectly. This would be a considerable challenge since Ca_i was known to be micromolar or less in the face of mM Mg, and much higher levels of Na and K. (By the early 70s others had managed to measure Ca_i with the luminescent protein aequorin or the organic dye Arsenazo III microinjected into large cells such as squid giant axons or barnacle giant muscle fibres.) Roger set out to design superior indicators based on the colourless Ca-selective chelator EGTA. This took quite some time to accomplish.

In the meantime he collaborated with me (then a young researcher recently come to Physiology and wanting to look at the role of Ca_i in stimulus-response coupling in cells where aequorin or Arsenazo would be unfeasible or inadequate) using his organic, inorganic and physical chemistry insights to design suitably sensitive and selective Ca-sensitive microelectrodes. As well as adapting a selective resin recipe from macroelectrodes, by for example adding PVC, we refined the production of the glass microelectrode itself. We cleansed micropipettes in ethanol-nitric acid, with some trepidation as this is an explosive mixture if not managed correctly, silanised them absolutely dry in an oven and painted them with silver paint to reduce capacitance, finally bevelling them on a rotating disc of diamond dust layered on an agar gel.

We had no adequate high impedance electrometers available to record from these ultra-high resistance microelectrodes, and so Roger promptly designed and built one to his own design (it was the topic of a communication to the Physiological Society) and it worked perfectly for at least a couple of decades thereafter. He saw nothing unusual in being able to accomplish this task; it was just another intellectual challenge to be met by some calculations, clear thinking, and maybe a focussed literature search. Working with various colleagues (including Richard W Tsien) we used these electrodes in skeletal and heart muscle, snail neurones and Xenopus embryos. This work was arduous, time resolution was poor, inapplicable to most mammalian cells and needed highly skilled researchers to perform the electrophysiology, which neither of us were.

So, further motivated, Roger pressed on with the work to design and synthesise fluorescent Ca_i reporters. His first successful fluorescent molecule was quin2 which was derived from a parent molecule, DAPTA, which gave only an absorbance, not a fluorescence signal. However the experience with Ca microelectrodes showed the critical need to design a method for introducing fluorescent probes, which were hydrophilic and membrane impermeant (as they needed to be, to stay in the cytosol as reporters) into populations of intact cells. Thinking through this problem and perusing the literature on making penicillins orally bioavailable, Roger made acetoxymethyl (AM) derivatives as a non-disruptive technique for loading hydrophilic molecules into cell. This technique for dye-loading intact cells soon became very widely used, and its invention was a major technical advance.

Having in hand quin2 and a method for trapping it in intact cells of any size, Roger and collaborators proceeded to make the first measurements of Ca_i in many cell types such as lymphocytes, platelets, sperm, neutrophils and macrophages. They started to explore the role, and sometimes the absence of a role, of Ca_i, in stimulus-response coupling, and also to investigate cellular regulation of Ca_i. This work led to numerous requests for samples of these probes, too numerous for him to supply with the available facilities.

To satisfy these requests Roger made two moves. First, he tried via the NRDC (the then mandated government agency that performed patenting and technology transfer for universities) to apply for patents, but they ruled that intracellular Ca was not commercially relevant (an error, though not so severe as later their failure to patent monoclonal antibodies) and they suggested he should work on probes for serum Ca. Second, he looked for a reagent company to synthesise and distribute the quin2 and quin2-AM to researchers world-wide. It turned out that these molecules were not that easy to produce and it took a while to find a company capable of doing a decent job. Lancaster Synthesis became the supplier and soon these probes became up to 50% of its business! Important further developments in Ca probes would come later, but while still at Cambridge, Roger designed and made a superior fluorescence cytosolic pH reporter, BCECF, which could be trapped in cells using the AM trick. In 1977 Roger finally wrote his thesis and was awarded a PhD.

From 1977 to 1981 he was a research fellow at Gonville and Caius College. He remained interested in fluorescence probes of membrane potential and worked with Steven Hladky and me on two classes of molecules that could report membrane potential due to redistribution across the plasma membrane. We worked out the physical chemistry of these systems in some detail and they gained moderately wide acceptance by cell biologists. However, they were not fast enough to report action potentials; Roger came back to that problem many years later.

Move to UC Berkeley

In spite of his accomplishments at Cambridge, and his manifest intellectual brilliance, Roger had difficulty in finding a permanent position. Cambridge had provided in many ways the ideal unstructured environment for him, with its permissive atmosphere and wide variety of visitors, to refine the many interdisciplinary skills he later exploited so well, but he was neither a 'card-carrying' biologist nor a 'properly' qualified chemist. In those days such boundary conditions were important to appointment committees; but after some searching, he received an offer to move as an assistant professor of Physiology and Anatomy to the University of California at Berkeley. Physiologists there such as Robert Zucker were keen to collaborate, and there were some, if primitive, facilities for doing his chemistry.

At Berkeley he was able to recruit synthetic chemists to his lab, one of whom, an ex-pat Englishman Stephen Adams, has worked with Roger throughout the remainder of his career. He continued to invent many further probes of intracellular ions, including a new generation of Ca_i probes (fura2, indo1, and fluo3) each of which had specific virtues. The most important was fura2 which was designed to give stronger signals than quin2, and also provided Ca-selective FRET (fluorescence resonance energy transfer)-based colour change. These improvements gave a probe that had much less background interference and much faster responses. Next came the development of intracellular Ca imaging for which Roger and his team were key pioneers. Among his many skills he was good at optics and computing and, working with Nikon, his team made one of the first systems for real-time, two wavelength, ratio imaging to research cell heterogeneity and Ca_i gradients within cells, and also rapid transients. His team also created the ratiometric Na_i indicator SBFI.

Roger had a pithy phrase for research in cell signalling 'show it, block it, move it', using 'spies, saboteurs and messengers'. With the aforementioned probes he had made major advances in 'show it'. It had also been possible to trap enough DAPTA or quin2 into cells to greatly curtail Ca_i changes and thus to 'block it'. Of course there were also pharmacological agents for blocking various signalling events. The Berkeley team produced a series of photo-labile Ca chelators, 'caged calcium', and collaborated with several neuroscience groups to study the role of Ca in control of neuronal ion channels, and with other groups in a variety of cell types. He also devised a photo-labile chelator that became more avid after illumination and so could locally reduce Ca_i. Roger's practice at this time and henceforth was typically to publish a new probe by exemplifying its use to answer some significant biological question, either with expert collaborators, quite frequently local colleagues, or with some of his own post-grads and post-docs. As far as practical, Roger would then distribute probes to the scientific community from his lab or arrange that they were available from a commercial source.

Move to UC San Diego

Despite these continued successes, support facilities and funding at Berkeley were quite limited; so Roger decided to move to UCSD in 1989, where until his death he was professor of Pharmacology Biochemistry and Chemistry with a well-funded Howard Hughes Investigatorship. Inventions made early on at UCSD included intracellularly trappable forms of inositol tris and tetrakis phosphate – a far from trivial chemical challenge; a caged inositol tris phosphate, and a caged nitric oxide; and highly effective intracellularly trappable cAMP and cGMP.

'He was very special, touched the work and lives of many, and will be missed by those who knew him, as a generous friend, and for his wonderful mind'

Given more facilities for chemistry and molecular biology he branched out into broader aspects of molecular and cell biology. In collaboration with Susan Taylor, Roger and his team devised an intracellular FRET probe for cAMP based labelling engineered versions of the regulatory and catalytic units of cAMP dependent kinase with different dyes

Roger had been seeking ways to use genetically encoded molecules to serve as his intracellular 'spies'. He recognised that the majority of cell and molecular biologists were well versed in cloning, transfection and genetic engineering, rather than the somewhat arcane techniques of cell physiology, and that the broadest use of new tools would likely come from those that could be delivered to cells by suitable transfection methods. He was initially intrigued by the intensely fluorescent phycobiliproteins from cyanobacteria but the need for an accessory co-factor was a major drawback . He discovered in 1992 that the gene for the green fluorescent protein, GFP, from the jelly-fish that provided aequorin had just been cloned by Douglas Prasher. Roger greatly appreciated Prasher's openness in supplying the GFP cDNA which allowed him and his colleagues to get to work rapidly. GFP was potentially highly attractive because it did not require an accessory co-factor. GFP produced by transfecting cells was intrinsically fluorescent. The development of many variants of GFP to probe multiple aspects of cell structure and function was a major turning point. Roger's laboratory led in this venture as recognised by the 2008 Nobel prize, awarded to Roger together with Shimomora who first isolated GFP and Chalfie who pioneered its use in intact organisms to follow cell fate. Roger ensured that Prasher attended the Nobel celebrations and received much appreciation for his key contribution in first cloning the gene. The applications devised for GFP by Roger and his collaborators are far too numerous to even list here and in any case an excellent account of progress through 2008 can be found in the Nobel lecture. By a mixture of rational design and random mutagenesis many different coloured GFPs were generated (often called GFPs even if they glow actually blue or yellow). To further extend the 'palette' of colours Roger followed up the discovery of a new class of red fluorescent proteins by detailed investigation of their physical chemistry and the production of new longer wavelength colours and superior biophysical properties. He took great pleasure in naming these variant FPs after fruits of different colours, such as honeydew, tomato cherry and plum. One ingenious new tool he developed to produce superior variants of interesting proteins was to subvert the genetic apparatus in B lymphocytes that normally hypermutates antibodies in the process of affinity maturation.

A few of the applications of GFPs Roger's team introduced to perform what he called 'intracellular biochemistry are tools that allow study of: inositol tris phosphate, Ca_i, cAMP, cytosolic pH, specific protease detection, kinase and phosphatase activity, and mitosis. Each demanded thoughtful and careful choice of the engineered proteins to which the appropriate GFP would be attached. Another aim was looking at cell signals in specific sub-cellular compartments by targeting the probes to e.g. mitochondria, initially with his longstanding colleague Tullio Pozzan at Padua, who originally worked with Roger on quin2 in Cambridge days.

The astonishing success of the GFP family of sensors and the renown it brought did not inhibit or even slow down Roger's desire to create yet more ways to 'peek and poke' into biology. One drawback of the GFPs is their large size that might interfere with the molecular events they are reporting. The solution was called FlasH, wherein a small peptide (much smaller the GFP) with four carefully positioned cysteines was the genetically encoded part of the probe that could be encoded in the DNA attached to that for any desired protein. The other component was a membrane permeant arsenical compound that could be applied to the transfected cells and becomes fluorescent only when complexed to the four SH groups.

In the 1990s he returned to devise better probes of membrane potential. With these probes he showed that one could follow fast action potentials with decent signal-to-noise, a step up from the previous two component system. He also worked out a way to make a FRET-based gene expression reporter that signalled from within intact living cells. This method provided a bacterial enzyme, beta-lactamase, which would have zero natural background in mammalian cells as the element to be inserted at the desired place in the genome of the cells to be studied. Then he and Gregor Zlokarnik invented a substrate with a FRET pair of fluorophores separated by a beta-lactam linker, as an acetoxymethyl ester so that it could be incorporated in living cells. Now expression of the gene in question would be reported non-destructively by ratiometric fluorescence in populations of cells or one cell at a time by imaging microscopy. This technology is now sold commercially as GeneBLAzer and has been used highly effectively in drug discovery for creating and screening cell-based assays.

With Stephen Adams, Roger developed a series of probes for protein localisation that gave both a light and electron microscope stain of the same molecules in the same sample to allow correlation at micrometre and nanometre scale. He also recently produced far red responsive variants of channel rhodopsins to extend the range of optogenetic technology for neurobiology.

The two projects that most engaged him in recent years were very different. One aimed at designing probes that targeted cancers in patients, as optical aids to surgery, MRI or positron emission imaging, or potentially as vehicles selectively targeting anti-tumour agents to the cancers. These were ingeniously designed molecular gadgets which on injection into a subject with cancer, were cleaved to produce either an increased signal due to de-quenching or a colour shift due to release of the FRET. Either way suitable imaging systems can show the operator (surgeon) where in the operating field is cancer and where the cancer-free margin is. After showing effectiveness in preclinical models, one such probe is now in clinical trials with a San Diego biotechnology company, Avelas. Inc. Roger's team also has preclinical data indicating that this approach can deliver anti-tumour drugs with increased therapeutic index.

The other big new project brought him back to the brain. He had long pondered what could be a basis for long term memory. He did not think that long term potentiation or synaptic and dendritic spine alterations could survive months and years as accurate long term engrams. As he read the neurobiology literature and pondered what long term store might be based on, he was intrigued by a structure with a set of proteins that are highly stable and closely connected with synapses and dendritic spines. This structure is the extracellular perineuronal net which surrounds neuronal processes, and indeed through holes in which dendritic spines must communicate. To summarise, he proposed the elegant, and in principle simple, concept that very long term memory stores are created by the number and pattern of these perforations (which for those old enough to recall he likened to a three-dimensional version of the punch cards we used in early computer programming up to about 1975). He adduced some interesting data that fitted with this idea and had embarked on a series of clever experiments to begin to support, or contradict, this radical notion. The requisite enzymes for making holes in the fibrillar network are present and subject to various biochemical controls. One neat point he raised is that the timing of the earliest of childhood memories fits roughly with the first development of the perineuronal net in infants. Even as a brilliant Nobel laureate he had difficulty getting any traction for this idea or support for the research. To publish the concept, he used his privilege as a member of the National Academy of Science to publish his hypothesis in PNAS. Unfortunately, now time, not Roger, will tell whether this is another example of aging Nobel laureates wanting to explain the brain, or a true breakthrough.

Roger was a brilliant research scientist. He is an author of over 400 papers and major reviews, with frequent publications in *Nature* and *Science*. He also did his fair share of reviewing papers and grants, supporting recruitment, and was also a fine educator and mentor, and trained over 100 graduate students and post-docs from many different disciplines. While he was an introverted, somewhat shy person, he was a superb lecturer using everyday plain language to explain complex ideas and avoiding jargon. He also had wonderful and colourful slides and videos and would many times give colourful practical demonstrations like the famous chemistry lecturers of old. He was a wry and insightful participant in Q&A after presentations or in symposia. His breadth of knowledge and expertise meant there were few presentations the he could not cannily interrogate no matter what the field of biology and indeed beyond. He did not wish to be distracted from the science that he and his group were doing and so did not take on administrative tasks such as a departmental or faculty chair. His achievements were recognised by dozens of prizes and awards and scores of plenary or keynote lectures. Aside from the Nobel Prize, other major awards included: Javits Neuroscience Investigator; Gairdner Foundation International; Foreign Membership of the Royal Society; HP Heineken Prize; Max Delbruck Medal; Wolf Prize; Golden Goose Award.

In addition to his tireless pursuit of academic excellence, Roger was a master translational scientist, before that became usual (or even acceptable) and encouraged. There are over 160 US patents in which he is named (and usually was the lead) inventor. While he was naturally keen to participate in or lead the first application of his new tools and produce the first publication he was generous in providing materials to the scientific community. Many of his reagents were manufactured and distributed by licensees of the patents, in particular Molecular Probes of Eugene OR, which was founded and run for years by a creative chemist, Richard Haughland who became a valued colleague, if occasionally also a competitor, of Roger. Roger consulted for many biotechnology and pharmaceutical R&D groups over the years and was founder or co-founder of three San Diego companies. He once semi-seriously commented that one motivation for founding these companies was to provide good jobs for his post-docs. He recognised that the kind of innovative cross-disciplinary science he got them doing in his labs was great training for the challenges of high level applied research in science-based industrial ventures. One company's biggest success, coming to fruition after it became part of Vertex Inc., where Roger remained on the scientific advisory board, was the launch of two drugs that enhance the defective chloride channel in cystic fibrosis. With his colleague Charles Zuker and the renowned biochemist Lubert Stryer, he also co-founded Senomyx in 1998, which aimed to use the new knowledge of taste receptors and the developments of the Tsien technologies applicable to compound screening to discover food additive compounds that could potently modulate taste receptors to for example, enhance sweet flavour or block bitterness. More recently he founded Avelas Biosciences to develop the cancer illuminating structures mentioned above.

Roger worked hard and intensively at his science. At home in the evening he would often sit cross-legged on the floor after dinner, with a weather eye perhaps on some TV drama, but his ever-present note book on his lap, pencil in hand, designing the next probe, or deep in a biophysical calculation. Away from work, Roger applied himself quite intensively to his other interests. He was a fine pianist and had briefly even considered a musical career. As soon as he had the space and funds, he acquired his own grand piano. He travelled with a Walkman, or modern equivalent loaded with the classics. He enjoyed somewhat down-market thrillers – John D MacDonald was a favourite author. Fitting with his joy in colours and imaging, he was a gifted amateur photographer, and enjoyed vacations in the wild outdoors, taking arduous treks, camera in hand.

In 2014 he suffered a stroke that left him with significant disabilities including a right hemi-paresis and some minor dysphasia. His intellect was not impaired, and with determined efforts in rehabilitation he was able to continue his science and inventions and indeed to travel and continue to give outstanding keynote lectures. But it was burdensome and tiring, and he had begun to wind down his research team in last year or so. He and his wife Wendy moved from San Diego to a delightful spot outside Eugene to start a new quieter existence. Sadly, one year after the move, Roger died while exploring on his tricycle in a local park.

Roger was for many the brightest person they ever met. He was generous with his time and intellect and in his own way totally non-elitist, not that he suffered fools gladly, especially if they had position and pretensions. But he was very supportive of motivated young scientists and had a major impact on so many careers, naturally those who worked for or with him, but also many thousands whose work was enabled by his inventions. He was very special, touched the work and lives of many, and will be missed by those who knew him, as a generous friend, and for his wonderful mind. Roger is survived by his wife Wendy, and his two brothers Richard and Louis.

Timothy Rink
Cambridge, UK

Obituary:

Alan W Cuthbert FRS, FBPhS, FMedSci 1932 – 2016

Alan Cuthbert in April 2008
Photo: Ivor Williams

Alan Cuthbert was born in Peterborough and educated initially at Deacon's Grammar School Peterborough, then at Leicester College of Technology where he studied Pharmacy. His growing interests in biology led him to the University of St Andrews where Alan was one of the first students to study the newly introduced BSc in Pharmacology. Following a three year service commission in the Royal Navy, Alan was determined to pursue a career in research and after writing letters of introduction to some eminent biologists of that time, he recounted that he spent an inspirational half day with Sir Henry Dale (at the Wellcome Foundation), who then introduced him to Professor Wilhelm Feldberg and then to his eventual supervisor, Gladwin Buttle, Professor of Pharmacology at the School of Pharmacy (Brunswick Square, London). A Pfizer Fellowship evolved permitting Alan's PhD research on acetylcholine receptors in chicken amniotic smooth muscle, with additional funds from the British Egg Marketing Board.

During his time at 'The Square' Alan impressed visiting scientists most notably Professor Edith Bulbring who invited him to undertake sucrose gap experiments to characterise the electrical activity of different smooth muscle preparations in her laboratory in Oxford. Whilst there Alan met Arnold Burgen, a pharmacologist visiting from Canada, and this contact lead Alan a few years later to apply for a University Demonstratorship in Professor Burgen's then embryonic Department of Pharmacology within the Physiological Laboratory at the University of Cambridge. Alan began publishing his research in 1964, one of his first papers on the electrical and mechanical properties of chick amnion being a single author paper in Nature. His career-long interest in epithelial ion transport processes and their modulation by hormones started in the late 1960's utilising a range of preparations such as frog skin, toad bladder, fish gills, rodent and human intestinal epithelia. This focus continued over four decades resulting in more than 250 publications, with much of this work being published in the Journal of Physiology and the British Journal of Pharmacology.

Alan was promoted on the basis of his research to Reader in Pharmacology (1973-1979) and then to Sheild Professor and Head of the Department of Pharmacology (1979-1999) which was then located at the Addenbrooke's Hospital site near the MRC Laboratory of Molecular Biology. His research at that time focused on electrogenic epithelial sodium and chloride ion transport, while as Head of Department his energies aimed to establish the department's financial independence. In 1989 the department moved back in to Cambridge city centre to a new building on Tennis Court road, where it remains today. This relocation to purpose built accommodation closer to other biomedical science departments was probably Alan's greatest legacy. It catalyzed academic-industrial interactions via the embedded Glaxo Institute of Applied Pharmacology (headed by Patrick Humphrey) as well as with other University departments and was geographically preferential for undergraduate Pharmacology teaching.

Professor Cuthbert was Fellow of Jesus College Cambridge (1968-1991) and then Master of Fitzwilliam College (1991-1999). He was Deputy Vice-Chancellor, University of Cambridge (1995-1999). Other positions included: chair of the Editorial Board of the British Journal of Pharmacology (1974-1982); Vice President (1997-2000) and then President of the Federation of European Pharmacology Societies (2000-2002); Foreign Secretary for the British Pharmacological Society (BPS: 1997-2000). In 2005 he was awarded the BPS Wellcome Gold Medal for his outstanding research achievements.

Alan retired in 1999, but as a true experimentalist he continued working at the bench (within the Department of Medicine) collaborating with Dr Lesley MacVinish and assisted by his long-term technician, Margaret Hickman. He continued an active international collaboration with Professor Jeff Wine (Stanford University) pursuing novel cystic fibrosis pharmacotherapeutics and published his work up until June 2015.

Always a strong proponent of the disciplines of Pharmacology and Physiology, his demise at the age of 84 is a shared loss to both the Pharmacological and Physiological Societies alike. He died on 27 August 2016 and is survived by his wife, Hetty and their sons, Adrian and Bruce, and four grandchildren.

Helen Cox
Kings College London, UK

Obituary:

Constancio Gonzalez MD, PhD 1949 – 2015

Constancio Gonzalez, who died in June 2015, was an eminent physiologist who made important contributions to the field of chemoreception and particularly to our understanding of the carotid body. He was instrumental in the major developments that generated the membrane hypothesis of oxygen sensing that recognized a seminal role for O_2-sensitive K channels and an author of the first report of Type I cell O_2-sensitive currents in Science in 1988. Additionally, Constancio contributed significantly to our understanding of the hypoxic transduction cascade of the carotid body and was the leading contributor to our appreciation of the complex role of catecholamines, particularly dopamine, in chemoreceptor synaptic transmission. His almost 40 years of published works reflect a scientific career that journeys from the study of the most fundamental aspects of the physiology of the carotid body chemoreceptor cells to the translational and covers papers on neurotransmission, the molecular identity of the oxygen sensor and the pathophysiological mechanisms behind the development of several obstructive sleep apnea associated-comorbidities. Constancio was also a great synthesizer of the emerging and often perplexing data arising from the early studies on chemotransduction literature and his review articles were always comprehensive and insightful. For many entering the field, his Physiological Reviews article 'Carotid body chemoreceptors: from natural stimuli to sensory discharges' was a valuable and authoritative introduction

Constancio was born in 1949 in the Spanish village of Renedo de Valderaduey in the province of León. He had an incredible pride in being *Leones* and never lost the opportunity to invite his friends to his village. Many will remember him as an amazing host who loved his Country.

He received his medical degree in 1974 from the University of Valladolid in Spain and in 1977 he pursued his PhD at the same University with a thesis entitled *Neurotransmission in the Carotid Body*, under the supervision of Professor Carlos Belmonte. From 1976-1980 he went to the University of Utah in the USA to pursue postdoctoral training under Professor Sal Fidone, with his beloved wife, Ana Obeso, with whom he shared all his life, scientifically and personally. After his post-doctoral training, he returned to Valladolid and between two further stays as a Visiting Professor in the United States, he advanced to the rank of Professor of Physiology, becoming the Director of the Department of Biochemistry and Molecular Biology and Physiology of the Medicine Faculty in 1995, a position he held almost until his death.

Constancio received enormous recognition and awards. He served as President of the Spanish Society of Physiological Sciences and supported successful joint meetings between the UK and Spanish Societies. He also held the President role for the International Society of Arterial Chemoreception (ISAC) and was Editor of several scientific journals, including *The Journal of Physiology*. He was awarded with the Severo Ochoa Award for Biomedical Research in 1999, with the prestigious Castilla y León Award for Scientific and Technical Research in 2011 and this last September he was posthumously awarded the Antonio Gallego Award for his dedication to teaching and research in Physiology. The approximately 200 refereed articles in international journals, books and monographs, as well as the many external collaborations reflected in these publications also tell of the remarkable and friendly scientist that Constancio was.

During his term as President of ISAC, of which he was a founding member, Constancio and his colleagues hosted a truly memorable Conference in Valladolid in 2008 on the occasion of the XVII Meeting of ISAC. He was proud to have been able to have the Conference opened by a talk given by F. de Castro, the grandson of Fernando de Castro whose anatomical studies during the 1920s in Spain, many believe, were the first to open the field of chemoreception. To us, Constancio can be viewed also as a descendent of that remarkable Spanish lineage in carotid body physiology that continues to this day. Those of us who were lucky enough to be in Valladolid with him and his colleagues that year enjoyed great science and exemplary hosting. In his own words in the Foreword to the published Proceedings, '*We like to remind you that Valladolid, Old Castile, is a land full of history, good gastronomy and excellent wines*'. We were reminded and we will not forget.

As a superb and enthusiastic teacher and mentor, he was the supervisor of dozens of physicians and researchers and contributed to generate high-level researchers not only in Spain, but also across the globe. He was an exceptional person who combined his remarkable intellect and ability with an enormous wisdom and many will remember him for his help in defining their own scientific trajectories, by the wise advices he offered and by the friendly words, always at the right moment.

The last years of Constancio's life were constantly shadowed by ill-health, which he bravely fought with a lot of strength and determination, without ever reducing his scientific activity. Constancio believed deeply in the value of physiology and in supporting physiologists and he was always a strong supporter of our Society and many of us will have fond memories of spending time with him and Ana when they attended the Physiological Society's main meeting in Manchester in 2012. Many of his friends would say that it was science and his insatiable thirst for scientific knowledge that kept him going in his last years. Definitely, in these last years his body did not follow his mind. He is survived by his wife, Ana and his children, Elvira, Ana and Constancio. He is much missed!

Prem Kumar
University of Birmingham, UK
Silvia Conde
Nova University of Lisbon, Portugal

Experimental Physiology

New Board members

Editor in Chief Mike Tipton has appointed the following to key positions on the Board:

Paul Fadel
Deputy EiC US

Jeremy Ward
Reviews Editor

Mike White
Deputy EiC UK

Virtual Issues

A compilation of Neuroscience related content made freely accessible to delegates at the sfN Meeting.

Articles on The Physiology of Temperature Regulation available for the PPTR Meeting in Slovenia.

Symposium Issue

The brain in hypoxia: curiosity, cause and consequence

With reports from Phil Ainsley, Damien Bailey, Sam Lucas, Sarah Milton & Peter Rasmussen.

New Editorial Assistant

EP is pleased to welcome Hannah Woolley to the journal team.

The Journal of Physiology

Focused issues

GI stem cells – new insights into roles in physiology and pathophysiology

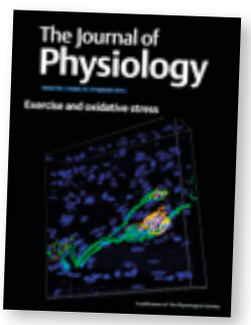
Volume 594, issue 17, September2016

These reviews illustrate the complexity of our current knowledge regarding physiology and pathophysiology of GI stem cells and point to remaining controversies and to gaps that still need to be explored.

Exercise and oxidative stress

Volume 594, issue 18, September 2016

Given that scientific interest in the field of exercise and oxidative stress has grown markedly during the past three decades, the goal of this special issue of *The Journal of Physiology* is to highlight research progress in several important areas of this field.



New Editorial Board members

We are delighted to welcome the following new Reviewing editors who started their roles in 2016.

Richard Carson – Trinity College, Dublin, Ireland. Development of novel approaches to the amelioration of age-related cognitive and behavioural dysfunction.

Hsiao Chan Chang – The Chinese University of Hong Kong, Hong Kong, China. Ion channels in spermatogenesis, sperm function, ovarian function, embryo development and implantation; epithelial transport mechanisms and epithelial ion channels in cancer development.

Sumantra Chattarji – National Centre for Biological Sciences, Bangalore, India. Synaptic plasticity in the amygdala: implications for stress & developmental disorders.

Bruno Grassi - University of Udine, Udine, Italy. The limiting factors, regulation and functional evaluation of skeletal muscle oxidative metabolism, factors limiting exercise tolerance, and muscle bioenergetics.

Paul Greenhaff – University of Nottingham, Nottingham, UK. Skeletal muscle mass regulation and muscle fuel metabolism.

Robert Harvey – University of Nevada, Reno, USA. The dynamic interactions between the sympathetic and parasympathetic branches of the autonomic nervous system and how this triggers abnormal electrical responses that can lead to the generation ventricular arrhythmias.

Karyn Hamilton – Colorado State University, Fort Collins, USA. Understanding the role of stress resistance, proteostasis, and maintenance of mitochondrial protein turnover and function in the context of slowing aging and age-related chronic disease.

Benedito Machado – University of Sao Paulo, Ribeirão Preto, Brasil. Neural control of the circulation and respiration, with emphasis on the neurotransmission of the cardiovascular reflexes in the nucleus tractus solitarii.

Janna Morrison – University of South Australia, Adelaide, Australia. How the fetal cardiovascular system responds to changes in nutrient supply before conception and during pregnancy.

Luis Fernando Santana – UC Davis, Davis, USA. Focuses on cardiac and vascular smooth muscle and determining how cell-wide (or global) and local changes in Ca^{2+} modulate the function of these cells.

Jolanda van der Velden – UV University Medical Center, Amsterdam, The Netherlands. Failure of the heart muscle caused by mutations in sarcomeric proteins in inherited cardiomyopathies.

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.

Physiological Reports

Physiological Reports transitioning to a mature publication

Physiological Reports continues to forge ahead, with submissions in 2016 to date up by 27% against this time last year. If the journal weren't online only we'd be running out of paper to print it on!

Our publishers at Wiley tell us that *Physiological Reports* is 'transitioning to a mature publication', which is a good summary of our progress, even if it hints at surly adolescence. With Julian Davies, a first-generation Associate Editor, standing down and expansion into publishing case reports and reviews alongside research articles, there are definite signs of time passing and growing maturity. We have welcomed Robert Semple a clinical endocrinologist to join us as an AE, and it is always good to have a fresh pair of eyes looking at what we are doing.

We are hoping that the next step will be acceptance by ISI into the Journal Citation Report, followed by calculation of a first Impact Factor. Hate them or hate them, having an Impact Factor will allow more international authors to submit to us and again signify that we are maturing as a publication.

The Editor-in-Chief of *PR* is always happy to receive any comments or suggestions members have about the journal, so please feel free to email her at **susan.wray@physiologicalreports.org**

Call for Nominations for the Editor-in-Chief of *Physiological Reports*

The American Physiological Society and The Physiological Society invite nominations for the Editor-in-Chief of *Physiological Reports* to succeed the current (and founding) Editor-in-Chief, Professor Susan Wray, University of Liverpool, whose term will end 31 December 2017. The Joint Managing Board of *Physiological Reports* will interview candidates in the spring of 2017.

The Editor-in-Chief receives excellent staff support from the societies and from the journal's publisher, John Wiley & Sons.

Nominations, accompanied by a curriculum vitae, should be sent to the Chair of the Joint Managing Board of the Journal via regular mail: Curt D. Sigmund, PhD., American Physiological Society, 9650 Rockville Pike Bethesda, MD 20814-3991

You may also send your nominations to Curt Sigmund via email, care of the APS Publications Department, Administrative Assistant, Charmon Kight: **ckight@the-aps.org**

Full information on *Physiological Reports* can be found online at **physreports.physiology.org**

Applications should be received before January 15, 2017

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