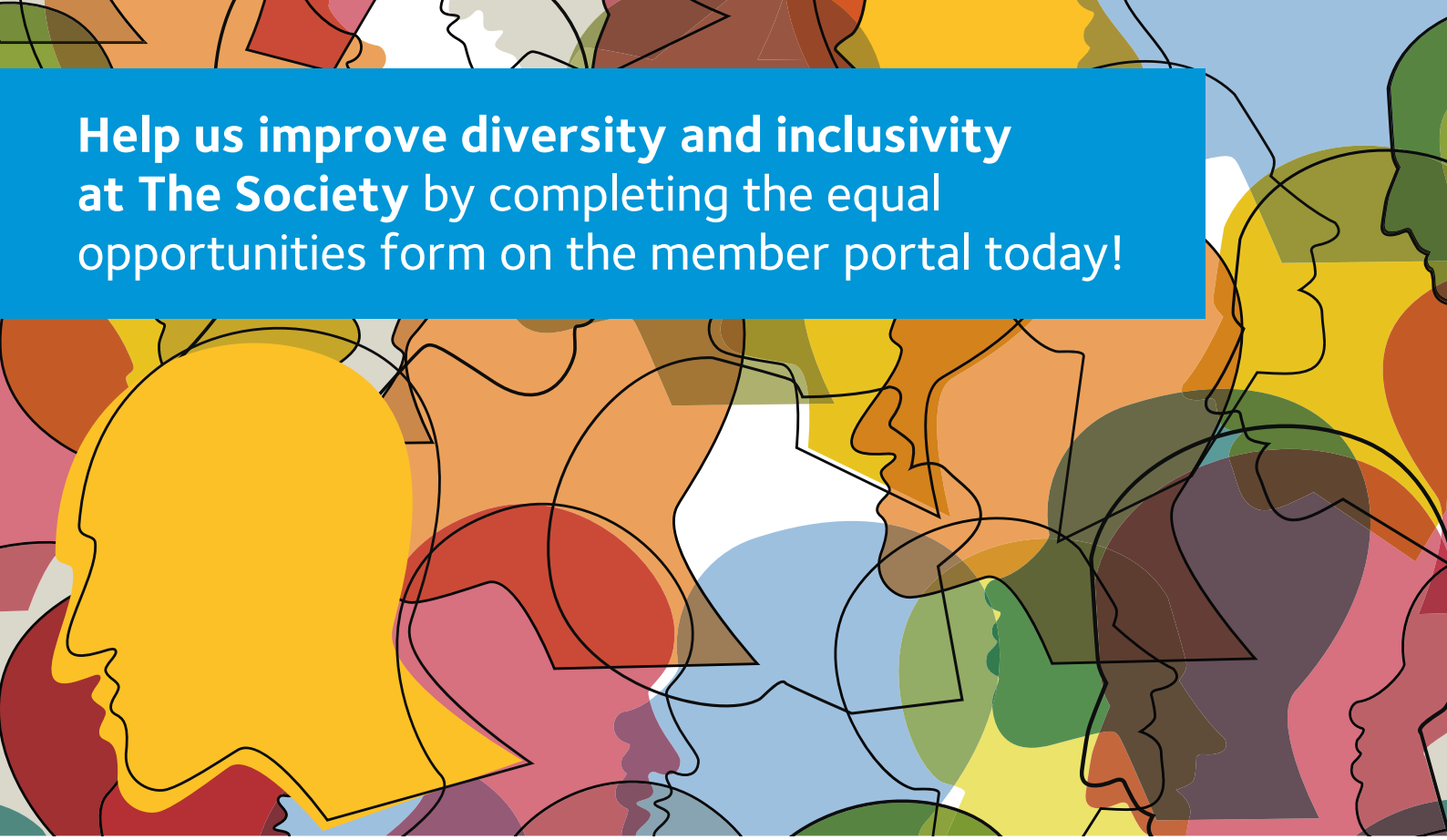
PN
Physiology News

Issue 114 / Spring 2019

My historical dive

The illuminating nature of science history

The Physiological Society



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The Physiological Society

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

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Welcome to the Spring 2019 edition of *Physiology News*

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News and Views

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Cover image: Drawings on front cover, and pages 24 and 26, by Marlon Vasquez. Instagram: @amargoelcanoero

Extreme Environmental Physiology: Life at the Limits

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The Physiological Society

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

The year ahead: Diversity and Space Special Issues

Keith Siew
Scientific Editor

Julia Turan
Managing Editor

2019 is set to be an exciting year for *Physiology News* (*PN*). As part of The Society's new website, *PN* will be also published as an online digital microsite in addition to the popular hardcopy and PDF formats. It is our hope that this additional format will enhance our readers' experience by improving *PN*'s searchability, shareability and accessibility on various device and browsers. In particular, we're excited to announce that a long-term pet project of many editorial board members, both past and present, will finally come to fruition with the completion of a searchable list of past *PN* feature articles and the return of the PDF archive of *PN* past issues.

Last summer, we enthusiastically welcomed both old and new members to the Editorial Board. We hail from around the world and bring together a variety of backgrounds in research, education, industry and clinical practice. Recently, a few of our Editorial Board members have stepped down or taken leave and we wish to extend our thanks for their time and service. We congratulate Fiona Hatch on her new job with Novartis (and recent engagement), Pete Aldiss on his new position at the Institute of Metabolism and Systems Research (University of Birmingham), and Katherine Rogers who is soon to be on maternity leave. If you are interested in science communication, and increasing engagement with physiology and The Society, please check the news section of our website or email **magazine@physoc.org** to enquire about applying for the vacancies.

Since the revamp of the magazine in 2011, we have aimed to produce two Special Issues of *PN* per annum, not only to draw attention to interesting areas of physiology but hopefully also stimulate discussion within our community. And given the tantalising success of companies like SpaceX, the historic first landings on the darkside of the moon and asteroid Ryugu, this year the Editorial Board have decided to focus one of our winter Special Issues on space. With plans already in the works for colonisation missions to Mars, regular space tourism and even the formation of a space force within the next decade, questions about how (or if) human physiology can adapt to the stresses of distant space travel or long-term inhabitation of other worlds are becoming ever more pertinent.

Another timely issue deserving of attention is diversity (Summer issue), as The Society's five-year strategy (approved last year) and the governance review (which is currently taking place) both seek to improve diversity and inclusion. Our hope is that this issue will not only explore the impact diversity issues have on our science (i.e. sex-bias in animal studies, overemphasis on Caucasians in clinical trials, etc.), but also allow those underrepresented or inequitably treated within our own community to share their experiences and engage the rest of us in much needed conversations about the challenges many face, be that due to race, age, sex, disability, religion, sexual orientation, gender identity, etc. As always, we welcome unsolicited contributions for any of our issues and if you have any ideas for content on these topics or others, please don't hesitate to reach out to us by emailing **magazine@physoc.org**.

In this issue of *PN*, we're delighted to feature an article by Jose Vega on his extraordinary journey into the history of the mammalian dive response and the hidden treasures he uncovered that have potential clinical significance (p. 24). Too often, many of us forget the lessons history can teach us, and in that vein Angus Brown's article stresses the importance of consulting the original literature which underpin seminal findings (p.32). As well as pieces on the more modern dilemmas faced by the medical communications industry (p. 36), the potential impact on learned societies by Plan S (p. 12), and the pros and cons of disruptive technology in the physiology classroom (p. 14 and p. 45). For those seeking something more light-hearted, a satirical piece the on perils of publishing is also quite an amusing read (p. 8).

The final focus of this issue, is on what a funny thing a career in science can be. On paper, the steps you're required to take can seem relatively straightforward – pick a STEM subject, study hard, get your PhD, do your postdoc rounds, and get an academic position so you can start climbing that ladder (p. 28). Yet when I think of my own career or those of Matthew Laye (p. 28), Ana Vujic (p. 40) or Bethan Phillips (p. 44), it's clear that things never go quite as planned but that's not necessarily a bad thing. To quote the Rolling Stones: "You can't always get what you want but if you try sometimes you just might find you get what you need."

The Society's governance review

Bridget Lumb

President, The Physiological Society

Hot on the heels of the newly adopted 2018-2022 Strategy, one of my first roles as incoming President was to oversee a governance review. At first, I imagined this would be a very dry and tedious overhaul of The Society's Articles of Association. STOP THERE – it's been far from it. To meet its charitable objectives, much of the scientific activities of The Society are organised through its Committees, which in turn report to and are advised by Council (the Board of Trustees). The governance review was the opportunity to revise the ways in which our Committees operate and, importantly, to establish structures that have the potential to increase participation of Members – that's YOU! The details of these changes will be made available for comment at the next Annual General Meeting.

To enable this review, the Chairs of The Society's Committees (Sarah Hall, Deborah Baines, Rachel Tribe, Susan Deuchars, Lucy Donaldson and Frank Sengpiel) have worked closely with the Governance Working/Implementation Group (Bridget Lumb [Chair], Guy Bewick, Lucy Donaldson, Sarah Hall, Matt Taylor and Charlotte Haigh), alongside an external consultant, Lucy Devine (Wellspring Consulting Ltd), and Society staff Rosie Waterton (Governance Manager) and Dariel Burdass (Chief Executive).

What is Good Governance?

Good governance is about the processes required for making and implementing decisions. It's not about making "correct" decisions, but about the best possible process for making those decisions.

Governance encompasses strategic leadership and direction, as well as accountability and ensuring the organisation is effectively and properly run. Governance is distinct from the day-to-day management and operations delegated to staff via the Chief Executive. Strong governance coupled with good management is fundamental to running a successful, confident and forward-thinking charitable organisation where Trustees are abreast of their duties and activities, and services are well planned and managed. A governance review is an opportunity to reflect on a charity's governance arrangements, in particular governance structures, which can often evolve without a coherent plan.

Why now?

There are two main reasons why this was an ideal time for a governance review:

Firstly, following the successful adoption of the 2018-2022 Strategy, which has provided a five-year framework for activities and a systematic approach to agreeing priorities (but at the same time flexibility and agility in The Society's focus), Council agreed that it was an ideal opportunity to bring in an external governance consultant to review both structure and processes of The Society's governance. The goals of the governance review were:

- To ensure transparency and accountability in the way decision-making and responsibilities are distributed and information flows across The Society.
- To ensure the governance structure supports the delivery of the strategy and provides a balance of agility, expertise and engagement through a series of focused, time-limited groups, allowing Council to focus on core strategic areas.
- To ensure improved inclusion and diversity within the governance structure.
- To enable efficient and effective decision-making through clear, delegated lines of authority.

> "The governance review was the opportunity to revise the ways in which our Committees operate and, importantly, to establish structures that have the potential to increase participation of Members"

- To ensure the legitimacy of governing documents of The Society, meaning that the Articles of Association and Regulations reflect best practice.

Secondly, with increased scrutiny of charity governance from regulating bodies it is also timely to review the governance of The Society to ensure we, as Trustees, are safeguarding the future of The Society from any kind of regulatory breach.

How will this affect Members?

As one of the goals for the review was to increase Member engagement, and diversity and inclusion, we will also want to bring in some new people, from inside and outside The Society. We will work to ensure that we are being diverse and inclusive, with a minimum expectation of 33% female representation on our committees and working groups, but working towards a target of 50%. To do this, there will be open calls for Members to join committees and groups, when new people are needed.

What is the timeframe for the governance review?

As with any complex project, the implementation will be via a phased approach to ensure we get it right. Therefore, we expect to realise the outcomes of the review throughout 2019 and into 2020. Following the principle of transparency, we will share more information with the membership as it becomes available.

We launched a Code of Professional Conduct last November to ensure interactions within our community are guided by our values. Below is a reaction from a Member and our President Bridget Lumb's response.

Of codes and conductors

Peter Kohl

Director of the Institute for Experimental Cardiovascular Medicine, University of Freiburg, Germany

Member of The Physiological Society since 1995

When I recently learned that "*our Council of Trustees has approved a new Code of Professional Conduct for all Members*" of The Society, I had a look for the "old" Code – as I felt quite guilty about not having considered its content before.[1] As it turns out, there was none: the Code of Conduct is a shiny new instrument. We have it, as "*Council wished to develop a mechanism*" to "*ensure that the charity's performance and interaction with its stakeholders are guided by the values, ethics and culture put in place by the board.*"[2]

I am not sure whether values, ethics and culture of The Society have been put in place by the board – but the new instrument to enforce them is neither meant to be blunt, nor merely ticking a box in the ever-increasing long list of rules-and-regs for charitable organisations. This is evident from the fact that a "*complaint against any Member should be submitted confidentially by email to the President and to the Chief Executive*".[2] If found to be in "*substantial breach of any part of this Code*" this "*could lead to [their] removal as a Member of The Society*".[3] So the Code of Conduct goes well beyond a statement on values and aspirations.

This raises some questions, in my view.

Firstly: do we need a Code of Conduct? For the past 140 years or so, The Society achieved its vision without formally requiring *"Members to be passionate advocates for physiology and to promote and preserve the reputation of the discipline and The Society*".[2] As a whole, they are, and they do.

Secondly: if we did need a Code – shouldn't it be as concise and realistic as possible? Why, for example, would half of the Code of Conduct for Members of The Society detail obligations of committees ("*Read the agenda and supporting papers*"; "*Arrive promptly and miss no more than two meetings"; "Where my absence is unavoidable I will send apologies…*").[3] And why would The Society try to define Members' interactions with the world at large, such as by stipulating that "*I will* […] *be considerate and polite to all those I come into contact with*"?[3]

Thirdly: if we did need a Code, and if we had one that was worded in a way that matches the significance of such a document – shouldn"t it be put to the Members of our distinguished Society to decide on its introduction? After all, the Members are the sovereign of The Society.

The matter is not a formality, given that "*breach of any part of this Code*" can have severe consequences.[3] And, even if you don't breach the Code, it does affect your rights as a Member of The Society, as Council decreed that "*if you really don't want to sign up [to the Code] then you won't be able to complete your membership application, or renewal.*"[2]

I am all for good conduct – but I do object to being conducted in this manner.

References

1. Email from our President, 26/11/2018, and physoc.org/news/2018/launch-membership-code-professional-conduct

2. physoc.org/membership-code-professional-conduct-faqs

3. physoc.org/membership-code-professional-conduct-faqs#code

Bridget Lumb, President of The Physiological Society, responds:

As President, I am proud to be part of a community who share common ideas and values, made up of Members who are actively engaged in supporting each other to make physiology flourish. Members are at the heart of our 2018-2022 Strategic Plan which was approved by Trustees in May 2018 and circulated to all members in mid-June. The Strategy, as well as setting out the Vision and Purpose, also defines The Society's values and the guiding principles which apply to the way we work, and it is the behaviours and expectations that this relies upon that are outlined in our new Code of Conduct.

The Code is intended to foster a positive, supportive community in which all Members can enjoy the freedom to interact, collaborate and learn, and celebrate the discipline, and although some values are aspirational as stated in the online FAQs, these are indeed generally things that Members are most likely doing anyway. The Code is not designed to impose stringent rules or unrealistic expectations but, created out of respect for our Members, their diversity, opinions and aspirations, formalises the points of common decency and professionalism that we are lucky enough to experience in this community and protects and nurtures these for the future community we endeavour to engage and build on.

The Code was developed and approved by The Society's Council. The Society Articles of Association, the document (approved by Members at the 2016 Annual General Meeting) by which The Society is governed, delegates the oversight of such a code to the Council. "5.1.2 - to operate a membership register and to require such Members to abide by a Code of Professional Conduct which shall be published, amended as necessary, and regulated by the Council."

A majority of the Trustees on Council are elected by the membership to be legally entrusted with oversight and decision-making on behalf of the membership, and, as part of this Trusteeship, Council is responsible for the good governance of The Society. Codes of Conduct are a common governance best practice tool for membership organisations and are designed to safeguard both Members and The Society from misconduct. Following the launch of the new Strategy and after undergoing a full governance review carried out in the context of increasing scrutiny on charities, Council felt it was an appropriate point to put in place a transparent, realistic and proportionate Professional Code of Conduct.

I am delighted that members have engaged with the Code and given thoughtful feedback, almost all of which has been entirely positive and strongly in support of the Code. Council is always, and will continue to be, willing to hear the views of the membership and respond to any observations or questions.

The Devil's Dictionary of Publishing (with apologies to Ambrose Bierce)

As Jane Austen almost said: "It is a truth universally acknowledged, that a single researcher in possession of a good grant, must be in want of a publisher", and while publication is the life blood of research – by ensuring the circulation of ideas it ensures the health and vitality of the body scientific – an up-to-date understanding is essential...

Abstract

1. *Of work presented at a scientific meeting*
   Evidence to the granting body that you are doing the work they funded. Honestly.
2. *Of a scientific paper*
   A summary of the main findings of the paper for those not sufficiently interested to read it.

Acknowledgements

A list of those who would be offended if they weren't mentioned; alternatively of those who didn't want to be an author.

Author

Progenitor of published research; or their boss.

Author contribution

Post hoc justification for inclusion as an author.

Citations/h-index

How you will be judged. Despite denials.

Clinical relevance

See Emperor's new clothes.

Copyright

Something given, in lieu of your soul, to see your work published.

Cover figure

An accolade, for reasons that are unclear.

Creative commons license

Permission to abuse the work however you wish. No, we don't understand the phrase either.

Editor

Academic acting as a conduit for documents between authors and reviewers until one or the other surrenders.

Editorial Board

A group of academics recruited by publishers to provide scientific credibility for their business.

High impact journal

A journal publishing high impact papers (q.v.).

High impact paper

A paper that provides the conclusion the field wants without considering alternatives.

Literature search or review

A visit to PubMed, downloading PDFs, and psychically absorbing their content.

Negative results

Possibly important but unpublishable waste of resources, leading to unpublishable duplication and bias in the literature, except in disciplines that review the study before execution, rather than the subsequent results.

New & Noteworthy

A summary of the main findings of a paper for those whose knowledge of the field or concentration span don't stretch to the abstract.

Online publishing

A method of decreasing time to publication, increasing access and reducing costs without reducing prices.

Open Access publishing

A method of increasing access to scientific literature to the general public (most of whom aren't interested) at a higher cost than pay-per-view, for an additional payment to the publishers (who are).

Publishing

Process by which academics provide material, reviewing and editing expertise for publication, free of charge; then pay to publish their work, which is subsequently bought by their institution for a price justified by the production of paper copies that nobody reads.
See also *Online* and *Open Access publishing*.

Reprint/Preprint (arch.)

Paper copy of article sent to colleagues to let them know you are still here.

Review

1. *Article*
   A method of increasing citations by providing a summary of the field, so that others don't have to read original sources.
2. *Of a manuscript*
   A summary of how the study and manuscript presented for publication differ from those that the reviewer (q.v.) would like to see.

Reviewer

Somebody so expert that they know more than the authors about the aims of the work and can therefore suggest extra experiments that slow progress by delaying publication.

Society journal

Well at least the money goes to a good cause. See *Publishing*.

Statistics

A discipline to which all others are subservient and whose least tenets must be obeyed.

Teleology

Not an explanation of scientific findings; frequently used as such.

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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

The Chair of Meetings Committee, Sue Deuchars, reported on the great success of Europhysiology 2018 and feedback from the other organising societies which had also been very positive.

In particular, feedback from attendees reported that the satellite meetings had been very successful and it was agreed that this format should be replicated for Europhysiology 2020. The Society has also agreed to adopt this format of satellite meetings at Physiology 2019 in Aberdeen.

The Trustees watched a promotional video, produced by the Digital Content Officer, Areeba Hanif, which demonstrated through the voice of the membership, the benefits of being a Member of The Society and part of the wider physiology community. This video will be showcased on The Society's new website when it launches early 2019.

Council also agreed that Future Physiology should be organised annually as it provided an excellent opportunity for early career physiologists to gain exposure and showcase their work, as well as network with more senior scientists. It was also agreed to explore further how Undergraduate Members might be better included.

John Speed of Js2, The Society's chartered accountants who provide a specialist accounting service to the not-for-profit sector, gave a presentation on the purpose of a reserves policy and examples of models used within the charity sector. It included the change in emphasis from the Charity Commission and the increasing need to both protect The Society from risk of income failure and to provide demonstrable utilisation of funds to support current charitable objects, as well as safeguard those of the future. Trustees noted that reviewing the reserves policy and utilising the free reserves of The Society was an opportunity to undertake some additional strategic projects to further the charitable objects. A draft policy would be reviewed at the first Council meeting of 2019.

It was also agreed that a publications task and finish group would be formed in early 2019 to review the potential impacts of Plan S on The Society's portfolio. Plan S is an initiative for Open Access publishing that was launched in September 2018. The plan is supported by cOAlition S **www.coalition-s.org/**, an international consortium of research funders. Plan S requires that, from 2020, scientific publications that result from research funded by public grants must be published in compliant Open Access journals or platforms.

The Trustees also approved the new governance structure and supporting processes and procedures to ensure the governance of The Society supports its strategic aims. Members are at the heart of The Society's strategy, and as part of the new structure there will be smaller, focused, time-bound groups to work on specific activities. This means there will be more opportunities for members to be part of governance and offer their expertise by joining these groups. Council is also committed to Equality, Diversity and Inclusion, and this means that we will look for better ways to involve Members whom we might have missed before.

The Head of Professional Development and Engagement (Chrissy Stokes) presented a paper on Membership Trends produced in conjunction with Rachel Tribe, Chair of Meetings and Grants Committee. She highlighted the trends in the various membership categories and noted that moving away from a transactional engagement model to an emotional engagement model where the more intangible benefits of membership are identified should help The Society to grow its membership.

Council discussed the membership data presented and approved the following recommendations:

- To complete the Member Insight Project; in particular to understand the perceived value of membership to Members, and to compare this to the actual value available to Members, and as a result review the membership proposition.
- Review the membership categories and fee structure to determine whether there are any obstacles to conversion that could be addressed by The Society.
- Further investigate the career pathway of physiologists and review the membership categories and proposition in this respect.

Membership and Grants Committee

The agenda included updates on the Member Insight Project which is still ongoing and will be reported to Council in March and the success of the recent Society Rep meeting, as well as membership planning including review of categories and fees.

There was discussion on membership engagement with a focus on welcoming Undergraduate Members to The Society when they join with a welcome email and pack, and this was introduced at the end of last year.

A total of 20 Society Reps were visited in 2018, and this is something The Society will continue to carry out during 2019.

The Committee also looked into ways in which The Society can demonstrate impact of travel grants, as significant funding is allocated here. Following discussions, a revised travel grant allocation process was agreed and introduced for this year.

Policy and Communications Committee

The Policy and Communications Committee met for a teleconference for its first meeting of 2019. The Committee received updates on regular work areas. The Lifelong Health Project has now completed four workshops focusing on current biomedical research on ageing, the public's current perception of ageing, the state of funding for physiological projects related to ageing and how best to encourage interdisciplinary working that promotes physiology.

The joint *in vivo* curriculum project with the British Pharmacological Society continues with the two societies working on a feasibility study for the project in 2019. The Sports and Exercise Science project organised in conjunction with GuildHE began at the beginning of 2019, and the Committee received an update on the survey and the institutions that are currently being engaged with the project.

The Chair also gave an update on the outcomes of the governance review and how this was likely to impact on the composition of the Committee as it currently stands. The Chair noted the success of The Physiological Society Prize, which will feature for the first time as a standalone prize at STEM for Britain this year in Parliament. Of the 103 bioscience applications, 78 have also asked to be considered for this prize.

The Committee also noted the success of the call for authors to discuss issues of diversity with the physiological community and discussed how this could be best approached within *Physiology News* in 2019.

Publications Committee

The Publications Committee met in October 2018, chaired by Debbie Baines. Presentations by Editors-in-Chief Kim Barrett, Mike Tipton and Tom Kleyman (of *The Journal of Physiology*, *Experimental Physiology* and *Physiological Reports,* respectively) highlighted the generally good health and growth of the journals. Kim Barrett's term as Editor-in-Chief was formally, and unanimously, agreed to be extended by two years from the initial appointment of three years.

The next few years promise to be an exciting time for The Physiological Society's publications, with initiatives in the pipeline for innovative article types and social media strategies. Supporting authors remains at the forefront of The Society's journals' plans, but there will also be an emphasis on encouraging good-quality submissions from underrepresented geographical regions and subject areas. Finally, a more rigorous approach to the presentation of data and statistical analysis is likely to be rolled out in early 2019. From a marketing perspective, The Society's journals will continue to have a presence at relevant local and international meetings. The Committee pledged to keep an eye on developments with Plan S in early 2019. A transition to full Open Access, the goal of Plan S, could have a large impact on our journals' strategies, and that of The Society.

Policy focus: Big data and society

Tom Addison

Policy Manager,
The Physiological Society

Attending various health and innovation conferences, both in Westminster and around Europe, as part of The Society's project on lifelong health, one cannot help but be struck by the pervasiveness of "big data" as a powerful tool in the future to improve the health of individuals and society at large.

From the perspective of physiology, big data is indeed an attractive proposition for both research and patient care. It may be that in the not-too-distant future, researchers will be able to continuously monitor trial participants beyond the confines of the lab. New technology allows patients to collect and analyse their own health data, which has the potential to transform the way care is delivered. Big data also has a number of high-profile health-related supporters. Matt Hancock MP, Secretary of State for Health in the UK, used his first speech in the role to announce a £500m investment in "the rollout of innovative technology aimed at improving care for patients and supporting staff to embrace technology-driven health and care".[1] George Freeman MP, former Minister for Life Sciences and former Chair of the Prime Minister's Policy Board, recently spoke of his desire to see patients, charities and the NHS combine to create "patient portals" that include patient data that are visible to patients and can be sold to companies once charities have negotiated the terms of the deal. He pointed to Estonia as an example of where patient data is stored online and used to develop personalised healthcare such as exercise targets, expedited pharmacy prescription collections and screening the population for those most at risk of developing diseases such as breast cancer.[2]

The success of a data-driven health system and physiological interventions will rely on securing public trust that their data is being held securely and used responsibly. Neither governments, nor companies with the financial clout to be early adopters of big data, have a strong track record in this area. In the UK, the NHS launched "Care.Data" in 2013 with the aim of bringing together health and social care information from across the NHS to improve patient care, as well as enabling researchers to use anonymised data to develop new treatments. However, three years later it was cancelled because of concerns about the sharing of sensitive medical information with companies without patient knowledge or agreement. In the past 12 months alone, the NHS has blamed a coding error for 150,000 patients in England being involved in a data breach.

> "We will only unlock the immense value of patient data if we have open and honest discussions"

Indeed, the Estonia example gives us a clue as to the long-term education and normalisation that would be required for acceptable and successful adoption of data analysis in health. Rapid implementation of a digital government in Estonia began in the 1990s with electronic banking, a digital tax system and related digital services all going digital first. By comparison, only 64% of UK customers used online banking in 2016.[3] Those involved with the digitisation of Estonia's data have recognised that this gradual move towards online services has made Estonians more receptive to the sharing of their data for "patient empowerment and personalised health" but have also described the initial steps as "a blind leap of faith".[4]

Jeremy Farrar, Director of Wellcome Trust, has said "We will only unlock the immense value of patient data if we have open and honest discussions about how and why data can be used for care and research, what's allowed and not allowed, and how personal information is safeguarded."

Individual NHS Trusts are now working to improve sharing of data at their local level with the intention of learning the lessons from Care.Data and building trust with patients and communities. The UK's move to digital health has sufficient examples from elsewhere to make labelling it "blind" unfair but "faith" remains in short supply.

References

1. gov.uk/government/speeches/matt-hancock-my-priorities-for-the-health-and-social-care-system
2. e-estonia.com/exporting-health-digitally/
3. statista.com/statistics/380884/online-banking-penetration-in-the-uk/
4. sciencebusiness.net/news/how-data-fuels-estonias-economy

Plan S: What will the implications be for The Society?

Simon Rallison

Director of Scientific Programmes,
The Physiological Society

Widening access to the scholarly literature increases the literature's value to society. Keith Siew's article "The open science movement" (*Physiology News* 107, Summer 2017) passionately and persuasively makes the case for openness and transparency in academic research.

The movement has usually marched behind the banner of open access (OA) to journal articles, demanding that all research papers should be available for anyone to read and re-use immediately they are published. Why should access be rationed when it costs no more to let everyone read an article than it does to keep the article behind a paywall?

Since the first commercial OA journals were launched in the late 1990s, there has been a steady migration from subscription to OA. In 2018, 19% of articles were published as Gold OA (OA immediately on publication), either in fully OA journals or in "hybrid" journals, former subscription journals that publish OA papers alongside articles still only available to subscribers. A small number of the fully OA journals are former subscription titles that have "flipped" to OA.

This migration has, however, been too slow for many people's (including Keith's) liking. The OA advocates suspect the commercial publishers of deliberately dragging their feet in order to protect the high profit margins their subscription journals deliver. A succession of developments, each at the time heralded as a tipping point, have come and gone: *PLoS ONE*, institutional repositories, funder mandates, SciHub and others. Suddenly though, the fox is well and truly loose in the hen house. The latest initiative looks like being a genuine gamechanger.

Plan S, driven by Science Europe, was launched in September 2018. Fourteen national research-funding bodies across Europe (with UK Research and Innovation by far the largest) set out conditions for publication of the research they paid for. Non-compliance could lead to sanctions, including withholding instalments of grants.

Although Plan S was short on detail, the intent was very clear: to pull down the temple of subscription publishing and stop the publishers (and indirectly the societies) taking so much money out of the system. Publishing in hybrid journals would no longer be countenanced; only fully OA journals would in future be acceptable. That future wasn't far off either: January 2020.

While Plan S snowballs (the Gates Foundation and the Wellcome Trust have now aligned their own policies with it), through consultation with the publishers and societies Plan S's sponsors are joining up the dots. There will be some flexibility in the timing of implementation if journals are on a clear path in transforming from subscription to full OA. Although a figure hasn't been set, there may be a cap on how much journals are allowed to charge for OA publication.

There are of course serious implications for *The Journal of Physiology* and *Experimental Physiology*, both of which are hybrid journals (*Physiological Reports* was born fully OA). Currently, only 5% of articles published in *J Physiol* and *Exp Physiol* report work funded by Plan S signatories, but being unable to publish research paid for by MRC and BBSRC (or even work done in any British university, as Research England [the former HEFCE] comes under UKRI) would be a severe blow. On the other hand, a transition to full OA would almost certainly put a dent in the journals' financial return to The Society and therefore our ability to pursue our charitable activities.

While we make plans to secure the journals' financial future, developments are coming thick and fast. Our publishing partner John Wiley & Sons have just announced their ground-breaking, Plan-S-compliant agreement with Projekt DEAL, a national consortium of academic libraries and funders in Germany. The innovation is that what the institutions are paying for is turned on its head. The finances of the DEAL deal (as it were) are based on how much a university publishes, not on what its faculty and students read. Between them, the publishers, funders and libraries may have got some way towards squaring the circle.

"Although Plan S was short on detail, the intent was very clear: to pull down the temple of subscription publishing and stop the publishers (and indirectly the societies) taking so much money out of the system"

Congratulations to our newest Fellow Members

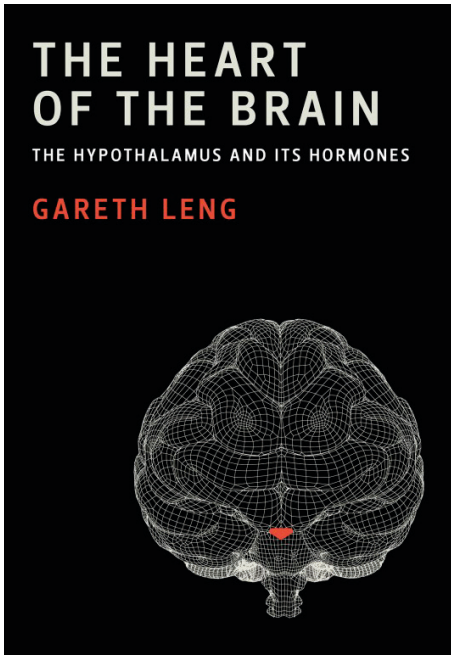
- Anthony Ebeigbe, University of Benin
- Shanta Persaud, King's College London
- Francis Stephens, University of Exeter
- Andrew Coney, University of Birmingham
- Dylan Thompson, University of Bath
- Dario DiFrancesco, University of Milan
- Sean Roe, Queen's University Belfast
- Raheela Khan, University of Nottingham
- John Mackrill, University College Cork

A complete list of our Fellow Members can be viewed at **physoc.org/fellowship** and to apply to become a Fellow Member visit **physoc.org/fellow-membership**

Book review

The Heart of the Brain – The hypothalamus and its hormones by Gareth Leng

Dervla O'Malley
University College Cork, Ireland



Gareth Leng
MIT Press; 1st edition (2018)
ISBN: 9780262038058

"The book title refers to the hypothalamus as 'The Heart of the Brain', and indeed, it also drives irrational behaviours such as passions, biases and instincts: essentially, all of the things that make us human"

With his long-standing research career focused upon hypothalamic function, Gareth Leng, a Professor of Experimental Physiology at the University of Edinburgh, illuminates, entertains and informs the reader on the multifunctional actions of the hypothalamus. Far from being the evolutionarily primitive organ that it is often regarded as, Leng explains that the hypothalamus is in fact a highly evolved structure, which regulates all of the base drives: hunger, thirst, metabolism, body rhythms, stress, growth and reproduction. The book title refers to the hypothalamus as "The Heart of the Brain", and indeed, it also drives irrational behaviours such as passions, biases and instincts: essentially, all of the things that make us human.

Apparently, if one curls the tongue back as far as it will go and presses it against the roof of the mouth, the hypothalamus will almost be resting on its tip. Leng alludes to the complex nature of the hypothalamus by describing it as the "Europe" of the brain, as it encompasses a confusion of small nations (neuronal nuclei controlling different functions), each one noisy, heterogeneous and sometimes strident. Each nation contains multiple clans (neuronal clusters) that use a variety of languages (neurotransmitters and neuropeptides) and other signals that act at diverse spatial and temporal scales to communicate with other clans and neuronal nations. The clan members differ from each other but are more similar to each other than to members from other clans. Leng goes on to contrast the actions of neuropeptides, which are striking in their ability to orchestrate complex behaviours by coordinating different systems, with the release of neurotransmitters. He eloquently describes neurotransmitters as "whispered secrets that pass from one neuron to another at a very specific time and place" whereas, "peptides are public announcements, broadcast to whole populations."

On the topic of obesity, Leng aims to dispel the dogma that the prevalence of obesity is due to over eating and under exercising. Indeed, actual caloric intake has not changed that much since the 1940s, and whilst sedentariness has certainly increased, more people now consciously exercise. Leng explains that obesity is primarily a disease caused by hypothalamic dysfunction, and is primarily down to our genes. When we are in a state of starvation, the hypothalamus defends our body weight by reducing metabolic rate and energy expenditure by inhibiting reproduction and immune activity, and by focusing on the search for food. In obese individuals, resistance to leptin is often accompanied by low mood, lethargy, susceptibility to minor infections and a continuous hunger. Leptin resistance is difficult to reverse and is probably exacerbated by weight-loss dieting.

However, Leng's interest in oxytocin neurons is the common thread throughout the book. The cell bodies of oxytocin neurons are aggregated in hypothalamic nuclei and their axons extend down to the pituitary gland, which more closely resembles a "chickpea" in size rather than a pea, as Wikipedia states. Leng describes the long and winding path which finally led to understanding the random complexity needed in oxytocin neural nuclei in order to regulate the milk-ejection reflex, an icon of neuroendocrinology. However, he often refers back to this neural cell type as he explores appetite and social behaviours.

The book aims to celebrate the hypothalamus, and in particular its role in regulating our sometimes erratic behaviours. However, Leng also wanted to use this book to display the imaginative part of science: how ideas begin, how theories arise from observations and how they are then tested. Although Leng hopes that his book should be comprehensible by "any thinking person willing to listen", the terminology and language used means that this book will be of most interest to the specialist reader. As a fellow lecturer in neurophysiology, each year I try to parallel the complexity of the hypothalamus with the mundanity of the functions that it controls. This book is both educational and enjoyable to read, and many of my learnings, both about the workings of the hypothalamus and the scientific process, will be shared with future neurophysiology students. In a quote that would resonate with many undergraduate students, Leng states that, "A message is only a message if it can be understood by its recipient. Neurons can't decipher long and complex sentences. They have a short attention span, are easily distracted, and much of the time they aren't even listening."

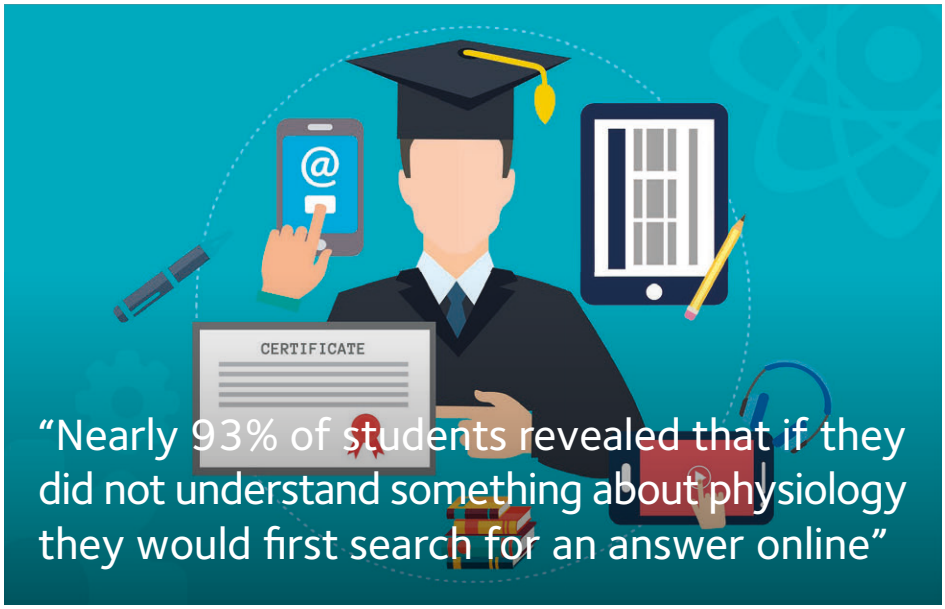
Physiology for the YouTube generation

Mark Rae

Universtity College Cork,
Republic of Ireland

The seemingly ubiquitous presence of the Internet and social media in the minute-to-minute existence of today's students is all too apparent to any lecturer that has had to navigate through an unseeing zombie swarm of students, completely absorbed, heads down, in whatever latest tweet, meme, gif or WhatsApp® message has appeared on their smartphones.

However, somewhat surprisingly, the extent to which students rely upon social media (which, in this context, includes all websites and applications that enable users to create and share content, and as such includes microblogging sites such as Twitter® and video sharing websites such as YouTube®, as well as standard social network sites) to supplement their educational needs in physiology has never been empirically quantified to the best of the author's knowledge.



Therefore, in conjunction with colleagues Dervla O'Malley (Physiology, University College Cork) and Dennis Barry (Anatomy, Trinity College Dublin), last year we decided to conduct our own study into this particular phenomenon by specifically surveying the social media habits of pre-clinical first year medical students (from both graduate entry [67 students from a class of 82] and direct entry [72 students from a class of 128] cohorts) in relation to their study of physiology. Below, I will discuss some of the main findings of that survey (which were also presented at the recent Europhysiology 2018 conference).

Possibly the least revelatory finding of the study confirmed what we already strongly suspected; that the majority of medical students surveyed did use social media tools to source physiology information. It was, however, a surprise to us just how much social media appeared to be an essential and integral study aid for physiology for most of our medical students. Specifically, an emphatic 90% of students indicated that they had used social media to study physiology at least once per week during term time, with YouTube® by far and away the most popular source of material (76% of students). Similarly, nearly 93% of students revealed that if they did not understand something about physiology they would first search for an answer online whereas, in complete contrast, only 38% of students would ask a physiology instructor a question in person (with nearly 50% disagreeing or strongly disagreeing). Not unreasonably, it was suggested that perhaps personality issues between lecturers and students might explain this particular issue (e.g. students disliking or feeling intimidated by their physiology lecturers). However, this idea seems to be undermined by the fact that even fewer students (13%) would ask their instructor questions by e-mail instead (with 70% indicating that they definitely would not do so). Although we weren't able to interrogate this finding any further in this study, the most parsimonious explanation for their reluctance to contact instructors by either mode of communication may be nothing more than a matter of simple expediency. Specifically, "Dr Google" will almost always provide a much quicker (although not necessarily correct) answer to their questions than their overburdened lecturers! As such, faced with the considerable study pressures pre-clinical medical students are placed under, one can sympathise with such pragmatism. However, given the largely unfiltered and unverified nature of most information available on the Internet, we wanted to determine if students were rigorous enough to apply their own "filter" to material garnered from such online sources. Worryingly, 35% of students indicated that they never doubted information that had been obtained from online sources. Although nearly 42% of students disagreed with this sentiment (with 24% neither agreeing nor disagreeing), only 31% actually "fact-checked physiology information obtained from online sources using textbooks, papers and/or instructors". Providing students with the benefit of the doubt, the lack of fact checking by students may simply be down, again, to time pressures (rather than, say, a decline in students' critical thinking abilities). However, if that is the case, and being all too aware that there is next to no chance of persuading students not to surf for information as and when the mood takes them, shouldn't we as academics take the lead and direct them instead to resources that we know to be reliable? Although LifeSciTRC.org, a searchable, digital library of peer-reviewed life sciences resources sponsored by The Physiological Society, fits this bill to a certain extent, it is a somewhat tricky site to navigate and appears to be primarily geared towards teachers rather than students.
I feel that something far more suitable for the purposes described above would be a Wikipedia®-style, editable webpage (hosted on The Physiological Society website perhaps?) that contained links to videos/resources (classified into distinct physiological systems) that Physiological Society members have verified as reliable and accurate (e.g. illustrative short videos on YouTube® that have been incorporated into lectures). Students could be provided with the link to such a webpage so that they would at least have a starting point for their searches.

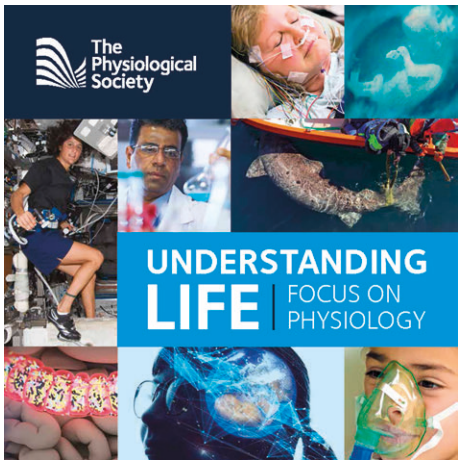
Of course, the idea and suggestion are the simple parts of any project. The difficulties begin when volunteers are sought to set up and maintain such a site.

Our careers booklet for 16–21 year-olds

We are delighted to announce the launch of our new careers booklet, Understanding Life, which is now available on The Society's website and to order in print.

Aimed at undergraduates and 16- to 19-year-olds, this resource is an update of an earlier version and showcases some of the latest and most exciting areas of physiological research, reflecting the evolving nature of this discipline and why we study it. By continuing to develop our understanding of normal body processes, physiology can provide useful insights into how we can maintain our health on Earth and in extreme environments such as space.

The booklet also includes profiles of early career physiologists working in an exciting variety of research areas; these case studies illustrate the career opportunities that are open to students who graduate with



physiology or a related degree. We hope this booklet will help students when choosing their next career step by distributing it at careers events, open days and outreach activities all over the UK and abroad.

If you would like to order any hard copies for upcoming events at your own institution, please email **education@physoc.org**

Does the menstrual cycle affect sports performance? Watch our latest journal video to find out

There's a real lack of scientific evidence about the effect of the menstrual cycle on athletes. Learn more in our video about research from *The Journal of Physiology* from Toby Mundel and his team at Massey University, New Zealand, which suggests that female cyclists are affected by the type of heat (humid or dry) in which they exercise rather than the phase of their menstrual cycle or whether they take the contraceptive pill. Watch the video here: **bit.ly/2TMDX0p**

Read the latest press releases from our journals at **physoc.org/news**

New blood vessels discovered in our bones

During emergency procedures when intravenous access is difficult or impossible to obtain, physicians may opt to introduce fluids via direct bone marrow injection; however, it has been unclear how intraosseous-infused medicines/fluids pass rapidly into the systemic circulation. Recent work by German scientists has revealed the presence of a previously unrecognised vast network of blood vessels, named trans-cortical capillaries, which originate in the bone marrow and pass perpendicularly through the shafts of long bones to connect to the periosteum, accounting for 83% of arterial and 59% of venous blood flow in the bones.

DOI: 10.1038/s42255-018-0016-5

Link between gut microbiome and depression strengthened

A study of two large European populations has identified two kinds of bacteria, *Coprococcus* and *Dialister*, to be significantly reduced in the microbiomes of depressed subjects but not those with a high quality of life, even when adjusted for confounders such as age, sex and antidepressant use. Of particular interest was the identification of the potential role of these differing microbiota in dopamine and GABA metabolism.

DOI: 10.1038/s41564-018-0337-x

The genetic advantage of the slim over the obese

Using a first-of-its-kind cohort of 1,471 clinically ascertained thin and healthy individuals, researchers from Cambridge compared the genetic makeup of the thin to that of those with either severe early onset obesity or normal weight. Their work shows for the first time that healthy thin people are generally thin because they have a lower burden of genes that increase a person's chances of being overweight, and that thinness, like obesity, is a heritable trait with a polygenic component.

DOI: 10.1371/journal.pgen.1007603

Meeting preview

Physiology 2019: Something for everyone

8–10 July 2019,
Aberdeen Exhibition and Conference Centre, Aberdeen, UK

physoc.org/physiology2019/

Guy Bewick

University of Aberdeen, UK

Whatever your interest in physiology, be it in research of systems (cardiovascular, respiratory, musculoskeletal, neural, etc.), tissues (epithelia, adipose) or nuclear receptors, or be it in teaching, we have it covered at Physiology 2019 in Aberdeen. If the Annual Conference does not quench your thirst for knowledge, why not extend your stay in Scotland's north-east to attend one of the five Satellite Symposia covering fatigue, obesity, cancer drug cardiotoxicity, and renal and placental physiology.

The Annual Prize Lecture by Silvia Arber (Basel Biozentrum, Switzerland) will describe her elegant work elucidating the function, assembly and plasticity of motor circuits. The Hodgkin-Huxley-Katz Lecture by Stephen Traynelis (Emory University, Georgia, USA) reveals the characteristics of neuronal glutamate receptors in health and disease. In the Joan Mott Prize Lecture, Claire Hills (University of Lincoln, UK) presents important discoveries in diabetic nephropathy and kidney disease mechanisms. And, finally, the Sharpey-Schafer Lecture by endocrinologist Roger Smith (University of Newcastle, Australia), a leading expert on pathophysiology of human pregnancy, will expound on the idiosyncrasies, interactions and inner workings of the body across species but especially in humans.

A particular teaching highlight will be Dee Silverthorn, whose textbook is a staple of many physiology degree programmes, who will provide insights into best teaching practice from an international perspective.

Aberdeen's local representation is by Lora Heisler, recent winner of the Outstanding Scientific Achievement Award from the American Diabetes Association. She will present the Annual Public Lecture describing her work on the neural control of appetite, looking for new targets to tackle the current global epidemic of obesity.

So, please come and join these world-class speakers from across the globe and all stages of their careers who are coming to sample the renowned Scottish hospitality. We look forward to welcoming you to Aberdeen for a memorable summer scientific conference.

Attend our Satellite Symposia, free to Physiology 2019 attendees

Our Satellite Symposia increase the involvement of underrepresented sub-disciplines of physiology at our flagship Annual Conference, Physiology 2019. This year, join us for one of the following five Satellite Symposia. Free to Physiology 2019 attendees, all held on Sunday, 7 July 2019. Keep reading for more detail about each meeting, and don't forget to sign up when registering for Physiology 2019 on our website **physoc.org/physiology2019/satellite-symposia**

Cellular Mechanisms of Anticancer-Induced Cardiotoxicity

Organisers: Susan Currie & Margaret Cunningham from the University of Strathclyde, UK

Cardiovascular disease and cancer are the leading causes of death in the industrialised world. Anti-cancer therapies have dramatically improved over recent years with increased patient survival rates following diagnosis. Kinase inhibitors in particular have had a major impact on cancer patient survival. However, a number of these agents have been reported to cause serious adverse effects on cardiac function, leading to increased numbers of cancer patients with cardiovascular complications that can, in some cases, lead to death. The true extent of the overall risk to cancer patients is unknown, and the underlying mechanism(s) responsible for the cardiotoxic effects remain to be fully identified.

Strategies to prevent or mitigate cardiotoxicity resulting from cancer treatment are urgently needed to ensure the best cancer care possible. Future management of anticancer-drug-related cardiotoxicity will rely on improved understanding of the cellular effects of these agents in the heart. This, combined with improved biomarker identification along with cardiac imaging for monitoring purposes, will be crucial in an overarching strategy to design effective targeted cardioprotective agents. This symposium will be a forum to bring together basic scientists, cardiologists and oncologists to present recent findings that will work towards this overall goal. Ultimately, collaboration across these disciplines will be essential for promotion of evidence-based research that can relate to clinical practice in the area of anticancer cardiotoxicity.

Fatigue as a Limitation to Performance

Organisers: Derek Ball, University of Aberdeen, UK, and Ron Maughan, University of St Andrews, UK

The complex nature of fatigue is a function of single or multiple mechanisms that result in the failure to produce or maintain the required or expected muscle force/power output. Models to explain the underlying causes of fatigue range from single cell, to organ, to whole body examples and bring together the many different aspects of physiology represented through The Physiological Society.

This symposium will discuss potential limitations to performance imposed by the cardiovascular and respiratory systems, muscle metabolism and the central nervous system and how these factors are modulated by training, environment and nutritional status. In addition, a discussion of the strategies aimed at offsetting fatigue from the perspective of training adaptation and nutritional and pharmacological intervention will be invaluable.

Physiology of Obesity and Diabetes

Organisers: Lora Heisler, University of Aberdeen, UK, Peter Aldiss, University of Birmingham, UK, Daniel Brayson, University College London, UK, and Jo Lewis, University of Cambridge, UK

Obesity is an increasingly common disorder of energy homeostasis and has become a leading cause of type 2 diabetes, cardiovascular disease, human morbidity and mortality worldwide. Exciting new scientific discovery continues to propel the understanding of the molecular, cellular and neural mechanisms underlying the control of metabolic health. Dysregulation of these and other processes underpin the development and progression of obesity, type 2 diabetes and cardiovascular disease.

This symposium will bring together breaking research advances from the basic science and clinical realms with the objective of sharing novel insights relevant to human obesity, type 2 diabetes and cardiovascular disease. Specifically, the meeting seeks to integrate existing knowledge with novel discoveries on appetite, cognitive drivers of feeding behaviour, the gut-brain axis, the neurobiology of ingestive behaviour and energy expenditure, adipogenesis and lipolysis, glucose sensing and glycaemic control, cardiovascular disease and the genetics of obesity and type 2 diabetes. Several new areas will also be addressed, including state-of-art technologies for neuroscience and physiological research, ageing, anorexia and metabolic resilience.

The primary goal of this meeting is to provide cutting-edge research related to the control of body weight and glucose homeostasis. The maintenance of stable body weight involves the biological process energy homeostasis that matches cumulative energy intake to expenditure. The discovery of critical integrative systems that underpin energy homeostasis and glucose metabolism has important implications for the future of obesity and type 2 diabetes treatment. This symposium will highlight the latest advances in the cellular and molecular mechanisms whereby brain circuits modulating physiological appetite and the cognition of food intake are integrated with systems controlling gut function and insulin sensitivity. We will explore the cross-regulation of these circuits by adiposity- and nutrient-related signals.

Renal Physiology: Recent Advances and Emerging Concepts

Organisers: Morag K Mansley and Robert W Hunter from the University of Edinburgh, UK

Renal physiology is flourishing in the UK and beyond. In recent years, physiologists have made fundamental advances: we now know the molecular basis of oedema formation in nephrotic syndrome, how renal sodium and potassium excretion can be controlled independently and how glomerular capillary permeability is regulated. We are also learning much about the influence of the kidney on whole-organism physiology, in particular blood pressure homeostasis including advances in understanding the (renal) mechanism underpinning circadian control of blood pressure.

These recent advances have not only allowed us to better understand renal physiology, but have opened up an array of potential targets for novel therapies in a range of kidney diseases and fluid-electrolyte disorders.

The clinical impact of renal physiology research has been demonstrated recently where Vallon and colleagues published a series of papers showing that sodium-glucose co-transporter inhibitors (SGLT2i) can attenuate glomerular hyperfiltration in diabetic rodent models. In 2017-2018, large-scale clinical trials demonstrated that these agents can delay progression of diabetic nephropathy, meaning that – in large part because of basic renal physiology research – we now have the first new effective treatment for this common condition in 15 years. This symposium aims to bring together scientists from across the UK and beyond to discuss the latest advances in renal physiology.

The Placenta and Maternal Metabolic Regulation in Health and Disease

Organisers: Luis Sobrevia, Pontificia Universidad Católica de Chile, Chile, Raheela Khan, University of Nottingham, UK and Abigail Fowden, University of Cambridge, UK

During pregnancy, many physiological changes occur in the mother, which are designed to support fetal growth and to sustain the baby during lactation. These include changes in the cardiovascular, pulmonary, immune and metabolic systems. A failure to appropriately adapt maternal physiology can lead to pregnancy complications, including abnormal birth weight, pre-eclampsia, and gestational diabetes, which can be traced to poor placental development in early pregnancy. The placenta is the place for bidirectional materno-fetal crosstalk involving transfer of metabolic substrates and epigenetic regulation, about which little is known. Amino acids, lipids, glucose and other substrates such as nucleosides and nucleotides are vital for fetal growth and maturation. However, our understanding of the physiological and pathophysiological aspects of placenta transport mechanisms and the potential consequences for fetal physiology in diseases of pregnancy is still fragile.

The overall goal of this Satellite Symposium is to explore the nature and wider biological significance of placental endocrine function in adapting maternal physiology during pregnancy to support fetal growth in both normal and compromised environments. Discussions will cover insights into regulatory epigenetic mechanisms within the placenta, placental structure and vascular/trophoblast function, contribution of the placenta to disease, placental transfer of nutrients and possible translation to the clinic, and potential consequences of human placenta pathophysiological transfer of nutrients for fetus and newborn health.

"So, please come and join these world-class speakers from across the globe and all stages of their careers who are coming to sample the renowned Scottish hospitality"

Meeting preview

Extreme Environmental Physiology: Life at the Limits

2–4 September 2019,
University of Portsmouth, UK

Mike Tipton

Extreme Environments Laboratory, Department of Sport and Exercise Science, Portsmouth University, UK

"Ecology", from the Greek "oikos" meaning home or place to live, is the branch of biology that deals with the relationships of organisms and their physical surroundings. It encompasses the impact of animals on their environment, and the environment on animals. Both sides of the ecology coin are becoming increasingly important and linked.

On one side we are careering, largely unfettered, towards the man-made abyss of the end game of global warming; we are threatening our direct descendants, but at a rate and distance that doesn't provoke us to action.

On the other side, only 15% of the surface of our planet is not water, desert, ice or mountain. For a tropical, low-altitude, air-breathing human, this means most of planet Earth represents an extreme environment, defined as a place where it is difficult to survive. The link between the two is, of course, that global warming will make our planet even more extreme with flooding, erosion, heat waves, cold snaps and desertification.

Perhaps, therefore, there is no better time for The Physiological Society to plan a specialist conference on Extreme Environmental Physiology (EEP) on 2–4 September.

From origins where EEP research was largely undertaken for occupational groups such as miners and the military, as well as those attempting expeditions to remote parts of the globe, EEP has now become much more "mainstream". The greatest number of submissions and publications in the journals of The Physiological Society come from the areas of "environmental" and "exercise" physiology; both of which have extreme environmental components.

EEP research continues to examine the responses of humans to environmental stressors such as heat, cold and altitude; these remain important areas in themselves with, for example, at least 1,000 people dying from drowning every day around the planet. But EEP research is now also providing insights into a wide range of other conditions such as responses to hypoxia on intensive care ("survivor phenotypes"); ageing; peripheral vascular disease; osteoporosis; and debilitation caused in critical care patients by bed rest.

> "...most of planet Earth represents an extreme environment, defined as a place where it is difficult to survive"

In addition, as we take greater and greater control of our environment through technology, it is becoming increasingly apparent that we need to challenge our homeostatic mechanisms in order to remain functional. At one time we did this naturally by exercise and exposure to the natural world; now we have to employ thermal therapies for a wide range of physiological and mental health pathologies, from microvascular function through autonomic function to depression.

The specialist conference at Portsmouth in September will reflect all of the above, with sessions on cold, heat, hypo- and hyperbaric physiology, micro-gravity and cross-adaptation. To remind us what an eclectic discipline physiology is, each session will include short keynotes on physiology, pathophysiology and comparative physiology, as well as plenty of time for free communications. Finally, it seems appropriate that we should "flip the coin" and spend some time on what the environment might have in store for us if we continue to damage it.

Our exciting keynote speakers include:

- Chris Imray **case-medicine.co.uk/Chris-Imray**
- Sundeep Dhillon **xtreme-everest.co.uk/Dr-Sundeep-Dhillon**
- Larry Kenney **news.psu.edu/expert/w-larry-kenney**
- Kevin Fong **en.wikipedia.org/wiki/Kevin_Fong**
- Andreas Fahlman **tamug.edu/mmbeg/_cv/Andreas%20Fahlman.htm**
- Dominic McCafferty **gla.ac.uk/researchinstitutes/bahcm/staff/dominicmccafferty/**
- Hugh Montgomery **iseh.co.uk/consultantdetails/basic-science-research/42/Hugh-Montgomery**
- James Pawelczyk **en.wikipedia.org/wiki/James_A._Pawelczyk#Education**

Further reading

1. Martin & McKenna (2017). High Altitude Research and its Relevance to Critical Illness. *ICU Management & Practice* **17**(2), 103-105.
2. Tipton MJ (2015). GL Brown Lecture: "Extreme Threats" Environmental extremes: origins, consequences and amelioration. Experimental Physiology. doi: 10.1113/EP085362.
3. Tipton, M. J. (2018) Humans: a homeothermic animal that needs perturbation? *Experimental Physiology.* https://doi.org/10.1113/EP087450.

Meeting notes

African Association of Physiological Sciences goes to Rwanda

2–4 December 2018
Kigali, Rwanda

Soga Sofola

President, African Association of Physiological Sciences (AAPS)

The African Association of Physiological Sciences (AAPS) organised its "Fourth Physiology Education Workshop" in Kigali, Rwanda, from 2–4 December, 2018. This Workshop was also preceded by an AD Instruments hands on activity on PowerLab and Kura Cloud, on 1–2 December. The Workshop had as its theme "Physiology Education in Africa and Other Resource-Challenged Regions: Reflections on Current Practices and Charting the Way Forward". The gathering was declared open by the Vice Chancellor of the University of Rwanda, Phillip Cotton, a Brit resident in Rwanda!

The choice of Rwanda for the Workshop was an attempt to use a country that is in the middle of the African Continent in order to attract a larger audience. Our previous Workshops in Cairo (2013) and Lagos, Nigeria (2017), attracted only the usual four countries – Egypt, Nigeria, South Africa and Sudan. However, this Workshop had over 70 participants from 11 countries: Benin Republic, Egypt, Ethiopia, Kenya, Nigeria, Rwanda, South Africa, Sudan, Tanzania, Zambia and Zimbabwe. We were also privileged to have amongst us Keynote Speakers from the USA (Dee Silverthorn, Gary Sieck and Rob Carroll), Japan (Nori Kiobuchi), Taiwan (Sam Chan and Julie Chan) and New Zealand (Tony Macknight). We were particularly delighted by the presence of the IUPS President, Julie Chan.

The topics discussed were quite varied and relevant and included items on assessments, curriculum design and novel teaching methods as well as practical classes, encouraging exchanges among African postgraduate students including south-south research cooperation as well as publishing in the Journal of African Association of Physiological Sciences (JAAPS) among others. The Workshop was a mix of Keynote/ Plenary Lectures followed by group assignments and discussions which really encouraged interaction and exchange of ideas, under the direction of our guests and senior African physiologists. The feedback from the participants was positive and encouraging, while our foreign guests were quite impressed with both the attitude and enthusiasm of the participants, our future African physiology Professors. Hopefully, the formation of more National/ Regional Physiological Societies in Africa will increase in the nearest future.

It was not "all work and no play" though – on the first night, we had a well-attended cocktail party with about 80 attendees. The night was electrified by the performance of a dance/theatre troupe from Rwanda, "Intare", which in Kinyarwanda (Rwandan language) means "Lions". It was a marvelous display that also attracted some guests to join in the dancing. There was also some city sight-seeing as well as visit to the Rwanda Genocide Museum, organised by our host/LOC Chair, Bosco Gahutu. The last night had the farewell dinner with exchange of pleasantries.

The AAPS would like to acknowledge the donations towards the Workshop from AD Instruments, American Physiological Society (APS), Axiology Labs, Canadian Physiological Society, International Union of Physiological Sciences (IUPS), Kesington Adebukunola Adebutu Foundation (KAAF) of Nigeria, The Physiological Society (UK) and the Wellcome Trust. The University of Rwanda provided most of the support facilities – venue, multimedia support, conference materials as well as transport facilities for guests. The choice of Nobleza Hotel as the venue, chosen by the LOC, was quite appropriate.

"African physiology is definitely on the march"

Meeting notes

Epithelia and Membrane Transport Symposium

13 September 2019
Newcastle University London Campus, London, UK

Kim Barrett

University of California, San Diego, USA

Immediately prior to Europhysiology 2018, a talented group of organisers (Debbie Baines, Morag Mansley, Mike Althaus and James Garnett) mounted a one-day Satellite Symposium entitled "Epithelia and Membrane Transport" (EMT) focused on various facets of epithelial biology in a wide range of clinically relevant tissues.

The event had three thematic sessions – wbut thereafter, the vast majority of oral presentations came from students and postdocs hailing from all over Europe, as well as from as far afield as the US and New Zealand.

The day was capped off with a large and lively poster session, with free-flowing discussions doubtless further stimulated by the concurrent drinks reception – indeed, the session ran well past its expected ending time even though it was programmed at the end of a long day of epithelial science. After the meeting, attendees dispersed to enjoy the numerous pubs and eateries in the City area – I particularly appreciated the chance to lead a group to sample Indian fare in Brick Lane, an old stomping ground from my days as a student at UCL.

The various presenters at the meeting focused their research on a variety of target tissues – including the gastrointestinal tract, airways and kidney. And the focus of their research spanned from detailed biophysical analyses in reductionist models to translational studies in patients and even clinical trials. But the common themes of epithelial biology and membrane transport ensured a robust exchange of ideas and technical approaches, with insights from one system clearly being relevant to others.

In this vein, and from a personal perspective, I was particularly excited by the scientific journey of Gabriela Krasteva-Christ and her efforts to define roles for the enigmatic brush cells of the trachea, including sensing and responding to changes in the airway surface microenvironment. The ability of these epithelial cells, which express TRP channels as well as taste receptors, to release acetylcholine and thereby regulate both nerves and immune cells, characterises them as an intriguing hybrid of neuronal and endocrine lineages. Their properties are also clearly analogous to another poorly-understood cell population, the tuft cells of the gut epithelium. Krasteva-Christ's findings and approaches thus have clear implications for gastrointestinal physiology, and likely for the biology of other externally-facing epithelia.

Overall, therefore, this was a rewarding day of epithelial science, especially because of the early career researchers who played such a crucial role in the programme (read on for reflections from two such speakers). The caliber of not only the research, but also the presentations (oral and poster) that reported it, was outstanding. The discipline is greatly served by meetings like this one, when we come together to draw common themes across a variety of systems and thereby gain often unexpected insights.

"My experience at the EMT Satellite Symposium was fantastic," said Alexandra Hochstetler, a first year PhD student at Indiana University–Purdue University Indianapolis.

"I felt honored to have been selected to give a talk on my current research. This was by far the best conference I have been to; the science was top-notch and collaborative, and everyone was amicable and genuinely helpful. I was able to hear relevant science and to make connections that I hope to cultivate over the duration of my PhD and throughout an academic career," she continued.

"While all of the talks were related in some way to my research, hearing André Dagenais of the Montreal Clinical Research Institute speak on the role of scratch injury on barrier function and ion transporters was one of the most interesting. His talk gave me several important clues as to how our TRPV4 ion channel may be behaving in the hydrocephalic state. Overall, this meeting attested to the quality and accessibility of epithelial biology research in Europe," she also said.

Maximillian Woodall, a final year PhD student at St. George's University, London said, "The EMT Satellite Symposium was an excellent opportunity for specialists to share research and early career students to communicate their ideas and establish connections worldwide with speakers from Montreal and New Zealand."

"The symposium was unique to any other meeting I have attended; the quantity of top researchers present in this intimate conference allowed for thorough communication of my research ideas whilst receiving valuable critique and advice. It was nerve-racking presenting my work to an audience containing a number of principal investigators in whose labs I am sure I will be pursuing postdoctoral positions with next year – Rob Tarran, Michael Gray, Margarita Amaral and Yves Berthiaume! However, my methods of using patients' sputum in cell models and implementing droplet digital PCR for quantification of a cell population were well received and discussion around the subject has birthed new ideas for my project," he continued.

A highlight for Maximilian was Guy Moss's talk entitled "Rapid, label-free measurement of airway surface liquid (ASL) and epithelial cell function". "The micro-electrode developed seems to be the Swiss army knife of *in vitro* epithelial model functional analysis. A single system in which one can measure ASL height, cilia beat, pH and mucosity is incredibly desirable and relevant to work in cystic fibrosis treatment and analysis, a field which was well represented at the symposium. With talks ranging from basic science all the way to development of a therapy for pre-clinical trials, the symposium was exciting and relevant for all attendees," he said.

The organisers would like to thank Newcastle University School of Natural and Environmental Sciences, *The Journal of Physiology*, Corning and ThermoFisher Scientific for their sponsorship.

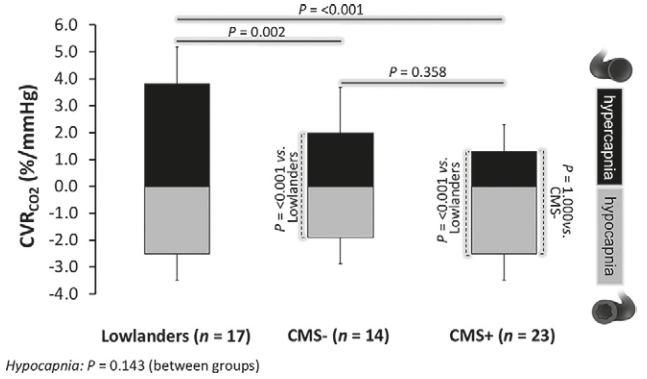
"This was by far the best conference I have been to; the science was top-notch and collaborative, and everyone was amicable and genuinely helpful"

The Journal of Physiology

Exaggerated systemic oxidative-inflammatory-nitrosative stress in chronic mountain sickness is associated with cognitive decline and depression

Bailey DM et al. (5 November 2018)
DOI: 10.1113/JP276898

Individuals at high altitudes who succumb to chronic mountain sickness (CMS), characterised by severe hypoxaemia, are at increased risk of stroke and migraine, with elevated morbidity and mortality. This cross-sectional study of high-altitude dwellers in Bolivia with or without CMS and lowlanders in the UK found elevated markers of oxidative, inflammatory and nitrosative stress in blood and this was further exacerbated in highlanders with CMS. Moreover, the highlanders exhibited some impaired cognitive abilities compared to lowlanders, and those with CMS presented with more depressive symptoms compared to non-CMS and lowlanders.



Values are mean ± SD; CMS–/CMS+, highlanders without/with chronic mountain sickness; *different vs. lowlanders for respective challenge (P < 0.05).

Simulated shift work disrupts maternal circadian rhythms and metabolism, and increases gestation length in sheep

Gatford KL et al. (22 January 2019)
DOI: 10.1113/JP277186

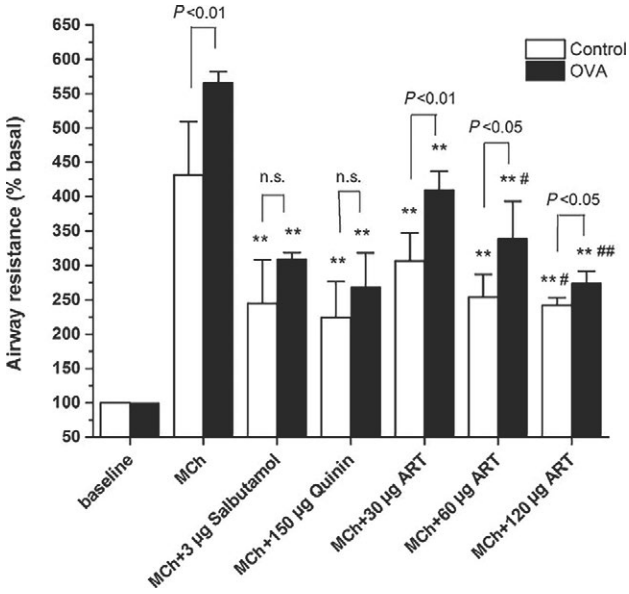
Circadian disruption caused by shift work is associated with impaired metabolic control. Epidemiological studies have reported that working shifts during pregnancy increases the risk of miscarriage, preterm birth, and intrauterine growth restriction, and experimental work has shown impaired metabolic health in offspring of rodents exposed to shift-work-like light schedules during pregnancy. This study investigated the impact of modifying light exposure and feeding times (i.e. simulated shift work [SSW]) on maternal metabolic health and pregnancy outcomes in sheep. SSW phase-shifted hormone and peripheral clock gene rhythms and transiently impaired maternal glucose tolerance in early pregnancy. SSW was also associated with reduced birth weight in singleton lambs and increased gestation length in twin pregnancies. These findings highlight the need to better understand the impact of shift work on maternal health.

Experimental Physiology

Artesunate attenuates airway resistance *in vivo* and relaxes airway smooth muscle cells *in vitro* via bitter taste receptor-dependent calcium signalling

Wang Y et al. (11 December 2018)
DOI: 10.1113/EP086824

Obstructive airway diseases are characterised by increased resistance to airflow. The mainstay of therapeutics in this area has been beta2-adrenergic agonists such as salbutamol, but these are associated with tachyphylaxis and long-term desensitisation. A large number of orphan and unexpected G-protein coupled receptors have been identified in the airway including the bitter taste receptor (TAS2R). Using the TAS2R agonist "artesunate", these researchers demonstrated that stimulation of this receptor led to an increase in intracellular $Ca2^+$ and decreased tension in airway smooth muscle cells *in vitro*, and attenuated airway resistance in a mouse model of experimental asthma, with an efficacy similar to salbutamol. Based on these results, the authors suggest artesunate may be a viable additional option for the treatment of asthma.



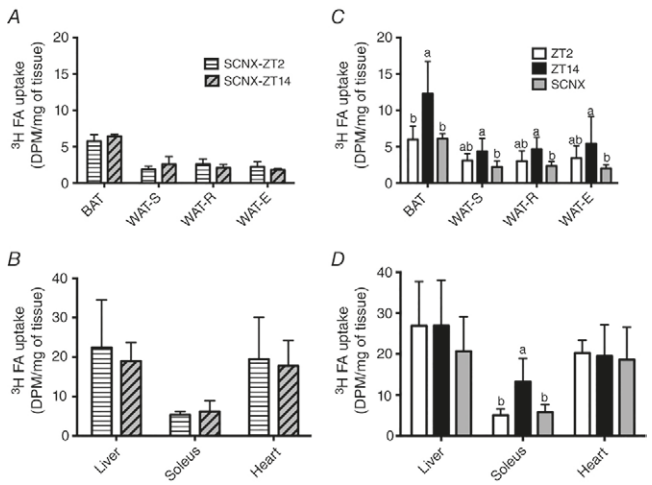
Artesunate attenuates airway resistance *in vivo* and relaxes airway smooth muscle cells *in vitro* via bitter taste receptor-dependent calcium signalling

Effect of artesunate on reduction of airway resistance of normal or OVA-treated mice. Reduction of airway resistance as a percentage of the baseline value (% basal) when treated with various drugs. Normal mice were used as control animals, and data are shown as the means + SD. $n = 5$. $^{**}P < 0.01$ versus corresponding methacholine (MCh) group. #P < 0.05, ##P < 0.01 versus corresponding MCh + 30 µg artesunate (ART) group.

The suprachiasmatic nucleus drives day–night variations in postprandial triglyceride uptake into skeletal muscle and brown adipose tissue

Moran-Ramos S et al. (7 November 2017)
DOI: 10.1113/EP086026

Metabolism has a clear circadian pattern, which is largely controlled by the suprachiasmatic nucleus (SCN) of the hypothalamus. Since metabolic disturbances are a feature of shift workers and those with disrupted circadian rhythm, these researchers tested whether the SCN is an important regulator of circulating triglycerides. After lesioning the SCN in rats, the authors compared how they handled a triglyceride challenge at the beginning of the day and night (the rats' rest and active periods, respectively) compared to non-lesioned controls. With an intact SCN, uptake of triglycerides into skeletal muscle and brown adipose tissue was higher at night compared to day resulting in lower circulating plasma triglyceride concentrations. This diurnal variation was absent in the rats with lesioned SCNs. This work suggests a role for the SCN in the temporal regulation of plasma triglyceride levels and/or differential diurnal responses to a high fat challenge following a fasting period.



Lipid tracer uptake 2 h after the oral fat challenge in intact rats and rats bearing bilateral lesions of the suprachiasmatic nucleus (SCNX)

A. lipid tracer uptake in adipose tissues of SCNX rats at ZT2 and ZT14. *B.* lipid tracer uptake in non-adipose tissues of SCNX rats at ZT2 and ZT14. *C* and *D.* lipid tracer uptake in intact rats at ZT2, ZT14 and SCNX rats at both time points in adipose tissues (*C*) and non-adipose tissues (*D*). Values are means ± SD of n = 3–6 per group. Different letters indicate significant differences between groups, $P < 0.05$. BAT, brown adipose tissue; WAT-S, subcutaneous white adipose tissue; WAT-R, retroperitoneal white adipose tissue; WAT-E, epididymal white adipose tissue; FA, fatty acids.

Smoking during pregnancy increases chemerin expression in neonatal tissue

Reynolds LJ et al. (22 November 2018)
DOI: 10.1113/EP087307

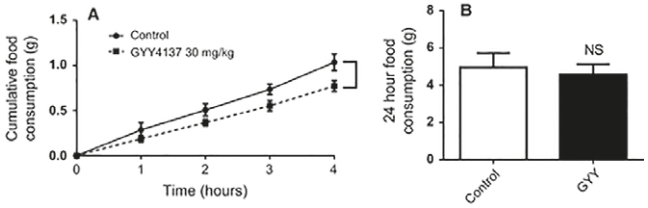
Intrauterine environmental exposures may increase risk of obesity and cardiometabolic diseases in the offspring. Chemerin is an adipokine that regulates adipocyte differentiation, which has previously been shown to be altered by smoking and obesity. These researchers looked at whether differences in chemerin expression and DNA methylation were detectable in neonatal tissues of children born to smokers and non-smokers. Differential gene expression and DNA methylation were observed suggesting chemerin is a candidate adipokine on the causal pathway between smoking during pregnancy and offspring obesity risk.

Physiological Reports

Hydrogen sulfide suppresses ghrelin secretion *in vitro* and delays postprandial ghrelin secretion while reducing appetite in mice

Slade et al. (7 October 2018)
DOI: 10.14814/phy2.13870

Ghrelin plays many important roles in metabolism; therefore, understanding how this hormone is regulated is of key importance in metabolic health and disease. Circulating ghrelin fluctuates around meal times, and ghrelin plays an important role in meal cues and postprandial metabolism. This article explores the effect of modulating levels of the gasotransmitter hydrogen sulfide on ghrelin secretions and appetite in mice. Using a hydrogen sulfide donor molecule, the authors demonstrate *in vitro* and *in vivo* regulation of ghrelin secretion and activity. The authors conclude that modulation of hydrogen sulfide has potential as a therapeutic target in treatment of metabolic diseases.



H_2S reduces short term food consumption in mice

Cumulative food consumption was examined in fasted mice after administration of a H_2S donor up to 4 (A) and 24 h (B). *$P < 0.05$ versus control animals.

A1899, PK-THPP, ML365, and Doxapram inhibit endogenous TASK channels and elicit calcium signalling in carotid body type-1 cells

O'Donohoe PB et al. (04 October 2018)
DOI: 10.14814/phy2.13876

The carotid body provides vital information concerning blood gases and pH to both respiratory and cardiovascular control centres in the brain. The ion channel complement that underpins the coupling of chemosensing to excitation in type-1 cells is the focus of this study. Using isolated rat type-1 cells and compounds with selectivity for TASK and BKCa channels in electrophysiology and Ca^{2+} imaging experiments, the authors add more weight to the evidence supporting a role for TASK 1/3 channels in chemosensing in type-1 cells. That selective TASK channel inhibitors could provide clinical use as respiratory stimulants with particular reference to overcoming the respiratory depression that accompanies the use of a number of general anaesthetics and analgesics is promoted.

"Science history holds much more than engaging anecdotes with which to embellish the introductions to our manuscripts"

My historical dive

The illuminating nature of science history

Jose L Vega

Department of Neuroscience and Stroke, Novant Health, Forsyth Medical Center, North Carolina, USA

A few years ago, after a stressful day at work, I found myself glued to a television news segment about freediving, which inspired a personal journey from the ocean, through historical archives, and into the heart of a fascinating medical enigma. The news segment, titled *Death-defying free dives*, featured a man who could plunge over 100 metres into the ocean and return to the surface, unassisted, *on a single breath of air*. As a neurologist who had often witnessed the devastating effects of even brief episodes of respiratory arrest on the brain, I wondered how he managed to remain unharmed by his extreme diving. But what really puzzled and even captivated me was the paradoxical tranquility he emanated during his risky dives.

Later that year I decided to enroll in a recreational weekend-long freediving course in which I learned about the mammalian dive response (MDR), a collection of oxygen-conserving reflexes that allows aquatic air-breathing mammals, like dolphins and whales, to remain submerged for extended periods of time. These reflexes 1) slow down the heart rate (i.e. diving bradycardia), 2) shunt a large portion of the body's blood volume towards the lungs (i.e. the blood shift), and 3) release splenic red blood cells into the systemic circulation (i.e. the splenic contraction) (Panneton, 2013). Although I found this to be a fascinating biological response, I questioned why it was relevant to the course; after all, humans are not aquatic mammals. But then the instructor unleashed a bewildering revelation: humans also possess this response. I was fascinated, yet alarmed. This was the most robust set of neurological reflexes I knew, and yet I had stumbled upon it fortuitously at a recreational freediving course. *Why wasn't the MDR part of the formal medical curriculum?*

The following day, we practised the actual mechanics of freediving at a local Olympic diving pool. Unlike the other students, who were excited to freedive, I was mostly excited to experiment with my newly discovered MDR. During one of my dives I stayed at the bottom of the pool long enough to test my diving bradycardia reflex by aligning my index and middle fingers over my radial artery. Within thirty seconds, I witnessed my pulse dwindle from 60 beats per minute to 12. I then felt a mixture of fear and euphoria; I had only seen such dismally low pulses in unconscious patients going into cardiac arrest. Yet, there I was, enwrapped by the tranquility of submersion, counting from one to five between heart beats.

After the course was over, I adopted freediving as a hobby, and decided to learn as much as I could about the human MDR. Unfortunately, this simple goal turned out to be much more difficult than I expected because, compared with other species, the number of human MDR studies was minuscule. The majority of them pertained

"This was the most robust set of neurological reflexes I knew, and yet I had stumbled upon it fortuitously at a recreational freediving course"

to the exercise physiology of professional freediving, but some–written in the second half of the twentieth century–exclusively addressed the therapeutic implications of "the diving reflex," (Wildenthal *et al.*, 1975), as diving bradycardia is known to physicians. This curious treatment strategy involved controlling frantic heart rhythms by immersing patients' faces into buckets full of water. While, its impractical nature led it to be dropped from routine medical practice, the diving reflex's fascinating physiology earned it a permanent place in the medical curriculum. However, it did so in isolation of the rest of its parent response, the MDR. Since then, aspiring physicians are taught about the diving reflex, but not about the MDR.

As I continued to scour articles for human MDR literature, I noticed that their introductions occasionally included historical morsels about Paul Bert (1833–1886) being the "father" of diving bradycardia (Harding *et al.*, 1965). One day, out of sheer serendipity, I picked up an article that discussed the experimental circumstances of his discovery. Bert had set out to compare the survival times of ducks and chickens subjected to forced water immersion (i.e. drowning). About a duck that survived longer than 16 minutes, he wrote: "... the heart, which was beating 100 times per minute before immersion now only gives 14 regular and deep beats" (Foster *et al.*, 1986). This description would later be uniformly embraced as the discovery of diving bradycardia, and as the first evidence of the MDR. But as I read it, I wondered how it illustrated the reflex given that the endpoint of the experiment was death. To show that his observation was a reflex, Bert needed to demonstrate a normalisation of the heart rate in ducks removed from the water while still alive. Without such a demonstration, the duck's slowing heart rate could simply reflect its natural progression towards death. Curious, I enlisted a French-speaking colleague to review Bert's original publication and learned that none of his ducks survived. More importantly, his celebrated quote turned out to be a singular remark, detached from his methods and conclusions (Bert, 1870).

The following year, while freediving in Dahab, I surfaced from a dive feeling uncharacteristically tired and decided to rest for the remainder of the day. Walking back to my hotel, I also felt congested and short of breath, as if I had suddenly developed a severe cold. My symptoms reminded me of Nick Mevoli, a fellow freediver who had died in 2013 while attempting to set a U.S. record in the Bahamas. Nick's was the first competition-related death in the entire history of the sport. His autopsy revealed a frothy residue and frank blood inside his alveoli, which suggested that high pressure within the pulmonary blood vessels had caused him to drown in his own fluids and blood. Suspecting I could be suffering from a mild version of such a deadly process, I decided to suspend freediving for a few weeks and spend my remaining time in Dahab relaxing, reading, and enjoying the awe-inspiring scenery.

One afternoon, while contemplating the Arabian Desert across the Red Sea from my favourite café, a question suddenly popped into my head: if Bert was not the father of diving bradycardia, then who was? I figured that the best place to start looking for this answer was in Bert's own background literature. Three espressos and one bottle of water later, I had read through a doctoral dissertation originally published in 1786 titled "The connection of life with respiration," (Goodwyn, 1788), which was cited in Bert's original text (Bert, 1870). This ancient document was freely available on the Internet and contained a clear and complete description of diving bradycardia (Goodwyn, 1788). In it, the author – Edmund Goodwyn (1756–1832) – showed for the first time that forced water immersion, and other forms of suffocation, caused death by preventing dephlogisticated air (i.e. oxygen) from entering the bloodstream (Vega, 2018a). One experiment described the gradual deceleration of a toad's heart rate during forced immersion, until it came to a halt. Thinking the toad had died, he removed it from the water, where moments later it took a few breaths, normalised its heart rate, and began walking about "without any expressions of uneasiness." Goodwyn then repeated the experiment in the same unfortunate toad, and in other animals, noting that "in all examples the contractions of the heart were diminished in frequency" (Goodwyn, 1788). Thus, my serpentine journey through the MDR literature had amounted to a diving bradycardia paternity test which pointed to Goodwyn as the reflex's new father (Vega, 2017).

When I finally arrived home from my trip, a small pile of miscellaneous envelopes and medical publications awaited in my mailbox. One of the journals in it contained an article about an unfamiliar neurologic mystery: the sudden and unexpected deaths of epileptic patients (SUDEP) (Devinsky e*t al.*, 2016).

Up until then, neurologists had considered seizure-related deaths to be rare, but a much higher frequency of such deaths was beginning to surface in the epidemiological literature, especially among patients who suffered from uncontrolled convulsive seizures. The typical SUDEP case involved a young and healthy victim who convulsed during her sleep, and was found dead in the morning, in bed. Witnessed cases invariably involved one or more convulsions during which victims ceased to breathe for prolonged periods of time before their hearts slowed to a halt. Mysteriously, autopsy reports were normal, with one salient exception: more often than not, their lungs demonstrated acute pulmonary oedema and pulmonary haemorrhage (Terrence *et al.*, 1981).

Still influenced by my recent experiences with freediving, I could not help but wonder whether these autopsy findings might stem from the same process that took Nick Mevoli. After all, both Nick and SUDEP victims ceased to breathe for prolonged periods of time before they died: Nick while diving, and SUDEP victims while convulsing. I quickly realised that these physiological conditions might relate back to the three reflexes of the MDR, and to the blood shift in particular, as excess blood in the lungs could increase the pressure inside the pulmonary blood vessels and cause pulmonary oedema and pulmonary haemorrhage. I tried to discuss this notion with other neurologists but I invariably lost their attention at the word "pulmonary". After some time and a great deal of thought I decided to propose a mechanistic hypothesis to investigate a possible role for the MDR in SUDEP (Vega, 2018b).

The outcome of my retrospective reading exemplifies a notable, yet rarely discussed aspect of science history. Goodwyn's thesis remained in obscurity for almost a century before it finally helped Bert advance the very line of research that gave us the MDR. In turn, the human side of this robust physiological response has escaped the attention of physicians for decades, despite its potential role in medical conditions like SUDEP. It seems, therefore, that the history of science holds much more than engaging anecdotes with which to embellish the introductions to our manuscripts. At its very core it holds illuminating concepts that can further our investigational pursuits and, with a little luck, provide the missing pieces to our scientific puzzles.

References

Bert P (1870). *Leçons sur la physiologie comparée de la respiration*. Paris : J.B. Baillière; Londres: Hippolyte Baillière.

Devinsky O *et al.* (2016). Sudden unexpected death in epilepsy: epidemiology, mechanisms, and prevention. *Lancet Neurol* **15**, 1075–1088.

Foster NK *et al.* (1986). Leukocytosis of exercise: role of cardiac output and catecholamines. *J Appl Physiol (1985)* **61**, 2218–2223.

Goodwyn E (1788). *The connexion of life with respiration,* London, T. Spillsbury.

Harding PE *et al.* (1965). Diving bradycardia in man. *J Physiol* **181**, 401–409.

Panneton WM (2013). The mammalian diving response: an enigmatic reflex to preserve life? *Physiology (Bethesda)* **28**, 284–297.

Terrence CF *et al.* (1981). Neurogenic pulmonary edema in unexpected, unexplained death of epileptic patients. *Ann Neurol* **9**, 458–464.

Vega JL (2017). Edmund Goodwyn and the first description of diving bradycardia. *J Appl Physiol (1985)* **123,** 275–277.

Vega JL (2018a). The Connection of Life with Respiration: Edmund Goodwyn's unexplored treasure of cardiopulmonary physiology. *J Appl Physiol (1985)* **125**, 1128–1130.

Vega JL (2018b). Ictal mammalian dive response: A likely cause of sudden unexpected death in epilepsy. *Front Neurol* **9**, 677.

Wildenthal K *et al.* (1975). The diving reflex used to treat paroxysmal atrial tachycardia. *Lancet* **1**, 12–14.

An N of 1

When science meets sports

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As an undergraduate biochemistry major and cross-country runner I wanted to get faster. I had heard about altitude training as something that professional runners did and wondered if a summer at altitude would speed my improvement. Luckily, at the University of California, Davis (UC Davis) we had William Adams, an expert on the effects of altitude training on performance. I asked Adams: "Should I go to altitude for the summer to get better?" His response? "You should take my class on environmental effects on human performance and figure it out for yourself!" So, like any easily persuaded undergrad I did and it changed my academic and athletic trajectory.

Scientific beginnings

At UC Davis I majored in exercise biology, studying exercise physiology alongside biochemistry, molecular biology, genetics, and organic chemistry. I thought of it as sports science with rigor. My roommate, Steve Laurie (who now works at NASA as a PhD physiologist) and I eventually did go to altitude to train, and with the help of one of our Professors we performed "case studies" on ourselves to look at how we adapted to altitude training over the summer. Turns out that dedicating yourself to training all summer is great for improvement, with or without the altitude. After that summer, my interest in sports science was piqued. Back at school, I worked in a lab studying skeletal muscle physiology, but using molecular biology techniques. Funding to do straight sports science was relatively scarce compared to funding for health sciences and basic biology, so I applied to a graduate school where researchers study how exercise improves health. I ended up in the lab of Frank Booth at the University of Missouri where we studied the molecular and physiological changes that occur in response to short periods of physical inactivity. Our goal was to determine the initial physiological changes in response to physical inactivity in order to identify the underlying mechanisms which link physical inactivity to 30 plus different chronic diseases (Booth *et al.*, 2012).

After graduating, I continued studying exercise as it pertains to health during my first post-doctoral position at the Centre for Inflammation and Metabolism in the laboratory of Bente Klarlund Pedersen in Copenhagen, Denmark. We published several papers on the role of microRNAs in health and disease, and I developed a muscle cell culture model of exercise. On the side we had several studies more related to sports science for fun. In the first we conducted pre- and post-testing on a small cohort of runners who ran a marathon a day for seven consecutive days. One hypothesis we had was that excessive exercise might accelerate ageing. So we looked at markers of ageing such as telomere length, telomerase activity and different components of the shelterin complex, the

Undergraduate students at The College of Idaho completing metabolic testing.

protein cap that protects telomeres from damage. The runners had seemingly no detrimental effects on telomere length or telomerase activity, and actually increased the amount of some proteins associated with and a part of the shelterin complex in either skeletal muscle or peripheral blood mononuclear cells (Laye *et al.*, 2012).

A second research question we attempted to untangle was the relationship between VO_2 max and health. If you look at a large population, higher VO_2 max is associated with a lower risk for many chronic diseases and even mortality. However, VO_2 max is also subject to genetic influences, with some people born with a high VO_2 max, others not, and some born with the ability to dramatically improve their VO_2 max, others not so much. We wanted to know whether VO_2 max and health could be uncoupled from each other. The experiment we did was a case-controlled experimental design which matched long-term marathon runners (5+ years, 10 marathons) with healthy, sedentary, non-runners of similar age, BMI and gender. Because of the intrinsic variation in VO_2 max, a third of the runner–non-runner pairs actually had similar VO_2 max values despite one of them running multiple marathons a year. When we looked at health and metabolic parameters we nevertheless found that the runners were more healthy with better blood lipids, body composition, and oxidative capacity in their muscles (Laye *et al.*, 2015). Essentially, your VO_2 max is not your health destiny, but how much physical activity you do might be.

My second postdoctoral position took me further away from the sports science area, as I worked at The Buck Center for Research on Aging (Novato, CA). There we tried to understand how dietary restriction and specific metabolites increased longevity in *Drosophila Melanogaster*. The science was interesting and challenging but as I continued to compete in endurance events and ventured into ultramarathons (any distance over 26.2 miles) it felt less connected to my own interests and was certainly more difficult to apply.

Putting the science to practice as an N = 1

Each athlete is their own experiment. You can't control for all the variables nor definitively prove that any specific training is "best". Instead, as an athlete, coach and scientist I try to weigh the scientific evidence and current coaching best practices against time constraints, potential benefits, and risks for a specific athlete. My goal is always to apply the most effective training stimulus given the situation. One example is how I used the existing science to support my own training for my first mountain ultra-race, 100 kilometres long with 6,000 metres of climbing and descent at altitude. While many athletes may look at those details and worry about the climbing, I was worried about all the descending and muscle damaging eccentric muscle contractions (i.e. muscle lengthening as it contracts) that occur when running downhill, especially since I was living in Copenhagen, a flat city, at the time. The science on eccentric exercise says that after each bout of muscle-damaging eccentric work it will take 2–3 weeks to adapt, but that the same amount of eccentric work the next time will elicit far less damage and lead to significant increases in muscle strength (Vogt and Hoppeler, 2014). Several months prior to the race I used the treadmill in the lab and set it to a -5% grade rather than up; 40 km later my quadriceps were destroyed (I wish I had an electron micrograph of the sarcomeres!) and I was sore for 2 weeks. A similar workout after a few weeks of normal running left me sore for 4–5 days, and then a third eccentric workout for only about 2 days. From 2 weeks to 2 days my quadriceps had adapted. Weeks later I completed the race and finished a respectable 25th given I lived at sea level in a very flat city.

"Several months prior to the race I used the treadmill in the lab and set it to a -5% grade rather than up; 40 km later my quadriceps were destroyed..."

The author competing in 2013 at the Ultraks Marathon, a 46 km trail race with 3,600 metres of climbing and descent, near the Matterhorn mountain in Zermatt, Switzerland.

When I prepared for my first 100 mile race I used a similar approach to training. This race was relatively flat, but I knew (and was told by other runners) that there was no way to mimic the eccentric demands of that distance by training on flat terrain alone. So I would climb our local mountain in the Bay Area and then bomb the downhills on the road to damage and then allow compensatory adaptations which hopefully would allow the muscles to complete 100 miles of running. I also used a periodised nutrition approach to maximise both fat and carbohydrate use. Some runs would have the goal of increasing my ability to use fat as energy and I'd take in no calories, while others I would practise taking in carbohydrates in the form of gels and food at 60–90 grams an hour. I managed to eat consistently throughout the race with good energy and strong legs the entire distance. My old roommate Steve paced me the last 20 miles as I ended up winning the race in 13 hours and 17 minutes, just under 8 minutes per mile for the 100-mile distance.

As a coach I've worked to apply and adapt the existing and new science. The simple principles of specificity, overload, and individuality guide my approach. For instance, many of these ultra-races can take place in hot conditions, with huge amounts of vertical gains, at significant altitude. I regularly prescribe 20–30 minutes of sauna time immediately after working out for my athletes to ensure they are heat adapted. The use of the sauna to transiently raise core temperature improves the body's ability to deal with running in hot conditions. My runners have not had significant problems with the heat while racing even when they train in the typically mild climate of San Francisco. Another challenge is for athletes who train at sea level and want to compete at altitude, but are unable to spend the time at altitude needed for proper adaptation. Sometimes you can't outperform the physiological challenges. I advise them to arrive as close to the race day as possible, and set lower goals than typical given the detrimental effects on performance. My athletes are not professional runners, and so training plans need to be individualised around their lives. When possible, I will "stack" workouts back to back to really stress the athlete when they have time to train, but then follow that up with a period of rest to coincide with the times when life is too busy for training. Sometimes this is two big runs on the weekend or a hard workout in the evening followed by a mellow, easier run first thing in the morning. Overload training stimulus when you can and build in rest around their day-to-day life.

From time to time I ignore the science to my own peril. For instance, a few years ago I fell and ended up damaging some knee cartilage and developing bone on bone pain that prevented me from training fully. I could still run, but instead of running 70 plus miles a week, I was reduced to under 30 miles a week. Nothing I tried could to get me back to normal training, so I looked to the science for some guidance on whether surgery might be an effective option for me. After reading the literature, I learned that most of the knee surgery techniques to restore or replace cartilage have very low long-term success rates and my particular surgery was inferior compared to others (Campbell *et al.*, 2016). Still, I justified surgery because my lesion was small and I was certain I could improve my outcome with added passive knee movement and supplements which had marginal efficacy. Over a year later I've worked back to running about 30 miles a week and I still have occasional knee pain along the same magnitude as prior to the surgery. Unfortunately, I was not special and I did not seem to beat the odds and existing science.

From scientist runner to teacher coach

Eventually, I decided to trade in the laboratory for the classroom and trade my own running pursuits for those of others. In autumn 2015, I started as an Assistant Professor in the Department of Health and Human Performance at The College of Idaho, a small liberal arts school (enrollment of approximately 1,000) in Caldwell, Idaho. While my primary job is to teach, I still have research goals. With limited time and resources, the type of research is different and I'm given lots of autonomy to seek out my own interests. Naturally, this freedom takes me back to running-related topics. For instance, I'm interested in whether I can reduce the high prevalence of gastrointestinal issues of ultra-runners during exercise. My current study is characterising the microbiome of ultra-runners prior to and after 100-mile races to try and identify microbial compositions that are associated with gastrointestinal issues. However, what's more important, is what my students want to research. These students are excited to do small research projects related to their own lives, and I get excited guiding them through the research project. The primary goal is not getting published or receiving grants but to show them how much fun, rewarding and sometimes hard research really is. Hopefully I provide my students with the same experience I had as an undergraduate.

I also volunteer coach and run with a local running group, The Boise Billies. Each week I write a short newsletter which includes a scientific study related to running or health. I also write a monthly column for *UltraRunning* magazine on the science of running. My goal is always to provide easy recommendations or takeaways on how to apply (or not apply) the research of the week. Writing about research to the general public helps me stay connected to the world of research and improve my ability to communicate how research might be applied.

Evidence-based performance science

Using scientific literature for sports science is a little like evidence-based medicine. In theory, these are concepts in which there is very little to disagree with. Base training or medical decisions on peer-reviewed science. It's a very simple concept and yet incredibly complex when you consider the details. Age, gender, genetics and countless confounding variables and conditions all make it extremely unlikely to find peer-reviewed science that applies to a specific athletes' or patients' unique situation. Coaches and practitioners have to use evidence combined with experience and sound judgement.

An added difficulty is that many training studies are done on sedentary subjects. For a group with low physiological functioning, almost any intervention improves performance. Conversely, highly trained elite athletes are near the top of physiological functioning and already do the most effective training protocols. For elite athletes, it is far more difficult to find an intervention to improve performance, even when just fractions of a percentage improvement may separate the podium at the elite level. Just as it's difficult for evidence-based medicine to tell us much about rare diseases of outlier patients, it's difficult for sports science to tell us much about improving the already stellar performance of elite athletes. Those that coach or compete at the elite level must be even more skeptical than most, not ruling out all data in elite athletes while not believing everything that improves performance of previously sedentary individuals. It's where the art meets the science at times.

For 10 years as an active researcher I spent a majority of my time doing things that were at best peripherally related to running and coaching. However, the skills I developed as a researcher – reading carefully, thoughtfully, skeptically, considering all of the confounding factors, isolating variables, and interpreting results in the appropriate context – were applied to every aspect of my training and coaching. Those are truly transferable skills, to whatever decisions and passions you have in life. I'm certainly grateful to all my fellow scientists, runners, and coaches who have taught me and continue to teach me how to create the best evidence-based training programs for an N of one.

References

Booth FW *et al* (2012). Lack of exercise Is a major cause of chronic diseases. *Compr Physiol* **2**(2), 1143–1211.

Campbell AB *et al.* (2016). Return to Sport After Articular Cartilage Repair in Athletes' Knees: A Systematic Review. *Arthroscopy: The Journal of Arthroscopic & Related Surgery* **32**(4), 651–668.

Laye MJ *et al.* (2015). Physical activity enhances metabolic fitness independently of cardiorespiratory fitness in marathon runners. *Disease markers* **2015**, 806418.

Laye MJ *et al.* (2012). 'Increased shelterin mRNA expression in peripheral blood mononuclear cells and skeletal muscle following an ultra-long-distance running event. *Journal of Applied Physiology* **112**(5), 773–781.

Vogt M, Hoppeler HH (2014). Eccentric exercise: mechanisms and effects when used as training regime or training adjunct. *Journal of Applied Physiology (Bethesda, Md. : 1985)* **116**(11), 1446-1454.

The sodium hypothesis of action potential generation

A classic updated or an act of electrophysiological sacrilege?

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In 1972, Stephen Kuffler asserted students should consult original sources (Kuffler, 1972), a viewpoint with which I concur. By the time experimental information has reached textbooks, the inevitable dilution, interpretation and editing may obscure the researchers' original intentions. For neuroscience students interested in membrane excitability there is a rich history of such information, a considerable amount of which is freely available via *The Journal of Physiology*. However, there is one major impediment that stands in the way of students' appreciation of these papers: the conventions used to present and describe data differ radically from those used today, which can be confusing even for the experienced researcher.

In an effort to surmount this I have dared to update one of the founding classics of electrophysiology, namely "The effect of sodium ions on the electrical activity of the giant axon of the squid" (Hodgkin and Katz, 1949). The difficulty in reading this paper stems from Hodgkin and Katz using the accepted norm in physics that an inward movement of positive charge is depicted as an upward current deflection, with the resulting change in voltage depicted as a downward deflection (Patton, 1982). Hodgkin and Katz treated the resting membrane potential as a positive quantity and the action potential (AP) as a negative deflection; thus, the action potential was displayed as an upward deflection with the y-axis defined as negative volts (–V).

Modern practice deviates from this convention, showing inward current as a downward deflection and membrane potential as "positive-up, negative-down" (Patton, 1982). The modern convention is illustrated in Fig. 1, where an electrode is shown inserted into a cell submerged in a bath, the amplifier is grounded (0 mV), and a resting membrane potential of about -70 mV is recorded, leading to the classic physiology teacher's formulation where, if the membrane potential (Em) moves towards 0 mV this is considered a depolarisation (a decrease in polarisation), a move towards the resting potential is considered a repolarisation, and a move to a potential more negative than the resting potential is considered a hyperpolarisation (an increase in polarisation; Hille, 2001).

The convention used by Hodgkin and Katz is based upon a reference system where changes in Em were considered relative to rest, with increases or decreases, respectively, being equivalent to hyperpolarisation or depolarisation, respectively. This was due to technical considerations, since the junction potentials created by switching from seawater to the test solutions made accurate measurements of the potential difference across the axon membrane unreliable. Indeed, Hodgkin and Katz spent a considerable amount of the paper discussing junction potentials and

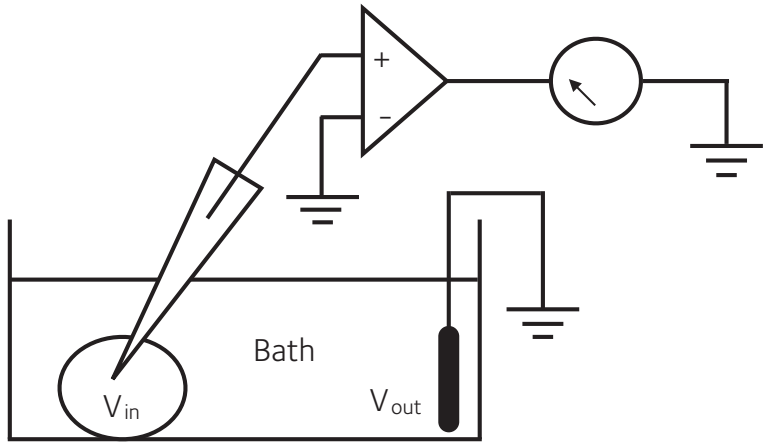

Figure 1. The modern convention in use when referring to the membrane potential (Em) recorded using intracellular recording techniques. The amplifier is connected to ground which is 0 mV. The membrane potential (Em) is defined as equal to $V_{in} - V_{out}$ (ground) and routinely has a value of about -70 mV.

"Reading the complete paper evokes an unmistakable sense of place and time – a time when the unfolding of a scientific story included leisurely discourses"

their effects on Em. A source of confusion is that the manner in which Hodgkin and Katz displayed the Em was inconsistent. Although resting potential is shown as +45 mV in Fig. 4 of the original paper, in Fig. 3 it is shown as 0 mV with the action potential shown as a positive voltage deflection, and in Fig. 5 both the resting potential and the action potential are shown as positive values. This confusion is compounded when deviations of Em from rest are variously described as "depression, decrease, diminution, reduce, lowered, raising, larger", each description being context-dependent. In addition, some of the terminology in the paper is antiquated e.g. the "positive phase" refers to the after hyperpolarisation (AHP), and "membrane reversal" refers to the degree by which the action potential exceeds 0 mV, i.e. overshoot, terms that are now redundant. The differences between the historic and modern convention are illustrated in Fig. 2.

The history of the paper's origin is captivatingly described in detail elsewhere (McComas, 2011), but may be briefly summarised as follows. The dogmatic view, proposed by Bernstein at the beginning of the 20th century (Hille, 2001), was that the resting neuronal membrane is predominantly permeable to K^+, but this selective permeability collapses during an action potential. This theory predicted that Em should approach 0 mV at the peak of an action potential. However, the first intracellularly recorded action potential, obtained from squid giant axon (Hodgkin and Huxley, 1939), famously showed a peak that exceeded 0 mV and approached E_{Na}. It is often forgotten that Hodgkin and Huxley made no reference to E_{Na} in the original paper, or indeed in a later more extended account (Hodgkin and Huxley, 1945), but instead provided four possible explanations for the membrane reversal, none of which mentioned Na^+ permeability.

Their reluctance to make the obvious connection between the action potential and E_{Na} lay in a paper published by Curtis and Cole in 1942, in which the authors described action potentials whose peaks occurred at potentials more positive than E_{Na} and, more worryingly, showed that removal of Na^+ from the bathing solution did not significantly affect the AP amplitude (Curtis and Cole, 1942). Despite this, Bernard Katz suspected an important role for Na^+ in action potential generation, and showed in 1947 that decreasing bathing [Na^+] decreased the conduction velocity in extracellularly recorded action potentials in single fibres of the crab *Carcinus* (Katz, 1947). Hodgkin was subsequently joined by Katz at Plymouth in the summer of 1947 (Huxley was busy preparing for his wedding), where they quickly and satisfactorily resolved the issue by recording the Em with intracellular microelectrodes in squid giant axon exposed to various dilutions of seawater, such that the data was acquired by September 1947 and submitted for publication in January 1948.

Although the main interest in the paper was the effect of [Na^+] on the action potential, the effect of [K^+] on the resting potential was of equivalent importance although of a less dramatic nature. The main findings of the paper were:

- AP amplitude was dependent upon [Na^+]
- Rate of AP rise was dependent upon [Na^+]
- Conduction velocity decreased in low [Na^+]
- Rate of AP fall was independent of [Na^+]
- Resting Em was dependent upon [K^+]
- After hyperpolarisation amplitude was dependent upon [K^+]
- The permeability changes underlying the AP could be quantified using the Goldman–Hodgkin–Katz equation, an extension of the Nernst equation, and supported a transient increase in Na^+ permeability underlying the AP

From an historical viewpoint, the paper is the foundation from which flowed the subsequent papers that gained Hodgkin and Huxley the Nobel Prize in 1963. In hindsight, the paper is not above criticism. It is rather verbose and repetitive by modern standards, and could easily be condensed to one third of its original length without losing any impact. The authors are circumspect in describing the now obvious relationship between Em and reversal potentials for Na^+ and K^+, and only in the discussion do they tentatively speculate on this subject, likely due to uncertainties of the values of the internal ion concentrations. For this reason, in appropriate figures, I have judiciously added reversal potentials for K^+ and Na^+ for illumination. It is notable that the resting membrane potential recorded by Hodgkin and Katz was depolarised compared to values recorded later with less intrusive methods (-45 mV compared to -70 mV; in Chang, 1986). This resulted in the resting potential being between 40 and 50 mV more depolarised than E_K, at odds with the central tenet proposed by Bernstein, and expounded by Hodgkin and Katz, of the membrane being selectively permeable to K^+ at rest.

Reading the complete paper evokes an unmistakable sense of place and time – a time when the unfolding of a scientific story included leisurely discourses. The paper is without doubt a classic, my personal

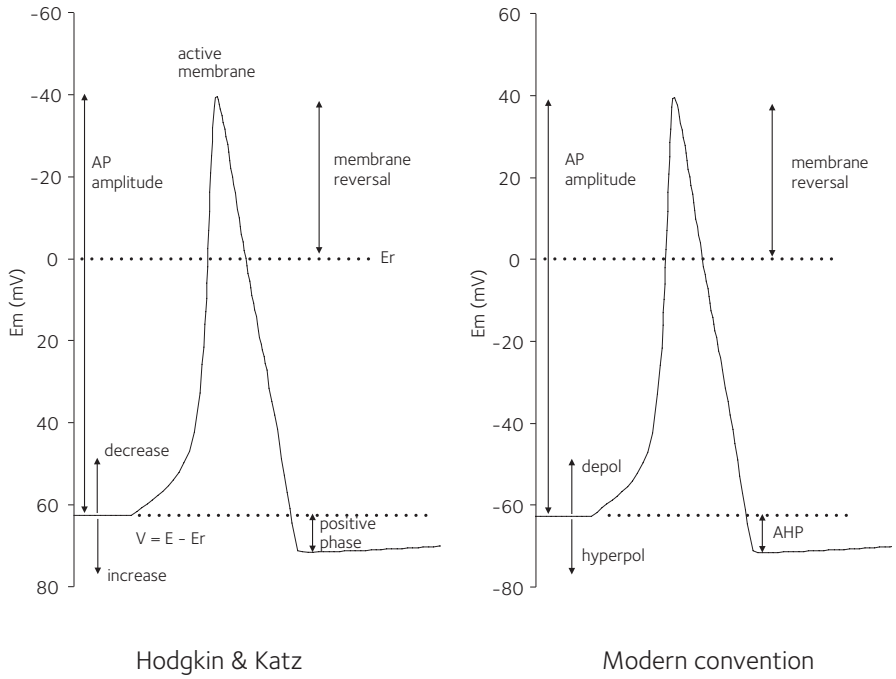

Figure 2. A comparison between the conventions used by Hodgkin & Katz and the convention currently used. In the historic convention the resting membrane potential is a positive voltage and the action potential is a negative deflection. However, the AP is shown as an upward deflection, thus, the voltage scale is –V (mV). An increase in resting potential equates to a membrane hyperpolarisation, decrease meaning depolarisation, the positive phase equates to the after hyperpolarisation and the membrane reversal refers to the degree by which the membrane potential exceeds 0 mV.

favourite in the entire electrophysiology canon. Updating it has been a labour of love, not a chore (though some might consider it more of a sacrilege!). The logical sequence of Hodgkin and Katz's figures is masterly at revealing critical data that is described later. For example, a glance at Fig. 3 reveals that the AP falls on exposure to Na^+-free seawater. However, hiding in plain sight is the fact that the falling phase of the AP, the AHP and the resting potential are all relatively unaffected by changes in external Na^+. In Fig. 8, one of the most reproduced images in all of neuroscience, the AP amplitude is shown to increase in axons exposed to supra-physiological concentrations of Na^+ – simple, brilliant and entirely convincing evidence that the peak amplitude of the AP follows E_{Na}.

I will not list all the changes I have made to the paper, but will only state that they comply with modern convention and should be readily understood by all students raised on current textbooks. I have inserted equations that illuminate calculations in the text, included only averaged data in the Tables, added explanatory columns in Table 4 relating to ratios of $[Na^+]$ relative to seawater, and redrawn graphs where appropriate. A thorough understanding of the practical implementation of the Nernst equation is recommended for optimal appreciation of the paper (Sawyer *et al.*, 2017). I have omitted the Appendix on the derivation of the equations, as this does not require extensive conversion and is of limited interest to the majority of undergraduate students.

In conclusion, the classic electrophysiology literature of the 1940s and 1950s is at risk of becoming a museum piece; admired and respected, but ultimately inaccessible, as the contemporary scientists age and no longer pass their knowledge on to succeeding generations of students. It would be a terrible shame if this were to occur, but hopefully this article may tempt qualified and dedicated individuals, with sufficient spare time, to proceed with equivalent updates of their favourite classic papers.

"Hopefully this article may tempt qualified and dedicated individuals, with sufficient spare time, to proceed with equivalent updates of their favourite classic papers"

References

Chang DC (1986). Is the K permeability of the resting membrane controlled by the excitable K channel? *Biophysical Journal* **50**(6), p.1095–1100.

Curtis HJ, Cole KS (1942). Membrane resting and action potentials from the squid giant axon. *Journal of Cellular and Comparative Physiology* **19**, 135–144.

Hille B (2001). *Ion Channels of Excitable Membranes*. Sunderland: Sinauer Associates Inc.

Hodgkin AL, Huxley A (1939). Action potentials recorded from inside a nerve fibre. *Nature* **144**, 710–711.

Hodgkin AL, Huxley A (1945). Resting and action potentials in single nerve fibres. *J Physiol* **104**, 176–195.

Hodgkin AL, Katz B (1949). The effect of sodium ions on the electrical activity of the giant axon of the squid. *J Physiol* **108**, 37–77.

Katz B (1947). The effect of electrolyte deficiency on the rate of conduction in a single nerve fibre. *J Physiol* **106**, 411–417.

Kuffler SW (1972). Introduction. In: *Cellular Neurophysiology*, ed. Cooke I & Likin M, pp. 1–3. Holt, Reinhart & Winston, Inc., New York.

McComas AJ (2011). *Galvani's Spark*. Oxford: Oxford University Press.

Patton HD (1982). Special properties of nerve trunks and tracts. In *Physiology and Biophysics: IV Excitable Tissues and Reflex Control of Muscle*, ed. Ruch T & Patton H, pp. 101–127. W.B. Saunders Company, Philadelphia.

Sawyer JER *et al.* (2017). The critical role of logarithmic transformation in Nernstian equilibrium potential calculations. *Adv Physiol Edu* **41**, 231–238.

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Medical communications in a changing world

Interesting times ahead

Krish Kapoor

Bedrock Healthcare Communications

Medical communications ("medcomms") agencies supply the pharmaceutical industry ("pharma") with communications and marketing materials to help these companies better connect with patients and healthcare professionals. With trends for international harmonisation and consensus competing with resurgent nationalism, along with falling trust in the industry and the rise of emerging markets, the robust pharmaceutical industry is likely to face significant challenges in coming years. How will pharma and medcomms weather these changes, and what will medcomms look like in the years to come?

Performance pressure: pharma and medcomms today

In recent decades, biomedical science and the pharmaceutical industry in particular have made great strides in addressing a wide range of diseases, many of which were once terminal. Formerly untreatable diseases such as HIV, haemophilia or rheumatoid arthritis are now chronic conditions, managed through long-term use of medication, along with monitoring and support from healthcare professionals. During these transformational decades, healthcare has developed into an incredibly competitive and noisy market. With the low-hanging fruit of drug discovery already picked, pharmaceutical companies are finding the return on investment from their research and development is falling, increasing pressure to invest in only the most promising products, and to ensure that everything possible is done to ensure a drug's success, even before launch. Accordingly, pharmaceutical companies spend a significant and ever-increasing proportion of their revenue on sales and marketing activities, often more than is spent on R&D (Fig. 1) (BacterioScan, 2016; Dobrow, 2016).

The medcomms industry offers marketing consultancy services to pharmaceutical and healthcare companies, advising them on how best to deliver accessible information about medicines and their use, and supporting the formulation and delivery of promotional and educational campaigns. While this includes pharmaceutical advertising, it is much broader including topics such as disease awareness, and unlike consumer advertising, these campaigns are obliged to be firmly backed up by clinical data.

Medcomms agencies offer their clients a wide range of services, commonly including the publication of clinical trial results, organisation of conferences and symposia, creation of educational assets for healthcare professionals, promotional materials for prescribing physicians, or educational leaflets or websites for patients. With a broad client base, and an even broader range of audiences, many in the industry are armed with both postgraduate qualifications and expertise in science communications – i.e. the ability to dissect clinical data, and turn it into a coherent message for the audience in question, be that in spoken, print, or digital

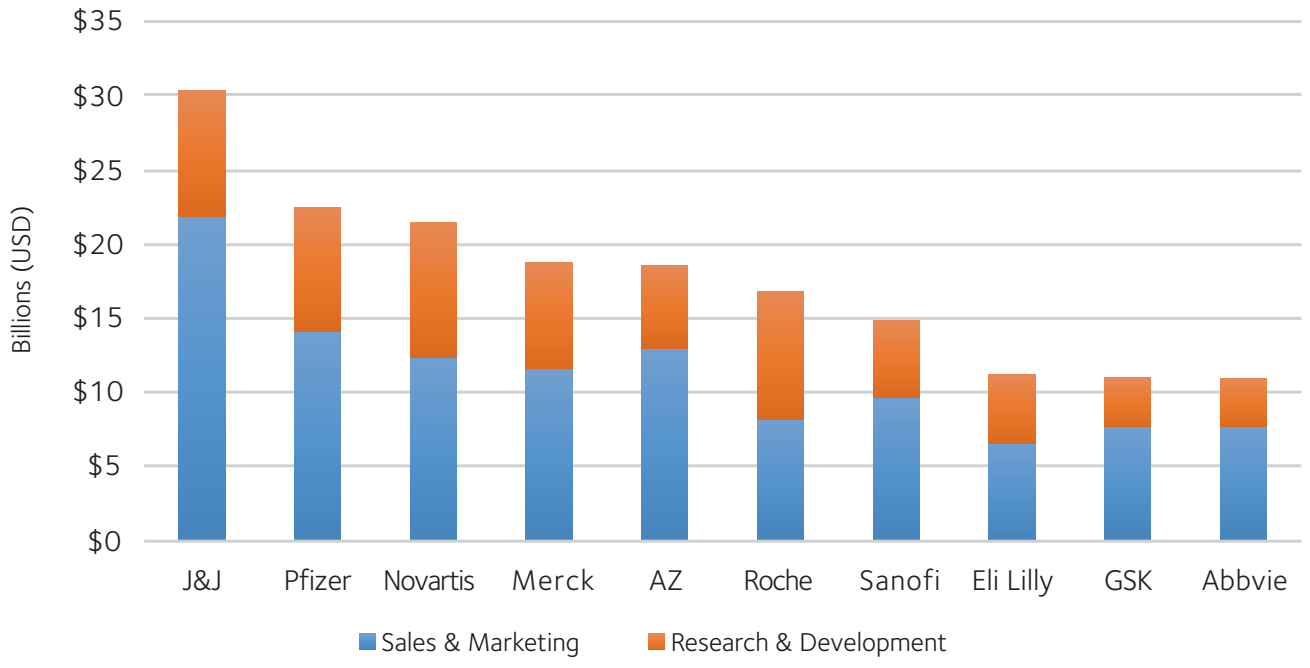

Figure 1. Global spending of ten of the largest pharmaceutical companies on R&D vs sales and marketing (2016). Adapted from: BacterioScan. *The financial barrier to developing antibiotics: no big payday for drug companies.*

media, all of which have distinct places in medical marketing campaigns (Fig. 2).

A changing world

Over the last few years, information technology has transformed communication, particularly internationally, by breaking down borders, slashing timescales. Accordingly, leading clinicians and researchers have influence which stretches across the globe, and everyone from politicians to healthcare professionals and patients increasingly aware of geographic discrepancies in drug approvals and healthcare delivery.

As a result of these trends, healthcare standards between the more economically developed countries of the world have increasingly harmonised. While the drug approval processes of the major regulatory agencies still differ (Van Norman, 2016) steps are being taken to bring their processes into alignment, particularly for urgently needed drugs such as novel antibiotics (Mezher, 2017). Adherence to international standards for pharmaceutical labelling (ISO 11238), medical device manufacture (ISO 13485) and conducting clinical trials (e.g. ISO 14155), for example, are all also increasingly important. This harmonisation extends into medcomms too, with three of the key bodies in medical writing, the American Medical Writers Association (AMWA), the European Medical Writers Association (EMWA) and the International Society for Medical Publications Professionals (ISMPP), collaborating to develop a global gold-standard for medical writing (Clifford, 2017).

Despite the above trends towards harmonisation, it is difficult to ignore recent shifts in political climates away from integration. Political opinion across Europe has shifted towards a more nationalist and Eurosceptic mood, most evident with the ongoing Brexit saga, and more recently the results of national and regional elections in Hungary, Italy, Sweden, Germany and Spain. On a more international level, tariffs are being raised and trade wars initiated between the USA and many other countries. At the time of writing, it's difficult to tell whether this is a mere hiccup in the shift towards a more interconnected world, or a new trend back towards the primacy of the nation state, but there is widespread concern regarding how these factors may impact on, international healthcare industry, including the movement of life-saving medications across borders (Liu, 2018). Within Europe, Brexit is likely to have significant impact on the medcomms and pharma industries, as the UK has been a leading player in both. With the planned departure of Britain from the EU, and the consequent move of the European Medicines Agency from London to Amsterdam, there are some who wonder if the Netherlands' pharma and medcomms industries will see a boost of investment. It's also possible that the global pharma

"The medcomms industry supports pharmaceutical and healthcare companies on formulation and delivery of promotional and educational campaigns"

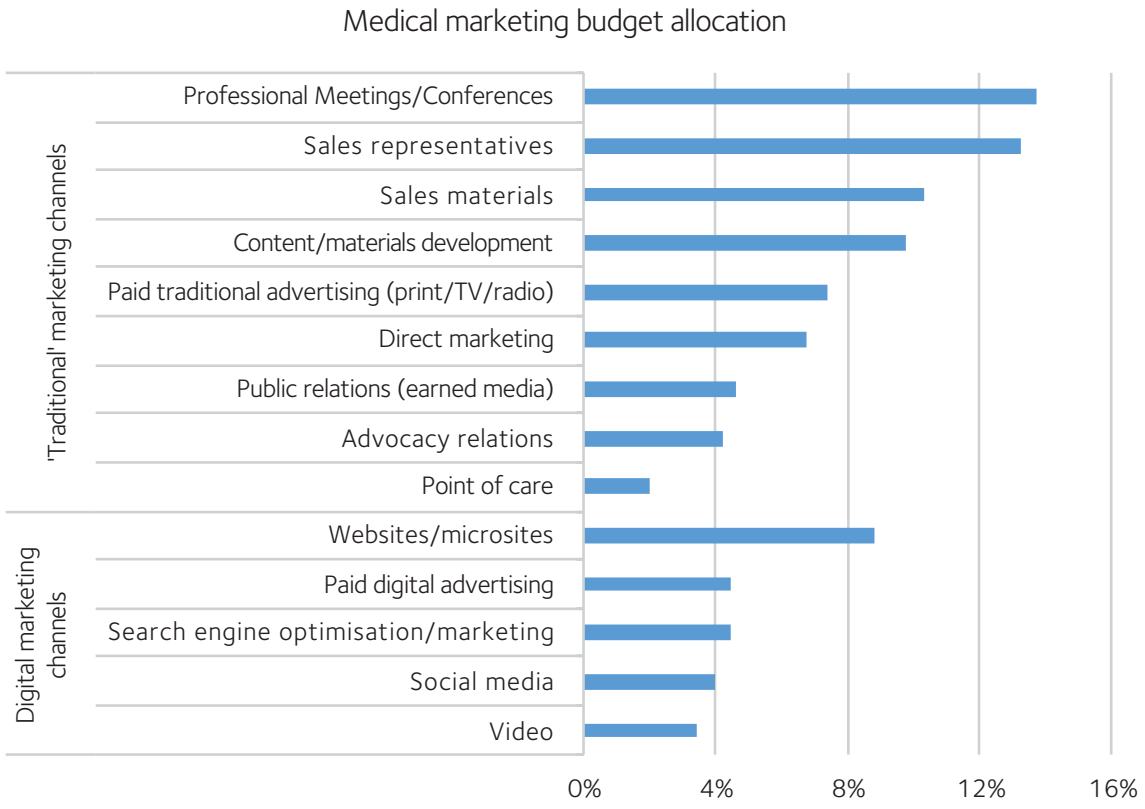

Figure 2. Medical marketing budget allocation. Based on a survey of 181 senior executives across the pharma, medical device, biotech and diagnostic sectors (2016). Adapted from: MarketingCharts. *Medical Marketers' Budget Allocations.*

"Between concerns about fake news and pressure for improved transparency, the traditional top-down mechanisms of communication are less and less fit for purpose"

industry will prefer to focus on the attractive tax rates of Ireland, the EU's soon to be largest remaining native English-speaking country. Many medcomms agencies are increasing their footprint on the mainland (PMLive 2017; Jones, 2018a; Jones, 2018b; McConaghie, 2018), to try to ensure smooth business no matter what outcome finally emerges. The medcomms industry already employs a significant cohort of freelancers, often working from home or across borders – and may increasingly rely on these groups until a more certain picture of the future emerges.

Expectation, trust and global opportunity

Healthcare also has another huge problem: while health literacy is (happily) on the increase, trust in the pharmaceutical industry is at an all-time low. This is against a much broader social collapse in trust. During the UK's Brexit referendum campaign, Michael Gove once stated that "people are tired of experts", and little since has cast doubt on that assertion. Between concern about fake news and pressure for improved transparency, there's no doubt that the traditional top-down mechanisms of communication are less and less fit for purpose. In terms of medcomms, this is leading to several transformational shifts. For example, key opinion leaders may be losing ground to the opinions of consensus groups, while patient representatives are finding the greater importance that they deserve. Both prescribers and payers are increasingly sceptical of clinical trial data (where non-adherence and patient comorbidities are the exceptions rather than the rule), favouring real-world evidence collected on larger everyday patient populations wherever possible (though this data is only available once a drug has been launched, and is also notoriously challenging to collect) (Taylor, 2018). More broadly, pharmaceutical companies are also regulated more tightly and scrutinised more heavily than ever before, which has led to a higher standard of communications and sales practices, meaning that the clinical data has never been more crucial to the quality of communications messaging.

Competition within the pharmaceutical industry also means that most companies no longer just market drugs, rather they are becoming suppliers of service packages, of which the drug is a single, albeit major, component – other aspects

may include enhanced patient support, physician education, fellowship grants, or patient monitoring and diagnostic services. Though increasing drug costs are probably not the biggest factor in the global rise in healthcare spending, healthcare providers are dealing with incredibly tight budgets so there is an enduring expectation of more for less. Medical communications agencies, insight organisations, and pharmaceutical consultancies can have major roles in helping their clients develop and deliver programmes with maximum impact for minimum cost.

"The accelerating pace of technological change is likely to significantly disrupt both healthcare and the practice of medical communications itself"

Any discussion of healthcare should never restrict itself to the situation in what might once have been referred to as developed nations (Europe, North America, Australia, Japan, etc.); these countries hold less than a fifth of the global population, and emerging markets have never been more important. Countries like India, China, Brazil, Kenya, Thailand, or Botswana have different healthcare needs (often younger, more rapidly growing populations; with less focus on chronic disease) and different healthcare systems to their historically (though not always contemporary) more economically developed counterparts. As a result, many also have poorer access to healthcare, particularly away from the cities. This means these countries may have half as many healthcare professionals per capita (World Health Organisation, 2018), while geographic and economic barriers may also restrict access to healthcare. Digital health interventions such as smart dispensers or wearables may not yet be totally suitable for large proportions of these countries' populations, but mobile health interventions such as apps, remote or peer-to-peer diagnostic technology, AI-based diagnostics, or SMS-based platforms offer huge opportunities. Medcomms has typically had less of a role to play in both emerging markets and in digital and mobile health interventions, but this will likely change as both fields mature and move to become more competitive.

Changing with the times

The pharmaceutical and healthcare industries are possibly the most robust industries in the world, together seeking to meet the basic human needs for health and longevity. As a subset of these industries, medcomms is a field with significant security. But while pharma has thrived despite weathering more than a century of change, it is far from immune to the international pressures of economics, politics and technology, and just as pharmaceutical companies have to change to keep with the times, so too will the medical communications industry. Medcomms is also an industry which trades on agility; being adaptable to the needs of different clients and of different markets, but adapting to changes in an international setting requires a different level of agility, and novel strategies may be required to overcome new trade barriers when seeking to win business, or to connect with a changing and more diverse audience worldwide. It remains to be seen whether this changing world will favour the large global communications groups such as McCann, WPP or Omnicom, or the smaller, more agile independent agencies. On top of this all, in years to come, the accelerating pace of technological change is likely to significantly disrupt both the pharmaceutical and healthcare industries, and the practice of medical communications itself. As long as medical communications agencies continue to add value and unique expertise to projects, they will remain an invaluable component of the pharmaceutical industry, but their role and how the pharma industry communicates with healthcare professionals and patients is ever-changing.

An apocryphal Chinese curse condemns the recipient to "live in interesting times". While working in medcomms has never been boring, the years to come will likely see some very interesting changes indeed.

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References

BacterioScan (2016). *The financial barrier to developing antibiotics: no big payday for drug companies.* [Online] Available at: bacterioscan.com/news/the-financial-barrier-to-developing-antibiotics-no-big-payday-for-drug-companies-2/ [Accessed 14 January 2019]

Clifford R (2017). Global standard for medical writing outlined. [Online] *PMLive.* Available at: pmlive.com/pharma_news/global_standard_for_medical_writing_outlined_1186333 [Accessed 14 January 2019]

Dobrow L (2016). How is pharma shifting its marketing budgets? [Online] *Medical Marketing and Media.* Available at: mmm-online.com/home/channel/campaigns/how-is-pharma-shifting-its-marketing-budgets/ [Accessed 14 January 2019]

Jones G (2018a). FCB Health expands into Germany. [Online] *PMLive.* Available at: pmlive.com/pharma_news/fcb_health_expands_into_germany_1254526 [Accessed 14 January 2019]

Jones G (2018b). Open Health merges with med comms services provider Peloton. [Online] *PMLive.* Available at: pmlive.com/pharma_news/open_health_merges_with_med_comms_services_provider_peloton_1271611 [Accessed 14 January 2019]

Liu A (2018). Biopharma caught in the crosshairs of U.S.-China trade tussle. [Online] *FiercePharma.* Available at: fiercepharma.com/pharma/despite-industry-wishes-biopharmaceuticals-caught-crosshairs-u-s-china-trade-war [Accessed 14 January 2019]

MarketingCharts (2016). *Medical Marketers' Budget Allocations.* [Online] Available at: marketingcharts.com/industries/pharma-and-healthcare-66049 [Accessed 14 January 2019]

McConaghie A (2018). Optimum expands comms offering to Switzerland. [Online] *PMLive.* Available at: pmlive.com/pharma_news/optimum_expands_comms_offering_to_switzerland_1273152 [Accessed 14 January 2019]

Mezher M (2017). FDA, EMA and PMDA Plot Harmonized Path for Antibiotics. [Online] *Regulatory Focus.* Available at: raps.org/regulatory-focus™/news-articles/2017/11/fda,-ema-and-pmda-plot-harmonized-path-for-antibiotics [Accessed 14 January 2019]

PMLive (2017). *Nitro Digital expands EMEA management team.* [Online] Available at: pmlive.com/pharma_appointments/nitro_digital_expands_emea_management_team_1190864 [Accessed 14 January 2019]

Taylor N (2018). The rise of real-world evidence. [Online] *PMLive.* Available at: pmlive.com/pharma_intelligence/The_rise_of_real-world_evidence_1226207 [Accessed 14 January 2019]

Van Norman GA (2016). Drugs and Devices: Comparison of European and U.S. Approval Processes. *JACC: Basic to Translational Science* **1**(5), 399–412

World Health Organisation (2018). *Global Health Observatory Data: Density of physicians data visualisation tool.* [Online] Available at: who.int/gho/health_workforce/physicians_density/en/ [Accessed 13 January 2019]

The good, the bad and the never ending quest

Maintaining persistence, focus, adaptability and passion in a scientific career

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Sometimes we win, but rest of the time we learn. Most of what we try fails, but these failures, which force us to grow, are often invisible because only the success stories are made visible. What are the core traits that make scientists stand out? There are a few that are always mentioned: persistence, focus, adaptability, confidence and passion. Yes, you must be smart and you must acquire knowledge of your specific area, but without the persistence and passion most ideas remain deeply buried while we distract ourselves with Candy Crush. I was always stubborn, passionate, uncomfortable with standing still, and I never liked Candy Crush.

In 2004, I was a 22-year-old biomedical laboratory scientist working in a clinical laboratory in Sweden. The job was meaningful and fun. I was great at my job, responsible, learning fast, and taking on long shifts. The rewards were instant both in terms of making a difference to someone's health, as well as the financial stability that came with the job. However, despite all that, I was still not satisfied. I had questions; I needed to be challenged. Those moments were defining for my research career. I didn't know much about pursuing a PhD or about funding, and even less about the career path that came after, but I knew that I was seeking knowledge and that I was willing to work hard. At the time, it was highly competitive to be hired as a PhD trainee in Sweden, since it was considered a job and not purely research training, and the academic job market was saturated. After two years of graduate coursework and research projects, a principal investigator (PI) agreed to take me on as a PhD trainee if I would work for him as a "shadow PhD trainee". After a year with minimal supervision, I had an unofficial interview where I was asked three questions: why do you want to do research? When are you starting a family? Can you commit to doing an eight-year, partly self-funded PhD, by working in a clinical laboratory part-time?

I failed my interview and I was told that there was not enough funding for my position. I was heartbroken and jobless. Having spent a year as a low-paid "shadow" PhD trainee and with a student loan to repay, my personal finances demanded that I return to the clinical laboratory. The job was interesting and well-paid, and within a few months I knew how to determine most of the disease-causing bacterial strains from different body cavities. There were occasional red flags – comatose patients or resistance to antibiotics – but the majority of the workload was routine, hence I was constantly re-assessing my goals and dreams. However, the unsettling feeling of repeatedly reaching the same answer to the question, "Is this me, 10 years from now?" haunted me. It was getting louder every day. Once the financial burden of my student loans was lifted I decided to change my career path. I pressed the submit button and four months later I was accepted to the prestigious

Marina Bay, Singapore

Wellcome Trust funded four-year PhD program at the University of Cambridge, UK.

In between beautiful, ancient colleges, there were paths that distinguished scientists had walked while pondering ideas that changed our perception of the world – and I was now following in their footsteps! With a strong passion for discovery and a drive to generate new knowledge, I dived into the unknown waters of the field of cardio-epigenetics. In 2008, the concept that terminally differentiated cardiomyocytes have dynamic epigenetic states, was wild and intriguing. Three years later I had contributed to several papers showing that the healthy human heart had specific DNA methylation patterns that were different from a diseased heart or cardiomyopathy. I set up *in vivo* models for cardiac imaging and surgery to test my hypothesis. I held workshops and formed new collaborations, yet my four-year PhD funding was coming to an end without a "first author" paper. In addition, my PhD advisor decided to take his science where there was more funding and more opportunity to create start-up companies, and left the UK to set up a new laboratory in Singapore. This decision was difficult since I was still gathering the *in vivo* data from the mouse strains that had to be transferred to Singapore. Working on genetic lineage mouse models takes a significant amount of time; strains need to be backcrossed and the correct controls generated. There is also biological variation to consider, and the data have to be highly reproducible, even if you transfer the strain across the globe. The paper was either to be finished in Singapore or dropped.

I had exciting results that I wanted published. In addition, a junior scientist has relatively low value in the scientific world without original, peer-reviewed, first-author papers. Without such publications, acquiring funding for a postdoctoral position becomes challenging. Mindful of these challenges ahead, I made the courageous decision to leave life as I knew it in Europe and move to Singapore to complete my study.

Within six months, I had transferred the mouse colonies, samples and myself to Singapore, and subsequently submitted and defended my PhD thesis. At the Singaporean research laboratories, which were highly technologically advanced, I had access to the latest equipment for transcriptomics and epigenetics. Still, to set up a new laboratory in a new country with a different administrative system, is challenging. There were protocols that needed to be approved and procedures to establish. I also had to train new staff and students. Building collaborative networks outside of Singapore, required enormous effort.

I tried to maintain the professional network that I established during graduate school in the UK, by reaching out to collaborators and attending international meetings. During an American Heart Association conference in the US, I was talking to one of the experts in the cardiovascular field and I was offered a postdoc position in his laboratory at Harvard. The project sounded amazing and I would have an opportunity to work with well-known researchers at a world-class university! I was elated but I also wanted to gather facts and think carefully about the job change. I visited a few other laboratories across the US before making my decision. I noticed that some of the labs were well-funded, published well and were also highly competitive and extremely challenging environments. Another interesting observation was the different lab structures that I came across, where priority was on hiring postdoctoral staff over graduate students and technical staff. Postdocs came already trained with various levels of independence and were prepared to stay between five and seven years for high-impact papers. Surprisingly, I also experienced that a lack of confidence is often interpreted as a lack of knowledge and this contrasts with the research culture that I experienced in European countries, where confidence is sometimes viewed as arrogance.

After considering all the pros and cons, I decided to accept the position at Harvard and moved to the US from Singapore. It is said that successful scientists must stay focused on achieving their goals, believe in their work and maintain a positive attitude. Every day

"The hard truth is that without original peer-reviewed, first-author papers, a junior scientist has very poor value in the scientific world"

The gate to Harvard

must be productive, in terms of fellowship applications, grants and experiments. Foreign postdocs in the US have only few options for postdoctoral fellowships, which means that they are highly competitive. It is usually a good idea to apply to fellowships within the first two years of your postdoc because of the five-year cap (post-PhD), with the success rate decreasing each year. The review board considers everything from your yearly productivity, to your mentor and the training program. Essentially, you should work on a project that already has preliminary data in a lab where people move on to successful tenured positions. Receiving a postdoctoral fellowship is not only a way to demonstrate that you are able to obtain grants but it also gives you more freedom in pursuing your ideas during your postdoctoral training since you are not depending on a salary from your PI.

I've been working in the same lab for five years now. The US-based labs create a fantastic opportunity for both professional and personal growth and provide access to superb intellectual capital from across the globe. They foster a dynamic environment that encourages creativity and out-of-the-box thinking. The pace of work is high, and vacation time is rare. Colleagues in the lab often become akin to your family since you spend most of your time together. Furthermore, living in a cosmopolitan city, such as Boston, often means that living costs are high and you have a tight budget.

I have not received any "on paper" professional benefits from my international career. However, it has enriched my professional and personal life, with large professional networks, new friends, new perspectives, and less fear of the unknown. Most scientists that I have met are indoctrinated into the educational system within the borders of the country where they are working and living. Despite science being a field that is forward thinking, there is surprising rigidness and lack of comfort regarding changes to the system. So, why would anyone expose themself to the challenges of an international career if it is not recognized as a valuable skill? The system only recognizes high-impact publications as productivity and not the ability to adapt to change and overcome failures. Nevertheless, I don't regret my international experience. I have developed a breadth of knowledge and a multidimensional view of my national identity; I see myself as more of a world citizen. Whether or not being you've been exposed to an international postdoc experience, on a personal level, many postdocs realise that hard work and talent do not always result in high-impact publications. These highly competitive environments can trigger anxiety due to a feeling of constant failure. Many postdocs are in their mid-to-late thirties and find they have stalled their life plans to reach certain career milestones, while their peers in non-academic or non-scientific fields have already progressed to higher corporate positions and a more settled lifestyle. Despite the huge desire to make a difference, many start questioning if they can truly fulfill the expectations of academia, or if they should instead change their career path. In most professions, increase of competence among staff is encouraged and promoted, but somehow this is not entirely true for the academic environment where the highly skilled trainees are forced to take alternative career paths or to start over.

The saving grace in these situations is to truly identify your passion, despite exhaustion from trying endlessly and receiving scarce rewards. There are countless mornings when I wake up with new questions that I want to answer and I feel that there is nothing else in the world that I would rather do. When I have lost more times than I have ever won and I am no longer sure of how many more times I can start over, it is persistence, focus, adaptability and passion that push me forward.

R Jean Bannister Prize winner: A rather winding road to research success

Bethan E Phillips

School of Medicine, University of Nottingham, UK

"We are delighted to inform you that you have been chosen as the recipient of The Physiological Society's inaugural 2018 R Jean Banister Prize Lecture … The Physiological Society would be greatly honoured if you felt able to accept our invitation."

I was sat in a University research sandpit event in August last year when I received an email containing the invitation above – they were delighted and so was I!

To me, this invitation was about much more than the recognition of my research by an external organisation (which was of course wonderful) and the fantastic opportunity that it provided (to present my research at numerous institutions); it was a proof that dedication, passion and perseverance (plus a lot of support and motivation from amazing colleagues) can lead to research success – even when the road to get there is far from straight. This was a message that I was keen to relay at a recent small-group "Transition to Independence Event" that The Physiological Society ran for post-doctoral members.

My story…

As a 17-year-old sitting my (rather unusual choice of) A Levels in Theatre Studies, Physical Education, Government & Politics, Biology (and the obligatory General Studies), I thought I had my life mapped out in front of me. I was going to do a degree (Sport Sciences), go through the Royal Military Academy Sandhurst and have a long, successful career as an Officer in the Army Medical Corps. Little did I know this was not to be.

Aim one went to plan and I gained an undergraduate place at Loughborough University to study a BSc (Hons) in Sport & Exercise Sciences and thoroughly enjoyed all aspects of University Life. However, for me, disaster struck when in my second year of University I went for Army Officer selection. At this, despite having passed with flying colours, they told me that my previous knee operation was an automatic bar from military service. I was devastated.

After a few weeks at home mulling things over, I decided to return to Loughborough and finish my degree while considering a number of graduate-entry options (medicine, physiotherapy, dietetics, teaching). I was then fortunate enough to be placed with Clyde Williams for my final year research project, exploring the effects of different glycaemic index breakfasts on substrate utilisation during exercise; an experience that sparked my passion for research and opened my eyes to a previously not considered career route.

However, I still wasn't wholly convinced that a PhD was for me, so like may recent graduates I moved back home (to the South West) to start my search for jobs. In amongst "exercise advisor" and "community well-being officer" roles was an advert for a Research Assistant at the University at Nottingham. Working on a BBSRC project grant, the job also encompassed a PhD – it sounded perfect. Looking through the job spec, all seemed ok: a 2i or above in a relevant BSc, a qualification in exercise instruction and human research experience, until I saw the dreaded words "a full, clean driving-license". Not willing to let this stop me, driving lessons commenced, I applied for the job and my research career journey began (having passed my driving test the day before my interview).

My journey through research hasn't been much smoother than the one I took to get there. A part-time PhD wasn't easy, even though it was so closely related to my full-time job role, and only my aforementioned fantastic colleagues got me through (eventually). Postdoctoral positions followed, each with their own challenges, which now with hindsight, I can see tested my resolve and heightened my desire to succeed in research. Similarly, failed fellowship applications provided both constructive feedback and fueled my desire to continue working towards independence.

Finally, in January 2015, I was appointed as an Assistant Professor in Clinical, Metabolic & Molecular Physiology at the University of Nottingham. Since this appointment, like most independent academics, I have had grant successes and (many) knockbacks; however, my winding journey to this point has taught me to pick myself up, dust myself off and head towards the next turn in the road.

Hear Bethan Phillips speak at lectures throughout the next few months. Her talk is entitled "Physiological adaptations to traditional and novel exercise interventions as a function of age." Learn more at: **physoc.org/events**

Blended learning in physiology: merging new technologies with traditional approaches

Louise Robson

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Learning and teaching in Physiology has undergone something of a revolution over the last 30 years, and as someone who had their very first teaching experience back in 1989 (running tutorials as a PhD student), I speak from experience! One of the biggest changes has been around digital technologies, bringing benefits and challenges to both students and staff. However, while there are challenges (e.g. information overload), for me the benefits far outweigh any challenges digital technologies generate.

I teach ion channel physiology, and aim for students to not only understand the ideas and concepts in this area, but also be able to apply these to novel experimental data. For this reason, I use data handling and interpretation exercises in my modules, i.e. students utilise mathematical approaches, interpret their data and draw on data from other sources. One thing that certainly hasn't changed is that students struggle with mathematics, and I suspect I am not the only academic to observe a sea of white faces when I have equations on my slides! However, my modules are very popular, despite the complex mathematics. The reason for this is due to my blended learning approach to teaching, matching traditional teaching with digital technologies.

In this approach, lectures introduce calculations underpinning physiological mechanisms, with lectures recorded, so that students can revisit to help their understanding. I have been using lecture capture for several years, and my experience is that it enhances learning. I have observed an increase in academic performance in my final year modules, and the types of questions students ask are more insightful. They utilise the captures to get to grips with the lecture content, and their higher level questions are then often about the published literature. Of course, if you are providing captures it is really important that students understand how to use these. Work by a cross-institutional group of academics, of which I am a member, has recently provided top tips for students and staff on using lecture capture, also presenting these in a student-friendly infographic format, Fig. 1 (Nordmann *et al.,* 2018). For me this work highlights an important but often forgotten aspect of learning and teaching, share your ideas and experiences and collaborate with others.

Overarching infographic on top tips for students on using lecture capture. More detailed tips can be found at: https://osf.io/edmzf/ (Nordmann *et al.,* 2018). Note, this figure is the front cover of the student guide produced by a collaborative group I am part of, and the study guide is freely available on the Internet.

The best way to learn is to do, and my students complete formative data handling workbooks that reinforce lectures and provide additional guidance. This allows students to develop skills in a low-risk environment, and feed forward and improve for the assessments. Problem-solving classes require students to apply their knowledge and skills, providing an opportunity for personal feedback. I also provide dynamic maths videos for them to view. Using a variety of approaches allows students to work in the way they find most beneficial (one size does not fit all in education). The final module session tests knowledge and understanding using the interactive Lecture Tools platform, allowing students to test knowledge and understanding. This blended approach provides an enhanced learning experience for the students, and is clearly appreciated by them, as they have voted me best Biomedical Science Lecturer at Sheffield several years in a row.

Many of you reading this article may be in the early years of your academic careers, and while there is lots of advice on developing your research profile, there is often less structured support on developing learning and teaching.

Here are my top tips:

1. Get experience early on. I started as a PhD student and continued to gain experience as a postdoctoral researcher.
2. Seek advice from experienced individuals.
3. Identify the key developments in learning and teaching, and give them a go.
4. Evaluate what you do. Some things will work (but not everything). Don't forget ethical approval if you want to publish.
5. Document innovation as you go. In research, outputs are easy to define. In learning and teaching, it's not so easy!
6. Always think about what is best for your students (it's not always what they want).
7. Share your ideas and collaborate as much as possible.

I hope you have found this article useful, and that you have been able to identify some ideas for your learning and teaching development (if you want more information, just ask)!

References

Nordmann E *et al.* (2018). Lecture capture: Practical recommendations for students and lecturers (pre-publication): 10.31234/osf.io/sd7u4

The pursuit of independence: Tips and lessons from our postdoc workshop

Hannah M Kirton

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So we want to establish our own independent research? But where do we start? Do we apply for a fellowship or a lectureship? What is the difference between fellowship and lectureship? When do we start applying? Do we have enough pilot data? What mentor should we select?

These are all daunting questions to consider in our journey to academic independence, but very important nevertheless; while variability in the available information and possible funding pathways pose yet further questions.

To provide some clarity on how postdocs can secure their first permanent academic position, The Physiological Society – with guidance from the Affiliate Working Group – developed a tailored workshop for postdocs, which took place in London on 23 November 2018. As a postdoc, I attended this workshop and quickly found the benefits of attending. The fact that the workshop had been tailored to address the specific needs of those attending was extremely invaluable to me.

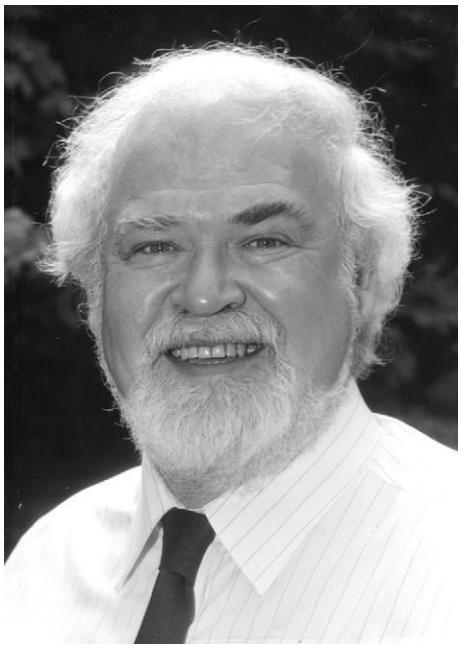
The friendly, informal approach of the event also helped to encourage discussion and future peer support.

Four speakers who had already made the transition to a permanent post were invited to share their honest expertise and knowledge to help us think more clearly about how we should execute the next steps in our careers. Katharine Dibb from the University of Manchester alongside Bethan Phillips from the University of Nottingham shared their experiences in securing funding. Their key take-home message was to accept rejections, and although failure is difficult to apprehend, it is a common concept in academia and one must never take it personally. Encouragingly, Phillips further explained how her failures lead to her most successful grants, and this was with thanks to the advice that most funding societies offer in terms of reviewers' comments.

Another fundamental aspect to consider was mentoring, and how important it is to find the right person for you and your career needs. It surprised me just how important a mentor truly is. Bryn Owen from Imperial College London spoke honestly about his pitfalls and successes, and that it wasn't until he found a mentor that he truly made clear concise decisions for his academic future.

Finally, Federico Formenti from King's College London challenged us to list the top three elements that we believe to be crucial in making ourselves more employable. Amongst this list were publications, citations, grant successes, what specialist techniques we are highly recognised for and our networking ability. The day was concluded with a roundtable discussion to ask *ad libitum* questions, which included the benefits and difference between applying for lectureships vs. fellowships, and barriers to career progression. At the end of the day, we were asked to make our own personal career pledge using what we had learned during the workshop to guide us. I pledged to seek both internal and external mentors to enhance and aid in my ability to gain academic success. Since the event, I have secured both mentors that I feel will prove instrumental to my next academic step.

Overall, this workshop has encouraged me to pursue my academic ambitions and helped to specifically tailor my needs to enable this. If you would like more information on maintaining academic success and gaining your next step in academia, I would strongly recommend you to visit The Society's website (**www.physoc.org**) or you can contact **education@physoc.org** for details of any future opportunities for postdocs.



"David was in many ways a Renaissance man; his contribution was in science, but he also had wide ranging interests in art and society"

Obituary:

David Millar Armstrong 1941–2018

David Armstrong was a pioneer in understanding how the central nervous system controls movement. He was amongst the first to recognise the importance of combining anatomical, physiological and behavioural methods to advance knowledge of the brain pathways and mechanisms that underlie voluntary movement.

David was born and educated in Cumbria where at school he met his life-long partner and wife Lucy. His academic talent was recognised at an early age, and he won a scholarship to study Medicine at the University of Oxford. However, he soon recognised that his true interests lay in understanding fundamental physiological mechanisms, and he transferred to a BA in Physiology and graduated in 1963 with a first-class degree, and subsequently a masters in Neurophysiology by research in 1964.

David's talent as a rising star in neurophysiology was recognised by Sir John Eccles who recruited him as a PhD student at the Australian National University in Canberra. Under the supervision of Eccles, David developed his long-standing interest in the mammalian cerebellum, and the critical importance of climbing fibre inputs from the inferior olive for the normal function of this major brain structure. He graduated from Canberra with a PhD degree in 1967 and moved the following year back to the UK to take up a lectureship at the University of Bristol where he remained for the rest of his career. He was an enthusiastic supporter of The Physiological Society, presenting numerous communications and chairing many sessions at The Society's meetings throughout his career. David was also on the editorial board of *The Journal of Physiology* between 1979 and 1986.

David obtained his personal chair in Physiology at Bristol at the young age of 43 and was Head of the Department of Physiology from 1990 to 1995, and also from 2003 to 2004. He was an outstanding and greatly respected Head, who managed to strike the right balance between being supportive but not interfering. He was always kind and generous with ideas and advice – he understood the importance of giving individuals the freedom and space to find their own way, at their own pace. He also had the rare gift of recognising what was important and what was less so.

During his research career David published 74 full papers (21 in *The Journal of Physiology* alone) and numerous other communications with a focus on the motor cortex and cerebellum. This body of work included key anatomical and physiological evidence to support the hypothesis that the cerebellum is modular in organisation. In the 1960s this was a controversial idea, but is now accepted as the framework to explore cerebellar contributions to movement control and indeed many other functions. David's neurophysiological studies in awake behaving cats were also ground breaking, and included compelling evidence that climbing fibre inputs to the cerebellum carry information about sensory errors. This is a concept that has shaped many studies since, and remains central to our understanding of how the cerebellum contributes to the coordination and modification of skilled movements.

Beyond research David was also a gifted and popular teacher of undergraduates, no doubt helped by his ability to understand and empathise with young people. David would tell the medical students that neurophysiology was in his blood and that his family coat of arms featured a pair of crossed tendon hammers!

David was in many ways a Renaissance man; his contribution was in science, but he also had wide ranging interests in art and society. For his inaugural lecture, rather than present his internationally acclaimed work on the motor system, instead he chose to give his talk on the plague in Cumbria in the early seventeenth century, including his own epidemiological research based on careful analysis of church records. After he retired he developed his interests in mediaeval church carved pew ends. He also had a life-long interest in photography. His favourite subject was sea birds on his beloved Orkney Islands, where he and Lucy owned a croft and spent their retirement enjoying summer holidays with their two children Catherine and James and grandchildren.

Several years ago David suffered the cruel irony of a cerebellar stroke, from which he never recovered, and Lucy cared for him until he died last August aged 77.

Good people are valuable, and David was a good person. We miss him.

Written by Richards Apps and Tony Ridge, with help from Judy Harris

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