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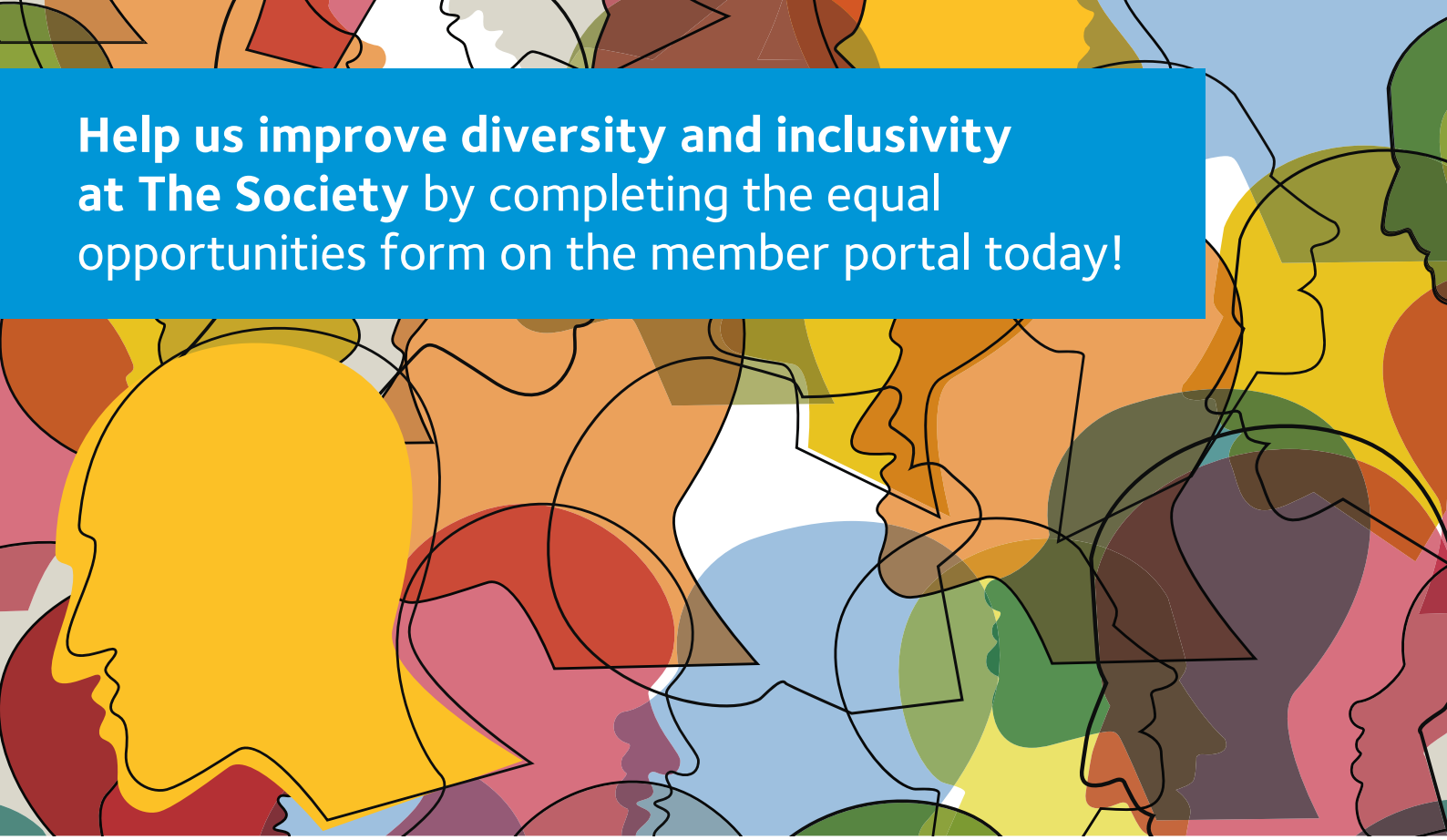
Physiologie Sans Frontières

International Special Issue

The Physiological Society



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The Physiological Society

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Physiology News

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Please email Julia Turan at **magazine@physoc.org**

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Cover image: The city islands represent interconnected neurons with a supporting oligodendrocyte shown as an island with air traffic control. Passport/immigration control (top) is illustrated as ligand-gated ion channels in the dendritic membrane of the synapse, while the microtubules and motor proteins serve as the conveyor belts moving about luggage (middle), and passengers exit their transports as neurotransmitters would exit vesicles via exocytosis at the presynaptic terminal (bottom). Design by Luke Brookes at Making Pictures, **lukebrookes.com/**

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Learn how meal timing influences our health, including connections to our circadian rhythm and the microbiome.

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The Physiological Society

Chrononutrition: From Epidemiology to Molecular Mechanism
13 November 2018
etc.venues, Marble Arch, London, UK

Keith Siew
Scientific Editor

Julia Turan
Managing Editor

7 January 1974 – Gombe, Tanzania. A young Kahama male by the name of Gobi was relaxing on a tree when he was set upon and killed by six male aggressors of the neighbouring Kasakela. This event marked the beginning of Gombe's 'Four-Year War', which saw the Kasakela systematically hunt down and wipe out the Kahama before seizing their territories. This was the first recorded incidence of war in one of our closest relatives, the common chimpanzee.

Humans are also an intensely tribal species; we thrive when surrounded by others of similar origin, habits and social graces. The desire to find one's tribe is so integral to us, it had become the driving force behind our hunter-gatherer ancestors move from wandering troupes to great nation states. While much beauty in the forms of music, art and poetry have arisen from our species' en masse tribalism, when faced with difference, we are not unlike our chimpanzee cousins. We too can wage war and seek to expand our empires, albeit on a grand scale like no other.

As the children of immigrants, we, Keith and Julia, both had the privilege of growing up exposed to many cultures, creeds and nationalities. To be different was to be normal; our tribes were many. We lived through a time when the 'troubles' in Northern Ireland were coming to an end, the EU was expanding and the internet allowed us to have friendships which transcended distance. Perhaps unlike our forebears, in this relatively stable and increasingly globalised world, viewing ourselves as citizens of the world as well as citizens of our own nations came quite naturally to us.

Like many before us, science gave us the opportunity to travel (*Crossing the pond; p. 24*) and we both left home for study and our careers. As the products of international collaboration of sorts, our citizenships meant transitions to life abroad were seamless. Other than the odd misunderstanding over pronunciation or terminology, we had no immigration visas to worry about and could come and go as we pleased. Attending international universities, we met students and lecturers from far-away lands and borders often seemed nothing more than an abstract concept. This view, shared by many of our peers was only bolstered by our study of science. After all, science – the pursuit of knowledge – had no nationality!

Fast forward to present day and things seem far less utopian: the Doomsday clock sits two minutes to midnight, resistance to globalisation is at an all-time high and the rise of nationalism is bringing about instability and uncertainty for all. As nations that were once friends see relations turn sour, and demagogues threaten the very foundations which have allowed international collaboration and science mobility to thrive, we should remind ourselves that moments of great division in our history have been much worse and yet we recovered (*War & Peace p. 36*).

In fact, as this very issue of *Physiology News* is hot off the press, the inaugural Europhysiology meeting will be held in London amidst significant concern from the scientific community about Brexit. No doubt some of you are reading this at Europhysiology. The topic seemingly unavoidable when surrounded by your European colleagues, a mere stone's throw from Parliament with barely six months until the UK must leave the EU and still no deal in sight! Many feel committed to protecting current collaborations, maintaining freedom of movement, or simply espousing their virtues, and we hope this international themed issue will give you food for thought in these politically uncertain times (*Together Science Can; p. 9 // CaSE on Brexit; p. 12 // Knowledge without borders?; p. 16 // Future Partnership Project; p. 11 // Brexit and animal legislation?; p. 19*).

Another goal of this special issue was to generate discussion around the virtues (and vices) of science mobility and collaboration, both at home and abroad (*Collaboration: friend or foe?; p. 27 // A global career from home; p. 47 // Inter-institutional opportunities; p. 48*). As proponents of mobility, we thought it important to highlight some of the great success stories that could only have been borne out of large-scale international collaboration (*International Mouse Phenotyping Consortium; p. 14 // Cardiac physiome project; p. 18 // Human Brain Project; p. 10 // Friends in high places; p. 30 // Hypoxia research; p. 34*). And if you feel passionate enough, we encourage you to get involved with the activities of your local and regional societies to promote the same (*The International Working Group; p8 // Physiology across borders; p. 39*).

In the end, perhaps our prevailing nature will prove to be closer to that of our other cousin, the bonobo. Known for their 'make love, not war' approach to conflict resolution, bonobos have evolved to reap the benefits of collaboration. When different groups meet, they socially mingle and form alliances; in fact, unrelated immigrating members are welcomed and even gain priority access to food and reach high social status.

So the question remains, which cousin are we truly closer to?

The best of times

David Eisner

President, The Physiological Society

I should begin by apologising that this, my final, President's view article is more self-serving than usual. My term as President ends at the Annual General Meeting so I think that this may be an appropriate time to reminisce.

Today's Society is very different from that which I joined in 1981. Then there were up to eight scientific meetings a year. The total number of meetings has not altered greatly but there is now one general Annual Meeting with the remainder being more specialised. The location of meetings has also changed. In the past, meetings were always held in universities. While it was always interesting to see where colleagues worked and, indeed, to be able to put on demonstrations, most universities cannot easily host the current large meetings and do not always have appropriate venues for poster communications, an increasingly used medium in recent years.

The introduction of posters is not the only change. Until the 1980s, meetings consisted entirely of oral communications, with the exception of a handful of prize lectures given over the year. Symposia, including invited presentations, began in association with meetings and now form the bulk of the science with free oral communications virtually absent from many Annual Meetings. Orals have made a comeback for Europhysiology 2018 due to encouragement from our partner societies, and it will be interesting to see what the reaction of Members is.

The Society (like the wider society in which it exists) has changed enormously since it was founded as a dining society for men in 1876. Attempts to allow women to join in 1913 were famously blocked with Ernest Starling pointing out that *'... it would be improper to dine with ladies smelling of dog'*. (I had always assumed that this meant that the ladies smelled of dog but, as pointed out by Lovatt-Evans in his inaugural Bayliss-Starling lecture, it referred to the men). The first female members were admitted in 1915, and The Society recently proudly celebrated the centenary. Some bizarre distinctions were still maintained and, even when I joined The Society, women were required to use their first names when submitting papers to *The Journal of Physiology*.

The Society has a past of which we should be very proud. It was founded in 1876 at a time when physiology was almost synonymous with what is now called biomedical science. Over the years, parts of the subject have split off to form their own Societies. One of the founders of the Biochemical Society (1911) was William Halliburton, Professor of Physiology at King's College London. The British Pharmacological Society was founded 20 years later, again by members of The Physiological Society, and held its first meeting in Oxford the day before that of The Society. Many other parts of physiology such as neuroscience, endocrinology, cardiovascular science, etc. have their own organ-based societies. A challenge for The Physiological Society is to ensure that these scientists continue to value their connections with other physiologists at least as much as those with people working on their favourite organ. This is not helped by the tendency (at least in the UK) for universities to increasingly organise staff into organ-based groupings rather than 'ologies'.

'The Society is now in the very good hands of a new President, Bridget Lumb, who has enormous experience of leadership'

The organisation and administration of The Society has altered out of all recognition. In 1981, the three main officers (Committee Secretary, Meetings Secretary and Treasurer) were supported by assistants based in their universities. There is now a centralised and professional staff under the leadership of our Chief Executive, Dariel Burdass. Such an arrangement is essential for handling the massive increase in regulation concerning businesses and charities with the financial size of The Society. As someone brought up in the previous incarnation of The Society, it has taken me some time to adjust to the idea that Council determines strategy and then hands it over to staff to execute. I have greatly enjoyed my interactions with the incredibly energetic Dariel and have only occasionally felt like the minister in 'Yes Minister'! More seriously, The Society is fortunate to have such a dedicated staff.

What have I learned in the past four years? When I began, I had little appreciation of the amount of time and effort that is required just to run the organisation, even before one produces journals and meetings. Perhaps Health & Safety and the Risk Register should not have been such a surprise but employment law, GDPR and the legalities associated with the fact that The Society has tenants in Hodgkin Huxley House were. I am sure that I have picked up many 'transferable' skills that may come in useful. Like many Members, I have long associated The Society with scientific meetings and publications but had little idea of the breadth of the various public engagement and policy activities that are carried out.

What am I most pleased with? Although I thought that I would never say it, it is good to see that The Society has a strategic plan which will be used to determine priorities and, in particular, avoid the risk of starting and stopping projects as members of Council and committees turn over. From a personal point of view, I am delighted by the establishment of the Europhysiology series of meetings. Several of my predecessors have tried to initiate similar projects; I was fortunate to find our European partners now very enthusiastic.

What other opportunities and challenges does The Society face under its new leadership? One obvious one is that more than 90% of income comes from *The Journal of Physiology*. This is used to subsidise scientific meetings as well as policy, educational and other outreach activities. There is considerable external pressure to move from subscription-based journals to those which are completely Open Access; this would remove the bulk of our income. Can an alternative income source be realised and, if not, what are the consequences for scientific meetings and other activities? This and other questions, many of which are unknown, will no doubt occupy Council in future.

It has been a real pleasure to work together with the other members of Council. Much is owed for their enormous effort. The Society is now in the very good hands of a new President, Bridget Lumb, who has enormous experience of leadership, both in The Society and University of Bristol. She will be an inspiring President. I wish her well!

Reports of The Society's recent Committee meetings

The purpose of these short updates is to keep you informed about the work of our Committees. The following summaries detail the meetings of the past few months.

Council

Following a presentation by the Honorary Treasurer, the Trustees approved the 2017 Annual Report & Accounts. The Chief Executive noted that the Impact Report 2017 (formerly Annual Review) would focus on the voice of the Members and the impacts of The Society to ensure '*Physiology is flourishing.*'

The Chief Executive reported that following on from March Council an International Working Group (IWG) Chaired by Trustee Stefan Trapp had been set up and a discussion paper circulated for its first meeting. The Chair of the IWG would report back recommendations to Council in October.

The Chief Executive presented both the implementation plans and roadmap for the approved 2018–2022 strategy. It was agreed that progress against the strategy would be reported to Council on a regular basis to highlight what had been achieved, in terms of outcomes and impacts.

Council considered and approved the proposal to join The Academy of Medical Sciences FORUM (AM Forum), a body which provides an independent, neutral platform to take forward discussions across sectors to facilitate constructive debate and drive collaboration on different science policy topics. It was noted that opportunities to participate would be communicated to Members as a benefit of membership of The Society.

Council approved the recruitment of a fixed-term History and Archives Project Manager. It was agreed that if The Society was to make more of its rich heritage and strengthen its position as a credible information source that the media, public and education providers could trust then an additional member of staff would be required to make the history of The Society and physiology more accessible and engaging.

A paper on diversity and inclusion which included Society data was presented to Council. This formed the basis of a discussion on how The Society could improve gender balance across all its activities.

Trustees approved the formation of an Equality & Diversity working group. The working group will research and advise on improving inclusion across all Society activities to encompass other under-represented groups such as members of the LBGTQ+ community.

Finance Committee

The Finance Committee discussed The Society's reserves and considered whether a new reserves policy should be formulated to better manage the two principal competing demands on The Society's financial resources: spending them to meet objectives today, versus investing them in order to meet charitable purposes in the future. This was recommended for Trustees to discuss further at the next Council meeting.

The Committee agreed to an accounting reclassification of Hodgkin Huxley House to reflect the investment property aspect. The stated charitable activities in the financial statements will be restated to align more closely with the strands given in the 2018–2021 Strategic Plan.

The Committee reviewed an internal controls self-assessment checklist, produced by the Charity Commission, and an updated expenses policy was discussed and approved.

To ensure due diligence in monitoring risk, the Committee approved a proposal to carry out additional audit work on the publishing income side. There was an update on the property project and two other key risk areas.

Letters to the Editor

A labour of love

Roger Thomas
University of Cambridge, UK

In *Physiology News* 108, p.15, Austin Elliott drew readers' attention to AV Hill's unpublished *Memories and Reflections* being made available as a digital file by Churchill College's Archives Centre in Cambridge. Sadly this was in the form of three large PDFs of what seem to be carbon copies of the original text, with a total file size of almost 900 Mb.

Since I found these hard to read but very interesting, I have laboriously converted them to a single word file, which is only 1.3 Mb, or 2.3 Mb as a PDF. Churchill College will add these to its website, as I hope will the History and Archives Committee of The Society.

There are many fascinating pieces, particularly those about anti-aircraft gunnery, immunisation and appeasement. I never met AV myself, but he was clearly a physiologist who could turn his hands to almost anything.

'There are many fascinating pieces … I never met AV myself, but he was clearly a physiologist who could turn his hands to almost anything'

The International Working Group – how can The Society use its international profile to realise its vision of physiology flourishing?

Stefan Trapp

University College London, UK
& International Working Group,
The Physiological Society

All members recently received by post The Society's **Strategy 2018–2022** with the overall objective to *'increase recognition that physiology is essential to solving the health challenges faced throughout life'*. Science is international, it thrives on open exchange and gathering information from as many sources as possible. However, we are now increasingly facing challenges from the current political climate in Europe and the US, which is building barriers for the exchange of knowledge and the free movement of scientists. It is strategically important to safeguard international collaboration in science, and The Physiological Society should play a clear role in promoting the international, inclusive and multicultural nature of science.

We are the oldest network of physiologists worldwide and currently have members in over 60 countries. In fact, 30% of our members are based abroad, and thus offer the perfect foundation to develop lasting international collaborative links and combat national isolation promoted by recent political tendencies. The Society has a rich international history and has always been an advocate of inclusiveness, even in difficult times, such as when The Society fought for the early readmission of German scientists to its meetings after WW1.

Whilst it was felt a decade ago that the world was growing together and the appointment of an International Secretary was deemed superfluous, times have changed and The Physiological Society's Council feels that we must develop a clear international strategy again for physiology to weather the current geopolitical turbulences as unscathed as possible and ensure that 'physiology flourishes'.

It is the remit of the International Working Group (IWG) to develop this strategy in order to make sure we maximise the benefits we gain from our international position for our membership and for physiology. So how will the IWG achieve this?

During the inaugural meeting in July, the IWG considered the international aspects of the four strands of The Society's strategy: Publications, Meetings, Engagement and Internal Processes. It was agreed that in the first instance we need to hear from our members what they would like from *their* Society. The Insight Survey that all members will have received by the time this article goes to print will inform us on some international issues, but we are additionally very keen to hear from you directly about your thoughts and ideas regarding our international activities. Please email any feedback/comments you may have to me, **s.trapp@ucl.ac.uk**, or to **membership@physoc.org** marking the subject international.

It was agreed that it would be desirable to enhance the information in the Society Members' directory by adding the possibility to link to publication lists (e.g. via ORCID), or institutional WWW profiles, and to add keywords to directory profiles, thus enabling easier identification of relevant collaborators at other institutions and countries from our directory. It was also recognised that the website needed to reflect better the international and inclusive nature of The Society, and this will be reflected in the new website when it launches in December 2018.

The IWG itself would like to become more international to reflect the interests of various member groups. To this end, we are interested in recruiting new members to the IWG, particularly those who are based outside of the UK. Currently, the IWG only has members from Ireland and the United States, in addition to the UK. The IWG recognised the importance of not replicating or competing with the home societies and sees the current positive collaborations with the American Physiological Society, the International Union of Physiological Societies and the Federation of European Physiological Societies, as well as Europhysiology, as an excellent model to connect widely and collaborate on the international stage. It was recommended that following Europhysiology and meetings with IUPS, the IWG should consider where else to establish collaborative relationships, including consideration of international groupings such as the Pan Americas. To strengthen The Society's presence in Asia and Oceanic countries, the IWG suggests that The Society attend the Federation of Asian and Oceanic Physiological Societies (FAOPS) 2019 Congress and the 2019 International Society for Developmental Origins of Health and Disease (DOHAD) conference.

Our mission is to make sure, that despite political obstacles, The Society continues to bring together the brightest minds on the globe to ensure physiological research and education is thriving, in order to solve the health challenges humanity faces now and in the future. We would like to galvanise our members worldwide to fight for this aim. So we would love to hear from you, our members, how we can support you most effectively.

United we stand: working together for scientific collaboration

Louise Wren

Wellcome Trust,
London, UK

In 1675, a 33-year-old Isaac Newton wrote to his friend and rival, Robert Hooke, *'if I have seen further it is by standing on the shoulders of giants'*. Newton was referring to the body of scientific literature that preceded the many discoveries he made throughout the 17th century. And what was true for Newton is even more the case now – scientific progress is rarely the achievement of one individual; rather, it is borne of the hard work of countless people.

Whether it's hundreds of researchers or just two or three people collaborating, teamwork is at the heart of modern science. Thanks to advances in travel and communications technology, it is possible for researchers and teams to work together from opposite sides of the world.

International collaboration of this type is on the rise. In 2014, a UNESCO Science Report noted that one in every four scientific articles were co-signed by a foreign collaborator, a number that had increased from one in five just a decade earlier. In the same year, an analysis of 1.25 million journal articles found that publications with authors from multiple countries are more likely to get picked up by influential journals and are cited more often.

Partnerships between researchers in different countries have helped to advance human knowledge and spur innovation. From the Human Cell Atlas to CERN, international collaborations have led to many feats of human ingenuity. But partnerships of this sort are not a given – rather, they depend on systems and processes that support working and moving across international borders.

Led by the Wellcome Trust and international partners, Together Science Can is a global campaign to celebrate and protect scientific collaboration at a time when it is particularly fragile.

Together Science Can is encouraging people to sign up to the campaign to create a unified voice, and is creating content and resources that supporters can use to advocate for scientific collaboration. Ultimately, Together Science Can wants to help the research community to make its voice heard and to secure the best possible outcomes for science.

Collaboration is at the very core of science. Throughout history, we have come together to do research, to push the boundaries of knowledge and to help create a better world; now, we must come together to speak up for collaborative science, because we are so much stronger when we work together. As Newton pointed out all those years ago, science relies on the work of many countless individuals.

Together Science Can
is a global campaign to celebrate and protect scientific collaboration.
Join the campaign and spread the word.
togethersciencecan.org
#TogetherScienceCan

Bringing you snippets of the latest intriguing research

Motherhood can make a woman's cells 'older' by up to 11 years

An analysis of DNA collected from nearly 2,000 reproductive-age women in the US reveals that those who had given birth showed evidence of altered genetic markers suggesting they'd undergone significantly accelerated cellular ageing. Adjusting for variables like chronological age, ethnicity, education, and smoking status, women who had given birth to at least one child had telomeres that were 4.2% shorter on average than those of women who had not borne children. The researchers predicted that this is equivalent to 11 years of accelerated ageing.

DOI: 10.1093/humrep/dey024

First biochemical classification test for autism proves highly accurate in second trial

One year after researchers published their work on a biochemical test for autism, a follow-up study confirms its exceptional success, 88% accuracy, in assessing whether a child is on the autism spectrum. A biochemical test that supports a clinician's diagnostic process has the potential to lower the age at which children are diagnosed, leading to earlier treatment. This algorithm predicts if a child has autism spectrum disorder based on metabolites in their blood.

DOI: 10.1002/btm2.10095

Big pharma dives into virtual clinical trials

Pharma companies are becoming increasingly attracted to a virtual model whereby patients feed data into a cloud-based platform. Not only is it efficient, but it also encourages patient participation. What's more, virtual trials run from a centralised platform that enables everyone involved to share study design, protocols and clinical trial management information online. Virtual trials will collect data more frequently, and potentially continuously from home, without placing burdens on the patient.

go.nature.com/2vO5gNg

Physiology Feed continues on p.13

The Human Brain Project – building the basis for collaborative brain science

Katrin Amunts

HBP Scientific Director, Forschungszentrum Juelich GmbH, INM-1, Germany

C&O, Vogt Institute for Brain Research, University Hospital Duesseldorf, HHU Duesseldorf, Germany

Meeting of the International Brain Initiative on 5 July 2018, hosted by HBP in Geneva, Switzerland.

The brain is the most complex organ we know of – and as scientists worldwide work to understand its organisation and dynamics, it becomes more and more apparent that much tighter international and interdisciplinary collaboration will be needed to tame this complexity. Neuroscientists throughout the world generate an enormous wealth of experimental data and models to understand specific aspects of brain function and dysfunction, but if we want to gain a comprehensive picture, it will be necessary to better link all this knowledge across scales and disciplines.

In the European Human Brain Project (HBP), more than 500 researchers from neuroscience and computing are working together to build up a digital research infrastructure for this endeavour. For this, we systematically link neurosciences, brain medicine, computing and information technology research. On our six online accessible platforms that we first opened to the public in 2016, scientists have access to innovative approaches in, for example, neuroinformatics, simulation, high-performance analytics and computing, neuromorphic computing, neurorobotics or medical informatics, including a set of brain models, large curated databases and atlas systems. Currently, we are working to unify them into a single Joint Platform, and are in the process of establishing a dedicated support team for external users. We hope that this infrastructure will drive the development to shape a community science approach for brain investigation, with routine data sharing and re-analysis – as is already common in fields like genetics and astrophysics, much to the profit of these disciplines.

‘The trend towards collaboration in neuroscience truly has gone global and is progressing’

Of course, the HBP itself represents an exercise in collaborative research which poses many challenges – both from the spread-out nature of the consortium, which spans 117 institutions in 19 EU member states, and from the high degree of interdisciplinarity. Many of our solutions in day-to-day work are facilitated by embracing the means of digitalisation: we coordinate via the HBP Collaboratory, which is the central web-based access point to the different resources and tools on the platforms, both for HBP members and external users. Anyone with an account can set up their own private or public virtual collaborative workspaces with other colleagues. Another way to ensure functioning collaboration is based in our project structure: we have established so-called Co-Design projects that are specifically set up to cross the different sub-projects, and in which neuroscientists and clinicians work hand in hand with computing experts to develop the joint platform. Simultaneously, they develop the infrastructure that is more and more being made available to the entire community.

The use of such new tools of course will depend on training a new generation of young researchers. To this end, we run a wide-ranging Education Programme that offers online courses and many learning events like advanced HBP Schools, an annual HBP Student Conference and Young Researchers Events in various locations across Europe. All educational offers are made available through the website: **education.humanbrainproject.eu/web/hbp-education-portal**

We also try to coordinate with the worldwide large-scale neuroscience projects that have been started around the world. Each of the large initiatives has defined its specific goals and areas where they can make unique contributions – and possibly be complimentary for each other. In December 2017, a declaration to establish an International Brain Initiative was made by representatives from HBP, US BRAIN Initiative, the Korea Brain Project, the Japan Brain/MINDS Project, Israel Brain Technologies and the Australian Brain Alliance. Since then we have been meeting and have established working groups for alignment of systems and data standards, sharing and interoperability, to name a few. The trend towards collaboration in neuroscience truly has gone global and is progressing. We hope that HBP can drive this shift to a collaborative workstyle across the borders of nations and disciplines and invite researchers worldwide to join us.

Please visit **humanbrainproject.eu** for more information and access to the platforms.

Future Partnership Project: an ambitious and close future partnership between the UK and Europe

Sophie Bennett

The Royal Society, UK

What do UK and European leaders of science feel is the most important issue for the research and innovation communities in the Brexit negotiations?

Since the EU referendum in June 2016, the Royal Society has been working hard to secure the best possible outcome for science and innovation in the Brexit negotiations. Earlier in 2018 the Royal Society and Wellcome Trust partnered on a joint Future Partnership Project (FPP) to explore what an ambitious and close UK-EU partnership on research and innovation could look like in practice, to inform the Brexit negotiations and keep the focus on international collaboration as a critical issue

This project was built on an evidence synthesis on the existing UK-EU relationship on research and innovation, and a wider consultation with the European research community, asking individuals and organisations from across the UK and EU for their recommendations about how future research and innovation partnerships should work in practice.

A residential meeting at The Royal Society at Chicheley Hall in January convened UK and EU science leaders. One output from this meeting was the Future Partnership Project statement communicating the science community's unified voice to inform the Brexit negotiations, and setting out a shared commitment to an ambitious and close future partnership between the UK and Europe.

The statement demonstrates the commitment of research communities across the wider European Research Area to a future partnership between the UK and the EU that enables excellent research and innovation to flourish across Europe, actively supports collaboration and cooperation, and avoids introducing barriers to them. We want to ensure UK and EU researchers continue to work closely to their mutual benefit and that of the wider global community. We hope that this statement is a valuable step forward in achieving this. The statement attracted support from 55 organisations across Europe, including other learned societies, higher education institutions and research organisations. Signatories range from the Academia Europaea, the European Union's Academy of Humanities and Sciences, and the French Académie des Sciences, to the Russell Group and British Council.

The enthusiastic support we have received in response to this work is testament to the UK's position as a leading global scientific nation which is committed to world-class research. However, we can only fulfil this role through international collaboration. Our research provides the foundation for new ideas and discoveries, and fuels economic growth and the creation of high-value jobs. Science and research are critical to the UK economy and environment, its place in the world and the wellbeing and flourishing of its citizens.

On 5 June, the Royal Society published a statement (**royalsociety.org/topics-policy/publications/2018/uk-future-relationship-with-eu-in-research-and-innovation/**) on the principles that should shape the UK's future relationship with the EU in the area of research and innovation. The statement made clear that science is a fundamentally collaborative and global enterprise. Scientists based in the UK must continue to be part of the shared European research endeavour and have the best possible access to international funds and the collaborations they support. We must not create barriers to practising scientists seeking to move across borders, but instead provide clarity and certainty, including through regulation and governance, but also through consistently signalling that the UK remains a great place to practise great science.

The EU Framework Programmes offer an opportunity for collaborative science that is unrivalled in scale and impact. Participation in such international funding programmes and large-scale scientific infrastructure delivers greater added value and leverage for investment by enabling the development of networks and collaborations. These networks allow involvement in programmes beyond the scope of individual groups or even countries; greater influence in the future direction of European and thus global science; and, from the point of view of the UK, give greater visibility to UK science and scientists, making the UK a magnet for top talent, start-ups and investment.

Contribution to and participation in Framework Programmes has therefore been central to the UK's global scientific effort and should remain so, both benefiting the UK and advancing European and global science. An international vision for science across Europe, with a strong emphasis on excellence, has been set out by the EU. The Royal Society supports this approach and will continue to work with partners across Europe, offering our expertise to help to shape the ninth Framework Programme, Horizon Europe, and in developing the European Research Area.

The FPP statement has support from organisations throughout Europe: **royalsociety.org/topics-policy/projects/future-partnership-project/**

It is vital that the European research community continues to work together for the benefit of the European research endeavour to tackle global challenges. Updates on the Royal Society's broader work on Brexit and UK science can be found at **royalsociety.org/topics-policy/projects/brexit-uk-science/**

Future Partnership Project meeting at Chicheley Hall, January 2018

Partnerships, pacts and politics – a view from CaSE on Brexit

James Tooze
Campaign for Science and Engineering

To scientists, it is no secret that collaboration facilitates the exchange of knowledge, ideas and ultimately, progress. The European Union has been a tremendous vehicle in allowing scientists and researchers to move freely and collaborate on international projects, and the UK has successfully received over €4.6bn of Horizon 2020 funding since 2014. International collaboration is key to research; 72% of UK-based researchers were internationally mobile between 1992 and 2015. Many of the freedoms currently enjoyed will be subject to change post-Brexit, posing obstacles to the UK's collaboration with EU partners. There have been warm words from both the UK and EU with regards to scientific collaboration after Brexit; most consider it a 'win-win' to continue to have a close bond. The Prime Minister, Theresa May, has consistently insisted that the UK will agree a comprehensive science agreement with the EU, while the European Commission have left the door open for the UK to participate in Horizon 2020's successor, Horizon Europe, and other R&D programmes.

The UK Government appears to understand that science is truly international. Discoveries do not respect borders, and the UK will need to continue to attract some of the finest minds from across the world to cement its position as a scientific superpower. We categorically hear that the UK has been an attractive destination for R&D-intensive organisations because of the strength of academia, ease of access to talent, and the depth of collaborative research between academia, industry and charity organisations. Worryingly for science and innovation, the biggest threat of Brexit is that the flow of people and ideas from across the world that has been crucial to the UK's success in research could become more difficult. Restrictive migration policy, divergence in regulatory frameworks from EU standards and changes in the ease of movement of goods and services are all threats to UK science.

At Campaign for Science and Engineering (CaSE), of which The Physiological Society is a member, we work on behalf of the sector to ensure that the UK environment enables science and innovation to thrive. CaSE have been working hard to represent the voices across our diverse membership on Brexit in Westminster and Whitehall. CaSE has a seat on the Science Minister's High-Level Brexit working group, which brings together key organisations from across the research sector and is attended by ministers from the Department for Business and the Department for Exiting the EU. We produced a dossier for this group on the interaction different parts of the sector have with EU regulatory frameworks. CaSE also takes part in an equivalent working group with senior civil servants in the Department for Business. In recent months, CaSE has also presented oral evidence in front of two Parliamentary committees on Brexit and science. Alongside this engagement, we hold meetings with parliamentarians and a vast array of civil servants on a regular basis to inform their work on immigration, research collaboration and the future of scientific prosperity in the UK.

Our political engagement is informed by our policy work. Ahead of the Brexit referendum in 2016, CaSE produced a report setting out what's at stake for science and engineering in the event of the UK leaving the EU. In addition, we sought the views of researchers through a survey. Since, we have listened to members such as The Physiological Society and set out the sector's priorities, concerns and proposals in consultations, proactive meetings and calls for evidence. These are all brought together in our recent Brexit policy review with recommendations focusing on two key areas: 1) the UK securing an ambitious agreement on research & innovation with the EU and 2) coordinating Government efforts to unleash the potential of UK science and engineering.

CaSE has developed as a respected, informed voice on immigration, and our Brexit work shows that current policies, including the arbitrary numerical cap on skilled workers from outside the EU, undermine warm words from Government on being an international science hub. Since December this cap has been reached preventing organisations from recruiting the engineers, doctors and professionals they need, damaging productivity and the UK's reputation. After a long campaign led by CaSE that garnered support across the UK, the Government announced a policy change to halt the recruitment crisis facing employers.

The Government's Brexit white paper, which is the Government's proposals for the UK's future relationship with the EU, demonstrates that the voice of science has been heard by the Government as the collaborative nature of science is well referenced and it sets out a desire to align with EU partners on several fronts. However, many concerns remain, not least that there is a lot of detailed work needed if there is to be a top-level agreement and science 'pact' by October – when it is expected that the withdrawal agreement will be finalised in order for the UK to leave the EU in March 2019 – and there is no confirmation that the positions set out will be viewed as tenable by EU negotiators or the UK Parliament. As negotiations rumble on and circumstances change, CaSE will continue to ensure the needs of science and engineering are well heard.

Physiological Reports: an international collaboration

Tom Kleyman

University of Pittsburgh, Pennsylvania, USA

There has been a remarkable growth in the number of open access journals over the past 15 years, led by the Public Library of Science (PLOS) and its open access initiative. The leadership of The Physiological Society and the American Physiological Society recognised the need to establish an open access journal with a physiologic focus, which led to the founding of *Physiological Reports* by the two societies in 2013, with Susan Wray as Editor-in-Chief. I was fortunate to have the opportunity to work with Sue on the journal's first editorial team for five years, and transitioned to Editor-in-Chief in January.

From its inception, the journal has had an international editorial team and editorial board. Our founding lead editors established an editorial team from the UK and US that provide oversight of journal activities. We initiated a collaboration with the Scandinavian Physiological Society, and asked Morten Thomsen to join our editorial team as its representative. Morten has transitioned to the position of Deputy Editor-in-Chief. Our new editorial team, as of January 2018, has members from the UK, Denmark and the US. We recently recruited a social media coordinator from the US. The editors also work closely with the Directors of Publication and Executive Editors of The Physiological Society and the American Physiological Society, Simon Rallison and Rita Scheman. Given the international composition of the leadership groups associated with the journal, face-to-face meetings are generally scheduled in the UK or US, often coinciding with meetings sponsored by The Physiological Society and the American Physiological Society. In fact, our next editors' meeting will be held in London at Europhysiology 2018.

Physiological Reports authorship and readership have broad international representation. Our submissions are from authors throughout Europe, including the UK, the Americas, Asia and other countries. Just under half of our submissions are from North America, and about 30% are from Europe. Our readership, based on downloads, also has an international flavour. About 30% of our readership are from Europe, and a similar percentage are from North America. In summary, the journal is clearly an international collaboration at all levels.

Congratulations to our newest Fellow Members

- Richard Apps, University of Bristol, UK
- Lothar A. Blatter, Rush University, USA
- Avijit Datta, York Teaching Hospitals Foundation NHS Trust, UK
- Ian Macdonald, University of Nottingham, UK
- Chris Peers, University of Leeds, UK
- Olusoga Sofola, University of Lagos, Nigeria
- Joern Steinert, University of Leicester, UK
- Gary Stephens, University of Reading, UK
- Jose Vina, Facultad de Medicina, Argentina
- Peter Julu, Central Middlesex Hospital, UK

Chris Peers is awarded his Fellow Membership posthumously having passed away before it was approved by the committee.

Early Investigator Prize 2017 winners

***The Journal of Physiology* Early Investigator Prize 2017**

Justin S. Lawley for his paper titled '*Effect of gravity and microgravity on intracranial pressure*'.

The Journal of Physiology **595**(6), 2115–2127 (15 March 2017).

***Experimental Physiology* Early Career Author Prize 2017**

Marcus Vinicius Machado for his paper titled '*Exercise training dose differentially alters muscle and heart capillary density and metabolic functions in an obese rat with metabolic syndrome*'.

Experimental Physiology **102**(12), 1716–1728 (1 December 2017).

Omega 3 supplements of little or no heart or vascular health benefit

A new *Cochrane systematic review* combines the results of 79 randomised trials involving 112,059 people. These studies assessed effects of consuming additional omega 3 fat, compared to usual or lower omega 3, on diseases of the heart and circulation. The risk of death from any cause was 8.8% in people who had increased their intake of omega 3 fats, compared with 9% in in the control groups.

DOI: 10.1002/14651858.CD003177.pub3

Scientists reverse ageing-associated skin wrinkles and hair loss in a mouse model

Researchers have reversed wrinkled skin and hair loss, hallmarks of ageing, in a mouse model. When a mutation leading to mitochondrial dysfunction was induced, the mouse developed wrinkled skin and extensive, visible hair loss in a matter of weeks. When the mitochondrial function was restored, the mouse returned to smooth skin and thick fur.

DOI: 10.1038/s41419-018-0765-9

Normalisation of 'plus-size' risks hidden danger of obesity

Normalisation of 'plus-size' body shapes may be leading to people underestimating their weight, thereby undermining efforts to tackle obesity. Analysis of almost 23,460 people who are overweight or obese revealed that weight misperception has increased in both men and women between 1997 and 2015. Men and individuals with lower levels of education and income are more likely to underestimate their weight status and consequently 85% less likely to try to lose weight.

DOI: 10.1038/d41586-018-03804-2

An orange a day keeps macular degeneration away

An Australian study has shown that regular consumption of oranges reduces the risks of developing macular degeneration. Researchers followed more than 2,000 Australian adults aged over 50 over a 15-year period and found that people who ate at least one serving of oranges every day had more than a 60% reduced risk of developing late macular degeneration. Flavonoids, found in oranges, appear to help protect against the disease.

DOI: 10.1093/ajcn/nqy114

The International Mouse Phenotyping Consortium – the creation of a complete catalogue of mammalian gene function

Steve Brown

Chair of the International Mouse Phenotyping Consortium &
Director, MRC Harwell Institute, UK

Despite the enormous advances in the characterisation of the human, mouse and other mammalian genomes, we remain remarkably ignorant of the function of the majority of genes. Much of the genome remains 'dark' and for many genes there is little or no functional knowledge. Moreover, while there have been advances in the identification of mutations in the human genome that lead to Mendelian Disorders and Rare Diseases, the identification of the genes and genetic variants that underlie common diseases has made slow progress. The functional characterisation of human genetic variation and its contribution to disease needs to be underpinned by a systematic effort to develop a complete catalogue of mammalian gene function. The International Mouse Phenotyping Consortium (IMPC) has risen to this challenge and in 2011 embarked on a global effort to identify the function of every gene in the mouse genome. The major mouse genetics centres from around the world have come together to develop the technologies and pipelines and build a genome-wide picture of gene function. It is expected that this catalogue will be transformative for biology and biomedical sciences providing a critical underpinning for our understanding of genes, genetic pathways and their impact on disease.

The IMPC is generating a null mutation for every gene in the mouse genome. Each mutant line undergoes a comprehensive phenotypic characterisation across many physiological and disease systems. Viable homozygous mutants enter an extensive and highly standardised adult phenotyping pipeline from 9 to 16 weeks of age. Homozygous lethal mutants enter an embryonic phenotyping pipeline which examines the timing of lethality and undertakes a detailed morphological analysis of embryological defects employing a number of sophisticated imaging platforms. From the generation of each mutant line to the acquisition of phenotyping data, considerable emphasis is placed on standardised procedures with stringent QC processes ensuring the development of a robust and reproducible dataset.

The IMPC comprises 19 research institutions and five national funders spread across 11 countries. 12 research institutions are principally responsible for mutant production and phenotyping and they deliver mutant and phenotype data to the IMPC Data Coordination Center (DCC) at the MRC Harwell Institute, UK. Following a stringent process of data wrangling and QC, data undergoes statistical analysis through the PhenStat tool to identify and assign phenotype calls to each mutant. All data is deposited at the IMPC core data archive at the EBI, Cambridge, UK, where it is made freely available through the IMPC portal. IMPC is an open access programme, and both the data and the mouse mutants are freely available to all academics. All the mouse lines are deposited in local archives and are available from IMPC and other national repositories around the world.

Since 2011, the IMPC has made substantive progress and has now analysed a third of the coding genome. It has generated over 7,500 mouse mutant lines, of which the majority have been completely phenotyped. This endeavour has to date generated a very large multidimensional dataset of genes and phenotypes comprising 62 million datapoints and 370,000 images. Already the IMPC programme is providing a series of extraordinary insights into the nature of the genetic landscape of the mammalian genome.

In 2017, the IMPC described a detailed analysis of the 410 homozygous lethal (essential) genes identified from the first 1,751 knockouts using a standardised phenotyping platform incorporating high-resolution 3D imaging. A large number of embryonic phenotypes were discovered for previously uncharacterised genes. An extraordinary and unexpected degree of variable expressivity was observed reflected in the large number of subviable mutations identified. Moreover, IMPC confirmed that human disease genes were significantly enriched for mouse essential genes. Building on this first major analysis of the genome landscape, IMPC undertook a comprehensive mouse-human cross-species analysis of data from Release 5.0 of the IMPC covering 3,328 genes. Ninety percent of gene-phenotype annotations had not been reported before and hitherto there had not been a mouse mutant available for 1,830 out of the 3,328 genes analysed. Moreover, for 1,092 genes the first functional knowledge was provided. Overall, the data demonstrate the huge fund of novel disease models that are being generated with wide implications for biomedical sciences and the major human and clinical genetics initiatives that are examining the genetic bases for disease, such as the 100,000 genomes project and the Precision Medicine Initiative. Moreover, the IMPC for the first time were able to take a comprehensive, genome-wide view of sexual dimorphism effects, particularly the interaction between genotype effects and sex. Extraordinarily, we found that for continuous parameters around one-sixth of phenotypes in mutants were affected by sex. Sexual dimorphism is pervasive across the mammalian genome, and it will be vital within the Precision Medicine Initiative and other programmes to take these findings into account. Finally, IMPC has focused on the identification of novel genes and pathways for diverse areas of physiology and disease, and two major reports have already appeared covering the auditory system and metabolism.

The IMPC has brought together the major mouse centres across the globe to tackle a major challenge for genetics and genomics and provide an increasingly comprehensive view of gene function and the role of genes in disease. The combined efforts and expertise of IMPC members have already generated a powerful dataset that is being used to generate transformative insights into the genome and disease landscape. The IMPC will continue its work over the coming years and complete the analysis of the coding genome. However, the consortium is already turning its attention to wider challenges as it continues to survey the need for functional genomic insights that will be critical in delivering a better understanding of the impact of human genetic variation on disease. A major priority will be to deliver an IMPC pipeline for the generation and characterisation of mice carrying human coding mutations. Such a pipeline will assist in the validation of putative human coding disease alleles as well as generating models for the pursuit of disease mechanisms and improved therapeutics. In addition, IMPC is considering plans to tackle a systematic effort to target and understand the function of the non-coding genome. One area of focus would be conserved non-coding enhancer elements (CNEs) which are highly enriched for human pathogenic variants in common diseases.

In conclusion, IMPC has created a highly productive international partnership to allow comprehensive functional analyses of the mouse genome with profound impacts on our understanding of the mammalian genetic landscape. IMPC will continue to address future challenges in the functional analysis of human genetic variation, aiming to bring further understanding and insight to this critical area of human disease studies, as well as uncovering opportunities for the development of therapeutic strategies.

To find out more visit
mousephenotype.org

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Knowledge without borders? The prospects for the UK's international research collaboration

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'*Every great British scientist could only reach new frontiers of invention because they built on the work of others, exchanged ideas with their contemporaries and participated in an international community of discovery.*'

The 'international community of discovery', as articulated by Theresa May (GOV.UK, 2018) earlier this year, is one of the most essential elements of science and research. Implicit in this statement are the benefits of being able to exchange ideas with a global community of scholars – intensified through increased physical and virtual connectivity – and the self-evident truth that knowledge and discovery is not limited by geographical boundaries.

However, in a world shaped by Brexit and Trump – not to mention the ongoing European migration crisis – geographical borders are in the spotlight. Many countries, including within the EU, are adopting rhetoric and policy measures that seem designed to close countries off, not open them up. This has potentially profound consequences for that 'international community of discovery', so it is worth considering what the implications of the current climate may be for the future of international research collaboration in the UK.

Many of my colleagues at UCL are acutely worried about the potential impact of Brexit on research mobility and their ability to collaborate with researchers in other European countries and beyond. Clearly, there are concerns about the short- and medium-term disruption and impact – both in terms of residency and future mobility and in terms of prospective future research projects and funding proposals. There is a very human element to all this, with people's families, friendships and future career prospects potentially being affected. Furthermore, there are frustrations at seeing successful partnerships disrupted, invitations to join collaborations declining, and anticipated difficulty in participating in international conferences, visits and training for EU researchers post-Brexit.

International research collaboration, however, relies not only on the availability of funding, but on networks and relationships built over many years, and on the ability to regularly interact with academic and researcher peers to identify shared interests and complementary expertise. I wonder if the as-yet-unknown longer-term impact on this activity – an effect that is compounded by the prolonged uncertainty, a greater voice for those opposed to immigration, and a gradual shift in attitudes and perceptions to the UK so that it is seen as a 'closed' country – is what will be most damaging.

Why does this matter? In the first instance, because international collaboration contributes to the productivity and quality of the UK research base. The increase in research output and quality over the past three decades has been driven almost entirely by international collaboration (Papers with international co-authors on average have higher citations; Adams & Gurney, 2016). The UK's internationally co-authored papers increased from less than 40% to nearly 60% of all papers between 2003 and 2016 (Marginson, 2018). In the context of Brexit, it is notable that since 2011 60% of UK universities' international co-authors have been from the EU, and growth in international collaboration has largely been driven by the European Framework Programmes (Adams & Gurney, 2016). The UK's research performance leads the world in terms of quality, but research quality (Elsevier/BEIS, 2016) and international collaboration are to some degree mutually reinforcing.

Secondly, international research collaboration matters for the UK's place in the world. The strength of the UK research base is a significant factor in attracting international investment (Hughes *et al.*, 2014), and the quality of our research and our universities (and their global links) are a key factor in the decisions of many global businesses to locate in the UK. As the Government's Science and Innovation Network website states: '*Maintaining our science excellence (and our reputation) and supporting innovation ensures the UK is a partner of choice, and helps UK companies with ambitions for rapid global growth.*' (GOV.UK, 2016)

The UK currently performs well in the global competition to attract a share of international research and development (R&D) investment (GOV.UK, 2014) and has the largest proportion of such R&D in the G7 Group of countries (Reid, 2014). This will be even more significant as the UK Government begins to consider how to meet its manifesto commitment of spending 2.4% of GDP on R&D; now is not the time to risk this international investment or to undermine our global partnerships.

Equally important is the role that our research strength plays in our ability to be a global leader and in our 'soft diplomacy'. Our current success in international research collaboration plays an important role in the UK's strategic global position and alliances, with research relationships offering a relatively harmonious means of forming partnerships. The Chief Scientific Adviser to the Foreign Office, in his categorisation of the different forms of 'science diplomacy' (Grimes & Hennessey, 2015), has emphasised the way in which research cooperation can enhance international relations – something which is particularly important as we see cooling and unpredictability in previously well-established diplomatic relations.

Finally, there is the increasing complexity and scale of the societal challenges we face. No single research discipline, institution or even country is able to address global challenges to deliver the solutions needed for humanity to thrive. Meeting these challenges will require the application of collective expertise; as UCL's Vice-Provost (International), Dame Nicola Brewer, has written: '*bringing together experts, irrespective of where they are in the world, means that the very best minds can be focussed on finding the solutions we all need*' (Brewer, 2018).

So, given its value across multiple spheres, what can be done to enable and strengthen international research collaboration?

There have been some positive policy announcements from the UK Government – the announcement soon after the 2016 Brexit referendum that they would underwrite participation in Horizon 2020 projects (GOV.UK, 2016), and more recently the Prime Minister's statement favouring a 'deep partnership' on research and indicating that the UK wishes to continue to participate in Horizon Europe (GOV.UK, 2013) (with terms and details still to be determined). This is important because it signals a continued commitment to research collaboration, and a recognition that collaborative funding

strengthens collaborative research. On a global level, the establishment of the £110 million Rutherford Fund to attract international researchers and the £900 million UKRI Future Leaders fund, accompanied by a new scheme to enable overseas researchers to come to the UK (UKRI.org, 2018), show recognition of the importance of attracting global talent (and enabling researcher mobility).

However, in the absence of a structure that brokers multi-partner collaborations, the UK may find itself confined to bilateral arrangements where national agreements can be formed. The current climate requires an ambitious response from universities and a clear statement that the UK must continue to foster partnership with EU member states and with the rest of the world. In particular, we can and should be more ambitious in responding to emerging opportunities for collaboration with rising research powers – not least to advance the global sharing of knowledge.

Universities can play a key role in strengthening international research collaboration. As an important counterweight to some of the more hostile rhetoric heard elsewhere, we must provide strong statements of our continued commitment to recruiting global talent, participating in international research endeavours and, above all, remaining open institutions committed to sharing knowledge and building common cause.

This positive rhetoric must be supported by concrete actions. University strategies – such as UCL's global engagement strategy – provide the overall framework, enabling environment, and specific levers (including internal funding support and management of partnerships) to support international research collaboration. UCL's own approach is characterised by a focus on building partnerships at all levels to deliver a number of academically driven strategic alliances, supported at the institutional level, under which a plethora of individual collaborations and relationships sit.

In the end, partnerships are forged by individuals. It is generally individual academics who are best placed to identify the experts in their fields (and beyond) with whom they want to collaborate and with whom strong partnerships can be established. So universities need to ensure that we put in place the right mechanisms and create the environment to support and strengthen this within our institutions, and to push for similar appropriate mechanisms to do so at a national level, including collaborative funding schemes and a sensible immigration system.

Yet this is about more than individual academics and individual institutions; international research collaboration ultimately should be about the global creation, sharing and application of knowledge to solve common challenges, not individual or institutional ambitions. To finish where I started, this global endeavour must be one in which the UK plays a full part. In the words of the Prime Minister: '*…the Britain we build together in the decades ahead must be one in which scientific collaboration and the free exchange of ideas is increased and extended…with partners around the world.*' (GOV.UK, 2018)

'The current climate requires an ambitious response from universities … the UK must continue to foster partnership with EU member states and with the rest of the world'

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The Cardiac Physiome project: the Oxford–Auckland connection

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The computational physiology link between Oxford and Auckland had its roots in 1972 when Peter Hunter began a Doctorate with a Commonwealth Scholarship at Oxford. The Oxford engineer Don Schultz (also a New Zealander) had begun a collaboration with the physiologist Derek Bergel a few years earlier to bring engineering approaches and technologies to the study of the circulation. Peter joined this team, under the supervision of Derek Bergel in the University Laboratory of Physiology – now the Department of Physiology, Anatomy and Genetics. Derek's lab was along the corridor from Denis Noble and Julian Jack, and although Peter's thesis topic was on ventricular mechanics, he became involved in Denis' modelling of cardiac cell electrophysiology, a collaboration that, 20 years later, led to the establishment of the Cardiac Physiome project.

Following a postdoc from 1975 to 1979 at the Rutherford Laboratory and St Catherine's College, Peter returned to a lectureship in the Department of Theoretical and Applied Mechanics (now Engineering Science) at Auckland University in 1980 and a new collaboration with Bruce Smaill in the Department of Physiology at Auckland on measuring and modelling the structure and mechanical function of the heart began. An invitation to Denis Noble to give a lecture in Auckland in 1985 established the Auckland–Oxford collaboration on bringing Denis' cardiac cell models into the context of the Auckland whole heart models and began the Cardiac Physiome project. At the invitation of the International Union of Physiological Sciences at the St Petersburgh Congress in 1997, this was expanded to become the IUPS Physiome Project under the leadership of Denis, Peter and, from the University of Washington, Jim Bassingthwaighte.

The next stage of the Oxford–Auckland link began in 1995 when David Paterson (who succeeded Derek Bergel at Merton College) bought a 256 electrode mapping system from the Auckland group and requested a postdoc to help use it for studies of cardiac activation. Marty Nash, who had been a PhD student in Auckland, came to join David's lab in Oxford (1996–2002), followed shortly afterwards by Chris Bradley (1999–2009). The late Andrew Pullan from Auckland then spent two sabbatical summers at Oxford as the team worked on experimental validation of the 'inverse problem' of electocardiography in the pig (1999–2001). At the same time (1999), another New Zealander, Nic Smith, came to take up a postdoc under Denis working on coronary flow. Nic returned to a lectureship in Auckland in 2001 and then returned back to the Computer Science Lab in Oxford a few years later in 2006, bringing another group of young kiwis with him. Following a period at KCL where Nic led the establishment of a new biomedical engineering programme at St Thomas' Hospital, he returned to Auckland, where he is now Dean of Engineering. Marty and Chris also returned to Auckland having benefitted from a fruitful collaboration in London with Peter Taggart where the Oxford mapping system found its way to human mapping during cardiac surgery.

A key milestone for the Cardiac Physiome Project was the award of a programme grant by the Wellcome Trust to David Paterson and Peter Hunter in 2005–2010. This provided the funding to establish the infrastructure for the modelling standards, software tools and model repository now underlying the Physiome Project. Peter Hunter was appointed a visiting Professor in Computational Physiology at Oxford. When David Paterson became Editor-in-Chief of *Experimental Physiology*, then *The Journal of Physiology*, he recruited Peter and Nic Smith to lead the editorial area of computational physiology, where several special issues were published highlighting the importance of modelling in the reassembly of physiological data to inform the next stage of experimental design.

Today, this long collaboration still continues with David Paterson having an Honorary Professorship at the Auckland Bioengineering Institute where he is a co-investigator on two long-running HRC programme grants led by Peter and Bruce Smaill. Ten years after Nash, Bradley, Pullan and Paterson published their experimental-modelling framework for the 'inverse problem', Bruce and David have revisited this area and refined the framework. Indeed, the collaboration between the Oxford and Auckland groups has been further connected by a new funding opportunity from NIH *SPARC* (Stimulating Peripheral Activity to Relieve Conditions), where the autonomic nervous system is being connected to end-organ function and modelled to understand how the nervous system controls physiological function in diseased states, as a prelude for target discovery and device therapy.

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Will Brexit have an impact on our animal legislation?

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As far as the regulation of live animal experiments in the UK is concerned, the short answer is 'no'. The EU Directive (2010/63/EU; **eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32010L0063**) was 'transposed' in 2013 into UK legislation as a modification of the existing ASPA (the Animals [Scientific Procedures] Act 1986; **gov.uk/government/publications/consolidated-version-of-aspa-1986**), and that will not be altered by the various stages of Brexit. Somewhat behind the scenes there will, though, need to be some tidying up of the legislation. This is because ASPA refers to various points in the Directive (e.g. the appendices) and those will need to be fully incorporated into ASPA; but that will happen by secondary legislation with no discussion of the contents. The end result is that Brexit will have no immediate effect on day-to-day regulation. Somewhat less certain is what will happen to ASPA after Brexit as and when there are changes to the Directive, although at the moment significant change isn't on the horizon.

As a response to the EU Citizen's Initiative 'Stop Vivisection' in 2015, the EU Commission produced a report (**ec.europa.eu/environment/chemicals/lab_animals/pdf/vivisection/en.pdf**) and subsequently convened a scientific meeting in 2016 on non-animal alternatives (for report see **ec.europa.eu/environment/chemicals/lab_animals/3r/pdf/scientific_conference/non_animal_approaches_conference_report.pdf**). The outcome of this process was that the Commission saw no need to deviate from the normal review process already embedded in the Directive. The first, inevitably rather preliminary, review was in 2017 (**ec.europa.eu/environment/chemicals/lab_animals/related_topics_en.htm**) and this concluded that the Directive was broadly doing a good job. There was also a meeting on the use of Non-Human Primates (NHPs) and a Commission report on the value of their use (**ec.europa.eu/environment/chemicals/lab_animals/scientific_committees_en.htm**).

As a result of all this (and other) activity (see **ec.europa.eu/environment/chemicals/lab_animals/index_en.htm**), no changes are currently proposed by the Commission that would cause substantive change to, or conflict with, current UK operations. That said, the Directive requires the Commission to keep various aspects under review; and when it initiates such reviews, this will no doubt trigger the animal protection groups to exert further pressure for restrictive changes. By the same token, the longer-term effect of Brexit on collection of the UK annual statistics is less certain; there are already minor amendments to Directive 2010/63/EU on this, but these are not substantively different from existing UK law.

'Any proposal for overt change to the UK regulations would open the door to political and public debate on the use of animals in research'

In its interactions with ASRU (the Animals in Science Regulation Unit in the Home Office), the sector, via UKBSC (the UK Bioscience Coalition; **rsb.org.uk/policy/groups-and-committees/uk-bioscience-sector-coalition**), has argued strongly for maintaining as much parity with the EU regulations as possible. This would not only avoid this becoming a hurdle to continued collaboration across the EU but would also give industry parity in the requirements for animals in safety testing of new therapies. Moreover, any proposal for overt change to the UK regulations would open the door to political and public debate on the use of animals in research – and given the risk that this could lead to further restrictions, that route is best avoided.

Depending on the hardness of Brexit, ASRU may or may not be permitted observer status at the EU's 'Contact Points' meetings in Brussels. Presumably, if the UK keeps that status then it will be a lot easier for ASRU to follow what's going on with the Directive and thereby to maintain full parity than if we are not present at the table.

A secondary aspect of a 'hard' Brexit might be delays in international transport, which could affect the duration animals spend in transit into or out of the UK. That would not be good for welfare, quite apart from likely additional costs.

Other possible legislative changes affecting international interactions

The Department for Environment, Food and Rural Affairs put out a consultation document in March 2018 on 'Health and Harmony: The future for food, farming and the environment in a Green Brexit', in which one proposal was the banning of export of live animals. While this was targeted at the export of animals for slaughter for food, it's important that the sector ensures that the export of research animals is not caught in the legislation. The Physiological Society contributed to a response from RSB (the Royal Society of Biology; **rsb.org.uk/policy/policy-issues/uk-biosciences-and-europe#Parliament**) drawing attention to this risk and the adverse welfare as well as scientific implications of getting the legislation wrong.

Meanwhile what's going on in the UK?

More parochially, the proposals for an Animal Welfare (Sentencing and Recognition of Sentience) Bill (**gov.uk/government/publications/draft-animal-welfare-sentencing-and-recognition-of-sentience-bill-2017**) are not aimed at the use of animals for research, but the sector needs to be aware of the possibility that the bill might catch animals that are studied in research projects outwith ASPA (i.e. not requiring a Project Licence, such as with environmental monitoring of wildlife). To that end The Physiological Society submitted a response (**physoc.org/sites/default/files/page/Sentience_Bill_PhySoc_response.pdf**) to the consultation drawing attention to the risks of collateral damage to research, supporting the slightly more general response submitted by RSB (**rsb.org.uk/images/RSB_response_Defra_draft_Animal_Welfare_Sentencing_and_Recognition_of_Sentience_Bill.pdf**).

The Society has an active 'animals in research' working group, chaired by Andrew Trafford (University of Manchester, UK). If you would like to contribute to the work of The Society in this area, or have views to express on any aspect of current/future animal regulation, please do contact the Policy team on **policy@physoc.org**.

2018–2019 *Forthcoming events*

13 November

Chrononutrition: From Epidemiology to Molecular Mechanism
Marble Arch, London, UK

physoc.org/chrononutrition/

16 November

Physiology and Medicine: First World War Perspectives
Thackray Medical Museum, Leeds, UK

physoc.org/ww1-medicine-physiology/

5–6 December

Sleep and Circadian Rhythms from Mechanisms to Function
Barbican,
London, UK

physoc.org/sleep_circadian/sleep-and-circadian-rhythms-mechanisms-function

17–18 March

Life Sciences 2019: Post-Translational Modifications and Cell Signalling
East Midlands Conference Centre, Nottingham, UK

physoc.org/lifesci2019/

Meeting Notes

Experimental Models meeting: giving your research a fresh perspective

26 May 2018,
University of Exeter,
Exeter, UK

Robert Menzies

University of Edinburgh, UK

The Experimental Models in Physiology meeting at the University of Exeter was a truly unique event. Over the course of these few days I learned not only from speakers within my field of cardiovascular and renal (patho)physiology but from many other physiologists investigating models and mechanisms that were thought-provoking and entertaining, sometimes giving me cause to ponder my own research questions with a fresh perspective.

Here's a snapshot of some of the insights I gleaned from this unique conference:

- Stuart Egginton gave us an honest account of the challenges you will be confronted with should you be planning to measure heart rate variability in fish in the coldest oceans on the planet. I can hardly imagine transporting my equipment by land for any great distance, let alone an entire lab across an ice ocean. Did you know that Antarctic icefish are so adapted to the cold that their hearts cannot function above ~15 °C? Now you do.

- Some adults have holes in their necks, and guess what – it's all the fault of our internal fish. Anthony Graham shared his fascinating studies into Hox control of the fish 'neck', orgill-area, I suppose. I found myself checking my neck, wondering if my darned Hox genes had been doing the right thing all those years ago when my preterm-self realised I wouldn't be spending forever underwater. Thanks to developmental biology for closing the right parts!

- This one was a visual treat: the magnificent madness of insect flight. Simon Walker has been developing some stunning X-ray approaches with the Swiss Light Source to capture insect flight in real-time. It was interesting to ponder other applications of his technology, but honestly it was all just so enjoyable to take in:

  'At conferences, I rarely have the chance to learn about something completely outside my field, let alone something hugely enjoyable and mind expanding. Simon Walker's @ThePhySoc #experimentalmodels talk on insect flight was just that!' **bit.ly/2vm2pe1**

- We learned about 'Frankenstein' computational models and that increasingly trodden path that binds mathematics with biology from Jeroen Jeneson and Emily Roashan. Can a biologist construct a radio? Do our parameters really matter when modelling with 10 – 100x range in our sensitivity analysis? Is life all differential equations? If your answers are 'yes' then great – let's talk.

All of this was in a beautiful setting of green, fresh air and walkability. There were sculptures and beautifully kept gardens. It was a real treat to wake up early and run in the sun. The social calendar was also importantly thought through to ensure folks actually had the time to meet, chat and reflect on each other's work.

I was surprised to hear many attendees state 'I'm not a physiologist, but…' before sharing their work which was almost always centred in physiology or pathophysiology. Maybe we need to reflect more on the vital role that physiology plays in our respective research. We're clearly all working in this area and have the support of a truly active and vibrant Society right on our scientific doorsteps!

Meeting Preview

Chrononutrition: From Epidemiology to Molecular Mechanism

13 November 2018,
Marble Arch, 86 Edgeware Road
& Garfield House, London, UK

physoc.org/chrononutrition/chrononutrition-epidemiology-molecular-mechanism

Perry Barrett & Julian Mercer

University of Aberdeen, UK

Circadian rhythms are ubiquitous in nature and underpin most physiological and metabolic process including the sleep wake cycle, body temperature, food intake and immunity. Over the last decade, evidence has emerged that most, if not all, cells within a mammalian system show a rhythmic expression of genes that is essential to the proper function of both the cell and the organism as a whole, while disruption of circadian rhythms can have a significant impact on physiology and metabolism. Feeding behaviour and associated metabolic responses in mammals have evolved to the 24-hour light-dark cycle, and the disruption of normal feeding behaviour can have profound effects on metabolism. Animal studies have led the way in this field, showing that disruption of a normal circadian pattern of food intake can lead to obesity and the onset of the metabolic syndrome. At the molecular level, identification of the molecular components of the circadian clock has enabled detailed studies of the consequences of the disruption of the clock at the tissue level. For example, the absence of the *Bmal1* gene in adipocytes, an essential component of the molecular clock, disrupts circadian rhythms in adipose tissue, leading to obesity and development of the metabolic syndrome.

Evidence is accumulating that in humans, our intrinsic circadian rhythm has consequences for the timing of food intake. When we eat during a 24-hour period may underpin a metabolic response dependent upon the size of the meal, leading to a view that there may be an optimal time to consume meals of different caloric contents (breakfast, lunch and dinner); for example, a higher caloric intake during the middle of the day may improve parameters of the metabolic syndrome and reduce body fat.

The gut microbiome may also have a role to play in meal timing. The gut microbiome is a recently identified essential component of mammalian physiology, processing, as it does, nutrients which are important to host metabolism. Disruption of the optimal composition of the gut microflora, for example by diet, can have consequences for host metabolism. It is also becoming evident that the gut microbiome undergoes circadian oscillations and consequently impacts on host metabolism. How this integrates and impacts upon circadian rhythms and metabolic health in humans is unknown.

The realisation of the importance of the timing of food intake across a 24-hour period has established the field of chrononutrition. This is a field where understanding of basic mechanisms can have translational benefit.

In this one-day symposium, we have gathered together some of the leading researchers in the field of chrononutrition from the UK, Europe and the USA, to share their latest research from human studies and animal models, and from epidemiology to molecular mechanisms.

We are pleased to highlight a plenary lecture to be given by Satchidananda Panda from the Salk Institute, USA, whose research on circadian rhythms and time-restricted feeding has brought to prominence the importance of this field to human health.

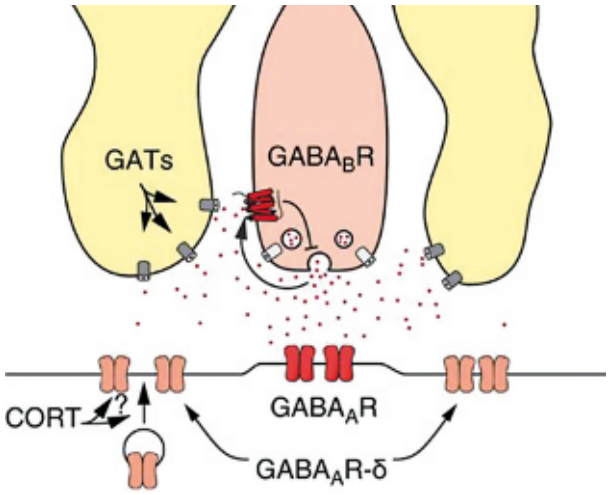
The Journal of Physiology

Balancing tonic and phasic inhibition in hypothalamic corticotropin-releasing hormone neurons

Phillip LW Colmers & Jaideep S Bains.
596(10), 1919–1929 (15 May 2018).

This study addresses the paucity of information surrounding how signalling is controlled at GABA synapses on corticotrophin-releasing hormone (CRH) neurons in the paraventricular nuclei (PVN). In the presence or absence of certain compounds, electrophysiological recordings of PVN CRH neurons – identified by prior genetic mutation to express CRH-tdTomato – revealed that GABA transporters affect neuron excitability via limiting activation of presynaptic $GABA_B$ receptors and postsynaptic $GABA_A$ receptors. Glucocorticoid upregulation of postsynaptic $GABA_A$ receptors to increase tone was observed but no effect on synaptic GABA signalling was determined.

DOI: 10.1113/JP275588



Extrasynaptic mechanisms regulate GABA signalling

Schematic illustrating that constitutive activation of $GABA_B$Rs restricts GABA release and that conditions promoting GABA spillover increase $GABA_B$R activation and elicit tonic $GABA_A$.

Temporal dynamics of circadian phase shifting response to consecutive night shifts in healthcare workers: role of light–dark exposure

Julia E Stone, Tracey L Sletten, Michelle Magee, Saranea Ganesan, Megan D Mulhall, Allison Collins, Mark Howard, Steven W Lockley, Shantha MW Rajaratnam. 596(12), 2381–2395 (15 June 2018).

Circadian phase-shifting due to shiftwork can result in transient periods of misalignment between circadian rhythms. Unanticipated light exposure associated with shiftwork is the likely causative environmental time cue. Factors that allow prediction of responses to unanticipated light exposures may allow effective designing of shift systems. The current study demonstrates, in ICU staff working multiple night shifts, that magnitudes of circadian phase shifting are highly individualistic. Circadian phase at the beginning of the shift period and individual light exposure patterns over the course of the shift period are highly correlative with the phase shift. This finding demonstrates that 'one size fits all' approaches for shiftwork interventions are unlikely to be successful.

DOI: 10.1113/JP275589

Cigarette smoke directly impairs skeletal muscle function through capillary regression and altered myofibre calcium kinetics in mice

Leonardo Nogueira, Breanna M Trisko, Frederico L Lima-Rosa, Jason Jackson, Helena Lund-Palau, Masahiro Yamaguchi, Ellen C Breen. 596(14), 2901–2916 (15 July 2018).

Cigarette smoking has myriad detrimental health effects including inducing skeletal muscle contractile dysfunction. The pathogenesis of smoking-induced skeletal muscle contractile dysfunction is incompletely understood but may involve changes in Ca^{2+} dynamics. The current study exposed mouse models to cigarette smoke and cigarette smoke extract for 8 weeks followed by, inter alia, isolating single fibres from the flexor digitorum brevis muscle, loading with a Ca^{2+} sensitive dye, and measuring intracellular Ca^{2+} transients following electrical stimulation. The 8-week exposure had no effect on lung airspace size, but single fibres from the extract exposure model were slower to relax – resulting from slowed Ca^{2+} reuptake by the sarcoplasmic reticulum. Additionally, function at muscle level was impaired alongside changes in vascular structure and depletion of satellite cells. Thus, components of cigarette smoke affect peripheral muscle Ca^{2+} dynamics, among other functionally relevant variables, before damaging the lungs.

DOI: 10.1113/JP275888

Experimental Physiology

Minocycline alters expression of inflammatory markers in autonomic brain areas and ventilatory responses induced by acute hypoxia

Talita M Silva, Laiali J Chaar, Reinaldo C Silva, Ana C Takakura, Niels O Camara, Vagner R Antunes, Thiago S Moreira. 103(6), 884–895 (1 June 2018).

This study investigated the effect of acute hypoxia on markers of neuroinflammation in brain regions responsible for the autonomic control of ventilation in Wistar rats. Acute hypoxia increased ventilation and the expression of pro-inflammatory mediators in the rostral ventrolateral medulla and paraventricular nucleus of the hypothalamus, but not in the cerebral cortex. The tetracycline antibiotic minocycline, which is known to inhibit microglial activation, attenuated the increased ventilation caused by acute hypoxia and the expression of proinflammatory markers in the brain nuclei regulating ventilation, suggesting the involvement of inflammatory mediators in the autonomic control of ventilation during hypoxia.

DOI: 10.1113/EP086780

Neopterin 7,8-dihydroneopterin is elevated in Duchenne muscular dystrophy patients and protects mdx skeletal muscle function

Angus Lindsay, Alexandra Schmiechen, Christopher Chamberlain, James M Ervasti, Dawn A Lowe. 103 (7), 995–1009 (1 July 2018).

This study investigated the involvement of the macrophage-synthesised molecules neopterin and 7,8-dihydroneopterin in Duchenne muscular dystrophy (DMD), as macrophage infiltration is a hallmark of the disease. The findings showed that levels of both pterins were elevated in urine samples from DMD patients. Furthermore, a potential protective effect of the antioxidant 7,8-dihydroneopterin in dystrophic muscle was uncovered. 7,8-dihydroneopterin reduced eccentric contraction-induced force loss and improved recovery of force in mdx muscle, suggesting the reactive oxygen species play a role in eccentric contraction-induced force loss and recovery in DMD and suggesting that enhancing 7,8-dihydroneopterin may provide a protective therapeutic strategy.

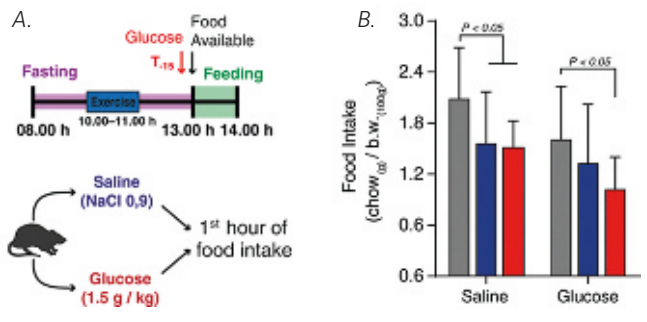
DOI: 10.1113/EP087031

Intense physical exercise potentiates glucose inhibitory effect over food intake of male Wistar rats

Joao Paulo Cavalcanti-de-Albuquerque, Grasielle Clotildes Kincheski, Ruy Andrade Louzada, Antonio Galina, Anna Paola Trindade Rocha Pierucci, Denise P Carvalho. 103 (8), 1076–1086 (1 August 2018).

It is well known that physical exercise can lead to weight loss by increasing energy expenditure. Additionally, it is suspected that physical exercise may aid weight loss by decreasing hunger perception. Using a treadmill, this study investigated the effect of moderate and high intensity acute exercise on food intake in Wistar rats and whether physical exercise had any effect on the anorexic effects of peripheral glucose injection. The findings show that both moderate and high intensity exercise reduced food intake in the first hour after exercise. In the moderate exercise group, the anorexic effect of glucose was similar to that of sedentary controls, but food intake in the high intensity exercise group was significantly less than controls, suggesting that higher intensity exercise may potentiate the anorexic effect of glucose, promoting weight loss.

DOI: 10.1113/EP086916



High-intensity exercise enhances peripheral glucose-effects on feeding

A. Schematic representation of the experimental day. Glucose (i.p., 1.5 g [kg body weight]$^{-1}$) or saline was injected in control (grey), MOD (blue) and HIGH (red) goups 2 h after the end of the exercise. *B.* After 15 min, food was available and the first hour of food intake measured. In *B.* the number of rats per group = 13–16. Statistical analysis was performed using two-way ANOVA and the Holm–Sidak multiple comparisons test to find post hoc differences among the groups. Differences were considered statistically significant when $P < 0.05$.

Physiological Reports

Resistance exercise stimulates mixed muscle protein synthesis in lean and obese young adults

Carl J Hulston, Rachel M Woods, Rebecca Dewhurst-Trigg, Sion A Parry, Stephanie Gagnon, Luke Baker, Lewis J James, Oonagh Markey, Neil RW Martin, Richard A Ferguson, Gerrit van Hall. 6(14), e13799 (July 2018).

Muscle protein turnover and myofibrillar protein synthesis in response to nutrient stimulation is attenuated in the obese state. New evidence, however, shows that while this is true for nutrient stimulation, the typical anabolic response to resistance exercise is unchanged in obesity. In a recently published human trial, physically active lean and obese men were infused with the stable isotope tracer [^{13}C6]phenylalanine prior to an acute bout of resistance training followed by serial biopsies (hourly for 4 hours) to determine muscle protein synthesis (MPS). Despite a deleterious metabolic profile (e.g. increased triglycerides, cholesterol and insulin resistance), resting and post-exercise muscle protein synthesis was not different between lean and obese individuals whilst exercise, stimulated MPS was similar at ~50%. Similarly, whilst resistance exercise increased phosphorylation of various intracellular signalling proteins these increases were not different between lean and obese participants. Taken together, this data would suggest that where MPS is concerned the response to exercise does not differ in the obese state.

DOI: DOI: 10.14814/phy2.13799

Similar degrees of obesity induced by diet or ageing cause strikingly different immunologic and metabolic outcomes

Kanthi B Krishna, Maja Stefanovic-Racic, Nikolaos Dedousis, Ian Sipula, Robert M O'Doherty. 4(6), e12708 (March 2016).

Obesity is associated with chronic, low-grade inflammation and insulin resistance. Ageing is also associated with increased adiposity and a deleterious cardiometabolic phenotype; however, there are relatively few comparisons between diet-induced obesity in the young and obesity associated with ageing. In new research, young animals were fed either a control of HFD diet for 14 weeks or fed the control diet for ~14 months and subsequently grouped into lean or obese aged animals based on fat mass. Interestingly, it is demonstrated and that despite similar body weight and adiposity, young obese animals were more insulin resistant and had increased liver triglycerides than their old counterparts. Further, the immunophenotype in adipose tissue and liver differs in these two obese states (e.g. young and old). Tissues of young, obese animals contained a greater number of macrophage and dendritic cells (CD11b$^+$ and CD11c$^+$ markers) in addition to the CD11b$^+$ CD11c$^+$ F4/80$^+$ (triple$^+$) cells common to obesity along with increased hepatic IL-6 and TNFα, with these changes not seen in age-induced obesity. In summary, these important immunometabolic differences in phenotype may represent the more gradual onset of obesity with ageing compared to the relatively rapid onset in response to diet.

DOI: 10.14814/phy2.12708

Crossing the pond for your academic career

Is the leap worth it?

Havovi Chichger

Department of Biomedical and Forensic Sciences, Anglia Ruskin University, Cambridge, UK

On 14–16 September 2018, a myriad of physiology researchers will descend on QEII centre in London for Europhysiology 2018. Conferences such as these allow the research community to network and collaborate on everything from the development of novel concepts to the sharing of technical expertise. Physiologists from around Europe and far further afield attend, bringing with them a range of diverse research ideas, academic cultures and backgrounds. In 2011, I moved to the USA for my postdoctoral fellowship, and I returned to the UK in 2015 with more experience and a wider perspective on academic research. As the conference nears, I have been reflecting on my own experience of the differences between academic research conducted in different countries and how it has shaped my career, highlighting how truly mobile you can be with your academic career.

What mobility in science meant for me

Scientific research, like so many other sectors, undoubtedly benefits from an international community. I would struggle to name a research group, my own included, which does not include researchers with a range of nationalities from across Europe and around the world. This is never more obvious than during 'potluck' lunches where we all enjoy a wide variety of delicacies from around the world. But exotic food aside, what does this diversity mean for the research community?

As a PhD student at University College London (UCL), I was part of a brilliant but relatively small laboratory at the Royal Free Hospital, with only one other PhD student and a postdoctoral fellow. I primarily worked on models relating to diabetes and metabolic disruption and studied the physiology of glucose transporters in the renal epithelium (Chichger *et al.*, 2016); my work was awarded the young author prize in 2016. Nearing the end of my PhD, I realised that I had significant experience in renal physiology and was keen to broaden my research skills, particularly with regards to studying the signalling mechanisms which regulate glucose transporters and epithelial barrier function at a cell and molecular level. Throughout my undergraduate and postgraduate studies, I had encountered many 'success' stories from supervisors, colleagues and collaborators about researchers who moved to US academic laboratories to further develop their expertise.

There are a slew of leading UK physiology researchers who have spent large segments of their career in overseas laboratories, particularly in the USA. With statistics in the UK indicating that only 3.5% of PhD graduates progress to positions as permanent research staff, and only 0.45% become professors (of which a mere 20% are female),

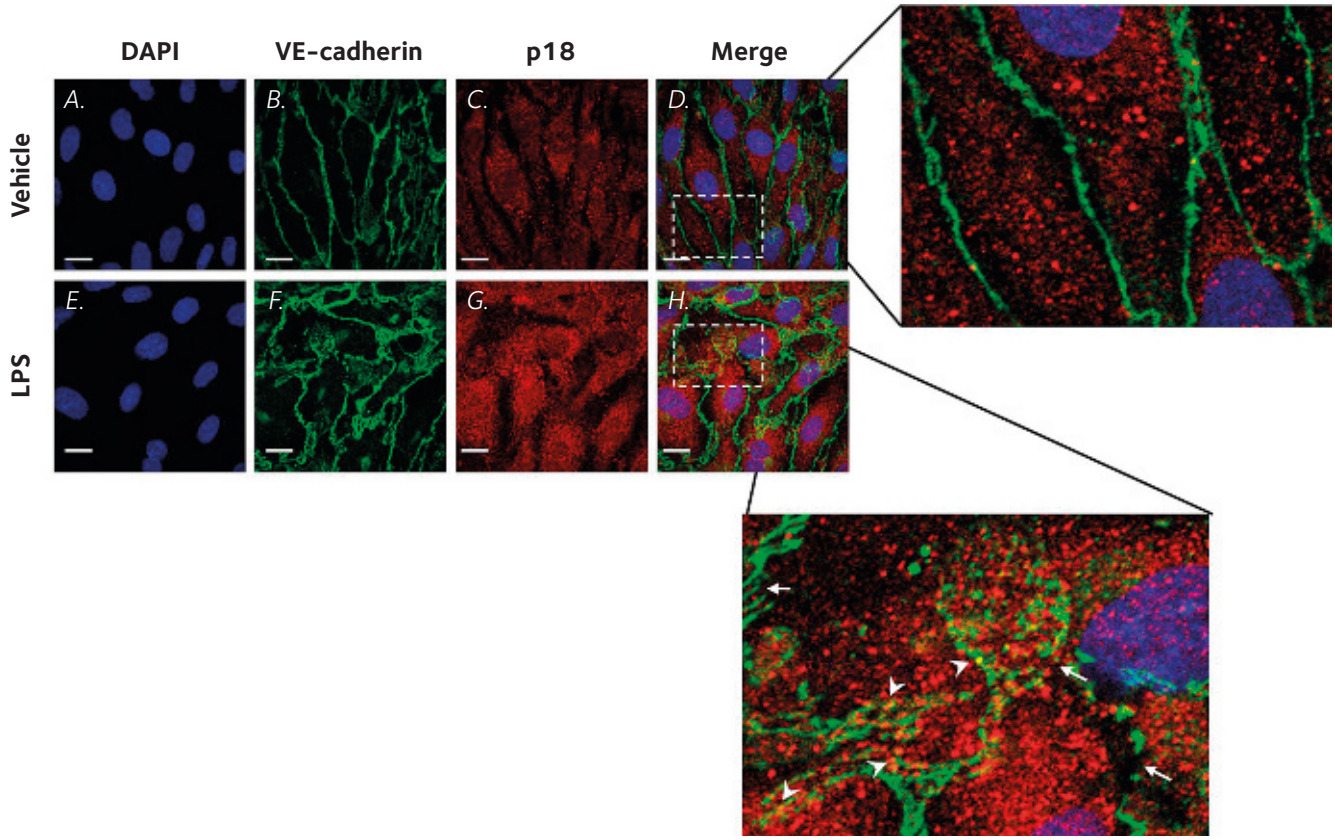


Figure 1. The first published experiments from my independent American Heart Association grant identifying the presence of p18/LAMTOR1 in the lung microvasculature. Studies such as these allowed me to develop my experience with cell signalling mechanisms whilst staying in the physiology field. Immunofluorescence studies show that LPS increases co-localisation of p18/LAMTOR1 with VE-cadherin positive endosomes (Figure adapted from Chichger, 2015).

I decided that any opportunity to strengthen my career had to be a good thing (Royal Society, 2014). I was happy to expand the scope of my research but I wanted to stay within the field so I applied for postdoctoral positions in physiology laboratories performing translational science on epithelial and endothelial barriers. Within weeks I found myself doing phone interviews and getting offers from a range of universities. A hop, skip and a viva later, I found myself in Providence, Rhode Island, starting a postdoctorate with Elizabeth Harrington at Brown University who recruited me on a 2-year contract to work on a National Institute of Health (NIH) grant studying cell signalling in the pulmonary endothelium in acute respiratory distress syndrome.

And then the fun started...

My first year at Brown University was a steep learning curve. I was working in a large laboratory with around eight technicians, four postdocs and five principal investigators. The pace of work was high, with a continuous push for publishing and working towards preliminary data required for grant submissions. The expectations of me as a postdoctoral researcher were high – because of the academic system, my peers in USA had all spent 5–6 years on their PhD, attending a variety of classes, being a teaching assistant and developing experience which I had simply not had time to achieve in my 3-year PhD. Working within such a high-paced team, with investigators all focused on pulmonary diseases, I had the opportunity to learn a wide range of technical skills using state-of-the-art equipment and disease models, like the electric cell impedance system (Chichger *et al.*, 2012) and pulmonary hypertension (Chichger *et al.*, 2014). Then there were the networks in the respiratory disease field which I had access to, opportunities to collaborate and connect with specialists in the field, and to present at conferences. To be clear, these opportunities are undoubtedly available in the UK, but only a small proportion of my peers who were early stage postdocs across the Atlantic were given these chances. In my experience, this was largely due to the higher expectations of a US postdoc, given the longer time to complete a PhD. After my first year, two papers and one published book chapter later, I was encouraged to apply for a postdoctoral fellowship award. As a UK citizen, with a J1 visa, I had limited options for where to submit an application with strict eligibility criteria from the major US funders. I developed an independent research project plan to study the role of a novel endosomal protein, p18/LAMTOR1, on vascular permeability in acute respiratory distress syndrome (Chichger *et al.*, 2015a; Chichger *et al.*, 2015b).

> ‘I would struggle to name a research group, my own included, which does not include researchers with a range of nationalities ...’

Funding	Be aware of your visa restrictions – many traditional US funders (e.g. National Institute of Health and National Science Foundation) have limitations on postdoctoral grants so ensure you check the small print before spending time preparing an application. Think outside the box for funders; for example, there are several foundations which are particularly supportive of overseas applicants (e.g. Human Frontiers Science Program).
Career progression	Mobility in science typically means joining different research communities and societies, expanding your mentor network, and having the opportunity to experience a range of different conferences. Whilst these are undoubtedly great advantages, it is important to remain a member of a UK society and keep abreast of the current research climate. This will allow you to keep an eye on the job market if you are looking to return to the UK.

Table 1. What I wish I had known.

'Many schematics of the future of UK research are dependent on a careful balance between the decisions made regarding UK migration policy and our access to international funding and infrastructure'

After three applications, I was awarded a two-year fellowship from American Heart Association to study p18/LAMTOR1. From this point onwards, I had greater freedom than I had ever experienced in my research. I had my mentoring team for support but suddenly I was independently developing my research, managing a budget, spearheading my papers and asked to review papers. Again, a luxury, which the majority of my UK peers may not encounter at my career level. So far, so good.

Before you start packing your suitcase

Of course, this works just great when the economic and political landscape remains stable. There may be many that feel the events of 23 June 2016 (Brexit) have abolished this mobility in science. Many schematics of the future of UK research are dependent on a careful balance between the decisions made regarding UK migration policy and our access to international funding and infrastructure (Royal Society, 2017). This has, and will, undoubtedly play a role in how freely scientists can move; however, there are also other pressures facing scientists, which differ greatly from those in the US, such as the REF (Research Excellence Framework) which assesses the quality of research in UK universities, and the resulting emphasis on research impact, as opposed to just high-impact papers.

Another consideration is the logistics of packing up and shipping to a different country. For me, this involved endless trips to the US embassy in London, saying goodbye to all my loved ones, learning to do the US dollar to UK pound conversion in my head, and learning to drive on the other side of the road. This was definitely part of the adventure, but if I had not loved the research and the laboratory I was working in, the adventure would have gotten old very quickly.

Would I do it again? Yes, in a heartbeat. Whilst there are some pointers which I would have liked to know ahead of time (Table 1), I am perpetually encouraging my PhD students and mentees to consider moving to a different country for a postdoctorate. There are the obvious advantages such as learning different techniques and skills; however, this does not typically require a new visa. For me, this mobility gives you a different perspective on research and lends opportunities to experience a different academic system, apply for different funding, attend different conferences, and network with different researchers, and it is these experiences, which I believe, make us more resilient and open-minded researchers and therefore shape our approach to our field of research.

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Collaboration: friend or foe

Grappling people to thy soul

Mike Tipton

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It can be argued that, in the broadest sense, we would not exist without collaboration. It is also easy to argue that our future health, prosperity, and indeed, survival will be dependent on collaboration. However, collaboration is something of a conundrum. Its meaning and usage are so broad as to be almost meaningless, and as a concept it covers a multitude of scenarios, not all of them good. So how do we foster enduring, productive collaboration in science?

Many people love the idea of collaboration; they pursue it with vigour, offering their services and proclaiming their interest in a project. Others are not keen on collaboration. For most, their view of collaboration largely depends on past experience or worries about future recognition. The problem is that there is a contradiction that runs through 'collaboration', right down to its definitions: a. *The action of working with someone to produce something* b. *Traitorous cooperation with an enemy*. Hopefully, academic collaboration falls under the former rather than latter definition, but perhaps not always.

Collaboration in nature: lessons for scientists

There is no doubt that collaboration can be a driver for advancement, and even optimal advancement. This is easy to demonstrate in biological terms; for example, over a billion years ago one bacteria became host to another, obtaining shelter in return for the production of energy from food and oxygen. Eventually the bacteria merged into a single cell that became the ancestral powerhouses of all multicellular life and the precursors to mitochondria. Today, examples of successful collaboration abound, from the African Oxpecker, and their aquatic equivalent, cleaner fish, to bacteria such as *Lactobacillus* that inhabit human intestines and help to relieve Irritable Bowel Syndrome, Crohn's disease and gut dysbiosis. As Darwin said, '*in the long history of humankind (and animal kind, too) those who learned to collaborate and improvise most effectively have prevailed*'.

What can we learn from the animal kingdom that might help our collaborations with other scientists? The obvious lesson is that those collaborations between organisms that endure are symbiotic rather than parasitic. That is, both collaborators bring something to the relationship and both gain. To coin a cliché, the sum is greater than its constituent parts. Collaborations fail when, in one way or another, they become parasitic. Perhaps we should focus on 'symbiosis' rather than 'collaboration'?

Scientific collaboration: the benefits

At one level, of course, all science is the product of a collaboration between colleagues within an institution, be they the technicians, students, academics or administrators that enable and conduct research. But what about collaboration across institutions? This is not an insignificant issue; even more so now

'Collaborations between organisms that endure are symbiotic rather than parasitic. That is, both collaborators bring something to the relationship and both gain'

than previously, successful collaboration is important for the advancement of research areas as well as scientific careers. As science moves unerringly towards complex, multifaceted studies employing advanced and highly specialised techniques, the need to collaborate nationally and internationally increases. This truth is increasingly being reflected in the published literature, where there is a positive relationship between the presence of international collaborating authors on top flight papers and citation impact (Adams & Gurney, 2016).

People are getting the message; as measured by co-authorship on refereed papers, international collaboration grew linearly from 1990–2005, or exponentially if international presentations are assessed (Leydesdorff & Wagner, 2008). In 1981 about 90% of UK published research output was domestic, by 2014 this figure had fallen to less than 50%; almost all of the growth in output in the last 30 years was produced by international co-authored collaborations (Adams & Gurney, 2016). In just the last two issues of *Experimental Physiology* we have published papers from 15 countries, and of the 22 papers published, 13 were collaborations between a total of 34 institutions. Leydesdorff & Wagner (2008) used network analysis to conclude that the growth of international co-authorship can be, at least in part, explained by the organising principle of preferential attachment ('the rich get richer'). Broadening collaboration should therefore be advantageous.

Figure 1. Collaborators seeing eye to eye: a symbiotic collaboration between the African Oxpecker and the African Cape Buffalo. One feeds, the other has parasites removed.

The major driver for collaboration is the need to share, be that ideas, equipment, facilities, techniques, resources or data. Without successful collaboration between experts within different fields, some major problems will either not be solved or will take much longer. For example, it is generally agreed that the battle against cancer cannot be won without such collaboration (Savage, 2018). Looking back, without collaboration we would have been less likely to know of the existence of the Higgs Boson or have sequenced the human genome. It is difficult to imagine the big questions of our time, such as understanding the working of the brain, the origin of the universe or the production of clean sustainable energy, being solved without interdisciplinary collaboration. The need for collaboration to provide the diversity of skills and techniques to answer these questions is paramount.

The UK Government is actively encouraging such collaboration through initiatives like the UK Research and Innovation (UKRI) Fellowships Programme (UKRI, 2018a). The Industrial Strategy Challenge Fund (UKRI, 2018b) looks to build collaborations between academics and business. One of the six key areas is 'Health and Medicine'. Research England recently invested £67m in 14 collaborative projects to 'drive forward world-class university commercialisation across the country' (UKRI, 2018c).

Promoting collaboration: opportunities and threats

So, how do we create the conditions that might promote successful symbiotic collaboration *within*, but even more importantly *across* disciplines? We start with an advantage; game theory (e.g. The Prisoners' Dilemma) research tells us that humans display a systematic bias towards cooperative behaviour in preference to otherwise rational self-interest (Fehr & Fischbacher, 2003). So, we need to foster this altruistic inclination and minimise the threats to collaboration.

Publishing has a role to play in promoting collaboration; since the first issue of the *Philosophical Transactions of the Royal Society* was disseminated in 1665, potential collaborations have been promoted by the publishing industry reporting what could be done by other people working in the same field. A relatively recent development is the publication of datasets that can be examined and used by others, a new and as yet not fully evolved form of 'collaboration'. On the other hand, publication can also be a barrier to collaboration: concerns about recognition of effort, authorship and ownership of ideas or data can introduce anxiety and suspicion. These problems can be minimised by early, open discussion, by scientists, and by

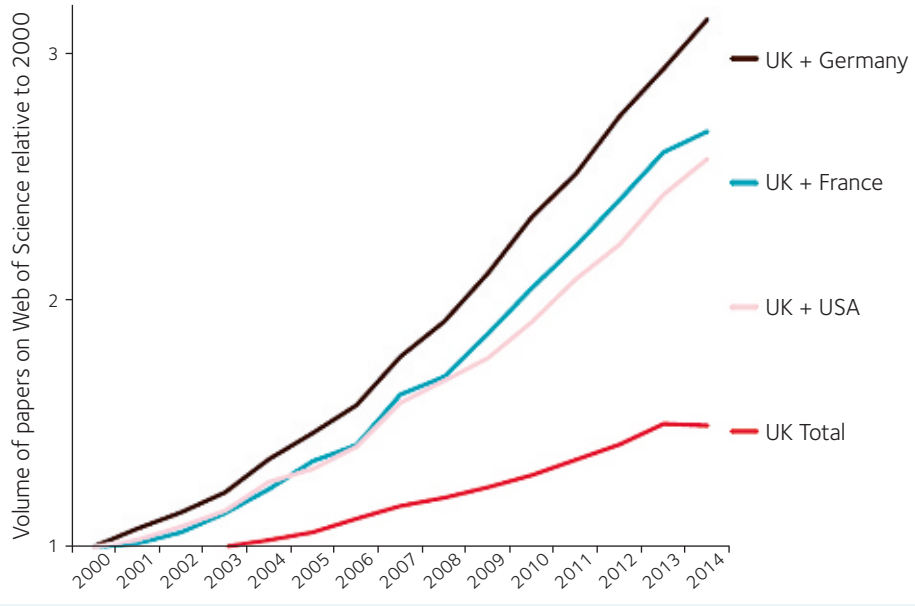

Figure 2. Relative increase in international collaborative publications (articles & reviews indexed in Thomson Reuters *Web of Science*) since 2000 (Adams & Gurney, 2016).

journals giving high value to ideas. Following established guidelines for authorship should also help (e.g. International Committee of Medical Journal Editors Guidelines, 2017).

Other threats to collaboration come in the form of international politics: Brexit and access to EU funding, the rise of nationalism, travel bans, language barriers and difficulties in getting work permits. This is a constantly changing canvas within which scientists and leading institutions must lobby and advocate the crucial societal benefits of international collaborative research. Hopefully continued access to international and pan-continental research funding that demands international collaboration will help.

The role of publishing in prompting collaboration is reinforced by scientific meetings where you meet, learn from and socialise with those working in your field. Having determined from the literature and scientific presentations those who you might work with, it is during social exchanges at meetings that you discover people you want to work with. One potentially negative consequence of subject-specific meetings is that they constrain the technical and academic cross-fertilisation, and consequent collaboration, that might be promoted at more multi-disciplinary meetings.

If we continue to use co-authorship with an individual from another institution as the index of collaboration, I have collaborated with 71 people from 15 countries over three decades (e.g. International Drowning Researchers' Alliance - **idra.world**). As far as I can recollect, all of these collaborations, and subsequent close friendships, were forged in the conducive atmosphere of a scientific meeting. It follows that any decline in funding to attend scientific meetings will stifle potentially critical collaborations. It also follows that although, as noted above, it is possible to encourage or require collaboration through targeted funding calls, in the absence of such funding it is very difficult to 'administer' long-lasting productive collaborations into existence from nowhere. They have to evolve naturally, through interpersonal contact and understanding of the skill sets and capabilities of different people.

That is not to say that people who do not get on personally cannot collaborate; it is simply that the holistic experience and durability of the collaboration is likely to be diminished. Because, in the end, it is about spending time with those you respect, like, need and can communicate freely with. As in so many other things, Shakespeare had it about right,

'Those friends thou hast, and their adoption tried, Grapple them unto thy soul with hoops of steel.'

For a scientist, as well as society in general, the benefits of collaboration go far beyond science.

Acknowledgements

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Friends in high places

Researchers go global to reach for answers at high altitude

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Global Research Expedition on Altitude Related Chronic Health, or Global REACH, is an international collaboration of academics and physicians from 14 institutions across Canada, the UK, the US, Peru and Nepal. While the 'Global REACH' title is relatively new, its leaders have conducted a multitude of expeditions over the last decade to Nepal's Himalaya, California's White Mountains and now Peru's Andes. With a collective interest in heart, lung and vascular health and altitude medicine, Global REACH's collaborations ultimately aim to understand how the human body adapts, or maladapts, chronically to the low oxygen environments of earth's highest altitudes.

I am writing this from 4,330 m, at the Laboratorio de Cerro de Pasco and Institutio de Investigaciones de la Altura in Peru. Our team of 40+ researchers, trainees, PIs and physicians are currently conducting ~20 studies examining heart, lung and brain physiology in lowlanders (us) and Andean highlanders with and without chronic mountain sickness. This article, however, does not intend to outline our experiments or specific scientific findings, which have been described in a recent issue of *Physiology News*. Instead, the reader will get a raw, 'behind-the-scenes' look at what transpires on these expeditions: the challenges we face, the experiences we gain, and most importantly the team values that drive the success of these international collaborations.

30 June 2018, day 1 at altitude.
Yesterday, the last of three groups of the Global REACH team drove from sea level in Lima up to 4,350 m in Cerro de Pasco, Peru. Amongst the team, some individuals are feeling 'okay' (say, a rating of 7/10), others have been in bed with splitting headaches for more than 24 h. We would later discover that one, in fact, had a bout of pneumonia. Nevertheless, one thing remains constant across the team – the excitement. It is palpable. Seven lab bays are set up, participants are being scheduled in, the equipment is (mostly) accounted for and working. Data collection has already begun today, and our first Andean participants are coming in tomorrow morning. This is what we came for, and we're ready for the fun to begin.

For those who haven't experienced the thin air of Earth's highest mountain ranges, a 7-hour jump from sea level to over 4,300 m altitude is significant, one which often leaves individuals feeling much worse than 'not great'. Yet, with advanced knowledge of the side effects of altitude and hypoxic exposure, Global REACH members have joined forces to answer a plethora of physiological questions. For many, this will mark more than four expeditions to high altitude, a select few even in the double digits. In the first few days, most – including our team leaders – will have headaches, nausea, sleep disturbances and apneas. The inter-individual variability of these symptoms is quite high, as a select few

Figure 1. Example of a centrifuged blood sample from an Andean participant with chronic mountain sickness. A normal, healthy lowlander's hematocrit (i.e. fraction of red cells in the blood) is ~40%; several Andean participants including this one had hematocrit values of 75–80%.

may feel fine, most will feel some magnitude and combination of the list, and others will be periodically out of commission.

So, why do we do it? Why do we involve ourselves with the potential suffering at altitude and any additional risks (i.e. transport, illness) kindred to these trips? From my experience, three fundamental elements outweigh the risks and define the success of expeditions and collaborations like Global REACH: the science; the experience; the team.

Science

1 July 2018, day 2 at altitude; 08:32 h
'MAS FUERTE MAS FUERTE, yeah Johnny!' Johnny, our first Andean participant is laying on the bed of testing Bay 1, currently practising a handgrip protocol for a vascular study. Johnny already has a venous catheter placed in his forearm and will be shuttled through a screening circuit: ultrasound imaging (cardiac, ocular and vascular), a maximal exercise test and assessment of total blood volume. Our Spanish skills are currently dismal, but we're managing to compliment the amazing work of our translators to collect a large cardiovascular dataset on ~50-60 Andean participants.

3 July 2018, day 4 at altitude.
Four of us are working in the bloods room to measure total blood volume, hematocrit and viscosity. We knew from previous reports that Andeans would have augmented total blood volumes and hematocrit levels compared to us lowlanders but seeing those bloods ourselves was staggering. 'A hematocrit of SEVENTY-EIGHT per cent!' a colleague yelled, astounded. For reference, a lowlander's normal hematocrit is ~40%. (Fig. 1)

An undeniable passion for physiology underpins collaborations like Global REACH. The energy amongst the group drives impressive productivity and allows us to complete multiple studies in relatively restricted time periods. During the 2016 Nepal Expedition our team conducted 18 major studies, including a total of 335 study sessions in just three weeks at 5,050 m (further to multiple sea level and ascent testing sessions). This high-density data collection is relatively uncommon outside of field work and is only made possible by the vast breadth of technical fluency, specific expertise and research experience amongst the team. The expeditions allow us to not only answer our current questions but further breed a multitude of ideas for future study. *'We could answer that one next, Ethiopia 2020? Another Nepal expedition?'*

Of course, these expeditions allow us as trainees and investigators to be productive, and to present and publish high-quality data and exciting findings. They strongly contribute to our development and career progression in academia. But what is undoubtedly most important is the greater aim of Global REACH: to understand altitude health on a 'global' scale. This collaboration and research ultimately aims to understand *why* chronic mountain sickness occurs, *how* different high-altitude communities have adapted (or maladapted) to low oxygen, and *what* might ultimately be done to improve the health of individuals exposed to acute or chronic hypoxia.

Experience

1 July 2018, day 2 at altitude; 13:17h
The viscometer is being set up in the bloods room and is a key weapon in our arsenal for primary outcome measures in multiple studies. Due to voltage differences (compared to Canada) the unit needs to be connected to a step-down. We connect the viscometer, water bath and the step-down, and at first all seems to be functioning well. A few minutes later, an odd scent emerges. Ah, the step-down is smoking, not good! This unfortunately is not the first fire hazard we've encountered. In Nepal, one of our technicians had to rewire most of the outlets to ensure they wouldn't catch flame. A few days ago, an outlet connected to a locally-made space heater went alight. We are constantly having to double- and triple-check that our equipment doesn't melt due to poor electrical wiring, or mismatched voltage inputs/outputs. At the same time, though, we more often find ourselves very thankful that we have electricity to power the large volume of studies being conducted in these remote locations.

Figure 2. Performing a carbon monoxide rebeathe test to measure red cell volume and total blood volume with an Andean participant in Cerro de Pasco. This method is technically challenging, and is made more difficult with a significant language barrier.

'This collaboration and research ultimately aims to understand *why* chronic mountain sickness occurs, *how* different high-altitude communities have adapted to low oxygen, and *what* might ultimately be done to improve the health of individuals exposed to acute or chronic hypoxia'

These expeditions provide comprehensive research experience and encourage growth amongst the team and its individuals. Things are not always sunshine, rainbows and unicorns, though the many logistical hurdles provide an opportunity for learning and developing our problem-solving abilities.

We often must think outside of the box and utilise our creative capacities to circumvent roadblocks, technical difficulties and unexpected challenges.

Aside from common technical conundrums, there are often cultural barriers that are both interesting and of course region-dependent. One obvious challenge is language – in Nepal, this was less obvious because many of the porters and Sherpa required some English for their work in tourism. Surprisingly to us, Peru has proved much more difficult, as virtually no one in Cerro de Pasco speaks a language other than Spanish. In fact, the local residents have an accent that is 'poquito' difficult for our translators to understand, so trying to explain protocols can be tricky. For example, measurements of total blood volume using the carbon monoxide rebreathe technique require the participant to complete a *few* steps: fully empty the lungs; attach to the spirometer mouthpiece; turn the valve; rapidly fill the lungs and hold for ten seconds; breathe normally for two minutes into the spirometer; then empty the lungs and turn the valve to close the system... all without breaking the glass spirometer (Fig. 2). Simple, right? Not so much. Despite our efforts to perform practice runs and explain the protocol several times over with physical demonstrations and translators, this is notably challenging.

While these international expeditions allow us to become immersed in a different geographical and cultural environment, certain local traditions or values unbeknownst to us can provide unexpected barriers. In Nepal, the Sherpa were incredibly kind, and almost always smiling. They would seldom show negativity or utter complaints. One of our prime focuses on these expeditions is to examine blood markers of inflammation, blood gases and hematocrit concentration. In Nepal we collected serial arterial and venous blood samples at every stop during our ascent, but in Pheriche, one stop before the Pyramid, the Sherpa began to show concern, some requesting to skip the blood draws. We would find out the Sherpa perceived blood as their lifeforce, and that once lost, blood could not be replaced. They believed the loss of blood would weaken them and impair their state of being. One translator mentioned the word 'vampire' and explained the concern that their blood might be sold. Luckily, with the help of our lead Sherpa and a few of the elders, we were able to convey that the bloods were solely used for research purposes and that we would never take more than necessary for study.

1 July 2018, day 2 at altitude; 16:05 h
I look over after completing one great blood volume test on the fourth Andean participant today (we're getting more effective at translating) and the viscometer is now working, with a step-down that isn't smoking! Turns out the previous step-down was pulled off the shelves of the Cerro lab. We've found one of our own from Canada and it has worked like a charm. With a bit of flexibility and a sprinkle of luck, these things often happen to work out.

Despite the aforementioned challenges, these expeditions provide overwhelmingly positive experiences, opportunities for personal growth and adventure. As researchers, we gain incredible organisational skills: much like a game of Tetris, we learn to schedule participants amongst multiple studies, ensuring a fine balance between efficiency and crossover, i.e. that no measures conflict with other studies. Our communication skills grow as we continually coordinate between our local contacts, the P.I.s and the rest of the team. Even when things go completely off-plan, we learn to utilise flexibility and make the best of challenging situations. This field-based research teaches us quick-thinking, adaptability (no pun intended) and resourcefulness. The challenges themselves provide strong learning experiences to be applied moving forward.

Perhaps the most obvious and enticing draw of these expeditions is the element of adventure. Not surprisingly, team leader Phil Ainslie's initial involvement in altitude research was borne from his job as a mountain guide before attending university. 'The first (trip) was when I was 22 or 23… I was running a trip in northwest India to some peaks at 6,000 m or 7,000 m. Damian (Bailey) was my instructor and he asked, *'would you collect some blood samples'? And I said, 'sure'. I spun samples down with a hand-crank centrifuge at 5,000 m on 25 people and took (saturation) measures, just me. And brought it all back. I've gone back (to altitude) every few years since.'* Following Phil's lead, these expeditions allow us to explore incredible regions and share awe-inspiring experiences with our international collaborators. Visiting Everest Base Camp or climbing a (slightly dangerous) hill to look out at the Andes creates a bond of friendship and provides the foundation for long-lasting international collaborations that define Global REACH.

Team

9 July 2018; 21:53 h
Myself, Phil Ainslie (University of British Columbia), Mike Stembridge (Cardiff Metropolitan University), Craig Steinback (University of Alberta) and Jonathan Moore (Bangor University) are sat in the lobby of our hotel, chatting over a few Cusqueña beers. While discussing the 2016 Nepal Expedition, I explained how impressed I was that a group of 37 individuals had worked so well together, with no obvious dramas despite living in a harsh environment.

'It's similar to the New Zealand All Blacks values… basically the 'no dickheads' rule', one of us said. We all laughed, then nodded in agreement. 'Well, much like in mountaineering leadership, a mantra of the All Blacks rugby team is that they 'sweep the sheds', meaning that it doesn't matter if you're the star player – everyone on the team cleans the dressing room. If you're a dickhead, if you're not a team player, you're not part of the All Blacks.'

Phil has explicitly provided permission to include this conversation in the article, because while blunt, this type of value characterises the core of our collaborations and ensures the success of the expeditions. When everyone works together, dismisses ego and shares positive energy, the team thrives. Sixteen-hour testing days become relatively easy when you're having fun.

Our team is at the heart of our success. We embrace collaborators with infectious personalities that border on the sides of eclectic and hyperactive: those with a genuine passion for research and zest for life. Team members remind each other to look beyond the academic pressures of funding and publication for the sake of career progression and light a fire and excitement for discovery. Our peers drive us to new heights, literally and figuratively, in our academic prowess. We find less pride in our individual successes than in those of our teammates.

Our leaders – Phil Ainslie, Mike Stembridge and the late Christopher Willie – continue to inspire us. Their energy brings the continents together to create impressively cohesive and brilliant multidisciplinary collaborations. Their teams will continue to go global and reach for answers to important health-related questions at Earth's highest altitudes.

Members of the Global REACH team in 2018 at the Institutio de Investigaciones de la Altura (4,350 m) in Cerro de Pasco, Peru.

Hypoxia research

Reaching new heights

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A constant supply of molecular oxygen (O_2) to every cell of our body is essential for the maintenance of health. However, we frequently encounter conditions where the oxygen demand by a tissue exceeds the supply, thereby leading to a dangerous state of oxygen deprivation (hypoxia). Because of our absolute reliance on oxygen, it is perhaps not surprising that we are equipped with multiple mechanisms which detect when oxygen levels drop and activate adaptive responses which help to increase oxygen supply and thereby overcome the hypoxic challenge.

The identification of the oxygen sensing mechanisms underpinning these mechanisms has proven to be a fertile ground for physiological research over the last quarter of a century and has recently identified a new class of therapeutic entities. The success of this rapidly growing field of research has depended heavily on the existence of a vibrant and well-structured multi-disciplinary international research community.

It is often said that we take for granted the air we breathe and the life-supporting oxygen which is contained within it. Indeed, a constant supply of molecular oxygen is essential for the maintenance of most multicellular life on Earth. However, this was not always the case. Early life on the planet, which was mostly composed of simple single-cell organisms, existed and thrived in an oxygen-free atmosphere. Indeed, when molecular oxygen (O_2) first appeared in the Earth's atmosphere it wiped out the vast majority of the planet's biomass, which could not deal with its reactive chemistry (Taylor & McElwain, 2010).

However, during the course of evolution, some organisms developed the capacity to not only withstand the toxic effects of molecular oxygen (O_2) but also to utilise its reactive chemistry for respiration (Taylor & McElwain, 2010). This represented a significant advance in the efficiency of metabolism. The step-up in bioenergetic efficiency and capacity that this enabled, provided the fuel to allow the development of multicellular animals (metazoans) and ultimately the expansion of higher organisms including vertebrates.

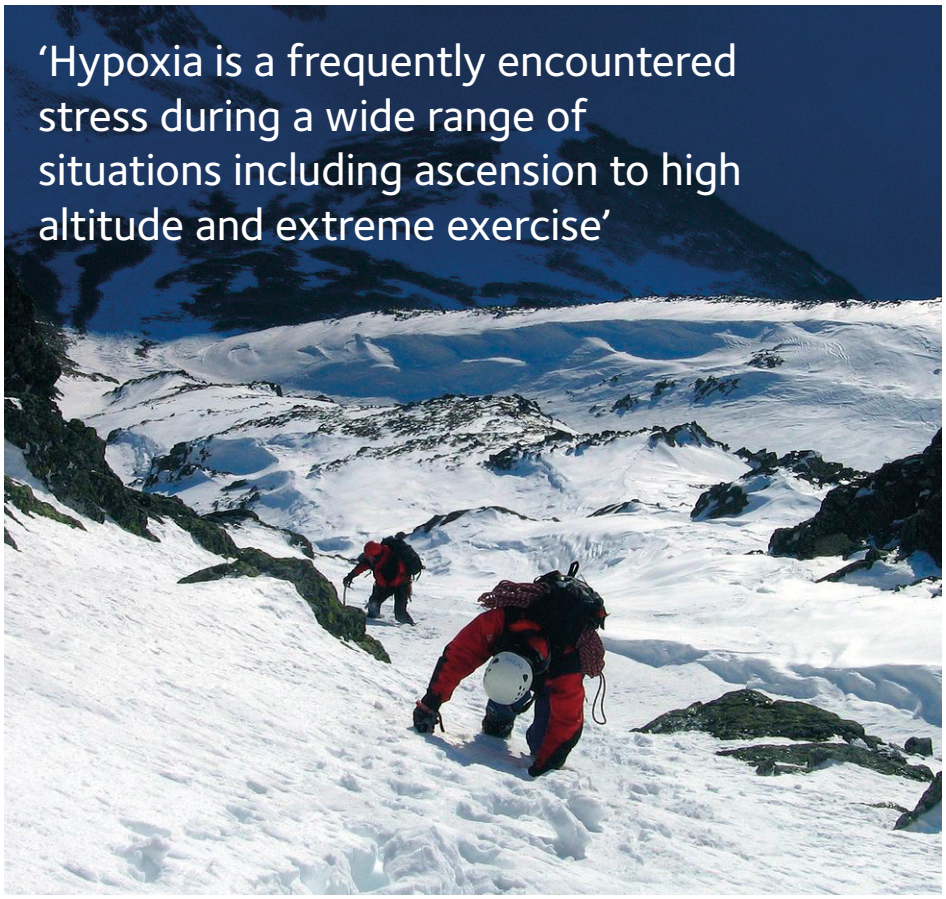
As such, the evolution of respiration as a metabolic strategy provided the fuel source to allow the development of complex life on earth. A payoff for this switch to respiration is that a constant supply of atmospheric O_2 is essential simply for the maintenance of life in most higher organisms. This requirement renders cells, tissues, organs and consequently organisms susceptible to bioenergetic crisis under conditions where oxygen demand exceeds supply (hypoxia). However, hypoxia is a frequently encountered stress during a wide range of situations including ascension to high altitude and extreme exercise (Semenza, 2012). Furthermore, in a range of pathological conditions including ischemic disease (such as heart attack or stroke), inflammation and

cancer, cells and tissues become exposed to hypoxia. Under these conditions, exposure of cells, tissues and organisms to hypoxia renders them at high risk of metabolic breakdown and death. Fortunately, we have also evolved mechanisms to detect when oxygen levels in the body begin to drop and to activate adaptive responses to promote survival during times of hypoxic stress. Because of our absolute reliance on oxygen, it is perhaps not surprising that much attention has been paid to studying the effects of this vital molecule on biological systems and how our systems adapt under hypoxia.

Two major breakthroughs mark our developing understanding of the biology of hypoxia. Firstly, the discovery and physiological understanding of the carotid bodies, two pea-sized organs located at the bifurcations of the carotid arteries which are responsible for monitoring blood oxygen levels and controlling the rate of and depth of breathing to keep them constant. The discovery of the physiologic role of the carotid bodies was recognised by the award of the Nobel prize in Physiology & Medicine to Corneille Heymans in 1939 (De Castro, 2009). Secondly, the discovery of the hypoxia-inducible factor, a ubiquitous master regulator of the transcriptional response to hypoxia, and the oxygen sensing mechanisms of the hypoxia-inducible factor (HIF) pathway opened up the field of cellular hypoxia. The latter was recently acknowledged by the award of the Lasker Award for basic medical research to Gregg Semenza, Peter Ratcliffe and William Kaelin in 2016 (Johnson, 2016).

A large part of the success of this field of research is fueled by the fact that interest in the mechanisms and consequences of oxygen sensing is shared by a diverse range of researchers including those interested in understanding the biology of high-altitude, comparative physiologists, sleep physicians, cancer biologists, physiologists, immunity researchers and clinicians. This diverse group has been well served by a strong sense of broad community as attested to a number of regularly convened high-level conferences around the topic of hypoxia which have a strong history of being inclusive of researchers with diverse interests.

As is the case in much of life, in the field of hypoxia research, embracing diversity has been key to its success. Initial studies into why numbers of circulating red blood cells are induced in climbers ascending to high altitude through the induction of erythropoietin led to the identification of the hypoxia HIF as a ubiquitous regulator of the cellular response to hypoxia. Subsequent studies revealed a general role for HIF as a master regulator of the cellular adaptive response to hypoxia and revealed roles for this pathway in cancer, ischemic disease and inflammation.



By developing our understanding of this pathway, a new class of pharmaceutical therapeutics (the HIF-hydroxylase inhibitors) are now in advanced clinical studies for the treatment of anaemia and other indications. It was through the presentation and discussion of the diverse aspects of the physiological response to hypoxia at regular international conferences that within 25 years of the first description of HIF, drugs will likely soon be approved for clinical use.

A key aspect to the success of this field of research has been a vibrant, active and well-organised community who meet regularly at dedicated international conferences such as Keystone symposia and the biannual Lake Louise hypoxia conference. At their most successful, the diverse interests of researchers in the field are well represented. This has promoted multidisciplinary studies involving clinical medicine, population genomics, cell biology, pharmacology and the application of state-of-the-art transgenic technologies to the field. Other funded initiatives, including two European Union funded COST actions, facilitated more dedicated conferences and provided support for lab placements and the promotion of international mobility for young scientists.

In a world where isolationist ideology appears to be on the rise in some countries, the success of the hypoxia research community represents a beacon of what can be achieved with goodwill, international cooperation and interdisciplinarity.

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War and peace

Physiologists during 1914–1919

Tilli Tansey

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At the 1913 AGM of The Physiological Society, the last before the outbreak of the first World War (WW1), it was noted with approval that membership reached a new peak – 272 – with 16 new Members elected that year. By 1919, however, membership had dropped back to 251. What had happened to British physiologists in the intervening years?

After the outbreak of the WW1 in August 1914, many British physiologists became directly involved with the War effort: some in uniform, some working in areas closely related to their pre-War research, others returning to (or continuing) medical practice, and a few working in completely new fields. Of the latter, two are of especial note; namely, Keith Lucas* (1879-1916, Member 1904) and the future Nobel Laureate A V Hill* (1886–1977, M 1912). Lucas, a Cambridge neurophysiologist with exceptional mathematical and engineering abilities, was encouraged by Horace Darwin* (1851–1928, M 1881), founder of the Cambridge Scientific Instrument Company and member of the Government's Aeronautical Research Committee, to join the Royal Aircraft Factory at Farnborough. As a captain in the Royal Flying Corps, Lucas worked on several projects including redesigning aircraft compasses to account for problems caused by engine tremor and the earth's magnetic field and creating a gyroscopic bomb-aiming device that eliminated vibration error. He was killed in a mid-air collision in October 1916, leaving behind a preliminary draft of his seminal work *Conduction of the nervous impulse*. This was completed in 1919 by his student ED (later Lord) Adrian* (1889–1977, M 1917) after his own return to Cambridge. In 1914, Adrian, like many, abandoned the Laboratory for accelerated clinical training, and worked throughout the War on nerve injuries and shell shock at the National Hospital, Queen Square, and the Connaught Military Hospital in Aldershot.

AV Hill had been another of Lucas' students. Originally a mathematician, he was recruited into the Physiological Laboratory by Walter Morley Fletcher* (1873–1933, M 1898). With the outbreak of War, Hill – a Territorial officer – was quickly invited (again, suggested by Horace Darwin) to create and lead an anti-aircraft experimental section of scientists in what later became known as operational research. Readers wanting to know more about 'Hill's Brigands', some of whose work resulted in the official manuals on anti-aircraft gunnery, are directed to the instructive work of Society Member William van der Kloot.

Physiologists in medicine

Lucas and Hill were unusual in stepping away from physiology. Many Members served in medical and scientific capacities: in hospitals on the battlefield, in military and civilian hospitals on the home front, and as specialist advisers to Government, military and professional committees. It should be emphasised that at this time the majority of Society Members were medically qualified, and a large proportion of those were engaged in clinical practice.

From left to right, the surnames of the physiologists are: Adrian, Brodie, Cullis, Dale, Barger, Sharpey-Schafer, Bayliss, Horsley, Fletcher, Loewi, Lucas, Barcroft, Sherrington, Starling and Hill. Images are from the author's own collection and are principally taken from The Physiological Society's archives, Wellcome Images, and the Royal Society

Indicative of this are Members addresses published in the 1905 pre-War Grey Book (the membership list of the Society), the last pre-War volume in the Society's archives. Such addresses include the Harley Street area of London and similar 'medical' areas of other cities (e.g. Rodney Street in Liverpool). Sir Victor Horsley* (1857–1916, M 1884), one of the most distinguished surgeons of his generation, did not live on Harley Street but on Gower Street close to the research laboratory he enjoyed as Professor of Surgery at UCL. He made numerous important discoveries concerning the thyroid gland, and his pioneering work in cerebral localisation included the invention of the first stereotaxic frame. At the outbreak of War, he joined the British Expeditionary Force to the Western Front and later the Mediterranean Expeditionary Force as Colonel and Consultant Surgeon to the British Army. He died of heat stroke near Baghdad in July 1916, a month before the death of Thomas Gregor Brodie* (1866–1916, M 1892). Brodie, an Englishman and then Professor of Physiology at Toronto, was serving with the Canadian Medical Services when he died suddenly of heart failure. The Minutes of the 1916 AGM record *'The Society has suffered heavily by deaths during the year, having lost three of its most distinguished members, Prof. Brodie, Sir Victor Horsley & Dr Keith Lucas, all of them members by whom much more & valuable work would undoubtedly have been produced'.*

Physiologists in physiology

In April 1915, a chlorine attack by the German Army on the Ypres salient on the Western Front marked the beginning of large-scale use of chemical weapons, and many physiologists were recruited to work on the new problems of gas poisoning, prevention and treatment. The Oxford respiratory physiologist JS Haldane* (1860–1936, M 1887) was immediately asked by Lord Kitchener, then Secretary of State for War (a position held previously by Haldane's brother Lord [Richard] Haldane who was by then Lord Chancellor) to visit the site and advise the War Office. Haldane subsequently worked, *inter alia*, on the development of respirators and remained a civilian throughout the War. With similar civilian status, Joseph Barcroft* (1872–1947, M 1900) from Cambridge studied the effects of gas poisoning at the Government's experimental station at Porton Down, Wiltshire. Barcroft claimed that as a civilian he could be much more assertive to the military top brass. Many of his colleagues, however, were commissioned officers in the RAMC (Royal Army Medical Corps) including Gordon Douglas* (1882–1963, M 1906). Douglas, of the eponymous Bag for respiratory gases, recalled Barcroft on a visit to France proudly demonstrating his status by eschewing a helmet and audaciously wearing his bowler hat within the range of German guns.

The Government's anti-gas department was established at the RAMC College at Millbank, London under the charge of the Professor of Physiology at UCL, Ernest Starling* (1866–1927, M 1890), then a Major in the RAMC. Like many of his generation, Starling had been immersed in the then dominant scientific culture of Germany. John Henderson's biography describes him as a 'man of passion' with 'teutonic enthusiasms', well known for his deep love of German and Germany. Profoundly distressed by the War, he vowed never to speak German again, becoming quite vociferously anti-German. Indeed, although in his late 40s, he tried to enlist as a combatant before being persuaded that he was more valuable in labs and on committees.

His brother-in-law and frequent collaborator William Bayliss* (1860–1924, M 1890) also diverted into War-related activities, but as a civilian. His lack of a uniform had one unfortunate consequence in 1917 when on a visit to France he became separated from his official host, was arrested, and held briefly as a spy. During that same visit he met the American physiologist Walter Cannon* (1871–1945, HonM 1934), Professor of Physiology at Harvard, then serving as a captain in the US Army Medical Corps. Bayliss' principal contribution was his work on wound shock, partly in collaboration with Cannon, which resulted in the use of gum-saline solutions to replace lost blood – a treatment calculated to have saved many thousands of lives. Bayliss was honoured with a knighthood in 1922, although he initially refused his investiture invitation because it clashed with a meeting of The Physiological Society.

Some Members remained in their Universities and labs, although many physiology classes were decimated. The future Nobel Laureate Charles Sherrington* (1857–1952, M 1885) stayed in Oxford working on the innovative student manual *Mammalian Physiology: a Course of Practical Exercises* (first published in 1919) which influenced generations of students over several decades. In the summer of 1915, Sherrington cycled to Birmingham and signed on for a short period as a munitions worker at the Vickers factory, working long shifts of over 75 hours a week. He proved a hard worker, his grateful foreman offering him a reference should he ever need one. Sherrington's subsequent report on his working conditions to the War Office contributed to the creation of the Industrial Fatigue Board of which he was appointed Chairman.

Others remaining in Britain were the first appointees of the newly created Medical Research Committee (later Council, MRC), established in 1913 as a consequence of Lloyd George's 1911 National Insurance Act. It was an inauspicious time for such a new venture. The key appointment of Scientific Secretary was accepted in early 1914 by the Cambridge physiologist who claimed his greatest contribution was introducing AV Hill to physiology, Walter Morley Fletcher. Reassured by Fletcher's appointment that this unfamiliar new venture would be scientifically robust, Henry Dale* (1875–1968, M 1900) and George Barger* (1878–1939, M 1909) accepted research positions, and in July 1914 were dispatched to Germany to meet eminent physiologists and examine equipment prior to the establishment of their own labs. In Strasburg (then a German city) they were privately warned that mobilisation was imminent, and hastily and with some difficulty got back to the UK shortly before War was declared on 4 August. Dale, recently appointed a FRS for his work at the Wellcome Physiological Research Laboratories and who would later win the Nobel Prize for the elucidation of chemical neurotransmission, spent five years studying amoebic dysentery, gas gangrene, wound shock, antiseptics, and the production of British alternatives to the many drugs previously obtained from Germany.

The Physiological Society

As these brief, but varied, vignettes suggest Wartime contingencies and pressures pre-occupied many, if not all, Members of The Society. Efforts were made to maintain the regular programme of 7-8 meetings a year but this had dropped to five and all held in London by 1917. Concurrently, the number of Members able to attend and present Communications fell with Wartime duties and transport difficulties being cited in The Society's Minutes. In 1915, the Secretaries reported that *'notwithstanding the fact that so many members have been occupied in various matters in connection with the War, the standard of communications has been kept up'*. The subject matter of some Communications did, however, give rise to concerns about published *Proceedings* being useful to the enemy. Immediately post-War, 10 meetings were held in 1919 and the Annual Report noted with satisfaction that the numbers of Communications *'are rapidly increasing to their pre-War numbers'*.

Membership decreased during the War years due to deaths, resignations and fewer new members. Importantly, however, a historic decision in 1915 allowed admission of the first six women Members. Ernest Starling had opposed the admission of women, arguing that the Society was primarily *'a dining society and it would be improper to dine with ladies smelling of dog – the men smelling of dog that is'* (details in Tansey 1993, reprinted 2015), and he was closely involved in another Membership debate. At the Committee meeting of March 1916, attended by only five members, a letter was received from de Burgh Birch (1852–1937, M 1892), then Professor of Physiology at Leeds and commander of a Territorial medical corps in France, protesting at the inclusion of German and Austrian subjects in the Grey Book. The meeting unanimously decided to take no action, and there the matter seemed to rest until the 1918 AGM at which, according to Sharpey-Schafer's *History of The Physiological Society*, *'[i]t was moved and seconded'* that enemy nationals should be omitted from the membership list. Somewhat coyly, Sharpey –Schafer, usually a diligent and reliable scribe of the Society's early archives, gives no further details of the proposers. The original Minutes record them to be Ernest Starling, seconded by Sir Henry Thompson, then Professor of Physiology in Queen's University, Belfast. The AGM voted eight in favour and eight against the motion, leaving the chairman William Halliburton to cast his vote to maintain the *status quo*. However, German and Austrian members were discussed again at the Committee meeting in March 1920 when the question of their outstanding subscriptions was raised. The 1919 Grey Book lists three such members (in addition to four Honorary Members), of whom two, the future Nobel laureate Otto Loewi* (1873–1961, HonM 1934) and Franz Müller, were alive. As neither could pay their arrears, the Committee Minutes of June 1920 record rather harshly, *'[they] therefore cease to be members'*.

Fractured international relationships between some individuals and organisations took time to repair. In March 1915, The Physiological Society had received a formal greeting from the Federation of American Societies for Experimental Biology sent to all combatant nations (the USA not then being in the War) with the *'hope of an early and enduring peace, which will leave the nations with no permanent cause of rancor towards each other'*. Sadly, some rancour and hostility did survive. As early as January 1919, Ernest Starling, his pre-War internationalism and use of German fully restored, reported proposals for an 'Inter-Allied Congress' by French physiologists. This was eventually held in Paris in 1920 but it was not until 1923 that the first fully 'international' post-War Congress, with no restrictions on attendance, was held in Edinburgh as Fernando Cervero has recently analysed. AV Hill, in his Nobel prize banquet speech in 1923, acknowledged that *'[t]he War tore asunder two parts of the world... Physiology, I am glad to know, was the first science to forget the hatreds and follies of the War and to revive a truly international Congress: my own country, I am happy to boast, was happy to be its meeting ground'*.

References & Further Reading

Details of Society committee meetings, correspondence, AGMs and membership records are taken from The Society's archives, housed in the Wellcome Library, London.

All named British physiologists, except de Burgh Birch and Sir Henry Thompson, have entries in the *Oxford Dictionary of National Biography.*

* Indicates a Fellow or Foreign Member of the Royal Society, for whom an *Obituary Notice* or *Biographical Memoir* has been published by the Royal Society, accessible via https://royalsociety.org/journals/

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Physiology across borders

A roundtable with your regional societies

IUPS

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FEPS

Bayram Yilmaz
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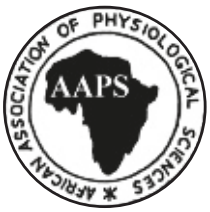

AAPS

Olusoga Sofola
President

Our national societies work to protect and promote physiology not only at home but also abroad, with many societies hosting or supporting travel to international conferences. However, none better personify the need to encourage increased collaboration than the international bodies that organize and coordinate activities between national societies. In recognition of the growing importance of these organisations, the *Physiology News* editorial board conducted an interview roundtable to capture their views on the current geopolitical landscape and the future of international collaboration.

Can you give us an update on the current state of physiology and its future as an academic discipline, in your region?

International Union of Physiological Sciences (IUPS): The current state of physiology is bright because it is returning to the limelight after falling off the centre stage of contemporary medicine over the last 30 years. As the academic discipline that studies the properties and functions of cells, tissues, organs and organ systems within all living organisms, IUPS (**iups.org/**) is optimistic on the future of physiology. In particular, this is an opportune time when physiology now embraces knowledge gained from genomics, molecular/cellular biology, and other disciplines to become an integrative discourse towards understanding the human life process under normal and disease conditions.

Federation of European Physiological Societies (FEPS): Physiology is alive and well in Europe! European physiologists continue to push scientific boundaries, while promoting scientific dissemination and education. Our physiologists remain highly respected both within the physiology field as a whole and within their sub-disciplines. Collaboration between European physiologists is more extensive than ever before, and made possible by several European platforms designed to foster this interchange of ideas and expertise. FEPS is one of these, which, through organisation of its annual meetings, allows scientific exchange in a broadly themed yet expert scientific environment. European agencies such as the European Research Council also continue to do a great service to European physiology by supporting large, collaborative projects spanning multiple nations, and allowing for exchange of students between groups. With the ongoing support of these agencies and European physiologists themselves, we look forward to continued excellence and relevance of European physiology in the coming years.

Federation of Asian and Oceanian Physiological Societies (FAOPS): Federation of Asian and Oceanian Physiological Societies (FAOPS) was officially formed in New Delhi in 1990 as a group representing physiological societies from 12 countries within the Asia and Oceania region. It included physiology societies from Australia, China,

‘Despite the mountains of genetic and molecular data, the ultimate existence of humankind roots in its functional expression that we call physiology’

India, Iran, Israel, Japan, Korea, Malaysia, New Zealand, Taiwan and Thailand, representing about 5,000-6,000 physiologists in the region. The Federation was later joined by Pakistan Physiology Society and more recently by Physiology and Biochemistry Subsection of Myanmar Medical Association and the Physiological Society of Sri Lanka. The Physiology Society of Nepal and the Physiology Society of Uzbekistan and the Physiology Group, United Arab Emirates are associate members. The main purpose of the Federation is to encourage the development and advancement of physiological sciences in the Asia and Oceanian region.

In terms of teaching, physiology is still taught as a distinct basic science subject or course (programme) at both undergraduate and postgraduate level in some of the institutes in the region. Yet in other institutes in the region it is mainly taught as a preclinical subject in integrated problem-based or case-based medical curricula with little distinction between physiology, biochemistry or molecular biology. It is also taught as a subject in pharmacy and other health-related sciences. At some other institutes it has been integrated with biotechnology to boost research between physiologists and biotechnologists. In other institutes, attempts are being made to integrate physiology with mathematics, engineering, information, social science, computation, and artificial intelligence. In general, the demarcation that existed between physiology and other disciplines in the past is gradually fading in some of the member countries. The departments of physiology that stood by themselves in the past are now gradually giving way to the cluster-based organisation in some institutes, housing most of the basic science disciplines. This is blurring further the boundaries between physiologists and non-physiologists.

Research in physiology is increasing in the region, albeit somewhat uneven and limited by budgetary constraints. There is more research in physiology in the developed member countries but somewhat less in the developing countries. But as the lesser economies grow and develop, and with the rapidly expanding economic activity in the Asian region, it is hoped that research in physiology will also grow alongside the economic development. FAOPS Congresses that are held every four years provide a platform for participants from member countries to meet and share their expertise and increase collaboration. In addition, a number of member societies have their own journals that are widely indexed, publishing state-of-the-art research.

Pan-American Congress of Physiological Sciences (PANAM): Physiology is growing up in the region of the Western Hemisphere. There are several universities in the continent where Physiology is one of the specialities studied by physicians. Also, in non-medical universities and in different careers, physiology is one of the disciplines that enhances their profile.

African Association of Physiological Sciences (AAPS): Physiology as a discipline in the African Continent has literally been in a state of flux. The African Association of Physiological Sciences (AAPS), from humble beginnings in 1989 to the present, has literally been hobbling. At the moment there are really four active members of the AAPS, i.e. Egypt, Nigeria, South Africa and Sudan, with occasional appearances of Morocco, Kenya, Ethiopia, Uganda and Zimbabwe at our meetings. However this observation does not detract from the fact that the teaching of physiology is actively promoted in about 120 medical schools in over 30 African nations. Physiology has always been a very popular subject and continues to be a very attractive subject in Africa.

What is your organisation’s biggest accomplishment, and the greatest challenge it faces?

IUPS: Accomplishments – 1) IUPS releases the landmark Board of General Assembly (BGA) Report, in collaboration with The Physiological Society, on ‘Physiology: Current Trends and Future Challenges’ (**iups.org/media/other_reports/Physiology--Current_Trends_and_Future_Challanges.pdf**) at the 2017 Congress in Rio de Janeiro. This report assesses the global strength of physiology as a discipline, highlights the similarities and differences within the international community of physiologists, and points out the challenges the global physiological community faces. 2) The quadrennial IUPS Congresses and scientific meetings organised by IUPS and its member societies provide wonderful opportunities for global physiologists to share cutting-edge knowledge and for networking with their peers. 3) IUPS is currently pursuing the mission to ‘return physiology to centre stage’. Despite the mountains of genetic and molecular data, the ultimate existence of humankind roots in its functional expression that we call physiology.

Challenges – 1) IUPS must continue to spearhead recognition of physiology as a key academic discipline in medicine. 2) IUPS must also advocate the importance of physiology to the funding agencies by emphasising the importance of functional implications of genetic manipulations or biochemical processes. 3) IUPS must make a relentless effort to attract young investigators to take up research in physiological sciences. 4) Finally, IUPS must make physiology a ‘brand name’ in contemporary medicine.

FEPS: FEPS has succeeded in bringing the vast majority of European physiology societies (34 in total) together under a single umbrella. No small task! Through our annual meetings, we have promoted an opportunity for members of these distinct societies to come together both scientifically and socially. We are proud to have celebrated our silver anniversary at the FEPS Paris meeting in 2016!

In the last two decades, physiology meetings have been challenged by evolving sub-disciplinary and thematic meetings. Every sub-discipline within physiology has of course witnessed impressive specialisation during this time. Indeed, the days are past when a trained physiologist could walk into a lecture in any field of physiology and understand the content. This makes the role of organisations like FEPS and physiology as a whole more important than ever! How else can we integrate findings from these disparate sub-studies? We must strive to keep scientists mindful of the benefits of a broad-minded and interdisciplinary scientific environment.

FAOPS: FAOPS holds its scientific congress every four years together with numerous pre- and post-congress workshops on laboratory techniques and in physiology education for participants from member countries. Workshops on research techniques have also been held in-between the Congresses. A small amount of financial subsidy is usually provided by FAOPS to the host Society organising the Congress, some of which is used to subsidise the travel and registration of young investigators from within the region and of members from the smaller physiology societies.

Since its inception it has held eight Congresses in the various member countries. Leaders in research in physiology from all over the world are invited to speak at these Congresses. Over the years, FAOPS has provided a good avenue to increase communications between physiologists in the member countries.

The member societies, or local institutes, of course, continue to have their own national-level activities promoting physiology in one way or another. For example, the International Medical Schools Physiology Quiz, a FAOPS independent activity, that was initiated by the Department of Physiology, Universiti Malaya, Malaysia, more than two decades ago has helped significantly in promoting interest in physiology in the region, if not the world. Such quizzes are now being held in a number of FAOPS member countries, and it is hoped that this activity will expand to more countries in the world.

Funding remains the biggest challenge for FAOPS as its current source of funding is mainly the contributions from member societies, which is based on their individual society's membership strength.

PANAM: The Second Pan-American Congress of Physiological Sciences is the greatest challenge. The II Panam is organised by several national societies from the continent. Our slogan is 'Physiology without borders' like in the first PANAM. You can find more information at **panam2019.com**.

AAPS: To our credit, we hold International congresses triennially with the last one in Lagos, Nigeria, in September 2016, following on the one in Cairo in 2013. African physiologists are recognised for their teaching quality but this has not been matched by our research output, which is meager and represents a big challenge. Recently, the International Union of Physiological Sciences (IUPS) during the presidency of Denis Noble, initiated the concept of 'Trading Post' that was designed for donation of or requisition for available but useful and needed equipment to laboratories, particularly in Africa. This is available on the IUPS website and should be actively patronised by our friendly donors.

At the last IUPS Congress in Rio de Janeiro, Brazil, in August 2017, there was a fairly large African contingent and there were discussions on the future direction of the African Physiology as well as the need to bridge the divide between the Anglophone and Francophone members. Thus it was decided to hold a meeting around Central Africa, in order to attract more countries, and based on this, AAPS decided to have its next Education Workshop in Kigali, Rwanda. This has been slated for 2–4 December 2018, and we are looking forward to this. However, the greatest challenge is funding especially to support the attendance of junior faculty.

Tell us about your most exciting upcoming project and the role your organisation plays in international collaboration

IUPS: 1) Increase the visibility of IUPS in the global biomedical community: Nominate 'physiology ambassadors' as IUPS representatives to deliver lectures in major basic and clinical biomedical meetings. 2) Outreach to fellow physiologists and young investigators: upgrade the IUPS website, establish social media, organise 'young physiologist forum'. 3) Interactions with other biomedical unions: sponsor IUPS Named Lectures or symposia in major meetings organised by other biomedical unions, or invite them to organise symposia in conferences organised by IUPS and regional federations. 4) Mentor-Mentee programme: this new initiative will bring together potential mentors and mentees at various career stages, and in both academic and clinical settings, to promote dialogues and aid career development. IUPS is in the best position to identify potential experts to serve as mentors in this program, particularly across national boundaries. 4) Physiology Education Workshop: IUPS Initiative: two Workshops have been planned for 2018: one in India in November organised by three local institutes in collaboration with the IUPS Education Committee; and another one in Rwanda in December organised by the African Association of Physiological Sciences.

FEPS: FEPS has played a significant role in the organisation and promotion of the Europhysiology project that was agreed upon in September 2015. It is hoped that this exciting initiative will attract the participation of large numbers of physiologists from across Europe, and thus enable organisers to hold specific sessions and thematic symposia to represent all aspects of physiology. The first meeting of the Europhysiology series will be organised in London in mid-September 2018, the second in Berlin in 2020, and the third in Copenhagen in 2022.

FAOPS: The next upcoming event is the 9th FAOPS Congress that will be held from 28 to 31 March 2019 in Kobe, Japan. It is hosted by the Physiological Society of Japan. In addition to the Congress pre- and post-congress workshops and internships will be organised. Participants at the congress will include eminent speakers for plenary and special lectures from all over the world. Plans are also underway to celebrate the 30th anniversary of FAOPS in Kobe. The 10th FAOPS Congress will be hosted by the Iranian Physiological Society in 2023.

PANAM: The upcoming project is the II PANAM and all the Societies play a key role in the success of this meeting. The organisations that take part in the PANAM are involved in a strong international collaboration.

Has international scientific collaboration increased or diminished across your region? How has this changed in the last decade or so?

IUPS: International scientific collaboration in biomedicine, across different disciplines and between basic-clinical-industrial entities, has increased significantly during the past decade. We now witness more published research outcomes from collaborative work by multi-national research groups with complementary research expertise. With the realisation that the primary goal of biomedical research is to provide the best solutions to unmet global human health issues, we anticipate that this trend of international collaboration will be sustained.

FEPS: FEPS has made a significant impact and contributed to international scientific collaboration in Europe. During the last decade, international scientific collaborations within Europe have become even more dynamic. Indeed, as the sub-fields of physiology have become ever more specialised, so too has the need to recruit collaborative assistance from other groups with distinct expertise. Very often such groups are not found locally or even nationally, making international collaboration essential. Young European scientists are particularly eager to travel and study in other countries, and this exchange makes for exciting, youthful, and international environments in the vast majority of successful European laboratories.

FAOPS: Formation of FAOPS has certainly increased the links between physiologists across the region. The Congresses have provided a good avenue for physiologists from within the Asia–Oceania region to meet. In addition, the involvement of speakers and senior invitees from Europe and America during these congresses provides for increased communications between physiologists in the Asia-Oceania region and those from Europe and America. Considerable collaboration exists between neuroscientists in the Asia–Oceania region and those in Europe and America, aided in part through FAONS and IBRO. Besides this, some of the FAOPS office bearers over the years have also held important positions in IUPS and other smaller regional organisations, like FAONS and South Asian Association of Physiologists.

PANAM: Because there isn't a Pan-American organisation, all the societies from the continent have to work together to organise the PANAM in Havana.

AAPS: African physiologists because of their colonial past, especially from Britain and France, have had some collaboration over the years with universities in these countries. Many of the older and upper middle age colleagues did cut their research teeth in our 'parent' countries especially in the 1970s and 1980s. The majority retained their contacts and were able to send out graduate students abroad, for some bench work. The same phenomenon is also occurring with universities in the United States. The advantages are the exposure to good research but, unfortunately, with little equipment to follow up with on return home. Thus, there will be the need to enhance more of these collaborations as well as stimulate increase in patronage of the IUPS Trading Post.

Recently, we have had some interesting initiatives from the American Physiological Society (APS) and ADInstruments. APS is in discussion with AAPS on how to get more Africans to attend Experimental Biology (EB) meetings, and hopefully this initiative will come to fruition soon. ADInstruments has made some funding available for sponsoring graduate students to visit other labs in Africa for their bench work. This is reminiscent of The Physiological Society initiative in 1993–1994 that gave grants for consumables and support for a graduate student to visit a UK Lab. We hope that more such avenues for support will reemerge. However, The Physiological Society and APS (EB) still provide some support for Africans with accepted abstracts to attend their conferences and hopefully the upsurge in attendance at these conferences will continue.

The AAPS is quite optimistic that with increased collaboration as well as improvement in funding and facilities, physiology in Africa will move to greater heights. We also need support for our meetings as well as for attendance at the big meetings in Europe and America, and maybe in China in the nearest future.

How do you navigate the cultural, political and economic differences between countries in your region?

FAOPS: The Asia–Oceania region has a huge cultural diversity, but most in the region speak the English language. The medium of communication at all FAOPS Congresses and workshops is in the English language. With the congresses moving from country to country within the region there exists a great opportunity to mix and learn about the cultural practices of the member countries. In addition, FAOPS congresses are open to participants from all parts of the world without gender, political or religious bias or prejudice. Social events are often held at the Congress dinners show-casing the culture and practices of the host country.

FEPS: At the end of the day, scientists speak the same language no matter their background. In our experience, any such differences are easily overcome and misunderstandings are rare. In fact, differences in background are celebrated! One needs only to watch the exchange of food between international students in the cafeteria to feel inspired. While there exist some economic differences between countries in Europe, organisations such as FEPS are designed to give special promotion to those whom may need extra assistance. We aim to include everyone.

Pan-American Congress of Physiological Sciences: In spite of the political and economic differences among the participant countries, working together on PANAM will be no problem at all. The Latin American countries have many cultural identities among them but, on the other hand, a common language and history. All of them have close contact with the North countries as well.

AAPS: The African continent is a heterogeneous mix of languages, culture and political diversity, ranging from the Arab North to sub-Saharan Africa, with English, French, Portuguese and Belgian former colonial masters. This diversity has been a challenge in forging a close identity among the scientific community, including physiologists. As for the political landscape, Africa has been a disappointment in terms of democratic norms. Sadly, after over 50 years of independence, there have not been any encouraging signs with most countries labouring under a perpetual one-man rule. These political scenarios combined with economic malfeasance have impacted negatively on societal and intellectual development as well as contributing to underfunding of research, hence resulting in the loss of talent or Brain Drain from Africa. However, the Republic of South Africa still has some semblance of quality research as evidenced by the positions of some of their institutions in the World University Rankings.

Extreme Environmental Physiology: Life at the Limits

Explore how our physiology allows us to visit other worlds, climb the highest mountains and swim in Arctic waters

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The Physiological Society

Extreme Physiology: Life at the Limits
2-4 September 2019
Portland Building, University of Portsmouth

Introducing our new Trustees

Council is delighted to welcome three new Trustees who will take office on 16 September at the AGM. Read about their research, and what inspired them to pursue careers as physiologists, or become involved in The Society.

Raheela Khan

University of Nottingham

What has been/was your most important scientific finding, or your most surprising finding?

As a postdoc in Cambridge, I was seeking to understand the molecular physiology of human pregnancy, specifically the triggers for transforming the uterus to an excitable state to enable delivery. The most surprising discovery was of a change in calcium-sensitivity of a large-conductance potassium channel. This channel is highly expressed in most types of smooth muscle and responds to acute increases in intracellular calcium levels. Our observation identifying a switch in calcium-sensing in uterine muscle came about at the time others reported the discovery of beta-subunits as modulators of this channel. The research direction of my lab is still very much in the realm of membrane physiology as my fascination with ion channels continues, focusing on links with inflammation.

What is your favourite aspect of your research/teaching/outreach work/ anything else in your work?

At the University of Nottingham, I teach undergraduate reproductive physiology to students on the BSc (Hons) Medical Physiology and Therapeutics, and Graduate Entry Medicine. I consider my role to be one of enthusing young scientists and sharing with them the underpinnings of physiology. My teaching is very much informed by research, and I try to encourage students to learn to value research. The Society's Summer Studentships are a great way for students to experience working in a lab and gain some insight into what a research career entails.

Equally vital is taking our message, on the benefits of research and participating in it, to patients and public. I have been fortunate enough to work on patient-centred research for most of my academic career. Through outreach activities, we have been able to share our research findings directly with patients. Working at this interface, discussing novel solutions for improving healthcare, is just one of the highlights of a research career.

Why did you become a physiologist? What drew you to this field?

I became a physiologist due to the intrigue of biology. As a child, one of my earliest memories is the wonder of observing the detailed, ordered structure within a piece of fruit. My work has spanned from understanding the neuromuscular junction of the cockroach during my PhD, to taking great steps in understanding the genomic regulation of function, for molecules thought to be 'junk'. Throughout the years, the sheer joy and diversity of seeing physiology in action continues to excite me.

If you were going to be marooned on a Desert Island, what luxury would you like to take with you and why?

It would have to be an iPad or mobile phone. I'm assuming I'd have 4G to keep me connected to the world of politics and science, preferably via Twitter.

David Paterson

University of Oxford

What has been/was your most important scientific finding, or your most surprising finding?

I guess this will be for others to judge. But I am most excited by our recent work that is concerned with understanding the molecular mechanisms of abnormal autonomic neurotransmission in cardiovascular disease. We have recently identified key transcripts (RNAseq) that have been validated against human neural tissue (qPCR). In studies using isolated neurons and cardiac neuronal co-cultures, we have found a key role for cyclic nucleotide-coupled calcium dysregulation of exocytosis in disease using a combination of FRET/Ca imaging, patch clamp, neurochemistry and viral vector gene transfer to drive phenotypes. The foundations of this work were developed by several talented doctoral students in the late 1990s where we were one of the first groups in the world to successfully gene transfer nitric oxide synthases (NOS) into cardiac autonomic neurones and change the release of the classical transmitters.

What is your favourite aspect of your research/teaching/outreach work/ anything else in your work?

Meeting interesting people in science and other walks of life. Being Editor-in-Chief of *Experimental Physiology* and then *The Journal of Physiology* exposed me to a lot of world-wide physiology. It is always exciting performing on this stage. Scientists are a bit like failed rock stars. They compose their single (paper), and then head out on tour to promote the work to gain applause (certainly not money). Then they return home and start another composition. Indeed, there are few jobs in the world where you can essentially decide what you want to do, how you wish to do it, and who you wish to work with. Academic freedom is such a civilised concept and is critical for discovery. Sometimes your work takes you into arenas that challenge you in different ways, e.g. when having to explain what you do to the public. I certainly found this out when we contributed in 2012 to the BBC4 documentary 'Of Hearts and Minds: What makes us Human'. The response I got from random people was really interesting (from mystics to philosophers).

Why did you become a physiologist? What drew you to this field?

By accident, really. I was an okay athlete at school and university and a pretty unremarkable undergraduate given outside interests. But I remember taking a course in

anatomy at the medical school in Otago and being exposed to physiology, which I thought was really interesting. So I got the bug then and somehow ended up in Oxford in the mid 1980s on a scholarship via Western Australia, and the rest is history. In those days I used to love mountains and was inspired by Sir Edmund Hillary and others, so the control of breathing I found fascinating, and still do.

My generation transitioned from analogue to digital so in many ways we got the benefit of the new with an appreciation of the old (fountain pens, typewriters, Letraset, early word processors). It was okay in the 1980s to go into the workshop and lathe away your porous plugs as we made ion-sensitive intravascular electrodes. Students don't seem to undertake the making of instrumentation anymore, but instead they have such advanced tech skills in computing which really highlights their digital base.

In many ways, physiology has been in a hole for several decades as molecular biology and genetics has been centre stage. We physiologists have had to learn to operate in a more reductive experimental environment and learn a new biological language. Today physiology has never been so critical as we reassemble complex biological processes from several spatial domains (molecular, cellular, tissue, organ) into *in vivo* systems. From my perspective, physiology is certainly the bridge to translation.

Who inspired or what inspired you to follow this career path?

I was fortunate to meet John Coote (fellow adventurer) in a bar in Kathmandu in 1984 (he had just been appointed Bowman Professor at Birmingham), and he kindly invited me to visit and stay with him and his family. John convinced me that Oxford would be a great choice given all the eminent respiratory physiologists there.

It was a thrill being accepted into New College where JS Haldane and JBS Haldane had been, and meeting Dan Cunningham and Bob Torrance. Dan introduced me to Roger Bannister so this sparked my interest in autonomic neuroscience. I also had a wonderful experience as a student in Oxford working on chemoreceptors with Piers Nye, and in human physiology with Ebbe Petersen and Dan Cunningham, and then Peter Robbins. Being exposed to the living history of physiology was formative. So meeting John Eccles, James Watson, Hermann Rahn, David H Hubel, Joseph Barcroft, Carlos Monge and others was certainly a thrill.

Sadly, I never met WB Cannon and Wallace Fenn, superheroes of mine in physiology as they had such insight. I was also fortunate to meet John West and spend time in his lab at UCSD as a postdoc. The Californian way of life was very agreeable.

What excites you about your work?

Watching young, talented students grow and flourish into outstanding young scientists and doctors, and growing the next generation. I still teach, and having the opportunity to update (with Neil Herring) Rod Levick's textbook, *Introduction to Cardiovascular Physiology*, gave me a real appreciation of the time it takes to give back in the form of writing a textbook. I have a great admiration for those people who have undertaken that journey.

Do you have a project or accomplishment that you consider to be the most significant in your career?

We all have our favourite papers, but I like to think I am best defined by my pupils over the past 30 years who have been absolutely terrific in the lab. Many have gone on to have stunning careers in medicine and science.

If you were going to be marooned on a Desert Island, what luxury would you like to take with you?

The Journal of Physiology from vol. 1 to date with an unlimited supply of Domain Road Pinot Noir 2006 from Central Otago, NZ, and a good hammock!

Matt Taylor

Generation Investment Management

Where do you work?

I work for a sustainable investment firm, Generation Investment Management. In our growth equity fund we support companies, through capital and our engagement, which are commercial but also helping tackle climate change and delivering positive social outcomes. These companies might be in mobility, like electric vehicles, the food system space, in energy, or consumer-facing brands.

What is your role at Generation?

I lead the support we give to companies on strategy, talent and governance, and commercial connections. That means that across our portfolio of investments, I help the management teams think about longer-term planning, and how they can improve both their financial performance and the social and environmental impact they are having. I also help share best practice on tracking and assessing that impact.

What was your academic background?

I studied Human Sciences, which combined elements of Genetics, Animal Behaviour, Physiology and Anthropology, followed by a Masters in Medical Anthropology. Much of my studies brought me into the same lecture halls as the physiologists, although my focus was on the broader development of health interventions in different country and cultural settings.

What attracted you to The Physiological Society?

I've always been keen to re-engage with academia in a subject that had been part of my multidisciplinary background. I think the work The Society does to advance physiology through nurturing the development and expertise of the membership, and the broader community, is critical and only going to become more important. Whilst there's an incredible history for The Society to be proud of, now also feels like a time when scientific study may see a range of disruptive factors, some for the good, and some not. I'm very excited to be a small part in helping The Society respond to some of those changes, to evolve to meet them, and continue to develop.

What do you do when you aren't working?

I spend time with my wife and two sons, and we all try and get as involved in sports and the outdoors as we can. I also spend time with a couple of other charities, specifically one focused on access to sanitation in the developing world, and another that focuses on conservation in the UK.

If you were marooned on a Desert Island, what luxury would like to take with you?

I'm not sure it counts as a luxury, but I'd feel a bit lost without my running shoes, so likely those and a decent supply of Kit Kats.

Making outreach relevant: sharing physiology in a small town in Nepal

Rajan Pandit

Nepal Medical College, Nepal

Attentive students and school principal at Shree Nabin Gram Shiksha Secondary School.

To address health awareness and potentiate an interest in physiology among school teachers and students, interactive outreach activities are instrumental. We strongly believe in teaching school teachers, linking physiology knowledge to real-life applications, and establishing good rapport between schools, youth organisations and medical college laboratories. This aims to widen participation and also to open the door to physiology-related study and career options among school students. Moreover, the interaction between the general public, especially those who are traditionally hard to reach, and researchers is imperative to establish a symbiotic relationship: the physiologists share their stories, passions and expertise in innovative ways, and the public can acquire life-changing health tips and knowledge from physiologists.

Nepal, one of the lesser developed countries of the world, is home to surreal geographical beauties. However, due to political upheaval and its challenging geographical location, most of the Nepalese are forced to live in an improvised condition. With generous support from The Physiological Society, we, five team members including school representative Mahesh Pd Timilsina, embarked with utmost zeal on our journey to the school on 27 April 2018. The school, Shree Nabin Gram Shiksha Secondary School, Naglebhare, is about 24 km north-east from central Kathmandu, located around 1,700 m above sea level.

‘Despite having travelled through muddy, bumpy narrow roads, we were uplifted by a warm welcome by the school authorities. The grade 9 and 10 students greeted us with curious eyes, seeing the bizarre instruments we brought with us’

Despite having travelled through muddy, bumpy narrow roads, we were uplifted by a warm welcome by the school authorities. Thee grade 9 and 10 students greeted us with curious eyes, seeing the bizarre instruments we brought with us.

We tailored the discussion around topics relevant to students, and had an interactive component where they had a chance to listen to their own heart sounds and breathing.

Firstly, we asked about their blood type, and most of the students were shy and hesitated to answer. Most of them did not know the answer. Students and even the principal were not aware of how to determine blood type. We demonstrated how to determine blood groups using antisera (A, B and D). Everyone was surprised to see the results.

When we asked them about doing blood transfusion without checking the blood, they knew this was a bad idea. The reason for their objection was the chances of transmission of diseases like AIDS and hepatitis. None of them mentioned blood grouping and cross-matching. We were happy and excited to know they at least had some knowledge on blood transfusion. We filled in the gaps in their knowledge with a brief discussion on the complications associated with mismatched transfusion.

Most of the students’ parents were farmers. Working in the field all day, they often have fainting spells, or syncope, and they do not know how to manage these. We demonstrated how to manage fainting in order to protect against head injury

Following these discussions, we showed the students how to listen to bronchial sounds, heart sounds and the sound of blood flowing (korotkoff). Students were elated to hear those sounds as it was the first time for them.

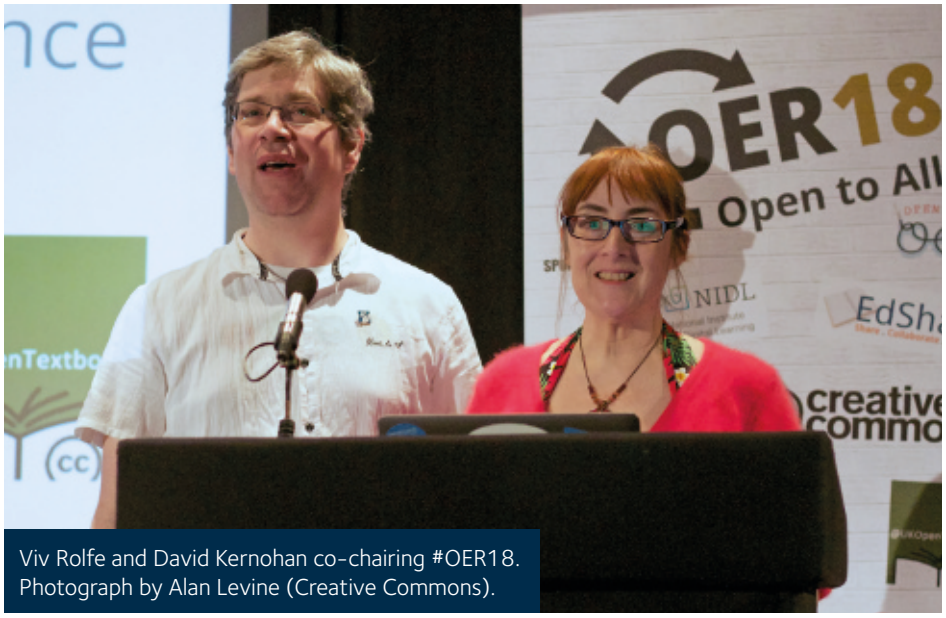
In the few hours we spent teaching the students, and discussing with them, we hope to have stimulated their interest in physiology. It also taught us how to deliver complex ideas using simpler words. The experience was surreal for us.

Our team decided to continue this programme and we hope to get generous support from The Physiological Society in the days to come.

A global career from the comfort of your own home

Vivien Rolfe

Head of Research, Pukka Herbs



Viv Rolfe and David Kernohan co-chairing #OER18. Photograph by Alan Levine (Creative Commons).

Thirty years ago I embarked on a degree in Physiology at the University of Sheffield, and I would never have believed that I would still be pursuing my passion for gut physiology all these years on. It has not been an easy journey and has required determination and reinvention. A common element from the start was my global outlook, particularly in my PhD where I explored the secretory mechanisms of *Escherichia coli* STa. I remember at the time being interested in the global epidemiological, social and political contexts as to why the bug caused diarrhoeal disease and was such a major killer, particularly of children. I have not spent time abroad as part of my career, but global connections and collaborations have always been central to my work.

After Sheffield I became a research fellow at the Institute of Child Health in London looking at fish oil for children with inflammatory bowel disease. Dame fortune and postdoc funding were not on my side, so in 1997 I took a permanent role with multinational Mars Incorporated heading up gut research for their Pedigree Petfoods division. I'm convinced my global perspectives and wide subject interest, including host-bacterial interactions and functional foods, made a good case for translating my knowledge of human gut health to that of dogs and cats. It was an international role working with global marketing, and research and development teams. It was fascinating to get a sense of global nutrition trends, for example the keenness for probiotics and pet care snacks in Asia, and markets focusing on wholesome food for their beloved pets – 'big baby' was one of the market segments – in Europe.

I then got the urge to teach and joined the University of Nottingham and subsequently spent 15 years in higher education. Strategically, we often talk of the importance of science mobility via international exchange, but I experienced how immobile I was through my transition from industry into academia. I had no publication track record, my product development and patent record were not obviously reusable, and my people and project management experience (managing budgets of up to £1 million and a team of over 30 at one point) was not understood, and I was given a position with no leadership.

I moved out of scientific research and over a number of years built a new career in science open education, leading national and international projects to create open educational resources and raise awareness of open textbooks. Through the use of social media I built new relationships that led to collaborative working – co-authoring papers, co-presenting at conferences, and participating in externally funded projects. These international links provided opportunities – for example, some of our open educational resources have been translated for use in Nigeria and Latin America. I gained a deeper awareness of socio-political issues, and global inequalities in education and research that then started to influence my own work

Physiology Graduates of 1990.

Years on, I did not envisage moving back into a full-time research role. This was a personal decision this time as I felt my values no longer aligned with the UK higher education system; the political changes were emphasising league tables over learners, and universities had become a commodity and less of a social good. How overjoyed I am to be in a new company that places global sustainability and wellbeing at its heart, where I can pick up my physiology interests and contacts, and develop new international ones. My role as Head of Research at Pukka Herbs now requires me to learn about all areas of physiology, although I'm pleased to see how current research is placing a huge importance on the gut and microbiome in human health.

As a scientist today I believe there is a huge need to understand global perspectives in order to deal with health challenges and to develop sustainable approaches to working; in this we have to learn from other regions and act as part of a responsible global community. There is much work to be done to open doors to knowledge and to create a more equitable science education and research community to address these questions.

Expanding inter-institutional opportunites for Masters research students

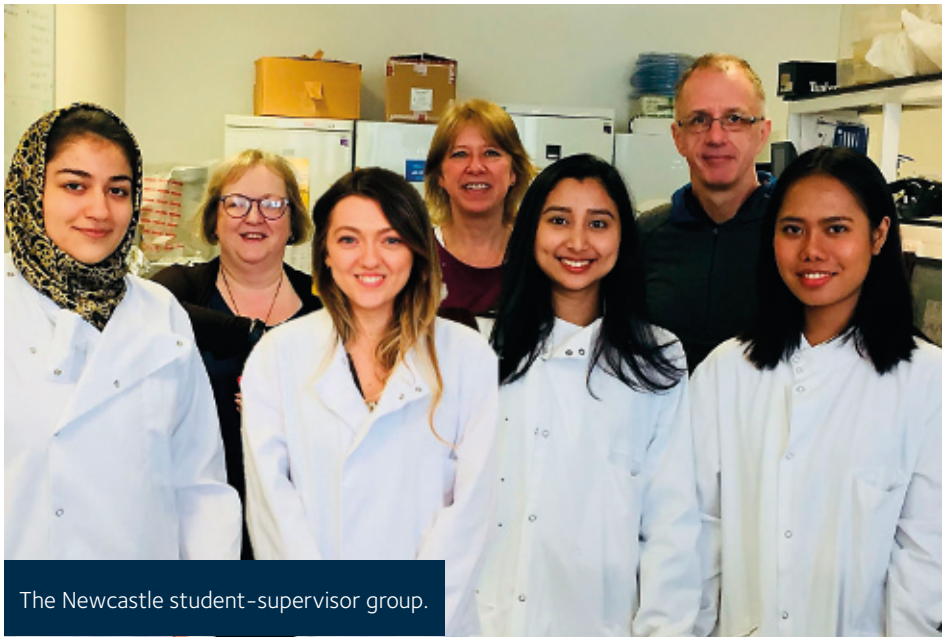
Michael Taggart

Newcastle University, UK

Tim Curtis

Queen's University Belfast, UK

In this article, Michael Taggart and Tim Curtis (previously co-Theme Leads for Vascular and Smooth Muscle) comment on the rise of Masters research programmes and the challenges this places on universities to provide courses suitable for the future careers of students. Fostering inter-institutional arrangements may therefore present opportunities to grow the physiology discipline.



The Newcastle student-supervisor group.

In the last decade or so there has been a notable change in the postgraduate research student landscape. Universities have increased not only the number but also the breadth of Masters degrees offered. This extends to incorporating lengthy research components and examinations by assessment of a substantive thesis/dissertation – typically as MRes (Masters by research) or MSc (Master of Science) programmes.

Numerous life science graduates are attracted to Masters degree programmes where the research project component is often 4–6 months in duration and individualised to each student. For many students enthused by their undergraduate final year research projects, this option helps them reach a better-informed decision about future steps. Also, in the competitive post-graduate training/career market, the acquisition of extra research training and skills may be beneficial to their next moves. The 1+3 years model of Masters/PhD training organised by many funding bodies including the MRC, BBSRC, Wellcome Trust and BHF recognises this to be so. Medical students too are choosing to intercalate in Masters degree programmes to increase their breadth of training relevant to clinical academic pathways.

There are evolving challenges, however, to the delivery of research-intensive Masters programmes. A principal one is that the trajectory of biomedical research is increasingly multidisciplinary. This raises the query: how can we best support student research training needs in this fluid setting? This question spurred the establishment of a pilot link-up between the Cardiovascular Research Centre (CVRC) and Institute of Genetic Medicine (IGM) at Newcastle University and the Centre for Experimental Medicine (CEM) at Queen's University Belfast (QUB)[1-3]. This academic year, four Newcastle students – studying for a MRes in Cardiovascular Science in Health and Disease[4] or MRes in Stem Cells and Regenerative Medicine[5] – undertook research projects with co-supervision by staff at QUB (Table 1). The students spent one week immersed in the CEM laboratories to get first-hand experience of the approaches used by the partner supervisors. Funds supporting the exchange were provided by IGM and CEM. Moreover, the co-supervision/collaborative arrangement fostered exchange of expertise (e.g. experimental protocols involving advanced electron microscopy and image analysis), materials (e.g. transfer of animal model cells and tissues) and data (e.g. single cell sequencing) between the respective laboratories, thereby adding breadth and substance to the research projects. Student feedback was positive, with suggestions for the exchange visit to be longer or more frequent consistently cropping up! Therefore, we hope to build on this pilot arrangement in future years. This could include: (i) establishing bilateral links whereby QUB-based students studying for an MSc in Experimental Medicine[6] have the opportunity of co-supervision by, and visits to, staff from CVRC/IGM in Newcastle; (ii) the possibility of awarding joint MRes degrees. Of course, these developments would require more secure funding arrangements.

Is there a role for physiology in expanding such inter-institutional opportunities?

There are 32 MRes programmes in Newcastle University – none feature 'physiology' in the title. This is despite the BSc physiology undergraduate degree programme consistently rating highly in national/international surveys[7]. Similarly, physiology forms a a key component of various undergraduate degree programmes at QUB (e.g. medicine, biomedical sciences, pharmacy, dentistry and nursing) but there are no Masters programmes specifically in physiology. Clearly, there are opportunities to (re)emphasise a positive role for physiology through Masters research degrees. Equally, the multi-disciplinary research environment favours the involvement of theoretical and practical contributions from physiology. Many Masters courses emphasise the integration of fundamental science with medicine in taught modules. This requires detailed consideration of the transition from physiology to pathophysiology. The students will appreciate this if we, as instructors, remember to call it so. Fostering inter-institutional arrangements may increase opportunities to grow the physiology discipline.

MRes Student	Research Project	NCL Supervisor	QUB Supervisor
Sarah Sugianto	The role of the Trpv2 channel in cardiac development	Deb Henderson	Tim Curtis
Alyson Macneil	Human cardiomyocyte differentiation from mesenchymal-derived stem cells: transcriptional analysis & proteomics	Annette Meeson	Anna Krasnodembskaya
Sarah Mehdi	Are cardiac mesenchymal stem cells (CMSCLC) capable of differentiating into endothelial cells?	Annette Meeson	David Simpson
Nabilla Kusuma	New perspectives on capillary structure as revealed by 3D electron microscopy	Michael Taggart	Tim Curtis

Table 1. Newcastle University-Queen's University Belfast MRes co-supervision.

How can The Physiological Society contribute to this research training landscape?

Many students wishing to foster research-oriented careers (whether it be for a PhD, industry or NHS-related clinical scientist positions) see a need for more research training and practical experience than is acquired at undergraduate level. It follows that much physiology-relevant research training now occurs during MRes/MSc postgraduate degree research projects. Therefore, it may make strategic sense for The Physiological Society to actively promote and/or engage in this area of student training. We offer the following suggestions for starters:

1. An application round for MRes/MSc research projects to be sponsored by The Physiological Society: PIs could flag physiology-related projects that could be submitted to The Physiological Society for consideration for sponsorship. If deemed within a remit (e.g. for skills training, topic, etc), The Society could, for instance, pick up the consumables tab (usually towards £3k). The student could write a report of the work for The Society at the same time as submitting their thesis for examination. This would have the added strategic value of embedding 'physiology' in the mindset of university administrators of MRes/MSc programmes.

2. Similar to (1) but the Society would sponsor students to carry out research across two institutions. With all the requirements as (1) in terms of physiology relevance, the sponsorship here would be to support student accommodation(s) when visiting the 2nd institution (predicted again to be in the £3k region). This would broaden the reach of physiology-sponsored projects across multiple institutions.

3. The Physiological Society would co-sponsor MRes/MSc research projects with industrial/healthcare partners. This could be in alignment with (1) or (2) whereby the project required access to, and use of, certain resources (hardware, software, drugs, antibodies, etc.) or visiting the outside partner. Students and universities are keen on these types of arrangements (i.e. developing transferable skills for the workplace), and companies would benefit from engaging with current university research activity.

We hope that this commentary encourages a broader debate on the delivery of MRes/MSc research-orientated programmes of study and we look forward to hearing of other experiences and suggestions for the promotion of physiology through these schemes.

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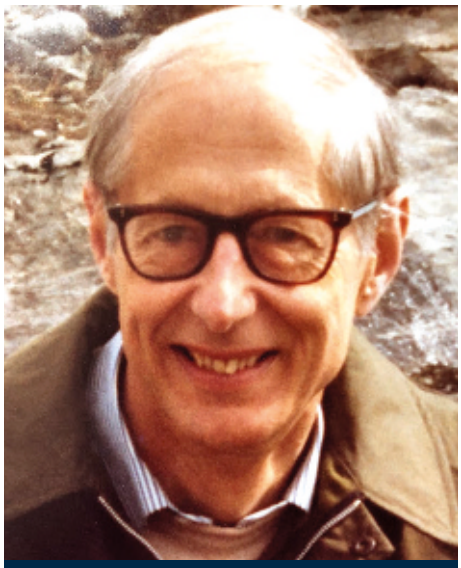
The QUB student-supervisor group.

Obituaries



John Cotes. Photograph kindly provided by Sarah Cotes.

John Cotes 1924–2018

John Cotes, who died in April this year aged 94, was a leader in the fields of respiratory physiology, exercise physiology and occupational lung disease. Cotes was born in Ashtead, Surrey, educated at Leighton Park School, New College, Oxford, and St Bartholomew's Hospital Medical School, London. He then became a respiratory physiologist at the RAF Institute of Aviation Medicine Farnborough in 1949–1951, and from 1952 at the MRC Pneumoconiosis Research Unit (PRU) at Llandough, near Cardiff. With the exception of a year with Richard Riley at Johns Hopkins in 1957, he spent the next 25 years at PRU working on the physiology of occupational lung diseases and on his celebrated book, *Lung Function*. He moved to Newcastle University in 1978 where he continued his work on lung disease in shipyard workers with DJ Chinn and JW Reed. Throughout his long career he focused on human physiology: his work was in the classical tradition of Haldane, Priestley, Douglas and others of the Oxford school of physiology.

In 1952, Cotes was asked by the Royal Geographical Society to consider oxygen equipment for the forthcoming British Everest expedition. It was his first project. Oxygen equipment had a dreadful reputation following its failure on the 1938 expedition to the mountain. Nevertheless, he persuaded the climbers to use close-fitting masks and an open-circuit oxygen system based on the equipment used by the Wartime RAF bomber crews. He modified the masks using additional large–diameter valves to reduce the resistance to breathing and designed a cowl to prevent them from freezing, testing them himself in a wind tunnel at minus 25 degrees and wind speed of 25 mph. These newly designed masks enabled Hillary and Tensing to make the first ascent of Everest. He later adapted this approach in the development of portable oxygen systems for patients with respiratory disease and he was one of the first to demonstrate the benefits of the oxygen concentrator in patients.

Cotes' work on lung carbon monoxide transfer factor has been a major and lasting contribution to what we know of how the lungs work. He developed automatic breathing circuits for administering small doses of carbon monoxide and introduced the term transfer coefficient, pointing out that the earlier term 'diffusing capacity' was inappropriate. His term, CO transfer factor, has been widely accepted by respiratory physiologists. Cotes published extensively on applications of this method in industrial diseases of the lung. His work on the role of haemoglobin and blood flow through the pulmonary capillaries in controlling the uptake of oxygen was a seminal contribution to the field. Cotes continued to work on transfer factor: a letter published in 2001 shows that at the age of 77 he had lost neither his capacity for critical comment nor his ability to suggest new lines of research.

Cotes' textbook *Lung Function* is a single-author work, first published in 1965. The sixth edition (2006) is still in print, and for more than 50 years it has been the leading work in its field. Cotes decided to write his book having read Julius Comroe's book *The Lung* (1955 and 1962). Comroe's was the first textbook of pulmonary physiology but Cotes was convinced that the subject needed a fuller clinical context. His textbook was certainly fuller, extending into pathophysiology and occupational lung diseases. Cotes was fascinated by the effects of disease on lung function and explored this in his book. Those who learnt their respiratory physiology from *Lung Function* never forgot it. Cotes' handling of the methods of testing lung function, of the distribution of ventilation and perfusion, of the subdivisions of dead-space could hardly be bettered. *Lung Function* is a lasting memorial to classical respiratory physiology in its full flowering and his work remains of permanent value.

John Cotes' manner, dress and speech patterns reflected his Oxford education. He was, at least at first sight, a rather formal, perhaps even forbidding, figure: tall, thin, immaculately dressed, precise in his enunciation and quick to detect errors of logic in conversation. His laboratory work was meticulous, emphasising calibration of equipment, and establishing normal values of pulmonary function in widely different groups of individuals. But behind that facade was a very different man. He laughed like a schoolboy when amused, he was endlessly helpful and he was an exceptionally active gardener. He was particularly good with young research workers: encouraging, looking for opportunities to help and generous with ideas, time and advice.

John was happily married twice, first to Patricia who died in 1976 and then to Sarah who cared for him until he died.

Written by Robert Maynard
Honorary Professor, Birmingham University, UK

& Gareth Jones
Formerly Cambridge Clinical School, UK

Christopher Peers

Christopher Peers 1963–2018

Christopher Peers, a leading cellular physiologist studying the carotid body, died on 20 May 2018. Chris had been courageously fighting against a rare form of lymphoma for over four years, maintaining until the very end his personal elegance, high spirits and love for science that were so characteristic of him. Although I always considered myself a long-standing colleague, over the last few years our relationship evolved into a solid friendship. In January 2014, I contacted Chris to invite him to participate in a meeting on hypoxia to be celebrated the following December in the newly created Institute of Biomedicine of Seville, IBiS. As I wanted the fields of carotid body physiology and acute oxygen sensing to be well represented at this meeting, I contacted him. Chris accepted, but in his response warned me that he expected to be undergoing chemotherapy and bone marrow transplantation in the intervening months. During this meeting, in which we had lively discussions about gaseous transmitters and carotid body physiology, I was deeply impressed by Chris' serenity and endurance. That visit to Seville was a milestone in our friendship for, although this was the last time I saw Chris, we kept in frequent email contact. Our exchange of scientific ideas and data was enriched with the sharing of opinions on the human condition and life's vicissitudes.

I first had knowledge of Chris Peers in 1990 when he published several seminal papers, in some cases as a single author, on the inhibition of potassium currents by hypoxia and other chemostimulants in rat carotid body glomus cells. Having obtained a BSc and PhD in Pharmacology at the University of London, Chris was finishing a postdoctoral stay in the Physiological Laboratory at the University of Oxford. This was a period of rapid and very exciting transformation in the field of peripheral chemoreception with the study of single chemoreceptor cells by patch clamp techniques. We along with others were in the early stages of the characterisation of glomus cell electrical properties and the recording of 'oxygen-sensitive' ion channel activity in several species. Chris' work was therefore received very enthusiastically. At 27 he was appointed as a Lecturer in the Department of Pharmacology at Leeds where he remained for his entire academic career. In 2002, he was promoted to Professor of Cellular Physiology and became Head of Division of the Multidisciplinary Cardiovascular Research Centre as well as Director of the Yorkshire Branch of the Alzheimer's Research Trust.

Chris carried out extensive work in related fields, including the characterisation of changes in cell excitability induced by chronic hypoxia and the interaction of several pharmacological agents with ion channels. Later on, he became interested in the pathogenesis of Alzheimer's disease and in this context performed a highly original piece of work on the amyloid peptide-mediated regulation of calcium channels in neurons and astrocytes. In the last decade, Chris was particularly focused on studying the actions of gaseous transmitters (carbon monoxide or hydrogen sulfide) and their role in cell homeostasis, searching for generalised effects of gases as ion channel modulators. As the author of more than 250 scientific publications and a participant at numerous meetings, workshops and lectures, Chris developed a strong reputation. Among other honours, he became an elected member of the Academia Europea and served for several years on the Editorial Board of *The Journal of Physiology*. In Leeds, Chris founded a very active 'school' of cellular physiologists taking under his wing numerous PhD and Master's students as well as postdocs who themselves continued independently in successful scientific careers.

For over two decades, before we became close friends, I met regularly with Chris at scientific workshops and visits to my laboratory in Seville. I was always impressed by the style of Chris' scientific presentations, his honesty, and his ability to defend his scientific opinions in an open and constructive manner. He always showed a profound respect for the person with whom he was debating and yet firmly defended his own position without causing offence.

Chris and I frequently discussed the role played by the ISAC (The International Society for Arterial Chemoreception) and in particular the relatively limited impact that this society was having due to its small size, despite the far-reaching medical implications of the study of hypoxia. To some extent we both shared the view that ISAC should merge with larger societies but so far this has not happened.

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We have lost Chris Peers, but his influence will remain. Accompanied by my grandchildren, I recently watched the animated film Coco, a beautiful story which poetically shows that, although we die, we remain alive as long as our relatives, friends and colleagues remember us. In this respect, Chris Peers will have a long life, as the memories of an outstanding scientist, teacher and companion will be recalled by generations to come.

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