PN
Physiology
News

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Ancient DNA:

What studying our archaic ancestors can teach us about human adaptation and disease

The Physiological Society

Physiology News

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Experimental Physiology

Open Access

Experimental Physiology is now fully Open Access

physoc.org/ExpPhysOpenAccess

Why become President of The Physiological Society?

Professor David Attwell

President,
The Physiological Society

As I step into the shoes of David Paterson, to be President of the Society for the next two years, it seems appropriate to give those of you who have never heard of me some background information on who I am, explain why I agreed to do this job, and state what I see as the challenges ahead for The Society.

I started undergraduate life as a physicist at Oxford but, on seeking a subject to do research in, for a PhD, was seduced into biophysics and electrophysiology, largely because all my friends doing physiology and medicine seemed much happier with their choice than those doing physics! I was fortunate to find an outstanding PhD supervisor (Julian Jack) who was willing to take a bet on a biology-naïve physicist, and a very patient college tutor (John Stein) willing to mentor me through the transition to a rapidly acquired degree in Physiological Sciences. Following my PhD, which was on nerve and cardiac electrophysiology in the labs of Julian Jack and Denis Noble, I did a post-doc in Berkeley working on the retina with Frank Werblin and Martin Wilson, before taking up a lectureship at University College London, where I still work. Since arriving at UCL I have been lucky enough to study a broad range of topics including retinal information processing, astrocyte biology, glutamate transporters, oligodendrocytes and myelination, cardiac and renal physiology, brain energetics, and control of blood flow in the brain at the capillary level, so I can reasonably claim to represent a broad swathe of physiologists.

From my earliest research years, The Physiological Society played a very important role as a venue at which one should aspire to present work and get feedback from others, despite (in those days) the associated "public viva" at the end of each 10 minute talk (including tiresome discussions of the punctuation in the abstract!) that almost inevitably led to a decision to accept the abstract for publication - except on those rare and terrifying occasions when the audience took against the speaker. It was experiencing the very positive aspects of participating in The Society that led me to accept to be its President for the next two years. The irrepressibly optimistic David Paterson is going to be a hard act to follow, and The Society has some serious challenges ahead, which I will dwell on below. But before that I thought it useful to assess the current state and likely future of physiology as a discipline, and how better to do that than to ask the new fashionable AI tool, ChatGPT, which has apparently digested (and can regurgitate) most text written up until 2021.

In response to the question: "What is the future of Physiology as a discipline?", ChatGPT replied (in about 3 seconds!) as follows.

Physiology is a broad and rapidly-evolving field that encompasses the study of the functions and mechanisms of living organisms. The future of physiology is likely to be shaped by advances in technology and new research discoveries. Some areas that may see significant growth in the future include: Systems Physiology; Precision Medicine; Neuroscience; Environmental Physiology; Biotechnology and Regenerative Medicine; Artificial Intelligence and Machine Learning. Overall, the future of physiology looks promising, with many new technologies and discoveries expected to shape the field and lead to new treatments and therapies for a wide range of diseases.

On starting as the new President, I greatly welcome this positive view, which even overlaps in part with The Society's strategy, but we need to be aware of some clouds on the horizon for our - and many other - learned societies. While, classically, it is traditional to talk of the fragmentation of disciplines into sub-disciplines, which then form their own societies, as a major risk to the future of learned societies, our current main problem stems from a much simpler cause: the move to Open Access publishing.

The Society is committed to the principles of the Open Science movement and at the start of this year we celebrated the occasion when *Experimental Physiology* became Open Access. Both authors and readers of the journal will benefit from this historic change and it represents a fantastic opportunity for research in *Experimental Physiology* to reach as wide an audience as possible.

Open Access publishing seeks to democratise and expand science by ensuring unfettered access to critical research to a whole scientific community without the restriction of a paywall. But the transition to a fully Open Access world is not necessarily a straightforward change to navigate, and the idea of a democratised scientific publishing landscape is not so easily achieved when the challenge of covering the cost of publication without penalising authors *or* readers remains.

From The Physiological Society's point of view, the main issue is that if, in the future, *The Journal of Physiology* is required to move to an Open Access model of publishing, then the journal will need to adapt to enable that change whilst ensuring that any income to support The Society's charitable aims, as has existed in the past, can be maintained. To protect The Society's income, we will need to publish more papers, either in the same journals (whilst balancing the focus on quality that the journals are renowned for) or in new journals, which will need to be carefully conceived to complement our existing portfolio of journals. Unlike some other societies, we have little endowment to raise income, so it would be desirable to develop extra income streams to ensure that we can maintain our core business of organising great meetings and publishing high-quality journals, while sustaining our Equity, Diversity and Inclusion plans and our engagement aims.

With all this in mind, I have been immensely impressed by the quality of The Society's staff and trustees and how they are addressing these issues. As we all know, physiology can Change the World, and the new Strategy for The Society sets out a clear plan for the next five years. We have excellent Journals to publish in, and there are some great Meetings coming up, including our flagship annual meeting Physiology 2023 in Harrogate. I look forward to meeting you in person at a meeting or, if that is not possible, do feel free to write to me to express your opinion on any Society-related matter.

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Building and strengthening our community

"The Society is well placed to bridge the gap between advances in basic science, translation research and their application to medicine – allowing for bidirectional dialogue by providing clinicians and physiologists with a platform to learn, connect, and inspire."

Dariel Burdass

Chief Executive,
The Physiological Society

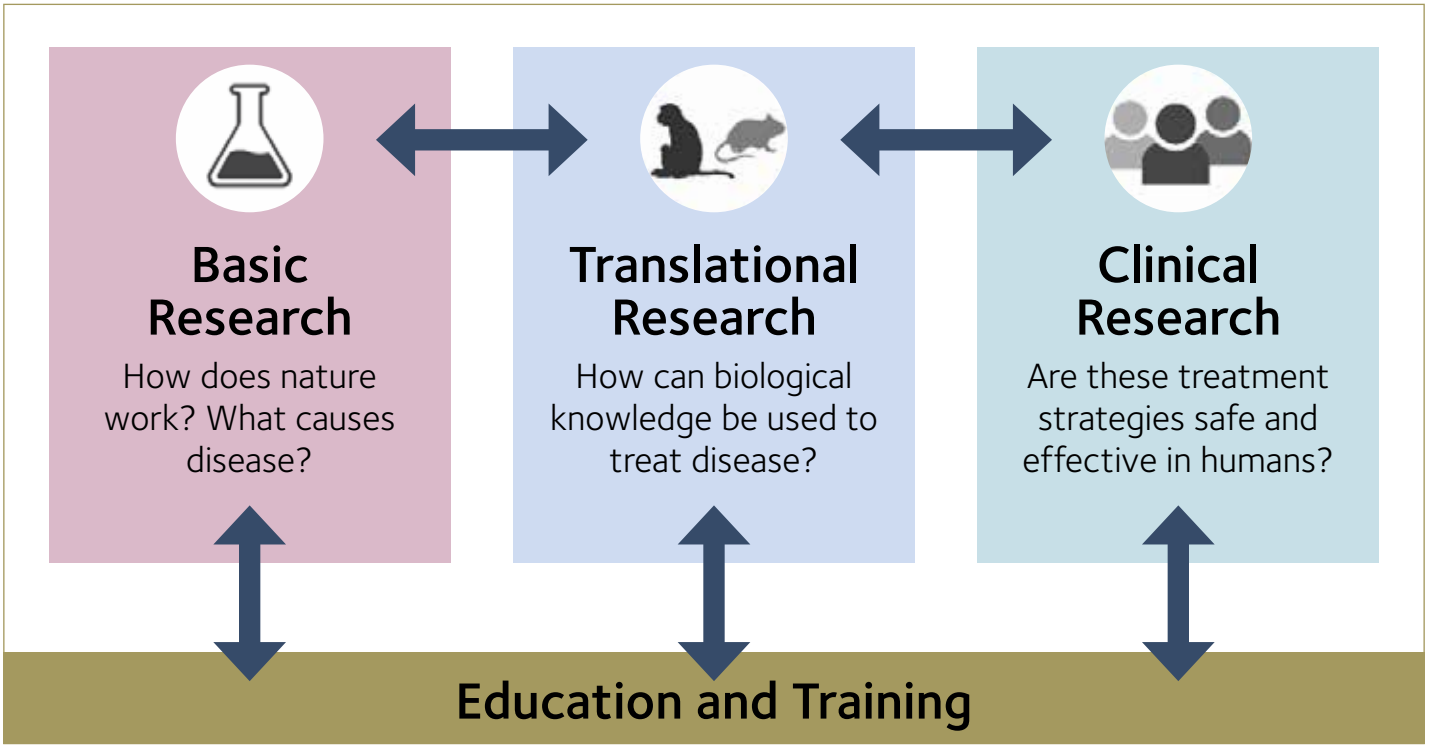
As David reflects in his President's View, this is a challenging time for The Society. We face financial pressures from a decrease in our publishing operations' income coupled with declining membership numbers. As I reported at the 2022 Member Forum, this fall in income has necessitated some difficult decisions to reduce expenditure across all our activities and operations so that we can move to 2024 with a balanced budget.

Over the last two years The Society has organised regional Roadshows focused on re-engaging with physiologists within their institutions. We will build on this foundation as we deliver the new 2023-27 strategy vision to support and inspire our community to advance the physiological sciences, enabling a world in which physiological discovery leads to healthier lives.

We are now in a stronger position to build our community and grow our broad church of physiologists.

Our members are active in a wide range of areas of Physiology from basic research through to translational and clinical, underpinned by education and training.

Several years ago, Sir James Black[1] was asked, "What is the biggest challenge in biology today?" His response was, "The triumph of physiology over molecular biology." The Human Genome Project will give us a book but learning to read it and understand what all its entries signify is the challenge of a lifetime, possibly several lifetimes. Thus, organismal physiology is the biggest challenge ahead in both basic and clinical research. The problem is who will accomplish this task, and why, given today's incredible opportunities, are we having such a difficult time bridging basic science with medicine?



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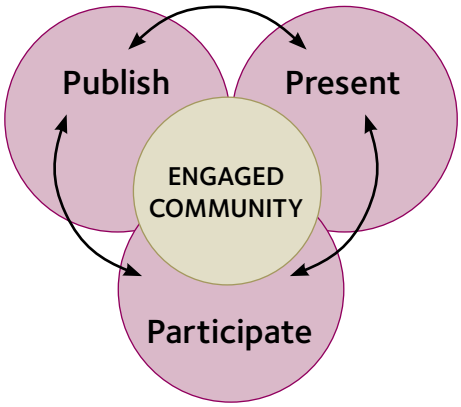
The Society is well placed to bridge the gap between advances in basic science, translation research and their application to medicine - allowing for bidirectional dialogue by providing clinicians and physiologists with a platform to learn, connect, and inspire.

One example of this is the success of Questions from the Frontline, which brought together a COVID-19 Advisory Panel to provide an evolving understanding of the physiological and pathophysiological mechanisms underpinning this disease in response to questions received from frontline clinicians. The Society recognised the need for a hub to enable effective communication and collaboration between the research-active clinical workforce and both basic and translational scientists. An outcome of this is that The Society will be launching a Clinically Focused Theme at our main meeting at Harrogate in July.

The Society pledges to strengthen and increase the visibility of the discipline by growing its numbers and providing greater networking opportunities. But we can't do this without your help. There are a number of ways that you can engage with The Society and help shape the future of physiology through the 3 Ps – *Present, Publish and Participate*.

Shaping future physiology & connecting our community



Here are some examples of ways you can *Present, Publish and Participate* at The Society, whether in person or virtually:

Present

We organise an extensive range of events, including scientific conferences, training events, interactive workshops and webinars, for example, our new two-day scientific meetings, annual main meeting and sandpit meetings. Whether giving an oral presentation or a poster presentation, these events provide the opportunity for physiologists to communicate their research, get feedback on their data, raise their visibility, network with other researchers, and develop their academic track record. To find out more about information on how to communicate your research, view our professional development resources.

Publish

Our three journals lead the discipline, promoting best practice and pushing the boundaries of scientific endeavour.

The Journal of Physiology is the leading general research journal in the discipline, with the highest number of citations of any physiology journal. Since 1878 it has published research that significantly advanced our knowledge of physiology and increased our understanding of how the body functions in health and disease.

Experimental Physiology is an open access journal publishing research papers that report novel insights into homeostatic and adaptive responses in health, as well as those furthering our understanding of pathophysiological mechanisms in disease. Research embracing the journal's orientation of translation and integration is encouraged.

Physiological Reports is a collaboration between The Physiological Society and the American Physiological Society. This is an open access journal, which publishes original research in all areas of basic, translational and clinical physiology and allied disciplines.

When looking to submit your next manuscript for publication please can I ask that you support your scientific society by considering our highly respected journals, which provide a home for physiology research. In addition, your help reading and citing relevant papers from our journals is most appreciated. Check out our YouTube Channel where we have a series of resources focused on Publishing for Beginners. By publishing with a Society journal, you support our community of physiologists, advance physiology and increase the influence of The Society with the public, policymakers, and other stakeholders.

Participate

The Society provides many opportunities to enable you to get involved with your community, which is a fantastic way to gain new skills, or use existing ones, and to build your network.

Volunteering opportunities include:

- Serving on our committees and working groups, which help deliver our activities
- Session organisers, chairs, and volunteers at our events
- Theme Leads and Society Reps
- Grant reviewers
- Contributing to our policy reports
- Sharing your research through our various communication channels including *Physiology News* and the blog

I am looking forward to talking to many of you at Physiology 2023 in Harrogate and through other activities that we have planned during the coming months, to understand and improve what The Society can do for you to strengthen our community.

Footnotes

1. Bridging the Bed-Bench Gap – National Academies of Sciences Engineering and Medicine Contributions of the Markey Trust Appendix A Bridge Building Between Medicine and Basic Science Irwin M. Arias, M.D. Department of Physiology Tufts University School of Medicine https://nap.nationalacademies.org/catalog/10920/bridging-the-bed-bench-gap-contributions-of-the-markey-trust

"The Society pledges to strengthen and increase the visibility of the discipline by growing its numbers and providing greater networking opportunities. But we can't do this without your help."

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Welcome to our new President-Elect Professor Annette Dolphin

The Society is delighted to announce that Professor Annette Dolphin is The Society's President-Elect.

Professor Dolphin's term as President-Elect began on 2 December 2022 at the Member Forum. She will become President in December 2024 and hold the position until December 2026.

Professor Dolphin said,

"The Physiological Society has been at the forefront of the life sciences for 150 years and it is a real honour to become President-Elect.

"From tackling the health issues around climate change to improving our understanding of the ageing process, physiology is at the forefront of finding solutions to many of the global challenges we face.

"This is an exciting time for The Society, especially following the launch of the new strategy. I look forward to meeting members at one of our exciting conferences and events over the next few months."

Annette Dolphin is a Professor of Pharmacology in the Department of Neuroscience, Physiology and Pharmacology, at University College London. In her academic career, she has made major discoveries with respect to neuronal voltage-gated calcium channels, their modulation and roles in disease. In recent years her work has investigated the involvement of particular calcium channel subunits in chronic pain. She has also elucidated the mechanism of action of an important drug class, the gabapentinoids, which are of therapeutic use in chronic pain. Her findings have significantly influenced our thinking in this field.

She has recently held the role of President of the British Neuroscience Association (2019-21), and she has been elected to the Council of the Royal Society (2023-25).

Letter to the editor

Using Game of Thrones to teach physiology

29 January 2023

Dear Keith,

I read with great pleasure the article on the use of *Game of Thrones* in physiology education by Professor Derek Scott (Scott, 2022). The paper elegantly shows how the use of pop cultural cases and examples can provide exciting narratives that provide a platform to convey various physiological (and here also pharmacological/toxicological) principles, while also enhancing student engagement, which was indeed quite a challenge for all of us during the recent pandemic lockdown. As mentioned in the article, I and my fellow stormtrooper, Ronni Plovsing, have also used pop culture in our teaching (see also pp. 27-29 in the current issue), particularly Star Wars, which we have also written about here in *Physiology News* (Berg and Plovsing, 2016; Berg, 2020).

It may be of interest that I set out to formally test the impact on learning of pop cultural cases a few years ago, that is, prior to the pandemic (Berg, 2018); one was a case from *Terminator 2* , and the other was a case from the *Star Wars* franchise. I randomised my physiology classes to be taught by these cases (intervention group) or by conventional clinical cases with identical themes (control group). By formal testing of the students at the end of the term using a multiple-choice test focusing on the physiological themes addressed in the cases, the intervention group achieved significantly higher test scores, and rated the quality of the teaching higher. Most of the students in the intervention group furthermore acknowledged that it made the teaching more fun, which is always good, and it also motivated them to participate more during class. Unfortunately, less than half of the students found that the approach led to more self-study, at least in my hands. Now, the results of this little survey of mine is hardly definitive evidence for anything, but it does nonetheless suggest that the use of pop culture is both amusing and probably also effective in physiology education. So, I for one will certainly start using *Game of Thrones* in my teaching this coming term!

Dr. Ronan M. G. Berg, Associate Professor

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Berg RMG (2020). Family ties in Star Wars. Is Force-sensitivity a matter of non-Mendelian inheritance? *Physiology News* **120**: 28-30.

Berg RMG, Plovsing RR (2016). Breath of the Sith: a case study on respiratory failure in a galaxy far, far away. *Physiology News* **103**: 30-33.

Scott D (2022). Using Game of Thrones to teach physiology. *Physiology News* **128**: 18-19, https://doi.org/10.36866/pn.128.18.

https://doi.org/10.36866/pn.129.8

It is nice to be important – but it is important to be nice![1]

Dr Peter Kohl

Editor-in-Chief,
The Journal of Physiology

Last spring, a colleague of mine started a prestigious appointment in physiology at a leading academic institution in the UK. She was delighted, of course, and impressed with the level of support in scholarly and operational matters that was promised. Then, the leadership at the institution changed, and so did the previously promised support: the budget allocated dropped by a third, citing the (genuinely difficult) financial situation of that institution.

Now – what would be your advice to my colleague?

Accept (mustn't grumble!) and get on with the job, even if this now was going to be much more difficult? Protest (grumble…), even if that is rarely productive and generally frowned upon? Leave, even if the academic fit remained near-perfect?

I don't know.

In my view, mutual respect and accountability in the way we conduct professional interactions form an essential basis for academic self-governance. 'Pulling rank' has no place in academia. When we debate science concepts and activities, it doesn't matter whose title indicates higher accolades, or who has been around for longer. This, I think, is one of the key aspects that makes our profession attractive, and we should keep it that way.

Mutual support is at the heart of peer review as well.

As authors, we should actively seek to exploit the productive impetus of criticism, even if it may be hard at times to separate this from emotions that arise from disagreement. As reviewers, we should refrain from judging authors and focus on the science at hand – ideally, with the clear aim of helping to improve both the research and its presentation.

Peer review involves a significant amount of work. Assuming that a manuscript goes through two rounds of revisions, involving two external referee reports each, we should act as a reviewer four times for each article we publish. And that is a rather conservative estimate, at least based on my experience of the journey towards an accepted paper. Food for thought.

As editors, we try to balance the arguments made and, hopefully, select the best papers for publication. This process is bound to involve mistakes. But I am unaware of a single research paper that hasn't been improved through thorough peer review. So, side-stepping it in favour of publishing more or faster doesn't seem prudent to me. One would simply delegate the task of reviewing a manuscript from a small number of expert colleagues to 'all readers', without the benefit of engaging authors in a dialogue that leads to an improved output for the benefit of all.

No doubt, it helps to get insight into all three aspects of the peer-review system: writing, reviewing, editing. With this in mind, *The Journal of Physiology*'s Editorial Board Fellowship offers up to 10 early career scientists per year an opportunity to experience the editorial process first hand. We warmly welcome our class of 2023, who will start their two-year term this July.[2]

I should like to finish by thanking all of you for engaging in academic self-governance though the various aspects of conducting and publishing science.

Even if *you can't always get what you want*.[3]

Footnotes

1. A saying variably attributed to Walter Winchell, Tony Curtis, John Templeton, Sidney Blackmer, Dwayne Johnson, Roger Federer, and others.
2. https://physoc.onlinelibrary.wiley.com/hub/journal/14697793/winners_editorial_board_fellowship
3. Jagger M & Richards K, The Rolling Stones: Let It Bleed, 1969.

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Mind and mend the gap: Women in physiology

Professor Damian Bailey

Editor-in-Chief,
Experimental Physiology

I'm writing this column a few days after 11 February, which marked the (eighth) International Day of Women and Girls in Science, an opportunity to celebrate creativity, innovation and achievements while continuing the global mission towards gender equality. In her opening address to this year's Assembly held at the United Nations (UN) Headquarters in New York City, Audrey Azoulay, Director-General of the UN Educational, Scientific and Cultural Organization (UNESCO) remarked, "Science is many things: a study of natural, physical and social phenomena; a process to test hypotheses and draw conclusions; a journey of discovery to understand the world's many mysteries. But what science should be is equitable, diverse and inclusive. It should be for all and open to all, especially women."

But as we know all too well, best wishes don't always stack up against the stark truths of reality, with the latest UNESCO Science Report highlighting a "leaky pipeline": only 35 per cent of graduates in Science, Technology, Engineering, and Mathematics (STEM)-related fields and 28% of all researchers are women (United Nations Educational, 2022). This is clearly out of kilter with what would be expected based on population demographics and an estimated 3.905 billion women that represent 49.58% (let's round this up to 50%) of the world's population (United Nations Department of Economic and Social Affairs, 2022). More needs to be done to "mend" the gender gap, and it's the steady drip, drip, drip of cultural change that will ultimately help wear away this stubborn stone.

The day's events have given me an opportunity to quietly reflect on our own specialist discipline and the common challenges facing our community. That women physiologists are underrepresented has not gone unnoticed by The Physiological Society (TPS), having led on a number of initiatives that challenge stereotypes and long-standing biases, while looking to raise awareness of those physiologists blazing new trails (Society, 2013). The recent launch of the TPS' Equity, Inclusion and Diversity Roadmap stands clear testament to its commitment to champion diversity, promote inclusivity, and strive for equity providing opportunities fairly and squarely for all.

A trip down memory lane helps put the challenges women physiologists faced into clearer perspective with a canonical example that holds special relevance to readers of *Experimental Physiology*. Dr Florence Buchanan (1867–1931) was one of our earliest "trailblazers" whose name will be forever etched into TPS' history books, given some "fearless firsts" that challenged the *status quo* (Burgess, 2015; Tansey, 2015; Ashcroft, 2022). Much to the disdain of others (male members), she was the first woman to attend a meeting of TPS in 1896 some 22 years after it was founded, although she did not join the men for dinner, which at the time hosted live animal experiments and was the highlight of the meeting. Ernest Starling (1866–1927) voiced his concerns, stating "it would be improper to dine with ladies smelling of dog – the men smelling of dog that is" (Evans, 1964). She was also the first to publish in the *Quarterly Journal of Experimental Physiology* that later became *Experimental Physiology* in 1990, with a 67 page (no less!) original article focused on the transmission of reflex impulses in the frog (Buchanan, 1908). And her third first, fueled by a relentless persistence that included at least ten communications to TPS and a smattering of papers published in the *Quarterly Journal of Experimental Physiology* (3) and *The Journal of Physiology* (2), she became the first (alphabetically) of six women to be elected for membership to TPS at the AGM in January 1915: much thanks to a postal ballot bravely proposed by J. S. Haldane (1860–1936) and J. N. Langley (1852–1925) that took place the year prior, culminating in the landmark "Rule 36": "Women shall be eligible for membership of The Society and have the same rights, duties and privileges as men." Dr Buchanan challenged tradition and broke the mould: she was surely made of the "right stuff"! Her legacy was celebrated by TPS on 4 July 2022, with the unveiling of a Blue Plaque at The Department of Physiology, Anatomy and Genetics at University of Oxford, UK where Buchanan worked as a research assistant under the tutelage of John Burdon-Sanderson (1828–1905).

We've come a long way since. A shining example that reflected modern society's changing attitudes towards sex and gender presented itself on 18 October 2019 when NASA astronauts Christina Koch and Jessica Meir performed the first "all-women" spacewalk on the International Space Station, a truly historic milestone (Fig.1). What's especially poignant is that Jessica Meir is a physiologist having studied vertebrate adaptation to extreme environments (there is no better example than humans surviving in the vacuum of space!): topics that she covered during her delivery of The President's

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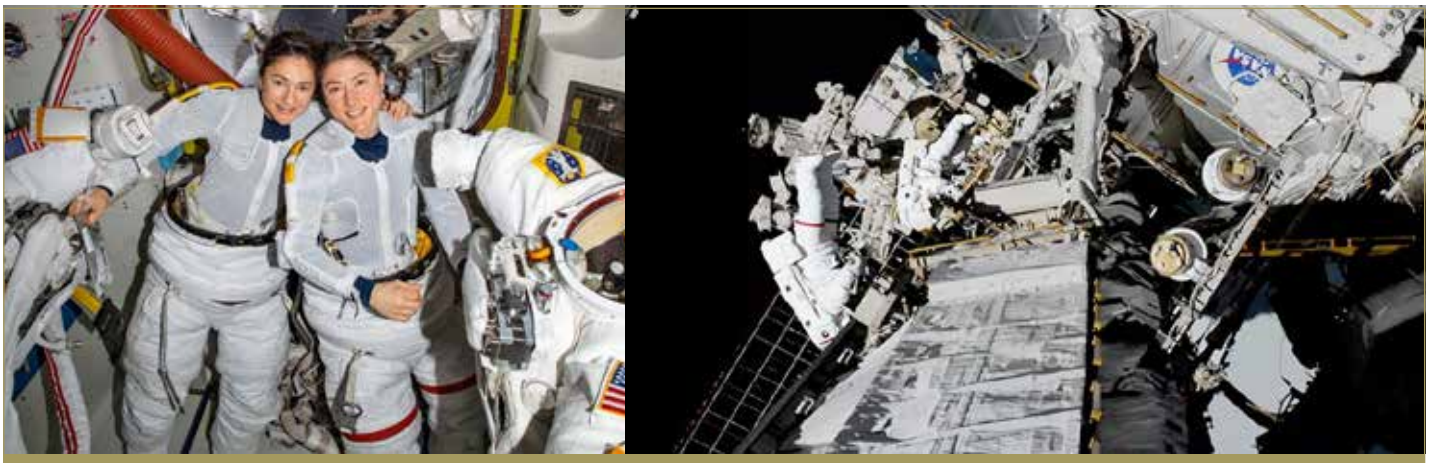

Figure 1. Giant leaps for woman-kind *Left photograph.* Physiologist Jessica Meir (left) and engineer Christina Koch (right) preparing for the first all-women extravehicular activity (spacewalk) on the International Space Station (ISS). Since the first spacewalk by Russian Svetlana Savitskaya who spent 3 hours, 35 minutes on 25 July 1984 outside the Salyut 7 space station, 15 women have participated in spacewalks (14 as NASA astronauts). *Right photograph.* Meir (14th woman to spacewalk) and Koch (13th, red stripes on legs of spacesuit in foreground) logged 7 hours and 17 minutes during their historic spacewalk performing repairs to the ISS. Koch later went on to break the world record for continuous time spent in space by a woman (328 days) surpassing the 288 days previously held by Peggy Whitson. Some of the fundamental contributions made by women in space can be found at nasa.gov (https://www.nasa.gov/feature/womens-history-month-2023-celebrating-women-astronauts), best summed up by Valentina Tereshkova, the first and youngest woman in space,
"A bird cannot fly with one wing only. Human space flight cannot develop any further without the active participation of women."

Lecture at TPS in 2021. And NASA's commitment, through its Artemis missions, to land the first woman (and first person of colour) on the Moon with an orbital outpost to support human exploration of Mars, will inspire future generations of like-minded trailblazing women. There's good reason why we need more women "astro-physiologists" to solve the complex challenges of deep spaceflight! (Bailey, 2022).

But there's still a long way to go as undercurrents of sex and gender bias persist (Barrett, 2019). Publishing papers, the primary currency of academe and established metric for tenure and promotion, highlights a systemic problem, with women much less likely than men to be credited with authorship (Ni *et al.*, 2021; Ross *et al.*, 2022). That their contributions are devalued or simply not recognised may account, at least in part, for the well established "productivity gap" understandably compounded by the COVID pandemic (Andersen *et al.*, 2020; Huang *et al.*, 2020) further discouraging career progression within junior ranks. And at the very sharp end of life and death, spare a thought for those (seemingly) obvious anatomical/physiological differences (Tarnopolsky and Saris, 2001; Ansdell *et al.*, 2020) best encapsulated by that famous saying, "men are from Mars and women are from Venus". Despite existing legislation such as the National Institutes of Health Revitalization Act of 1993 mandating the inclusion of women in studies of humans, the field of medicine consistently fails to account for differences in sex and gender. This puts women's healthcare provision at risk, with prescriptions and diagnoses confounded by approaches that overly favour male physiology (Miller, 2014; Nowogrodzki, 2017). On a more positive note, this is a rich plot for physiologists to plunder.

I've become acutely aware of this "unconscious" bias, borne through bitter experience and by taking the time to reflect and refer to the literature base as I write this column. The sobering reality of directing a male-dominated laboratory, reality checks when composing submissions to the Research Excellence Framework and only a handful of women scientists with whom I've collaborated in my specialist field highlights a personal failing. Even a cursory glance at the Editorial Boards of *Experimental Physiology* and the *Journal of Physiology* expose "fault lines" within their composition (Fig.2), which is commonplace across the life sciences (Palser *et al.*, 2022). Under-representation of women is equally apparent across a number of categories within TPS membership that appears to be compounded with age since the disparity is especially pronounced in the fellow, honorary and retired categories that typically attract older members (Fig.3). I wonder if this reflects the bitter aftermath of times gone past, with fewer women remaining in physiology, shackled by cultural constraints?

More steady drips needed, I hear you say? We all have a role to play and it's a long road ahead, after all, it's all about mutual respect and accountability (see Peter Kohl's column on p10). If the "leaky" pipeline is indeed age-related, there is a message of hope since we have an opportunity to provide (more) support to our younger women physiologists. This is a change that both Peter Kohl and I want to actively support and promote, indeed as those Editors-in-Chief that stood before us. We can look beyond our shores and take strength and learn from a number of new initiatives. The Royal Society of Chemistry's Joint Committment for Action on Inclusion and Diversity, mapping out the steps they will take to minimise bias across their family of (>1500) journals and sharing it with other publishers to make scholarly publishing more inclusive and diverse is a leading example. So too is the recent decision of a subset of *Nature* Portfolio journals where submitting authors will be prompted to provide details on how sex and gender were considered in study design (2022), encouraging compliance with SAGER (Sex and Gender Equity in Research) guidelines (Heidari *et al.*, 2016).

And on a more personal note, I'm keen to attract more women physiologists to the Editorial Board of *Experimental Physiology* to redress the current imbalance and ensure that women are visually represented alongside their male contemporaries: if you are interested in contributing either as a Senior or Reviewing Editor, please feel free to get in touch. In closing, I'll end this column with a simple equation, taken from António Guterres, Secretary General to UNESCO: ↑women + ↑girls in science = ↑volume + ↑quality science.

Simple.

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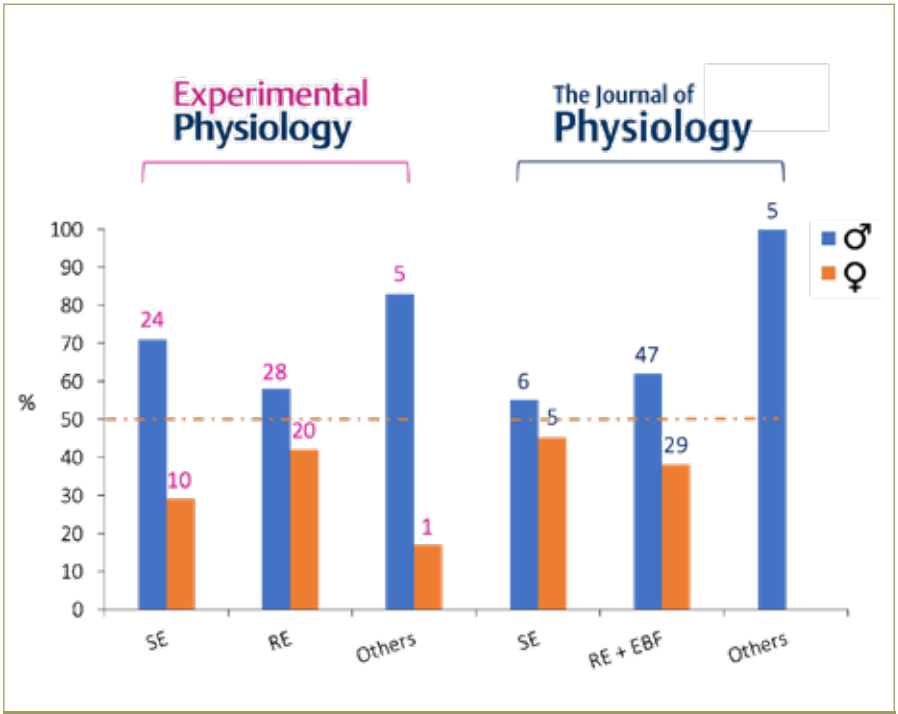

Fig.2. Sex composition of journal editorial boards Digits above histograms represent absolute number of members from which percentages were calculated. SE, Senior Editor; RE, Reviewing Editor; EBF, Editorial Board Fellow; "Others" includes Cross talk/Regional/Senior Ethics/Senior Reviews/Assistant Reviews/Statistical/Connections Editors.

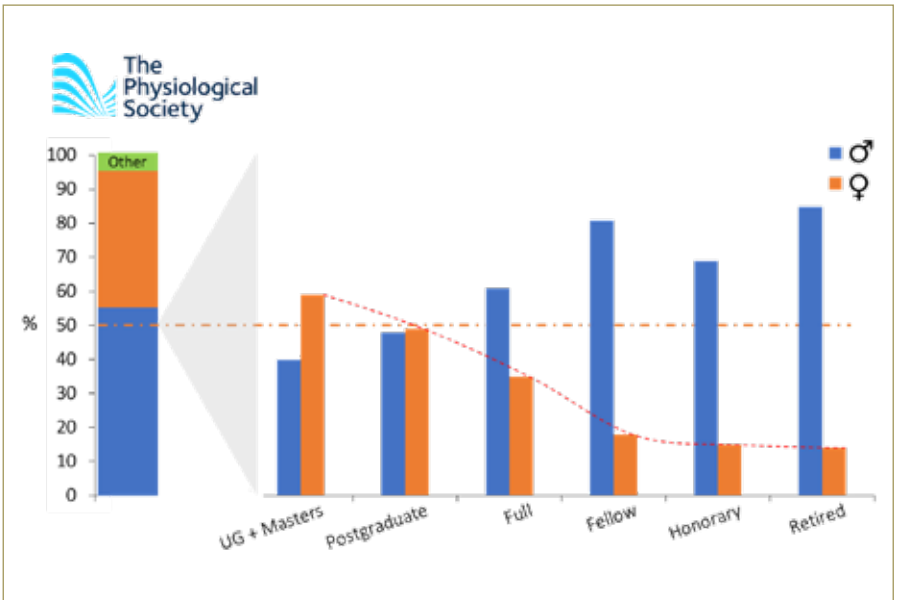

Fig.3. Sex composition of membership to The Physiological Society Left histogram represents differentiation across the entire membership (pooled categories). "Other" reflects members who do not identify as male/female or sex/gender is unknown, UG stands for Undergraduate. Stippled red line highlights the tendency towards more marked under-representation of women in those categories that typically attract older members (age differentiation not shown). This age-related "leaky pipeline" is especially apparent among fellow, honorary and retired members, perhaps a reflection of fewer women who have remained in physiology due to the cultural constraints imposed by the past.

Acknowledgements

I would like to thank Professor Peter Kohl (Editor-in-Chief of *The Journal of Physiology*) and Dariel Burdass [The Physiological Society (TPS)] for stimulating discussions and helpful reference to key literature sources. Josh Hersant (TPS) and Andrew MacKenzie (TPS) kindly provided the raw data supporting Figures 2 and 3 respectively.

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Celebrating the contribution of Scotland's research base to meeting the Sustainable Development Goals (SDGs)

Tom Addison

Policy Manager,
The Physiological Society

Scotland's research to meet the Sustainable Development Goals

Following the publication of Scotland's REF 2021 results and the Scottish Funding Council (SFC)'s *Scotland's research contribution to national and international challenges,* The Physiological Society partnered with the Royal Society of Edinburgh to showcase some of the research being undertaken in Scotland to elected officials in the Scottish Parliament that responds to the ambitions of the United Nation's Sustainable Development Goals (SDGs). The event was an opportunity to continue to "bang the drum" for physiology in another of the UK's four national legislative bodies while aligning with Scotland's national funding and policy priorities relevant to the work of our members.

Agreed in 2015, the *2030 Agenda for Sustainable Development* includes 17 SDGs. Building on the principle of "leaving no one behind", the SDGs emphasise a holistic approach to achieving sustainable development for all. They combine a number of initiatives targeting the end of poverty and other socio-economic inequalities with objectives relating to improving health and education, while tackling climate change and working to preserve the planet's oceans, agriculture, wildlife and forests.

Each SDG has a series of targets totalling 169 individual targets overall. Many of these goals have a direct health target, which will be informed by physiological research. For example, SDG 11 (Sustainable Cities and Communities) includes targets related to reducing deaths caused by flooding and improving transport systems. Additionally, SDG 3 "ensure[s] healthy lives and promote[s] well-being for all at all ages", a focus which clearly aligns with physiological research.

Over the last decade, a third of Scotland's research was directly related to the ambitions set out in the SDGs. Scotland is world-leading in the physiological sciences, with a proud history of Nobel Prize winners continued today by cutting-edge research and teaching.

The SFC's response to the SDGs

Scotland's research contribution to national and international challenges was published by the SFC in March 2022 and outlines how the funding provided by the SFC will address Scotland's ambitions in relation to the SDGs. The foreword notes that "The SDGs underpin the Scottish Government's National Performance Framework (NPF) and its ambition for a sustainable, just and prosperous future for everyone." The report also highlights that almost half of all Scottish SDG-related research contributed to an improved understanding of good health and wellbeing and this research aligns with the targets identified in SDG 3.

Given the strength of Scottish research related to the SDGs and the overwhelming focus on this research output on health and reducing health inequalities, the event was an important opportunity to recognise physiology's role within this and encourage the Scottish Government to continue to support physiological research that builds on the impact of previous research in these fruitful areas.

Names from left to right: Professor Derek Scott, University of Aberdeen, and The Physiological Society; Professor Charlie Withers FRSE, RSE Research Awards Convener; Clare Adamson MSP for Motherwell and Wishaw; Jamie Hepburn MSP, Minister for Higher Education and Further Education, Youth Employment and Training; Dr Cat Ball, Scottish Funding Council.

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Graeme Cook speaking to attendees.

The foreword of the report, co-authored by Professor Derek Scott and Catherine Ross, Scotland's Chief Health Science Officer, notes that "The SDGs underpin the Scottish Government's National Performance Framework (NPF) and its ambition for a sustainable, just and prosperous future for everyone."

Read the report at
physoc.org/policy/research-landscape-and-funding/scotland-at-the-heart-of-meeting-global-challenges/

As The Society launches its own updated strategy, The Society's policy team will be working closely on collaborations such as these to ensure that we play an influential role in shaping funding and public policy and continue to advocate for physiology's role in meeting often complex and deep-rooted problems such as health inequalities and healthy ageing.

To this end, we produced a short report for the event *Physiology in Scotland: Achieving the Sustainable Development Goals*, which characterises the role of physiological research in addressing the SDGs and also gives some tangible examples from across Scotland's higher education institutions (HEIs). One such example was from the University of Aberdeen, which highlighted researchers' work there in developing a low-cost COVID-19 vaccine, which could be rolled out globally.

Scotland at the Heart of Meeting Global Challenges

The event in Holyrood, kindly hosted by Clare Adamson MSP, brought together Scottish researchers, Members of the Scottish Parliament (MSPs) and policymakers from throughout the country, to celebrate the contribution that Scotland's HEIs have made to meeting the SDGs and outline the major challenges and opportunities yet to be addressed. We also heard from Jamie Hepburn MSP, the Minister for Higher Education and Further Education, Youth Employment and Training, as well as Dr Cat Ball from the SFC, Professor Derek Scott from the University of Aberdeen representing The Society and Professor Charlie Withers from the University of Edinburgh. In combination, their speeches demonstrate the breadth of impact that Scottish research has in meeting the SDGs. We would like to thank Catherine Ross for her valuable contribution and support for this project and its related report.

The event also included an exhibition from some of Scotland's HEIs and those physiologists who contributed to our report for the event.

Some examples of impact of the event have already been shared by members of The Society and MSPs. The University of Glasgow project "Science Travels", which promotes STEM among members of the Gypsy, Roma, Traveller, Showmen and Boater (GTRSB) communities was referenced in the Scottish Parliament debate on International Women and Girls in Science Day 2023. Similarly, the Scottish Parliament Motion "S6M-07768: Scotland at the Heart of Meeting Global Challenges", has been signed by 21 MSPs on a cross-party basis. Additionally, our event host met with representatives from the University of Edinburgh neuroscience team about research into chronic pain. The Society's policy team will be following up these and other connections to continue to promote Scottish physiology research among politicians and funders alike.

Mrs Natasha Price and Dr Allison Wood, Queen Margaret University.

Clare Adamson MSP, Motherwell and Wishaw.

The Society will be working closely with Scottish members and other physiologists to ensure that funding available exclusively to Scottish members can be secured to ensure that physiology continues to make an impact both within Scotland and through international collaboration.

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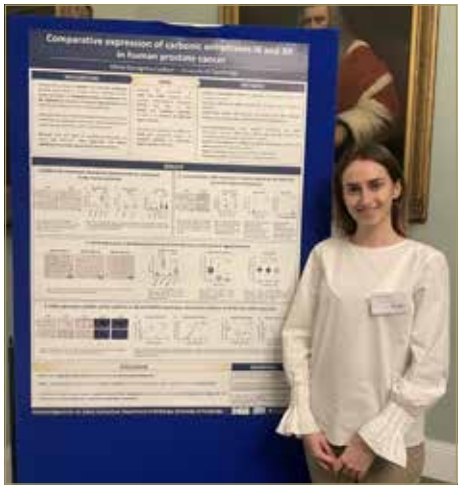
Congratulations to our 2022 Rob Clarke Awards Winners

The Rob Clarke Awards were one of the highlights of the Member Forum held on Friday 2 December 2022. The award recognises excellence in undergraduate physiology projects.

Last year, 11 students were shortlisted for an Abstract Award and invited to present a poster at the Member Forum for final judging. The judges were impressed with all the finalists but receiving the overall highest score was Elena-Georgiana Capbun from University of Cambridge, UK who presented her poster titled "Comparative expression of carbonic anhydrases IX and XII in human prostate cancer". The judges were impressed with Elena-Georgiana for the huge amount of work undertaken, the diverse techniques used and the depth of her knowledge on the topic, which she clearly presented.

We interviewed the winner and runners up to find out more about their projects. They share the inspiration behind their research and their experience of presenting to a panel of judges.

Award winner



Elena-Georgiana Capbun

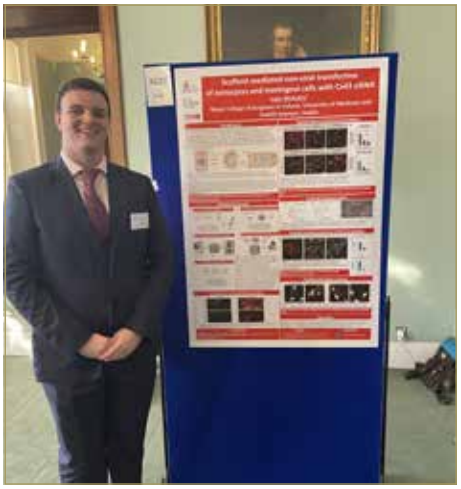
University of Cambridge, UK

My project focused on the "Comparative expression of carbonic anhydrases IX and XII in human prostate cancer", as potential biomarkers used in risk stratification, to allow better targeting of treatment with the intent of improving success and minimising adverse effects associated with therapy for indolent phenotypes. This was my first research project, completed during my intercalated year at university. Although challenging at times, given the amount of work and diverse techniques undertaken, I thoroughly enjoyed this experience: reading around the subject, thinking about data analysis, the significance of our findings and future paths that can be undertaken. I am thankful for the opportunity to work with my supervisor and other experts in histopathology and the field of carbonic anhydrases.

The poster presentation was enjoyable, from meeting other students and learning about their work, to presenting and being questioned by the panel of judges. It was an honour to be able to present my work to experts, to be listened to and questioned in a way in which interest was shown and ideas were discussed. The feedback from the judges was encouraging and it is a privilege to receive the award.

Motivated by my experience working on this project, I would like to work on clinical research and I am interested in pursuing a career in surgery.

Runner up



Luke McAuley

Royal College of Surgeons in Ireland

My project looked at ways to promote the regrowth of cells to improve healing and recovery following a spinal cord injury. To achieve this, we devised a scaffold-based delivery system capable of administering therapeutics directly to the injury site, which reduced scarring and promoted regrowth. I am a medical student and an avid rugby player, a sport where head, neck and spinal injuries are common. So, I was keen to research injury prevention and possible therapeutics leading to better outcomes following a spinal injury. I was fortunate to get the opportunity to partake in an eight-week summer project within the Tissue Engineering Research Group (TERG) Spinal Cord Injury team.

The poster presentation was an amazing experience and excellent learning opportunity for me personally. I had never presented to a panel of judges before and so was a little nervous to start. As the day went on, however, I grew in confidence, helped by the enthusiasm shown by both the judges and The Physiological Society members that came to view my poster and ask questions. Their questions made me think about alternative approaches to my work and consider other processes that would improve the efficiency and quality of the results.

The summer project has guided my decision to specialise in Orthopaedics. It has highlighted for me the need for further research into spinal cord injury repair therapeutics and the need for clinicians who are willing to bring these new revolutionising technologies to trial in their patients.

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Runner up

Peter Panizza

The University of Western Australia

My research focused on developing our understanding of the progression of Duchenne muscular dystrophy, with a particular focus on the aetiology of mitochondrial dysfunction in the pathology. Once I learnt about the devastating effects of this disease, I was drawn to research in this field, especially as I can relate to those affected as it affects primarily young males.

This was my first presentation of original research to a room full of accomplished scientists. It was truly an amazing and humbling experience. Leading up to my poster presentation I was quite nervous, however also extremely excited for the opportunity. When my presentation began, I started to relax as the judges were encouraging and patient. The conversations I had with judges during and after my presentation were stimulating and provided me with some new ideas for my future research. I thoroughly enjoyed the experience and the opportunity to network with the other presenters and more experienced researchers.

This project has deepened my interest in skeletal muscle disease and it is the field I wish to focus my career on. I am continuing my research into muscular dystrophy and building upon the interesting results of this project through an honours programme at the University of Western Australia. Next year I plan to apply to undertake a PhD.

Finalists – Rob Clarke Abstract Winners

Aaliya Ashik, University of Manchester, UK
Understanding structural alterations to the atrial microtubule network in heart failure

Alokya Balagamage, King's College London, UK
Maternal Obesity and the Effects of Sulforaphane on White Adipose Tissue Mass and Cell Size

Elena-Georgiana Capbun, University of Cambridge, UK
Comparative expression of carbonic anhydrases IX and XII in human prostate cancer

Louise Cope, University of Aberdeen, UK
Repurposing of a selective phosphodiesterase 1 inhibitor for pulmonary arterial hypertension

Anna Devari, University of Birmingham, UK
Exploring a potential extracellular action of succinate on carotid body activity mediated by gpr91

Roisin Dowd, University College Dublin, Ireland (not in attendance)
Assessing the Structure-Function Relationship of Obligatory and Accessory Respiratory Muscles in Early Dystrophic Disease

Luke McAuley, The Royal College of Surgeons in Ireland
Scaffold-mediated non-viral transfection of astrocytes and meningeal cells with Cx43 siRNA

Kamil Moosavi, Oxford Brookes University, UK
Effect of repetitive Transcranial Magnetic Stimulation (rTMS) of the Dorsolateral Prefrontal Cortex (DLPFC) on hypercapnic air hunger induced in healthy individuals

Peter Panizza, The University of Western Australia
In vitro cyclosporin A exposure does not prevent hypochlorous acid induced muscle weakness in the mouse extensor digitorum longus

Yashika Relan, University of Dundee, UK
Glutaredoxin-overexpression attenuates chronic angiotensin-II induced hypertension and changes cardiac dynamics

Parth Tagdiwala, University College London, UK
Development of contractile function and motility patterns within the intestine

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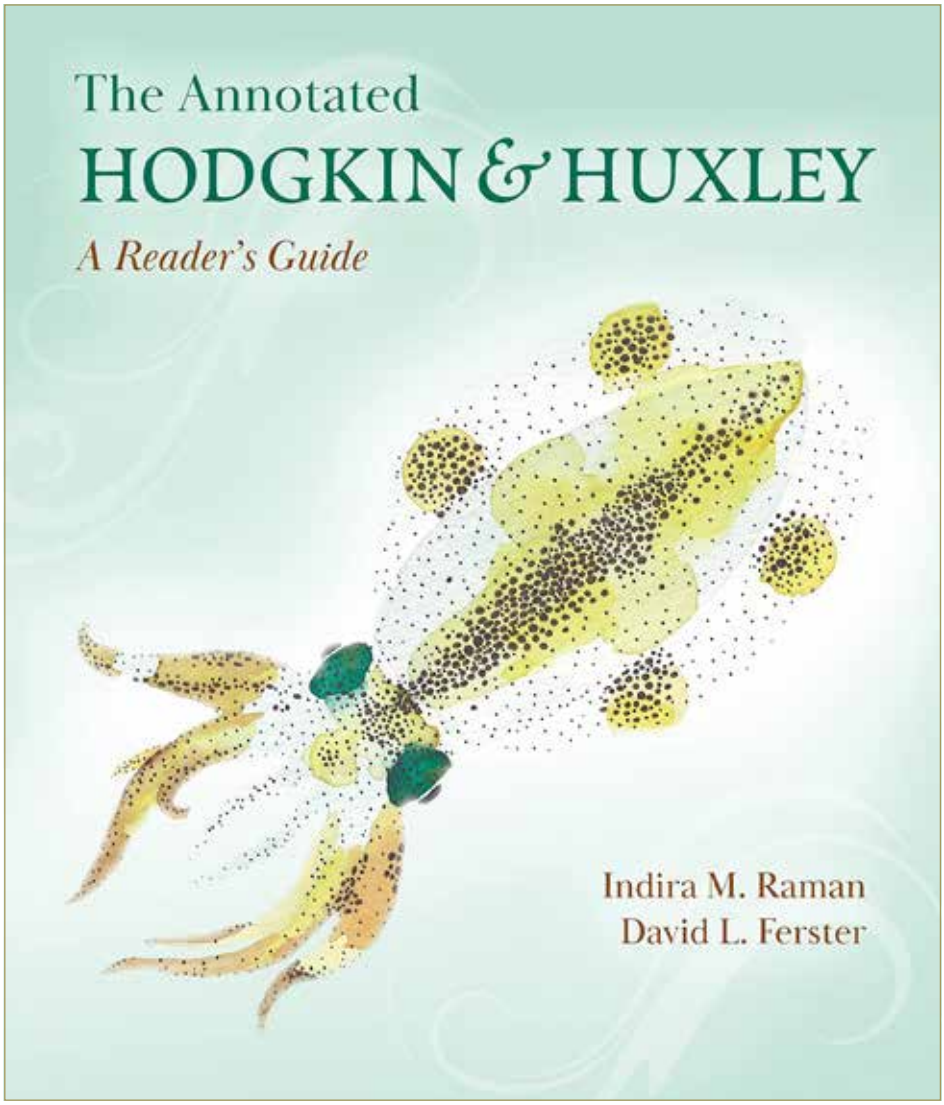
The Annotated Hodgkin & Huxley: A Reader's Guide

Indira M Raman & David L Ferster

Princeton University Press, US

Dr Angus Brown

University of Nottingham, UK



This book joins a long list of those dedicated to illuminating the work of Hodgkin and Huxley, contained in the five classic papers published in *The Journal of Physiology* in 1952 (Hodgkin and Huxley, 1952a, b, c, d; Hodgkin *et al.*, 1952). The need for such books emphasises two important aspects of the Hodgkin and Huxley work, its central role in physiology and its seemingly impenetrable complexity. The first academic to meaningfully address the work was J Walter Woodbury in the Department of Physiology and Biophysics at the University of Washington, Seattle, in the late 1950s. Woodbury, a physicist by training, realised the rich rewards offered by the work and ran a course where students were instructed in non-linear partial differential equations as well as the underlying physiological mechanisms. Based on this lecture series he was asked to contribute relevant chapters to the 18th edition of the textbook *Medical Physiology & Biophysics* edited by Ruch & Fulton in 1960. The rigour with which Woodbury approached the subject would horrify contemporary students, and one need only consult his section on "Potentials in a volume conductor" to realise how far standards and expectations have drifted since the 1960s. Woodbury was asked by the Nobel committee to nominate worthy candidates for the Physiology and Medicine Prize: his nomination secured the Prize for Hodgkin and Huxley in 1963. The 19th edition of the book was published in 1965 (Maynard, 2014) and Bertil Hille assumed duties for the excitable membrane chapters in 20th and 21st editions. The role of Hille in publicising the Hodgkin and Huxley work cannot be overstated, his own book *Ionic Channel of Excitable Membranes* published in 1984, with further editions in 1991 and 2001, reaching a vast and receptive audience ready to utilise the recently developed patch clamp and cloning techniques to study structure and function of ion channels. Every modern neuroscience textbook contains at least one chapter on the membrane potential and the action potential, which begs the question, what does this new book add?

Students approaching in-depth study of a research topic are routinely advised to consult original sources and in the introduction to this book seven convincing reasons are provided as to the wisdom of this advice. But what if the original sources are based on outmoded conventions and refer to redundant equipment and terminology? This book offers a very pragmatic solution by providing appropriate up-to-date explanations, interpretations and redrawn graphs based on information in the original papers. The format of the book is novel as the original Hodgkin and Huxley papers are printed on the left side of the page with updates and explanations on the right. This format runs the risk of blank

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pages where no explanation is necessary or text spilling over to the subsequent page, interrupting the narrative flow. The need for such updates stems from the conventions for reporting current and voltage used by Hodgkin and Huxley, which are different from those in use today. The movement of +ve charge into axons was depicted as an upward deflection, with the resulting membrane depolarisation a downward deflection. However, upward pointing action potentials were deemed more pleasing to view thus the voltage scale was depicted as –ve volts. This was compounded by reporting resting membrane potential as 0 mV, where adherence to the contemporary convention would depict it as +ve volts. For students familiar with modern textbooks, consulting the original papers is an exercise in confusion, frustration and inevitably capitulation. However, browsing through only a couple of pages of this current book reassures the reader they are in safe hands. Indeed, one gets the impression that if the authors were to uncover Hodgkin and Huxley's old equipment in a dusty cupboard, they would have it up and running by the end of the day. Further validation comes in the form of an enthusiastic recommendation from Beril Hille, and the recent award of The Physiological Society's Hodgkin-Huxley-Katz Price Lecture to one of the authors, Indira Raman.

Full appreciation of the Hodgkin and Huxley work requires understanding of the historical context, which is provided in the introduction, with a fascinating fuller account available (McComas, 2011). Thus, one must understand what Hodgkin and Huxley set out to do, the techniques and model available to them and the work of their contemporaries. Although the five papers in the canon are considered complete, it would have made sense to include the Hodgkin and Katz 1949 paper as a logical introduction (Hodgkin and Katz, 1949). Indeed, had it not been for Huxley being unavailable due to wedding commitments in the summer of 1947, Katz would not have been invited to participate in the experiments and the canon would consist of six Hodgkin and Huxley authored papers. The five papers comprise 126 pages, but contain a multitude of redundant information, and heretical as it sounds, about one third of the content could be happily ignored with no loss of impact or meaning. This refers principally to equipment and terminology that is obsolete and unknown to contemporary students, i.e. inductance, series resistance, guard systems, polarisation, cathode follower etc. The independence principle experiments, although important in suggesting that I_{Na} and I_K were separate entities, was not an integral component of the model, and the incorrect conclusions drawn from these experiments took several years to be corrected (Hodgkin and Keynes, 1955). In addition, the lack of a system for cooling the seawater bathing the experimental squid axons ensured the experiments in the Hodgkin and Katz 1949 paper were carried out at room temperature. The later introduction of a cooling coil, which was used in experiments described in the five classic papers, meant the seawater was at an appropriate temperature, but required reconciling with the room temperature data, thus there are eight figures at room temperature that could be deleted. Indeed, of the seventeen figures in the 1st paper (Hodgkin *et al.*, 1952) only five are essential to the model. Thus, the inclusive nature of this book, where every aspect of the original papers is updated, means considerable labour has been expended for information that will be of interest to a very few readers. Another important point to make is that students don't need to understand everything in the papers to appreciate Hodgkin and Huxley's work.

The book is aimed at graduate students, an appropriate target audience. Having undertaken a similar venture recently (Brown, 2020), I appreciate the enormous amount of work that goes into producing a book of this sort, where every word and graph must be minutely weighed for clarity and meaning and can happily report that this book is a very welcome addition to the Hodgkin and Huxley oeuvre. In covering such a vast subject there are inevitable omissions and a few minor grumbles, but I regularly dip into the book for pure pleasure, and it does not disappoint. Highly recommended.

A few observations

p.70 Update composition of salt solutions to mM rather than g/kg H_2O.

p.78 Confusing Nernst predictions. What should be straightforward Nernstian calculations include an additional step to account for reporting the resting membrane potential as 0 mV.

p.86 Given that only half of the page is used, some detail of the calculus required for isolation of I_K could have been included (Cronin, 1987).

p.93 Good graphical explanation of chord and slope conductance.

p.142 Polarisation of the voltage clamp – Hodgkin and Huxley mention a polarisation effect of unknown origin in their estimates of E_K. We now know this is due to accumulation of K^+ in the limited space between the axolemma and a surrounding tight membrane, where the longer the duration of the pulse, the more K^+ accumulation and the more depolarised E_K became. This only came to light with later experiments (Frankenhaeuser and Hodgkin, 1956).

p.199 The best explanation I have come across for gating particles.

p.230 The authors offer no explanation for the phrases "under a travelling anode ... under a travelling cathode", which have puzzled me for the last 35 years.

p.255 and p.259 Excellent graphical illustrations of membrane current to explain threshold and anode break excitation, respectively.

p.279 Excellent appendices on derivation of equations used to fit data

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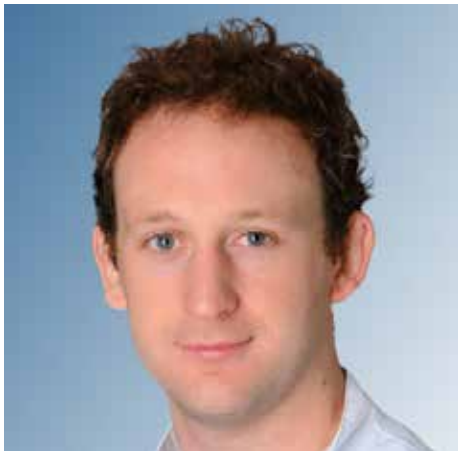
Is daylight worth saving or is it time to change?

The health controversies around daylight saving time



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Daylight saving time (DST) is an advanced official clock time, typically by 1 hour, and typically employed during months with longer durations of daylight (e.g. from the last Sunday in March to the last Sunday in October, in the EU and UK). The desired result is that sunrise and sunset occur at an official clock time that is 1 hour later. DST is then changed back to "standard time" (also known as "winter time") for months with shorter durations of daylight. This biannual transition is practised in most of Europe and North America and in some parts of South America, Oceania, and Asia. Many countries not currently employing DST have experimented with it in the past. The "spring forward" (DST onset) and "fall back" (DST offset) transitions have caused controversy for many decades and on many levels, including potential complex health and economic effects, and simple inconvenience and practicality. Furthermore, the manner in which changes in official clock times affect the relationship between social schedules, sunshine hours, internal "circadian" time, and health will differ by geographical, cultural, and individual factors. From a health sciences perspective, DST offers an incredible natural experiment opportunity to be explored. As DST debates (including whether to abolish the time change and to keep either standard time or DST) gather momentum, DST-policy changes, at least in some regions, seem inevitable. Therefore, this natural experiment must be appropriately utilised to help reconcile health controversies.

Brief history of (adjusting) time

The adjustment of clock time is nothing new. For instance, water clocks used in ancient Mesopotamia, Egypt, Greece, China, India, and Rome had different scales for different months, making time intervals within a day longer or shorter as necessary in alignment with daylight hours. Sundials could only indicate time when the sun was shining, and daylight hours vary with season. Furthermore, the gnomon of a horizontal sundial must be parallel to the Earth's axis for accurate time; this was not always the case. Sundials could be used to determine local solar time only, the reference for which is when the sun reaches its highest point (or zenith) in the location of the observer. Thus, towns and villages had their own local time zones. The use of equal hours (i.e. 60 mins in every hour) in a 24-hour day may have become more widespread with the development of spring clocks in the 14th–15th century and with traders needing more accurate, secular time keeping for commercial benefit.

Although equal hours were increasingly used, local solar time remained common (and a person would have to adjust their clock if travelling from e.g. London to Dublin). In 1884, "The International Meridian Conference" facilitated propagation of the time zones concept in scientific-political discourse in many countries. However, it took many decades before a significant number of countries adopted the time zone concept and the Greenwich meridian was taken as the reference point for universal times and time zones (longitude 0°, UTCs).

The first serious proposition of biannual adjustments to standardised clock time came about a decade after the 1884 conference. In 1895, George Hudson put forward the idea of a 2-hour shift in New Zealand so that daylight hours would overlap with his off-work entomology hobbies. The next known suggestion by William Willett in London (1907) involved four shifts by 20 mins each over consecutive Sundays after noticing many people slept after sunrise and yet he had not enough daylight for golf in the evening (Douma, 2008). None of these suggestions were implemented.

The first city to employ DST was Port Arthur in Canada in 1908, while the first states to employ DST were the German and Austro-Hungarian Empires during World War I – to conserve coal. Other countries quickly followed suit. More countries adopted DST during World War II and more again during the energy crisis of the 1970s.

The specific calendar days when transition to and from DST occurred and the size of clock change on transition days has varied by region and year. For instance, a 2-hour shift was employed in the UK during World War II and again in 1947. Currently in the EU and the UK, a 1-hour advance occurs on the last Sunday in March (DST onset) and DST offset occurs on the last Sunday in October. Different DST practices in Europe were considered disruptive to transport and communications, leading to directives from the European Commission for transition day alignment since 1981.

Brazil makes for a good case study in DST practice variability. In Brazil, DST transition dates were set one year at a time until 1968 when onset was fixed as the first day of November and offset as the first day of March, regardless of the day of the week. Note that the month–daylight relationship is inverse for the southern hemisphere, and most Brazilian states are south of the equator, hence, the inverse time-of-year onset and offset compared to the northern hemisphere. In 1987, transition days in Brazil were fixed to Sundays. By 1991, 15 of the 27 Brazilian states, all from the north and northeast regions abandoned DST practices. From 2008, DST onset was fixed as the 3rd Sunday in October and offset as the 3rd Sunday in February unless this coincided with Carnival, with offset then being delayed by one week. As of 2020, no Brazilian states employ DST.

		Biannual Time Change		Perennial DST		Perennial Standard Time	
		Dublin	Rome	Dublin	Rome	Dublin	Rome
21st Jun	Sunrise	~05:00	~05:35	~05:00	~05:35	~04:00	~04:35
	Sunset	~22:00	~20:50	~22:00	~20:50	~21:00	~19:50
21st Dec	Sunrise	~08:45	~07:40	~09:45	~08:40	~08:45	~07:40
	Sunset	~16:15	~16:45	~17:15	~17:45	~16:15	~16:45

Table 1: Comparison of sunrise and sunset times, in Dublin and Rome, with and without DST transitions.

Current debate in Europe and the USA

Following the results of a citizen survey in 2018 (European Commission, 2018) the European Commission proposed to end biannual clock changes. However, no approval by parliament and council has yet been made due to discrepancies between what member states favour, lack of impact assessments made by member states, and the COVID-19 pandemic delaying proceedings. Of note, a slight majority of the 2018 citizen survey were in favour of keeping DST all year round (i.e. perennial DST). However, the representativeness and generalisability of the survey results are highly debatable (Blume and Schabus, 2020).

In terms of public perception of DST, Coogan *et al.* (2022) use the example of Dublin and Rome to highlight potential differences; for instance, abandoning DST for perennial standard time may be more negatively appraised in Rome (with sunset before 8pm in summer) than in Dublin (Table 1) (Coogan *et al.*, 2022).

The UK leaving the EU in 2020 ("Brexit") throws another spanner in the works for Europe. The UK government has no current plans to abandon DST practice. If the EU abandons DST practice, there would be a 1-hour time difference between Northern Ireland and the Republic of Ireland for approximately half of the year, which is unfavourable to locals (Coogan *et al.*, 2022).

In the USA in 2022, the Sunshine Protection Act (US Senate, 2019) – which involves the implementation of permanent DST – was approved by the Senate but is yet to be approved by the House of Representatives. The name of the proposition – "Sunshine Protection" – is certainly non-neutral in terms of how it may be perceived.

In popular media, and often in scientific circles, the debate is framed as choosing between perennial DST and perennial standard time. Arguments for and against include both health and economics. Consumption of resources, as was central to DST origins due to the World Wars and energy crises, may again be an issue in some places. Reliance on Russian oil and gas in Europe has been highlighted since the condemned Russian invasion of Ukraine. Seemingly lacking from popular debate is whether biannual transitions should be maintained or even modified (such as changing transition dates).

Health controversy

Regarding health, the principal "exposure" talking points are: (1) acute transition to and from DST, (2) the DST period for a given year and across many years (as opposed to standard time during these periods), and (3) the standard time period for a given year and across many years (as opposed to DST during these periods). The principal "outcomes" studied mainly concern the acute effects of transitions, and include potential brief differences in the incidence of acute myocardial infarction (AMI) (Manfredini *et al.*, 2019), traffic and other accidents (Fitz *et al.*, 2020; Lahti *et al.*, 2011), and all-cause mortality (Levy *et al.*, 2022). The principally discussed "potential physiological drivers" linking exposures to outcomes are changes to sleep and circadian rhythms, and to stress and anxiety in the lead-up to transition days.

Acute transition

To the best of our knowledge, only studies of AMI have been subjected to a meta-analysis, with increased risk of AMI following DST onset but not offset observed (Manfredini *et al.*, 2019). Controversies behind these results include that two of the included studies providing high weight to the meta-analysis involve overlapping populations, that no critical appraisal of the studies involved was provided (including the extent as to whether pooling was justified), and that large differences in risk estimates between some studies suggest that at least some are heavily biased. There is evidence of increased traffic accidents following DST onset in the USA (Fitz *et al.*, 2020), but questions arise regarding how great a role was played by the consequent changes in illumination during major commute times (Martin-Olalla, 2020). DST offset,

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but not onset, was associated with a spike in all-cause mortality in Europe, which is in contrast to what might be expected given the observations regarding traffic accidents and AMIs with DST onset (Levy *et al.*, 2022). A study from Finland concluded effects of DST transitions were not harmful enough to have an impact on occupational accident rates (Lahti *et al.*, 2011). However, there are mixed findings for many outcomes in the scientific literature. Reaching a consensus on potential DST transition effects on health would appear to require a stronger evidence base. Effect sizes are small and not consistent, but this does not rule out causal effects. Identifying who is at risk of negative health outcomes is difficult when using registry-based information and taking the large and diverse EU or USA as the regions of interest as wholes. Geographical and individual differences may play a role and investigation of these factors may be useful in debate. The plausibility of the hypothesised mechanisms also come with some controversy; the section below deals with the mechanism.

DST in winter or standard time in summer

Consideration of DST in winter or standard time in summer comes with difficulty. Cohorts of individuals with sufficiently similar geography, culture, and sociodemographic characteristics, but who differ only by either DST or standard time are at a premium, and ruling out potential confounders in studies of these populations would be very difficult. The potential health differences are hypothesised based on circadian biology and potential changes in behaviour are discussed below.

Light, time and circadian controversy

Timing of social schedules and 24-hour rhythmic light-dark exposures are important for our circadian biology. In order to discuss potential biological mechanisms driving potential DST-associated health outcomes (mainly circadian biology-related), we must first understand the relationship between official clock time, time zones, local solar time, and individual internal circadian time – the examples below will help.

Official times and sun times

On standard time in Greenwich in the UK (time zone: UTC 0), the sun crosses the Greenwich meridian (or longitude 0°) at noon (or official clock time: 12:00), and is at its zenith in the sky. On DST, the sun reaches its zenith at official clock time 13:00. While the official time of sunrise and sunset will vary in accordance with seasonal trajectory, the official timing of the sun's zenith will be constant at 12:00 for standard time and 13:00 for DST along the longitude 0° meridian. On standard time, in the UTC +1 time zone (i.e. the clock time is 1-hour advanced compared with UTC 0), the sun reaches its zenith at the longitude +15° meridian (or 15° east) at noon. The +15° meridian approximately follows the German-Polish border and alongside Prague (Prague is located at +14.4°). On DST, the sun will reach its zenith at this meridian. As this meridian is 15o east of the Greenwich meridian, and the time zone is UTC +1, a given solar time (e.g. sun zenith) and corresponding official clock time (e.g. 12:00) at this location will occur one hour before these times occur at the Greenwich meridian.

Along the time zone meridian and during standard time, the solar time reference point – i.e. sun zenith – will be equal to noon. If we move east or west from the meridian but remain in the same UTC time zone, local solar time will occur at an earlier or later official clock time, respectively. In comparison to Prague, the city of Vigo in Gallician-Spain, at longitude -8° (or 8° west) but also in UTC +1, experiences the sun at its zenith at official clock time ~13:40 (1.67 hours after official clock time 12:00 when the zenith occurs at longitude +15°) on standard time

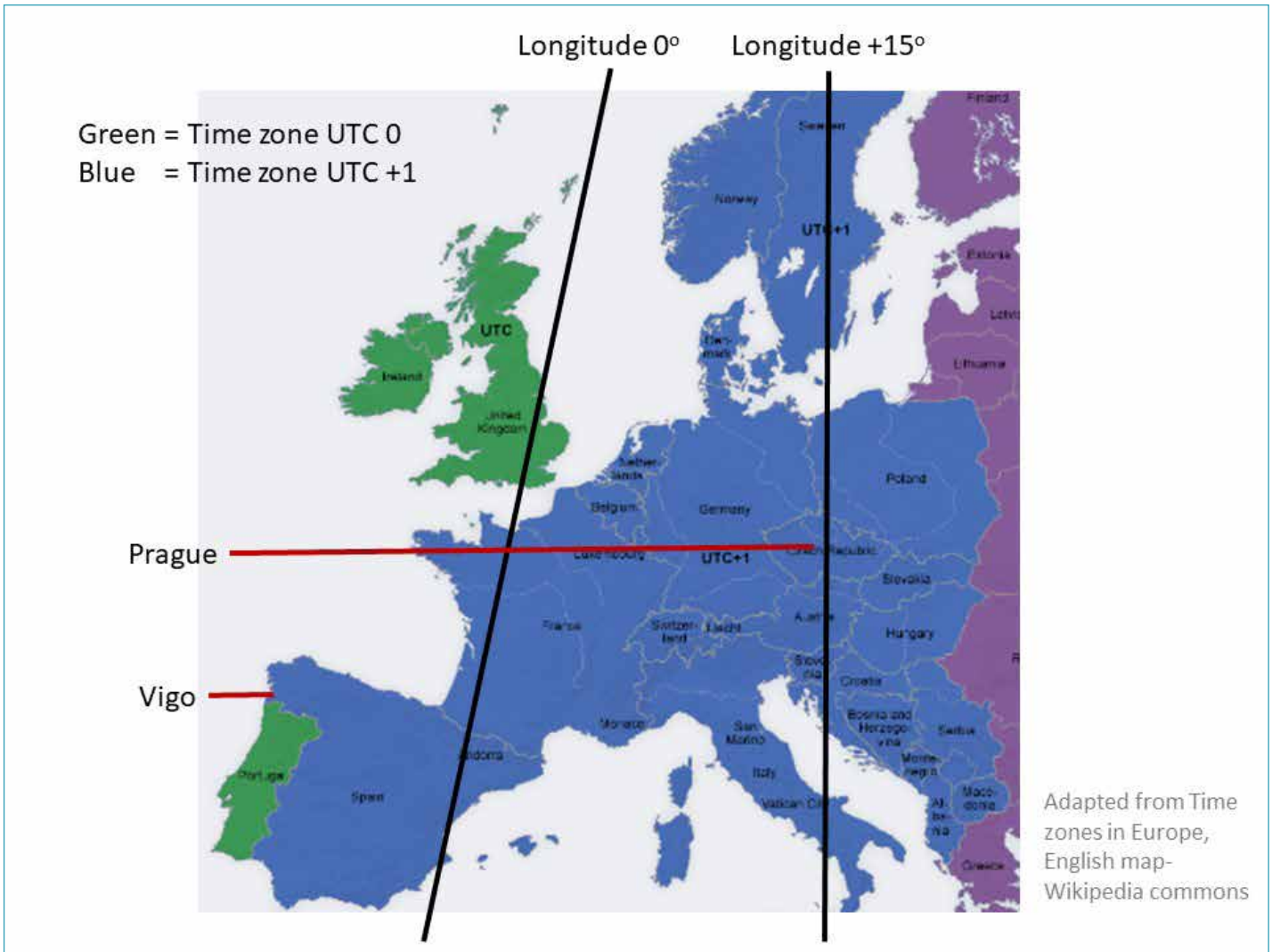

Figure 1. Time zones and longitude in Western Europe with Prague and Vigo highlighted.

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and at official clock time ~14:40 on DST. This discrepancy between solar time and official clock time (discrepancy insofar as compared to Prague) occurs because Vigo is some distance west of the +15° meridian for the UTC +1 time zone (Fig .1).

Internal time

The internal circadian timing system (CTS) receives light information from specialised light sensitive cells in the eyes that project to a "master" circadian clock in the suprachiasmatic nuclei of the hypothalamus. The master clock has direct and indirect neuroendocrine projections to the clocks in every other cell in the body (so-called peripheral clocks). Each cellular clock is composed of a genetic-transcription-translation-feedback-loop (the specific genes involved are known as clock genes) lasting approximately 24 hours that give rise to circadian rhythms in cellular physiology. The master clock receives information about the 24-hour light-dark zeitgeber (time cue) rhythm and entrains to it (it can take a few days to entrain to a new zeitgeber rhythm – which can cause the jet lag associated with rapid travel across time zones) (Lewis and Erren, 2021). The master clock will subsequently assist entrainment in the peripheral clocks. When entrained, cellular circadian rhythms will now be in-sync, and the highs and lows in rhythmic functions that are beneficial to our physiology can now occur and at an appropriate time relative to the external time cue. For example, metabolism will start ramping up for activity during the light part of the zeitgeber rhythm and slowing down when it is time to sleep during the dark part of the zeitgeber rhythm. It can be helpful to consider our circadian-entrained sleep time as the biological night and our circadian-entrained wakeful time as the biological day. The biological night and biological day make up our internal time.

In our modern society, our light-dark zeitgeber rhythm consists of different intensities of daylight, artificial light, and darkness. The latter is typically our exposure when going to sleep as we seek darkness and then close our eyes. The zeitgeber rhythm phase then typically includes higher light intensities after wakening, during waking hours, and lower intensities as we again approach the biological night. The timing and intensity of light experience is important. In times before artificial light, we would entrain to the natural light-dark cycle that occurs because of the Earth's 24-hour rotation on its axis. Nowadays, our biological nights and days do not necessarily follow local solar time because of social schedules and artificial light, but we still have a penchant for scheduling social activity to overlap with at least some daylight hours. Daylight intensity is often orders of magnitude higher than artificial light and can provide an important and stronger zeitgeber effect.

Thus, an advance or delay in clock time and consequent advance or delay in social schedules (as school, work, and appointment times

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are typically at set times) with transitioning between standard time and DST can affect our circadian rhythm because the rhythm phase when light is experienced will change. As the CTS entrains to the new zeitgeber rhythm (i.e. the zeitgeber rhythm phase is 1-hour shifted), there can be periods of internal rhythm misalignment as different internal clocks shift at different speeds, and this may cause damage (Pittendrigh, 1960). The acute CTS shift required for DST onset and offset may be considered minor and somewhat comparable to the shift needed to flying to a new time zone with a 1-hour difference from place of origin (Lewis and Erren, 2021). Of course, some individuals may be more susceptible to the impact of transient misalignment.

Sleep

Regarding sleep, if we do not try to adapt to DST onset in advance, sleep can be cut short by 1-hour for those who must get up at a certain time to fulfil social obligations such as work and school. Again, a 1-hour difference for 1 night only might be considered minor but some individuals may be more susceptible. If a few days are required for entrainment (i.e. setting our internal clocks to the shifted zeitgeber) the sleep-wake cycle may also be transiently perturbed as it is co-controlled by the CTS.

Controversy

Regarding circadian biology controversy, individual susceptibilities may explain acute health effects following transitions, but what about perennial DST or perennial standard time? Even though our light exposure may change by 1 hour at transition, the duration of time between zeniths of the sun does not (i.e. the sun zenith occurs almost precisely 24 hours after its previous zenith, regardless of official clock time change). Advocates against keeping the time change (and against keeping DST if the change is abolished) argue that our social schedules match solar time more accurately when we use standard time and that our internal times would then also (Roenneberg *et al.*, 2019). Now, the importance for the CTS of strong light shortly after awakening is probably the most often cited element of circadian biology for public health. This is certainly the case in mid-latitude winter and is why sleep and circadian researchers are against perennial DST. Sunrise would not occur until after 09:00 in London in mid-winter; the majority of people will waken between 06:00 and 08:00 for school and work. Sunrise may be as late as 10:00 in the city of Vigo in Spain if DST were used in winter. For summer months, DST may be more favourable than standard time and the "internal time more closely matching solar time" argument (indeed, whatever "closely matching" actually means) should be less problematic. Mid-summer sunrise in London will be ~04:30 on DST and would be 03:30 on standard time. The majority of people will not require first light exposure before 04:30 so potential morning light unavailability is much less of a problem compared to winter months. For those less well able to find or create darkness for sleep – for instance due to the cost of light-blocking curtains or requirement to keep curtains and windows open to let cooler night air inside in summer – 03:30 sunrise may be more detrimental to their circadian biology. Shift workers travelling home after the late shift are more likely to be exposed to the earlier sunrise before sleep, which may be detrimental to their circadian biology.

Beyond sleep and the circadian timing system

As mentioned already, illumination, or lack thereof, on commutes also presents dangers (Martin-Olalla, 2020). Depending on local sunrise and sunset times, morning or evening commutes may be affected by increased morning or evening daylight. Pro-perennial DST arguments also cite reduced crime with more evening daylight at the expense of less morning daylight, and more time for children to play outside during daylight hours on winter evenings. How these arguments are perceived is also likely to be affected by actual sunset times and outdoor temperature, in addition to individual factors such as sex and age. Additional pro-DST during summer arguments include that those attending animals, such as farmers and families with pets, may have to arise very early to tend to animals on standard time during the summer and this may hinder social obligations that occur later in the day.

What can we do?

For circadian biology, DST may be more preferable to sunrise and social schedule relationships during summer rather than winter for the reasons outlined above, and is contrary to the position of many sleep and circadian biology societies. Findings of acute health effects of transition are controversial and mixed findings need to be reconciled. Changing transition dates to prevent sudden and dramatic changes in illumination levels during commute rush times in some regions should be considered. In addition to reconciliation of controversies, trade-offs between potentially beneficial DST in summer and potentially detrimental health effects of transition to and from DST need to be weighed against each other. Use of resources and economics also need to be considered alongside health in terms of how DST or standard time may affect the consumption of resources. Local geography (in particular latitude and longitude), time zone, and culture (e.g. early and late risers) are also important aspects to be considered.

For the individual, step-by-step or gradual adaptation in advance of transition days, especially by those more susceptible to an acute health event, should help to reduce potential risks. In line with Willett's 1907 idea of gradual adaptation, four days of shifting sleep and wake times by 15 mins might be helpful (Douma, 2008). In some cases, it may simply help to reschedule the clock time of a social obligation to better suit local solar time. This may be facilitated nowadays following the increased use of home offices after the COVID-19 pandemic. Ultimately, the latter requires appropriate dissemination of advice from Public Health and requires agency on the part of individuals.

All-in-all, the jury is still out regarding the best policy decisions to make and this is before looking beyond circadian biology. Dropping the biannual time change may be neither beneficial nor necessary, but this is a controversial standpoint.

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Placebo and nocebo effects in sport

How physiologists can harness knowledge of placebo and nocebo effects to maximise an athlete's performance

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Placebo and nocebo effects can significantly influence sport performance (Hurst *et al.,* 2019). In the past two decades, research has identified various neurobiological mechanisms of their response and how an athlete's expectation and previous experiences can alter the effectiveness of various treatments, such as medications, nutritional ergogenic aids, and altitude training. Importantly, this research has highlighted how physiologists can harness knowledge of placebo and nocebo effects to maximise an athlete's performance during competition and training. In this article, I briefly review evidence for the magnitude of placebo and nocebo effects on sport performance, before providing a description of the mechanisms in which they can be induced. To help athletes perform at their highest level, I also highlight the ways in which physiologists can maximise placebo effects and minimise nocebo effects and propose future research directions to provide greater understanding of these putative phenomena on sport performance.

What are placebo and nocebo effects?

Placebos are often used as a control treatment in randomised controlled trials that are indistinguishable from the experimental treatment, but without the essential component. In their broadest sense, placebo effects are an improvement in a person's symptoms following the administration of a placebo, which cannot be attributed to the properties of the placebo itself. However, the placebo effect is a misnomer because in some cases there is no need to use a placebo to induce a placebo effect. Placebo effects can be induced after administration of a treatment (e.g. physiotherapy, altitude chamber, caffeine) and by factors that include the treatment context, expectations, and previous experiences. In short, placebo effects are the response to the psychosocial treatment context surrounding the athlete and the effect that this context has on their brain, mind, and body. On the other hand, nocebo effects are a negative response and are essentially the opposite of placebo effects, which relate to the negative aspects of the psychosocial context (e.g. negative experiences and expectations).

What is the evidence for placebo and nocebo effects on sport performance?

In the last two decades, a body of literature has examined placebo effects on several outcomes related to sport performance (Hurst *et al.,* 2019). This research has shown that when an athlete receives a placebo,

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but believes it is beneficial, this belief can significantly improve sport performance. Maganaris *et al.* (2000) showed that when national-level weightlifters received a placebo, but were told that it was an anabolic steroid, they improved to an international standard and increased the amount of weight lifted in bench press, deadlift, and squat by 3.8%, on average. Beedie *et al.* (2006) reported that cyclists given a placebo improved their time to complete 10 km time-trials by 1.3% and 3.1% after they believed they had received a moderate and large dose of caffeine, respectively, whereas they performed -1.4% worse when they believed they received a placebo. More recently, Hurst *et al.* (2020) found that when middle-distance runners received a placebo and were told it was caffeine, time to run 1,000 m was similar to when they received caffeine and were told it was caffeine. In fact, when runners received caffeine, but were informed it was a placebo, their performance did not improve compared to baseline (Fig.1). In short, evidence indicates that when an athlete believes they have received a beneficial treatment, their performance can significantly improve.

While a body of evidence has shown the influence placebo effects can have on sport performance, the evidence for nocebo effects is less developed. This is likely to be related to ethical constraints in deceptively administrating placebos to athletes and the harmful effects they can cause (e.g. increase in anxiety). Nevertheless, a handful of studies have shown that nocebo effects are powerful and can affect a treatment's effectiveness (Hurst *et al.*, 2019). Beedie *et al.* (2007) administered placebos to two groups of athletes and told the first group (i.e. positive belief) that it was a supplement that would improve performance and the second group (i.e. negative belief) that it was a supplement that would worsen performance. After running 3 x 30 m sprints, athletes in the positive belief group ran 2.8% faster than the negative belief group. These results were replicated in a follow-up study (Hurst *et al.*, 2017) and highlight that athletes' expectations about a treatment can negatively affect their performance.

What causes placebo and nocebo effects?

Several researchers in sport have examined the existence and magnitude of placebo and nocebo effects in the last two decades (see Hurst *et al.*, 2020 for review). However, there are few that have sought to understand the mechanisms that cause such effects. Most of our understanding of what causes placebo and nocebo effects comes from psychology and neuroscience. This research has identified not one, but many placebo and nocebo effects operating across different neurobiological pathways. While it is outside the scope of this article to provide a detailed explanation of each one (see Petrie and Rief [2019] for review), the main psychological and neurobiological mechanisms will be briefly discussed below.

Research over the past 30 years has centred upon two psychological mechanisms: expectancy and classical conditioning. Expectancy is underpinned by a person's belief that an effect will occur, which can be generated by, for example, verbal suggestions (e.g. this drug will improve your performance), environmental cues (e.g. having a degree certificate on the wall of a physiologist's office), and interactions with others (e.g. observing a competitor improve after altitude training). To put this into context, when an athlete is administered a placebo and told it is an anabolic steroid, that athlete is likely to develop the expectation that it will increase strength and power. These expectations, in turn, can influence psychological and physiological processes, which improve performance. Alternatively, classical conditioning indicates that a conditioned stimulus (e.g. placebo) elicits a conditioned response (e.g. placebo or nocebo effect) by virtue of its previous coupling with an unconditioned stimulus (e.g. the drug purported to be inside the pill). For example, an athlete with previous experience of caffeine can lead to a conditioned response (e.g. increase in heart rate), whereby a placebo on its own can create a similar response to caffeine. The placebo is thus the conditioned stimulus, and the placebo effect is the conditioned response.

In neuroscience, a plethora of evidence has identified that placebo effects act on the dopaminergic (i.e. reward) and endogenous opioid (i.e. pain) system. Using state-of-the-art technology, such as functional magnetic resonance imagining (fMRI) and positron emission tomography (PET), researchers have shown that when a person is administered a placebo and told it is a potent drug, this can have profound effects in the brain. For example, after participants were exposed to the opioid drug, buprenorphine, Amanzio *et al.* (2001) reported significant reductions in pain via activation of the endogenous opioid pathway when the drug was replaced with a placebo. Similarly, de la Fuente-Fernández *et al.* (2001) demonstrated that administration of a placebo, described as an active drug, increased dopamine within Parkinson's disease patients. In fact, the dopamine concentration increased by 200%, which is comparable to the response related to amphetamine use.

Our understanding of the psychological and neurobiological mechanisms of placebo and nocebo effects has rapidly increased in the last two decades. This has been reported across several conditions, such as pain, immune function, anxiety, and motor control, which have relevance for physiologists aiming to facilitate sport performance. In short, this research highlights that placebo and nocebo effects share similar mechanisms to those activated by actual treatments and can mimic the effects of those treatments. This has important implications for how physiologists support athletes and how they can capitalise on placebo effects and minimise nocebo effects.

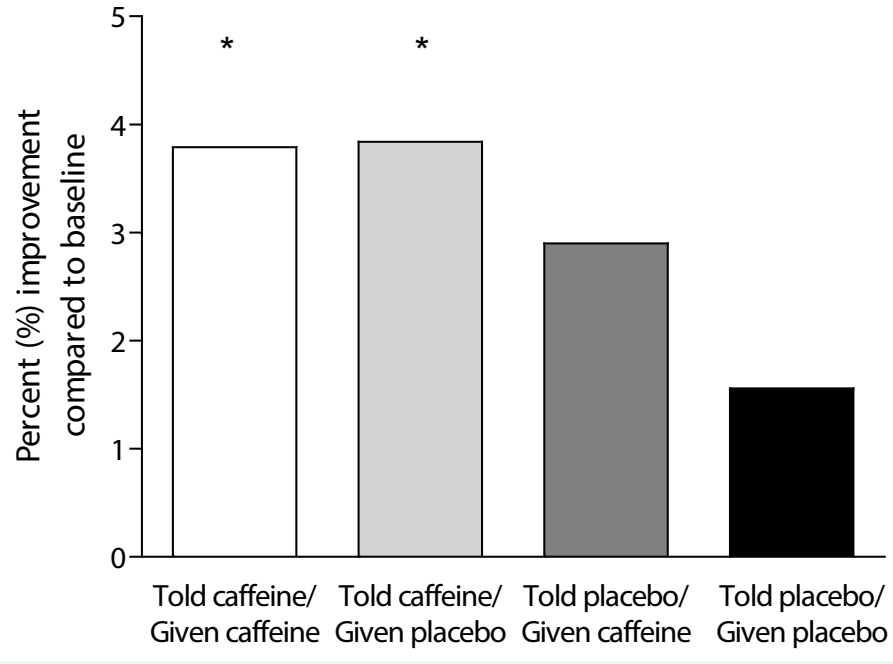

Figure 1. Data from Hurst *et al.*, (2020) reporting the percent improvement in 1000-m running time compared to baseline. * = p<0.01 compared to baseline.

How can I capitalise on placebo effects and minimise nocebo effects?

A large body of evidence has highlighted that placebo and nocebo effects are genuine psychobiological responses to the context surrounding the administration

of a treatment. This highlights that those administrating a treatment can shape how well, or not so well, it will influence performance. That is, when an athlete believes they have received a beneficial treatment, they are likely to report a greater improvement in performance than when they do not believe in it, and when they believe it is harmful, they are less likely to obtain the full benefits of that treatment and/or underperform compared with when they believe it is beneficial. Given this, it is important that physiologists consider the context in the administration of their treatments.

Evidence from placebo and nocebo effect research indicates that benefits of treatments are often due to the interaction between the verum (e.g. the physiological or pharmacological effects) and psychological (e.g. placebo effects) components of that treatment. On this basis, it is important that physiologists endeavour to maximise the placebo effect component of a treatment by engendering a positive belief in its effectiveness. The words used, the context it is delivered in, and previous experiences should be considered when administering a treatment to an athlete. Imagine for example, a physiologist aiming to implement heat-acclimatisation into an athlete's training programme. If that athlete had a negative experience of using it (e.g. underperformance) and did not believe that it is important for their competition preparation, the athlete is less likely to fully maximise from the purported benefits. To ensure that benefits are maximised, the physiologist can capitalise on knowledge of placebo and nocebo effects to provide that athlete with evidence of its effectiveness, what benefits it is likely to have and how it can be specifically tailored to that athlete's training programme. In short, a physiologist can apply an understanding of heat-acclimatisation and placebo effects to potentiate a beneficial response.

It must be stressed, however, that using a treatment, without evidence of effectiveness, should be avoided. For a physiologist to knowingly promote the benefits of a placebo, for example, through deception and false information, is unethical and counter to professional guidelines. Although evidence for the use of open-label placebos (i.e. administrating a placebo and informing the athlete it is a placebo) suggests a means by which to achieve this ethically (Saito *et al.*, 2020), evidence is limited and this could induce effects that are counter-productive, unstable and unpredictable (see Beedie *et al.*, 2017 for commentary). In short, the need for evidence-based treatments that are administered openly and honestly is fundamental to physiological support.

What is next for placebo and nocebo effect research?

In the past two decades, placebo and nocebo effect research in sport has grown substantially. At the turn of the millennium, little was known about their existence and magnitude on sport performance, and what factors may influence their response. Today, physiologists and the larger sport science community can harness placebo and nocebo effect research to ensure an athlete maximises their potential when competing and training. Placebo and nocebo effects are induced by expectations and prior experiences, which have a direct impact on neurobiological pathways, such as the dopaminergic and endogenous opioid system. However, while such advancement has been achieved, a need exists in understanding the mechanisms that can directly influence sport performance, and under which contexts they are more likely to be induced. For instance, placebo and nocebo research is often conducted in tightly controlled conditions, which have little validity to the actual demands an athlete would experience during competition and training. Similarly, with the advancement of technology that can directly examine neurobiological responses during exercise (e.g. functional-near-infrared-spectrometry) and more rigorous research designs that delineate the physiological and psychological effects of treatments (e.g. balanced placebo design), physiologists are in a position to further enhance insight and understanding of placebo and nocebo effects and the significant influence treatments can have on an athlete's brain and mind during performance.

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^{40}K: from ancient supernovae to bananas and beyond

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"We are stardust / billion-year-old carbon." Indeed, we are; as you sit down and read this article, I recommend that you put on Joni Mitchell's track "Woodstock" from 1970 in which she sings these lines, with a voice that appears to vibrate through time and space into the endless universe. However, this is not an article about carbon, but about potassium, which like carbon was formed in generations of dying stars way back when. A trace amount of naturally occurring potassium throughout our Solar System, including in our bodies, is the unstable and thus radioactive isotope ^{40}K. As it turns out, the presence of this isotope is a hint of the very birth of our Solar System.

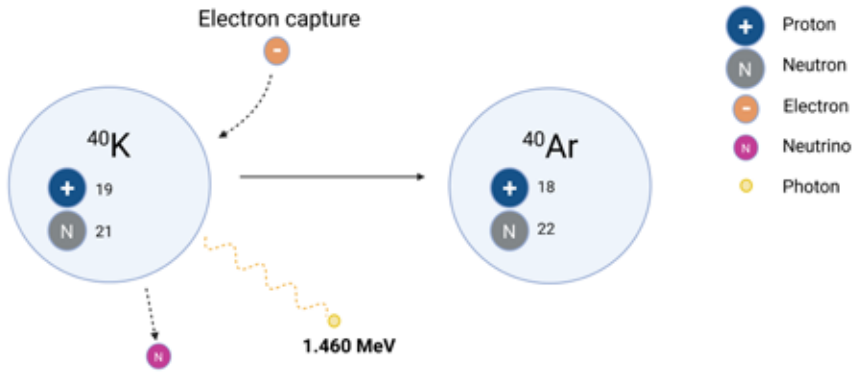

Figure 1. **Detectable decay of ^{40}K.** During 10.32% of its decays, the nucleus of 40^{K} absorbs an inner shell electron, whereby a proton is converted to a neutron, while the excess energy is released as an electron neutrino and subsequently a photon, of which the latter has the characteristic 1.460 MeV energy that may be captured by a scintillation detector. Prepared using BioRender.

Due to concerns that working with radioactive materials would result in internal contamination, the first scintillation detectors were built into whole-body counters in the immediate post-World War II period and used for routine monitoring of nuclear workers.

Somewhat surprisingly at the time, a high-energy peak of ionising radiation at 1.460 MeV was persistently noted, indicating the omnipresence of the same radioactive isotope regardless of the worker's exposure history to radioactive materials. It was subsequently

clarified that this "background peak" was caused by the decay of ^{40}K as it decays to ^{40}Ar by electron capture (Fig.1).

Curiously, ^{40}K has an astoundingly long – at least from a physiological perspective – half-life of nothing less than 1.251 billion years! So, at the current geological age (i.e. the Holocene), its proportion of total potassium is practically constant at 0.0117% (Bin Samat *et al.,* 1997). In the context of physiology research, the detection of ^{40}K by whole-body counting can be used to accurately determine whole-body potassium content without a need of any tracer injection or invasive sampling of any kind. It is a somewhat time-consuming procedure (it takes approximately 45 minutes including patient preparation for a single whole-body ^{40}K measurement at my own department), which largely hampers its use in clinical routine, and it is thus primarily used in research studies of electrolyte physiology and fluid homeostasis, in which it is particularly useful, because serum potassium is a poor proxy for the intracellular or whole-body potassium concentration (Blumberg *et al.,* 1997). Indeed, serum potassium barely changes even when vast amounts of bananas are ingested, even though bananas are enriched in potassium, as will be outlined later in this article (Miller, 1997). Before the emergence of dual-energy X-ray absorptiometry, the determination of whole-body potassium content in this manner was also used for determining gross body composition based on empirical equations that took advantage of the fact that most of the body's potassium, approximately 80%, is concentrated in the intracellular compartment of skeletal muscle. Meanwhile, ~18% is mainly present in the intracellular compartment of other tissues and only the remaining few % is present in the extracellular space (Forbes *et al.,* 2000).

A radioactive trace of our supernova past

The stellar origin of the ^{40}K present throughout the Solar System, including our bodies, is described in the so-called "supernova trigger hypothesis". Accordingly, the Solar System was created 4.6 billion years ago from a molecular gas cloud that consisted mostly of hydrogen and helium created in the immediate aftermath of the Big Bang almost 10 billion years earlier (Cameron and Truran, 1977; Podosek *et al.,* 2000). However, the gas cloud also contained isotopes of heavier and mostly stable elements that had been created by stellar nucleosynthesis in already ancient stars, which had spread them by bursting into supernovae. Of note, these elements included the stable potassium isotopes ^{39}K and ^{41}K. It was the shockwave from a nearby type II supernova (Fig.2), resulting from the core collapse and concomitant explosion of a star with a mass of 8 to 50 times that of the Sun, that caused the presolar molecular gas cloud to collapse into a disc with a protostar at the centre. This would eventually become the Solar System as we know it.

With the shock wave, also followed an ejecta containing elements created within the type II supernova, including ^{40}K, which was diluted within the existing potassium isotope pool, so that it initially made up 0.15% of the potassium. Due to its continuous decay over the past 4.6 billion years, it now makes up 0.0117% of potassium, while the stable isotopes ^{39}K and ^{41}K make up the remaining 93.1% and 6.88%, respectively. The healthy human body contains somewhere between 140 and 180 g of potassium (2.2–2.8 x 10^{24} potassium atoms), and thus ~0.2 g ^{40}K, the decay of which continuously produces between 4000 and 5000 disintegrations per second. This makes ^{40}K the single largest naturally occurring internal source of radiation in humans, responsible for approximately 5% of the annual natural background radiation in the UK, which is ~2.5 mSv.

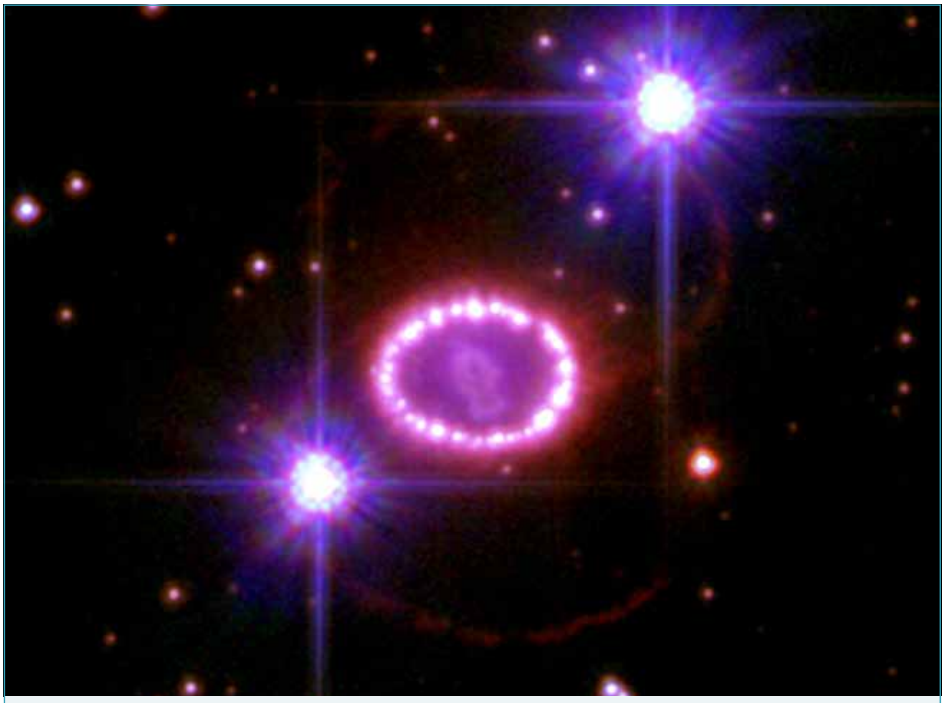

Figure 2. **The expanding remnant a Type II supernova in the Large Magellanic Cloud recorded by the Hubble telescope.** A similar supernova occurred in the proximity of the present-day Solar System. NASA image. Public domain. The material was created for NASA by Space Telescope Science Institute under Contract NAS5-26555, or for ESA by the Hubble European Space Agency Information Centre.

Discussing ^{40}K in the physiology classroom: a pop culture rendezvous

So, I am very fond of using case examples from pop culture when I give lectures in physiology (Berg, 2019). When I talk about electrolyte homeostasis and mention ^{40}K, it has happened more than once that an excited student has asked whether it is because of this isotope that Dr. Manhattan, from the acclaimed graphic novel Watchmen, emanates a blue glow from his skin. This is a feature he obtains after being trapped in a so-called "intrinsic field subtractor", which disintegrates him entirely on a subatomic level. After this, he somehow reassembles, and apart from his conspicuously glowing skin he then gains the ability to exist outside space and time. This would be a great story to pull off in the classroom, but unfortunately, this has nothing to do with ^{40}K! Firstly, if it were true, we would then primarily be seeing a blue glow from Dr. Manhattan's skeletal muscle and not his skin. Secondly, the decay of ^{40}K does not emanate a blue glow. According to an interview with James Kakalios, who is a physics professor at the University of Minnesota and a pioneer of using pop culture in communicating science, the blue glow reflects so-called Cherenkov radiation (Rogers, 2009), which occurs during the decay of certain radioactive isotopes that leak high-energy electrons that travel faster than the speed of light in a given medium.

During one of the abovementioned lectures where Dr. Manhattan was brought up, I mentioned that it may be the isotope ^{90}Sr that gives off Cherenkov radiation, and that it may somehow have replaced the calcium in Dr. Manhattan's body, since these elements have similar chemical attributes. A very bright student then remarked: "Ah, that would make it a bone seeker – that must be the reason Dr. Manhattan's bones are shown so clearly through the skin on *The Physiological Society's* website." Now, I do always recommend my students to look up *The Physiological Society* online and to follow us on social media, and kudos to this student for actually doing so, especially while also thinking critically about the things I say, even when I'm just trying to

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Figure 3. **Dr. Manhattan and Cherenkov radiation.** The avatar-like man with transparent bluish skin on www.physoc.org could pass for Dr. Manhattan. It is considered that Cherenkov radiation likely originates from the isotope 90Sr, which primarily binds in bone.

be a bit funny. I did have to look up what the student meant; and truly so, on our website, there is an avatar-like man with transparent bluish skin. He could pass for Dr. Manhattan any day (Fig.3).

Going bananas for an index of radiation exposure

Given that radioactivity is inherently linked to superhero powers, particularly in comics from the 1960s and 1970s, I have previously attempted to highlight *Bananaman* as a much more useful example of how ^{40}K may play into understanding phenomena in pop culture while also conveying some fundamental radiation biology with relevance for electrolyte homeostasis. However, while Bananaman is certainly a cult figure in the UK, he clearly does not have the same bad boy appeal as Dr. Manhattan, at least not here in Denmark. When I explained how he is a schoolboy who transforms into a caped (anti)hero when he eats a banana, and then gets a very diverse set of skills, ranging from intense stupidity to super strength (these two are not mutually exclusive in the Bananaman franchise), students just gazed at me with a blend of disappointment and distrust. My idea was to use this narrative as a vehicle for going into the concept of banana equivalent dose (BED), but since then I have just skipped the Bananaman part. Perhaps it will work better in the UK where he is better known and has a somewhat wider appeal.

But in terms of BED, the concept is that bananas have a high content of potassium, which is only outmatched by certain tropical fruits, such as avocado, guava and dates. In a Western diet, bananas are one of the major sources of dietary potassium along with potatoes, kidney beans, and nuts (Lanham-New *et al.*, 2012). A 150 g banana contains approximately 0.54 g of potassium, and thus 63 x 10^{-6} g of ^{40}K. Thus, eating one average-sized banana gives rise to a radiation dose of 0.1 µSv. This has thus been coined BED, an informal unit of radiation exposure. One BED corresponds to approximately 1% of the average daily background radiation exposure; a flight from London to New York corresponds to 320 BED, a chest X-ray up to 1,000 BED, and a chest CT to 70,000 BED. However, while BED may be used for general educational purposes, it is a flawed measure in practice that is neither used clinically nor in research (i.e. hits on PubMed on 29 January 2023: 0). This is because the radiation dose from banana ingestion is not cumulative, and given that whole-body potassium is tightly regulated to maintain homeostasis, any excess potassium is excreted through the kidneys within a few hours after ingestion (McDonough and Fenton, 2022).

Concluding your journey through space and time

The understanding of potassium homeostasis is paramount for understanding almost all areas of physiology, and for grasping the complexity of the mechanisms at play in various potassium disorders in the clinical setting. Here, I have taken you on a journey through space and time with ^{40}K, the isotope that is omnipresent albeit in miniscule amounts, and I hope that apart from reflecting on the fact that "we are stardust", you will think a little about how many bananas you theoretically need to spare next time you go for an overseas flight, and that you also have a renewed taste for revisiting Joni Mitchell, Watchmen, and (perhaps) Bananaman.

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What can Neanderthal DNA teach us about current humans?

The study of human evolution advances our understanding of the genetic architecture of disease

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A hundred thousand years ago, mammoths, woolly rhinoceroses, sabretooth tigers and cave bears roamed the icy expanses of Europe. They were hunted by small bands of large-brained, robust hominins, well-adapted to the difficult conditions of the last ice age: our cousins, the Neanderthals. They have recently been thrust back into the spotlight due to the 2022 Nobel Prize in Physiology and Medicine, which was awarded to Svante Pääbo "for his research in the field of genomes of extinct hominins and human evolution". While the hominins in question may be extinct, namely Neanderthals and Denisovans, their legacy still lives on in us intertwined with our DNA.

Neanderthals

The first remains to be recognised as *Homo sapiens neanderthalensis* were found in 1856 in Germany, in a cave in the Neander Valley (formerly *Neanderthal*, now spelled *Neandertal*) on the river Düssel. It is ironic that the remains of the "ancient" man were discovered in "the valley of the new man". The Neander Valley was named after a 17th century pastor, Joachim Neander, whose name comes from *neo* (Latin/Greek for "new") + *andros* (Greek for "man"). Quarrying for limestone in this valley led to the discovery of the fossils, and subsequently to the unfortunate destruction of the cave (Schmitz and Thissen, 2010).

Neanderthals are the best-known subspecies of archaic humans. Archaic humans are usually defined as being the group of now extinct human species that successively branched out of *Homo erectus* in the last million years. The two populations that would become Neanderthals and, respectively, anatomically modern humans (*Homo sapiens sapiens*) diverged about 550,000 years ago (Prüfer *et al.*, 2017).

Neanderthals probably evolved locally in Eurasia and disappeared about 40,000 years ago.

Compared to anatomically modern humans, Neanderthals had much longer to adapt morphologically, physiologically, and culturally to cold glacial climates.

Fossil records facilitate our understanding of Neanderthal morphology and can help us to infer information about their functional capacities. For the most part, Neanderthal morphology seems to follow the so called "ecogeographical rules", which describe the underlying relationship between morphology and climate. Short sturdy limb bones and broad stocky bodies with barrel-shaped chests are thought to be cold climate adaptations, which all served to increase their heat-conserving abilities via a high body volume to low surface area ratio (Ocobock, Lacy, and Niclou, 2021).

Before the sequencing era, scientists used to build their understanding of morphological and functional features on fossil records, and contextualised these with the information extracted from the archaeological settings in which they were found. Nowadays the availability of ancient genomic data has spectacularly enhanced our capabilities to infer physiological aspects of Neanderthal biology.

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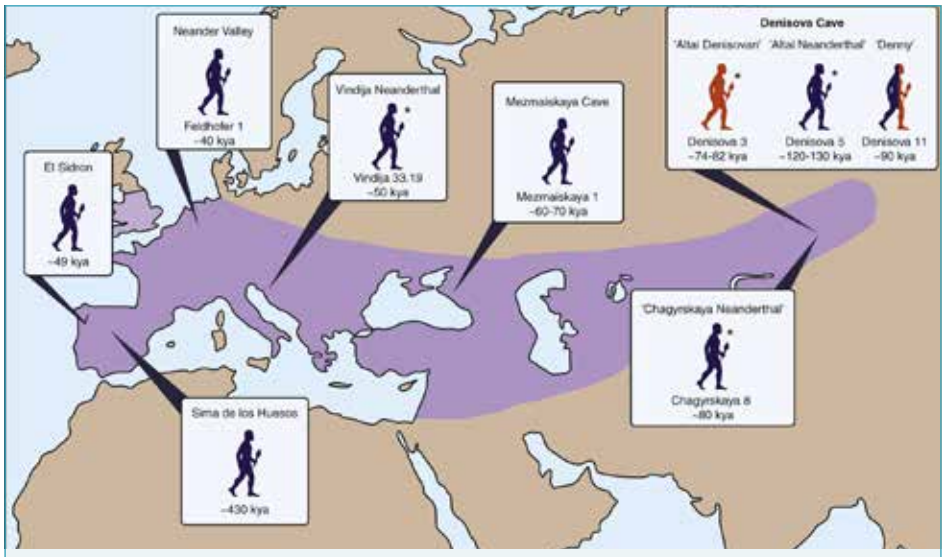

Figure 1. **Neanderthal geographic range.** Dating and location of some of the archaic hominin specimens (Neanderthal – Navy Blue; Denisovan – Orange) for which nuclear ancient DNA is available are also shown. Asterisks (*) indicate genomes sequenced at high coverage. *Reproduced with permission from © Reilly et al., 2022.*

Ancient DNA and modern technology

For a long time, scientists believed it would be impossible to extract usable DNA from historical samples, but in 1984 Higuchi *et al.* made an important breakthrough and sequenced 129 base pairs extracted from a 200-year-old specimen of an extinct zebra-like animal (the Quagga)! Around the same year Svante Pääbo also succeeded in extracting ancient DNA, this time from a millennia-old mummy (Jones, 2022). Extracting ancient human DNA is, indeed, difficult. In addition to the almost inevitable bacterial contamination and chemical degradation of the samples, DNA extraction and analysis of archaic and ancient human remains are made even more difficult by contamination with present-day human DNA from the researchers themselves.

The first complete Neanderthal genome to be sequenced was that of their mitochondria (Green *et al.*, 2008). The process of extracting fragmentary Neanderthal DNA was streamlined, improved, and standardised, borrowing heavily from clean-room techniques used in the semiconductor industry, with stringent physical contamination prevention augmented by contamination filtering software. These improvements in technique led to the publication of the first complete nuclear Neanderthal genome a mere two years later (Green *et al.*, 2010).

Thanks to these efforts, three good-quality nuclear Neanderthal genomes are currently available: one from the Vindija cave in present-day Croatia (about 50,000 years old), one from the Denisova cave (about 110,000 years old) and another from the Chagyrskaya cave (about 80,000 years old), both in the Altai mountains of present-day Russia (Fig. 1). These Neanderthal sequences, along with a large number of ancient and present-day *H. sapiens sapiens* genomes, can be publicly accessed through the *Allen Ancient DNA Resource* (Reich, 2021).

The mixing of DNA: introgression signals

Introgression is defined as the incorporation of stretches of DNA from one species into the gene pool of a second one. The presence of genetic material from a relatively recent admixture with an evolutionary branch that diverged a long time ago can, in principle, be detected with statistical methods, even in the absence of genetic information related to the donor population (in our case, the Neanderthals). Simply put, during the time they were separated from us, Neanderthals accumulated mutations (variants), not shared by modern humans. Introgressed material has a higher rate of variants than either the background or the subpopulations without introgression.

Another observation is that genetic material is more likely to undergo recombination at multiple points along its length over many generations, so only short contiguous fragments occur today. Comparatively, newer introgressed material has less time to get fragmented, so it occurs in longer stretches, which makes it identifiable.

The arrival of *H.sapiens sapiens*

About 45,000 years ago, modern humans started populating Eurasia, arriving from Africa via the Middle East. This allowed for an overlap between the two species of approximately 5,000 years (Hublin *et al.*, 2020). We currently believe that during that time interaction between the two groups followed all possible avenues: avoidance, conflict, and mixing – the latter scenario leading to introgression.

As a result, 1%-3% of the *H. sapiens sapiens* genome is believed to be of Neanderthal origin, except for genomes of sub-Saharan Africans, which is consistent with introgression having occurred outside Africa. While the average DNA fraction of Neanderthal origin in a non-African individual is around 2%, the fragments of ancient DNA do not occur at the same positions for everyone. It is believed that between 12% and 20% of the Neanderthal genome survives in modern humans today. This archaic DNA is not uniformly distributed within our genome. Neanderthal genetic material is particularly rich in some areas, and conspicuously absent in others, suggesting that both positive and negative selection pressures have affected the present-day distribution.

Although not the principal focus of this piece, it is worth noting that there is also evidence of another archaic human subspecies introgressing with previously Anatomically Modern Humans. The highest levels are found in individuals from Oceania who have inherited ~5% of their genome from Denisovans (Browning, 2018), and those in mainland Asia and Americas sharing ~0.2% of their genome with Denisovans (Prüfer, 2013).

Present-day consequences

The functional effect of Neandertal variants versus modern human ones can be assessed by computational analysis. For instance, the depletion of Neanderthal sequence in and around functional elements of the modern human genome suggests that a large proportion of the archaic variants were deleterious for *H. sapiens sapiens* (Dannemann and Kelso, 2017).

However, there are also some Neanderthal variants that have increased in frequency in modern humans. One possible explanation is that these variants have contributed to a better adaptation to new environments, having therefore been positively selected, and therefore retained in the recipient population. As such they are most likely the result of "adaptive introgression" (Reilly *et al.*, 2022).

The computational/statistical assessment of the correlation between Neanderthal alleles and modern human phenotypes, derived from large populational databases (Dannemann and Kelso, 2017) and electronic health records (Simonti *et al.*, 2016), has contributed to the definition of a set of traits that are influenced by archaic ancestry: hair and skin phenotypes (pigmentation, tanning, sunburn, skin lesions); psychological/behavioural traits (mood, depression, chronotype – morning or evening person, addictive behaviour – tobacco use); metabolic traits (obesity); height, blood disorders, heart rate, etc.

One of the main conclusions of the Neanderthal trait association studies is that a major influence of the introgressed alleles is exerted through their effects on gene regulation (Dannemann and Kelso, 2017). This effect can also be computationally interrogated genome-wide, given the accessibility of datasets from high-throughput studies of human gene expression (The Genotype-Tissue Expression – GTEx – Project; Geuvadis, etc).

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Most spectacularly though, the ultimate biological significance of the Neanderthal-associated traits can be tested by *in vitro* functional assays in the wet laboratory.

For instance, in Massively Parallel Reporter Assays (MPRAs), introgressed and non-introgressed alleles are barcoded and cloned into reporter vectors, in front of a minimal promoter whose efficiency they are going to influence. The vectors are then transfected into cells that will transcribe the reporter mRNA. The reporter transcripts can subsequently be sequenced and counted, allowing the comparison of the two variants' efficiency when it comes to gene expression (Jagoda *et al.*, 2022).

Genome engineering of induced Pluripotent Cell Stem (iPSC) lines can also be used to demonstrate causality of associated variants, by inserting them in model organisms or by organoid modelling. For example, a Neanderthal-specific non-synonymous substitution in the NOVA1 gene was assessed by CRISPR editing of iPSCs to generate cortical organoids, showing neurodevelopmental differences between Neanderthal and modern human-derived organoids (Trujillo *et al.*, 2021).

One of the first instances of comparing Neanderthal vs. modern variants, assessed the functionality of FOXP2, a gene previously involved in the evolution of language, in "humanised" mice. This historically important study showed that the mice bearing the modern human specific variant have altered vocalisations, modified behaviour and decreased brain dopamine concentrations (Enard *et al.*, 2009).

(Auto)Immunity

One of the most important effects of introgressed variants is manifest in the immune function of present-day humans. This importance is highlighted by the recent identification of Neanderthal variants associated with susceptibility to and severity of COVID-19 infection. Several of these variants have also been associated with lung or autoimmune diseases, and inflammatory responses to infection (COVID-19 Host Genetics Initiative, 2021).

Due to the strong mortality burden brought about by infections, genes involved in the immune response are under the strongest selection pressure. It has been shown that instances of variants from archaic populations have introgressed in modern humans in both adaptive and innate immunity genes, with the innate immunity genes having an even higher average of Neanderthal ancestry than the rest of the genome (Deschamps *et al.*, 2016).

Neanderthals were probably better adapted to the local regional pathogen spectrum when anatomically modern humans started their forays in Europe, hence introgression might have contributed to the adaptation of *H. sapiens sapiens* to the newly encountered pathogens (Kerner, Patin, and Quintana-Murci, 2021).

It is likely that the lag observed between the appearance of modern humans in the Middle East (~100,000 years ago) and their further dispersion into Eurasia (~45,000 years ago) was necessary for them to acquire, by introgression, the immune-related variants adapted to the local regional infectious conditions. This "epidemiologic transition" lag is observed in invasive species between the moment of their appearance in the new environment and the start of efficient population growth (Hawks, 2017).

Risk factors for autoimmune diseases probably originated as adaptations to the infectious diseases of the time, but what we see today might be an unfortunate rebalancing of the immune system. Many autoimmune disorders have been linked to variants inherited from Neanderthals. Some of these deleterious traits could have survived simply due to chance and insufficient negative selective pressure, especially those occurring later in life. It is also possible that they presented a heterozygote advantage with respect to a pathogen, even one no longer present (as is the case of thalassæmia/sickle cell in the Haldane hypothesis: wherein homozygous individuals suffer from the respective disease, while heterozygous individuals are unaffected and have increased resistance to malaria) (Haldane, 1949).

Concluding remarks

Thus, the study of recent human evolution contributes not only to our understanding of population history and adaptive physiology, but also to the genetic architecture of diseases. In the case of autoimmune diseases, it is becoming clear that the infectious context is a major source of evolutionary pressure, with effects seen over comparatively short timescales. Investigation of Neanderthal and other archaic human subspecies DNA can advance both our understanding of the complex genetic makeup of disease risk factors and, more generally, the way we conceptualise the relationship between environmental conditions and evolution. Our archaic ancestors have much yet to teach us about ourselves.

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Apply for one of The Physiological Society's grants

Conference Attendance Award
Funding to attend a Society and/or Society-sponsored conference

Deadlines: 31 May, 31 July, 30 October 2023

Unlocking Futures Fund
Funding is open to postdoctoral researchers who require additional support to help them achieve their full potential.

Deadline: 15 September 2023

Research and Knowledge Exchange Award
Funding to support members wishing to conduct pilot studies, develop a new technique or to finalise a project

Deadline: 30 April 2023

Education and Teaching Award
Funding to support members wishing to develop new educational resources or conduct a piece of publishable educational research

Deadline: 30 April 2023

Professional Development Award
Funding to visit a lab or attend a training course for the development of a specific skill or technique

Deadlines: 17 May, 22 August, 02 November 2023

Institutional Engagement Awards
Funding to support Society Representatives and members to co-host events at their institution

Deadline: 1 October

For more information about the grants programme, visit - physoc.org/grants

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The Physiological Society

Committee Meeting Report

Regenerating the Cardiovascular System: Mending Broken Hearts and Beyond (13 – 14 September, University of Oxford, UK)

Report of The Society's recent Conferences Committee meeting

November 2022

Dr Catherine Hall (University of Sussex, UK), as Chair, welcomed members of the committee, including new members, Professor Paul Greenhaff (University of Nottingham) representing *The Journal of Physiology* and also Dr Joe Costello (University of Portsmouth) representing *Experimental Physiology*.

The main agenda item, a continuation from CC22.01, centred on Society conferences and meetings for 2023 and beyond, and how these could best support physiology and physiologists, also engage the membership and their communities. The Committee noted that the 2023 meetings calendar had been populated with the following five meetings following the recent call:

- Innovation and Updates in Teaching and Student Education across Physiology and STEM in the UK (12 – 13 April, University of Leeds, UK)
- Membrane Transport 2023: Recent Research into Ion Channels, Transporters and Epithelial Physiology (24 – 25 August, University of St Andrews, UK)
- Cross-Talk of Cells in the Heart: Novel Mechanisms of Disease and Arrhythmias (11 – 12 September, University of Liverpool, UK)
- Regenerating the Cardiovascular System: Mending Broken Hearts and Beyond (13 – 14 September, University of Oxford, UK
- Neurophysiological Bases of Human Movement (12 – 13 December, King's College London, UK)

There was also some discussion on additional support for meetings organised by members outside of the two-day meeting format. These ideas will be developed and refined in 2023.

Finally, Professor Raheela Khan (University of Nottingham, UK) was warmly thanked for her time and commitment to the Committee during her time as a Trustee.

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Meeting Report

Energy Stress Meeting

15 September 2022, Liverpool John Moores University, UK

Dr José Areta

Physiological Society Representative and Ambassador for the Society for Endocrinology

Research Institute for Sport and Exercise Sciences (RISES) at Liverpool John Moores University, UK.

Dr José Areta organised and led the Energy Stress Meeting, supported by the Institutional Engagement Award by The Physiological Society and the "Meeting Support Grant"he received from the Society for Endocrinology. José summarises the meeting and its aim to enhance research on energy deficit and energy balance.

The "Energy Stress Meeting" took place on 15 September 2022 at Liverpool John Moores University, UK. It was the first meeting that brought together a group of international experts researching the endocrine, physiological and metabolic effects of dietary energy deficit and energy balance in humans. The topic is an important area of research considering the current obesity pandemic and the high prevalence of inadequate fuelling in many athletes. Through researching these seemingly divergent populations we seek to understand the underpinning physiological mechanisms in response to states of energy deprivation.

The meeting provided eight stimulating high-quality talks providing rich insights on the physiological effect of energy deficit from different perspectives. The speakers drew insights from divergent human populations, including athletes, overweight/obese and general population, discussing their responses to energy deficit, focusing on different levels of organisation from molecules to whole organism.

It was an honour to have prominent international speakers presenting at the meeting. These included Professor John Speakman from University of Aberdeen, UK and Chinese Academy of Sciences (Beijing, China), who is a fellow of the Royal Society and a "1000 talents" professor at the Institute of Genetics and Developmental Biology, Chinese Academy of Sciences.

Another international speaker was the highly regarded Spanish exercise physiologist, Professor José Calbet, from University of Las Palmas de Gran Canaria in Spain, who trained with Professor Bengt Saltin in Copenhagen in the 90s. Also, up-and-coming talent Professor Karsten Koehler, from Technical University in Munich (TUM), Germany, and Dr Eimear Dolan, from the University of Sâo Paolo.

In addition to the international speakers, established and up-and-coming researchers from the UK presented stimulating talks at the meeting. A prominent figure among these was Professor James Betts from University of Bath, followed by Dr Mark Hopkins from University of Leeds, Dr Carl Langan-Evans, and myself from Liverpool John Moores University.

The meeting was attended by individuals from the UK, as well as international delegates from France and Spain, seeking the latest information in this topic.

In addition to the one-day seminar, the meeting included a networking session on the morning after the talks to enhance research collaborations between the speakers and boost the current research agenda on the topic.

Group photo of speakers at the meeting. From left to right: Professor José Calbet (University of Las Palmas de Gran Canaria, Spain), Professor James Betts (University of Bath, UK), Dr Mark Hopkins (University of Leeds, UK), Dr Eimear Dolan (University of São Paulo, Brazil), Professor Karsten Koehler (Technical University of Munich, Germany), Dr Carl Langan-Evans (Liverpool John Moores University), Dr José Areta (Liverpool John Moores University), Professor John Speakman (University of Aberdeen and Chinese Academy of Sciences).

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Meeting Preview

Membrane Transport 2023: Recent Research into Ion Channels, Transporters and Epithelial Physiology

24 – 25 August 2023, University of St Andrews, UK

Dr Morag Mansley

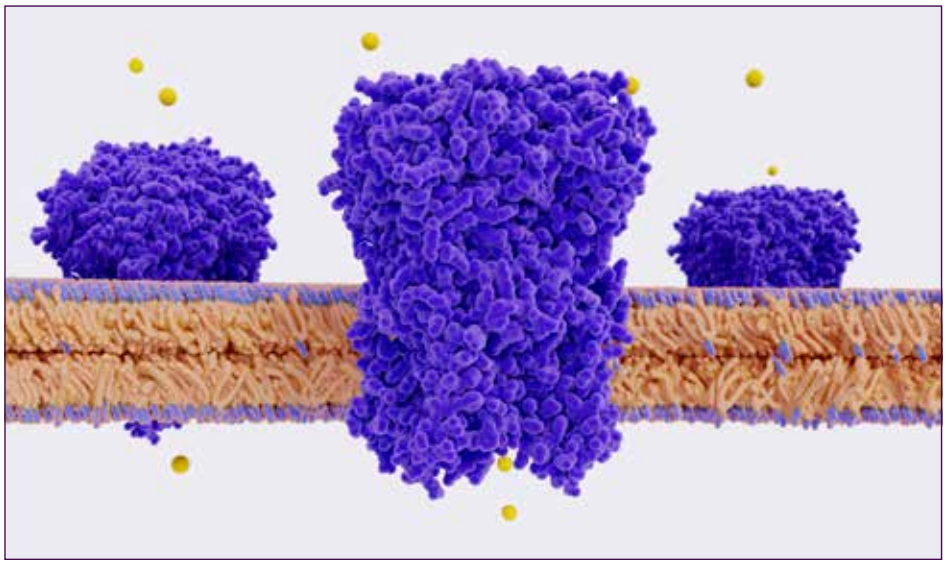
University of St Andrews, Scotland

Professor Mike Althaus

Bonn-Rhein-Sieg University, Germany

Dr Stephen Keely

Royal College of Surgeons in Ireland



We are delighted to announce a two-day themed meeting entitled *"Membrane Transport 2023: Recent Research into Ion Channels, Transporters and Epithelial Physiology"*, which will be held at the beautiful and historic University of St Andrews, Scotland on 24 – 25 August 2023. Since the discovery of cell membranes more than 500 years ago, scientists have been trying to understand how solutes traverse these structures to and from the cell, enabling them to survive and perform their distinctive functions. Through their efforts we now know, of course, that transport is mediated by specialised proteins embedded into the cell membrane, which function to facilitate the translocation of a myriad of substances, including electrolytes, nutrients, and metabolites, and that dysregulation of these proteins is a key factor in driving the pathogenesis of many disease states.

With the development of new and more refined techniques for studying membrane transport, along with the arrival of multiomics technologies, recent years have seen massive advances in our understanding of cellular and molecular mechanisms that regulate membrane transport and how we can potentially target these processes for therapeutic purposes. Against this background, *Membrane Transport 2023* aims to bring together scientists from multiple disciplines to discuss the most recent developments in this broad and exciting field of study, including sessions on *"Recent developments in epithelial transport physiology"*, *"New insights into structure and function of ion channels and transporters"*, and *"Dysfunction of ion channels and transporters in disease"*. There will also be a special session entitled *"The transport physiologist's toolbox in 2023"*, which will be dedicated to highlighting state-of-the-art approaches for the study of membrane transport in health and disease.

A key feature of this two-day meeting is that it aims to provide a platform for early career researchers to showcase their work in both oral and poster sessions and to give ample opportunities to network with more senior researchers in the field. The Taste of Scotland evening will undoubtedly be a highlight for this purpose! With speakers from across the UK, Ireland, Europe, and the US, discussing the latest advances in membrane transport across a wide range of organs and tissues, this meeting will be a truly international and interdisciplinary affair. We look forward to seeing you soon in St Andrews!

Key dates

Registration opens:
03 April 2023

Abstract submission:
03 April 2023 – 30 April 2023

Conference Attendance Award deadline:
31 May 2023

Early bird registration deadline:
06 July 2023

Online registration deadline:
10 August 2023

physoc.org/events/membrane-transport-2023-recent-research-into-ion-channels-transporters-and-epithelial-physiology/

https://doi.org/10.36866/pn.129.36

Meeting Preview

Cross-Talk of Cells in the Heart: Novel Mechanisms of Disease and Arrhythmias

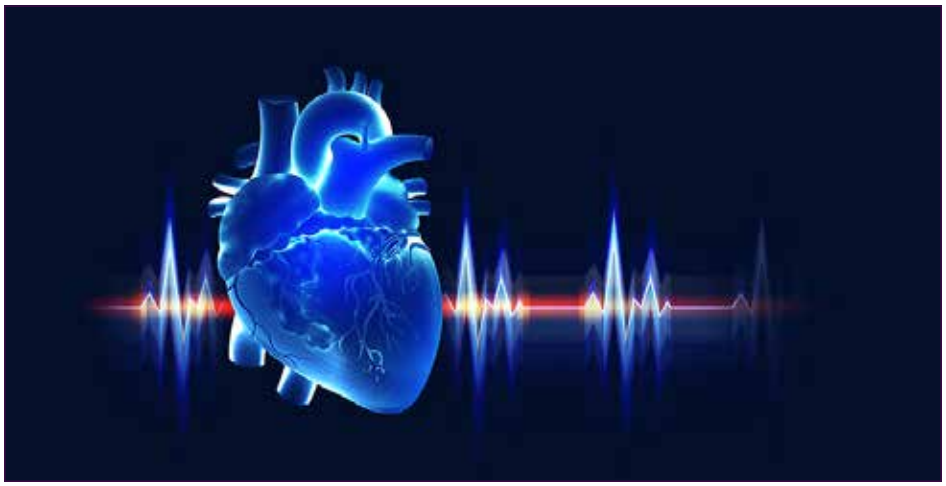
11 - 12 September 2023, University of Liverpool, UK

Dr Daniel Johnson

The Open University, UK

Dr Nordine Helassa

University of Liverpool, UK



Heart disease is one of the major causes of morbidity and mortality around the world. Until recently, arrhythmias, an irregular rhythms of the heart, were thought to be driven by dysfunction of cardiac myocytes alone. However, work over the last 10 years has started to show that the myocyte does not act alone and is highly influenced by its surroundings. For these reasons, this two-day Physiological Society meeting organised by Dr Daniel Johnson, The Open University, UK and Dr Nordine Helassa, University of Liverpool, UK, will provide a unique and timely opportunity to get together in person to discuss the extremely important topic of cell–cell interactions and links to arrhythmia and disease formation.

This conference will give us a chance to hear from a diverse programme of speakers, ranging from early career researchers to established professors, discussing myocyte interactions with various cell types, including fibroblasts, adipocytes, neurons and immune cells.

Furthermore, a number of presentations will discuss the potential of different models to investigate the effects of cellular heterogeneity in this field, including the use of cardiac organoids and slices as well as work in the computer modelling field.

The overall aim of this symposium is, therefore, to provide a platform for the discussion of cutting-edge issues in this field such as the cellular structural basis, intercellular signalling, physiology and pathophysiology.

In addition to the scientific programme, we hope to be able to offer an exceptional social programme that will allow researchers to network and cross-pollinate ideas while catching up with friends and colleagues, with the hope of re-establishing old working partnerships as well as discussing new ideas for future collaborations. The conference will take place in Liverpool, a city with fantastic transport links and which is known for pioneering buildings, its maritime history, as well as the music of The Beatles! Therefore, this meeting provides a unique opportunity for the community to "Come Together".

Registration is open from 1 March until 21 August 2023, with abstracts being accepted throughout the month of May.

We hope to welcome you to Liverpool in September!

Key dates

Registration opens:
01 March 2023

Abstract submission:
01 May 2023 - 31 May 2023

Conference Attendance Award deadline:
31 July 2023

Early bird registration deadline:
17 July 2023

Online registration deadline:
21 August 2023

physoc.org/events/thephysiological-society-event-cross-talk-ofcells-in-the-heart/

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Introducing Dr Nephtali Marina-Gonzalez, our General Trustee leading The Society's Equity, Diversity, and Inclusion (EDI) work

The importance of role models, advocates for diversity and the need for long-term commitment to EDI. In this Q&A, Nephtali shares the challenges to achieving a more inclusive scientific community and the changes he would like to see to achieve this. The gains will ultimately lead to greater innovation, creativity, and progress for all.

Tell us a bit about yourself

After completing my medical training from the National University of Mexico I decided to pursue a career in physiology research and I gained Masters and PhD degrees in Neurosciences before taking up academic positions at Cambridge and University College London. I have devoted my scientific career to the study of the autonomic control of cardiorespiratory physiology with a special focus on the pathogenesis of arterial hypertension. I am currently serving as Vice Dean (Equality, Diversity, and Inclusion) for the UCL Faculty of Medical Sciences.

What inspired you to get involved with Equity, Diversity, and Inclusion (EDI) work?

As an ethnic minority myself (born and raised in Mexico) I have witnessed the challenges of EDI inside and outside academic research. The social inequities and disparities brought to light during the COVID-19 pandemic inspired me to use my experience and resources to promote inclusion by empowering people who are often under-represented and ensure they have equal opportunities to succeed in their careers.

As The Society's EDI Champion, what would you like to achieve in the role?

The future of The Physiological Society will be shaped by the commitment of staff, Trustees and committee members to promoting EDI. I would like to see more initiatives aimed at increasing the representation of marginalised groups in Physiology research and education, as well as promoting equitable access to opportunities and resources within the field. As The Physiological Society community becomes more diverse, it will be better equipped to address the challenges of our rapidly changing world and create more effective solutions that benefit everyone.

What challenges do you hope to address?

A big challenge is the lack of adequate support. Promoting EDI is labour-intensive, and research institutions need to allocate resources required to implement, monitor and maintain these initiatives effectively.

The main change I would like to see is long-term support and commitment for EDI. Achieving short-term changes can be relatively easy but maintaining a diverse and inclusive culture over time can be challenging, and research organisations must continuously work to foster an environment that supports EDI.

What do you think is the main aspect of positive change in EDI that is happening currently?

I am excited to see that some organisations are starting to commit dedicated funding for under-represented early career researchers who face numerous obstacles in advancing their careers in science and academia. Providing dedicated funding will help mitigate these barriers and provide more equitable opportunities for under-represented researchers to succeed in their careers. This will also help to address the leaky pipeline issue and ensure that the next generation of researchers are more diverse and inclusive as well.

What do you think is the major obstacle that often goes unnoticed, that is keeping us from a diversity-inclusive and equitable scientific community?

One major obstacle is the under-representation of women and of racial and ethnic minorities at leadership and decision-making levels in many institutions. This creates a lack of role models for students and early-career researchers and limits their ability to advocate for diversity and inclusion.

Have you any words of advice for your colleagues on how to be an ally and actions to support more diverse communities?

I have a few!

Listen to the voices of under-represented communities, and use your networks to amplify their voices and perspectives.

Challenge discriminatory language and behaviour, and speak out against institutionalised barriers that limit opportunities for diverse communities.

Get more engaged and champion initiatives that promote diversity and inclusion in your institution and advocate for policies and practices that address systemic barriers and promote equity and fairness for all people.

Being an ally is a journey, not a destination, and it's important to continue learning, and advocating.

To finish, what is your favourite city and why?

I love San Sebastian in the Basque country. The friendliness of the culture and the beautiful gastronomy are unparalleled!

The Society will champion diversity, promote inclusivity, and strive for equity through its Equity, Inclusion and Diversity Roadmap. Find out more at physoc.org/about-us/diversity/

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An introduction to the *Physiology News* Editorial Board

We're excited to introduce the new members of the Editorial Board. Members join us from around the world, bringing expertise across physiology, including research, education, clinical and industry backgrounds.

Roslina Abdul Rahim

International Islamic University Malaysia, Malaysia

I am an Associate Professor of Physiology at Kulliyyah of Medicine, International Islamic University Malaysia (IIUM). Having completed my undergraduate degree in biomedical science at University Kebangsaan Malaysia, I went on to study a Master's in medical sciences majoring in physiology at IIUM and obtained my PhD in Biomedical Science in 2011 from University of Nottingham, UK.

For the past 12 years, I have been teaching Physiology focusing on the renal system, respiratory system, endocrine system, pain and thermoregulation physiology. My research interests are molecular mechanism of non-alcoholic steatohepatitis (NASH), polycystic ovary syndrome (PCOS) and male infertility in NASH animal models, which is strongly related to insulin resistance. I am also the Executive Committee Member of the Malaysian Society for Pharmacology and Physiology since 2021 to date. I have been a member of The Physiological Society since 2021 and recently join the *Physiology News* Editorial Board. Sailing aboard with this team will help me gain knowledge and recognition as well as meet and work with The Society's member community.

Yasser El-Wazir

Suez Canal University, Egypt

I am a medically qualified Professor of Physiology at Suez Canal University in Egypt, an institute well known for introducing an innovative medical curriculum in the 1980s. This motivated me to be quite involved in medical education, specifically curriculum design and quality assurance of education. In parallel, my career in physiology involved several research areas, mainly the autonomic control of cardiac rhythm in different conditions like intense physical training, diabetes, or obesity. Additionally, I have developed an interest in regenerative medicine, and my work aimed to explore the modulation of different types of stem cells on oxidative stress state and apoptotic mechanisms in various body organs. Like many physiologists working outside the UK, I have been a member of The Physiological Society for several years, and my recent membership of the editorial board of *Physiology News* aims to assume a more active role to serve the Society and to establish better ties with the local and regional physiological societies in my region.

Rachael Kemp

Swansea University, UK

My research interests centre around understanding the mechanisms underlying the benefits of exercise with the aim of optimising exercise protocols for the prevention and treatment of disease. Currently, I am completing a PhD at Swansea University, UK combining my background in exercise physiology with *in vitro* cell-based approaches to investigate the effects of exercise on cancer cells. Since joining The Physiological Society during my undergraduate course in Exercise, Nutrition and Health at Kingston University, UK, I have enjoyed learning about the latest developments and research across the different themes in *Physiology News*. I aim to bring an early career perspective to the Editorial Board and promote opportunities for early career physiologists to share their views and research updates alongside more senior authors.

https://doi.org/10.36866/pn.129.39

Zoran Redzic

Kuwait University, Kuwait

I am a Professor in Physiology at College of Medicine, Kuwait University. I am a medical doctor by training, having completed an MSc in neurosciences and a PhD in Medical Sciences. I started off my career with choroid plexuses (CPs) and blood–brain barrier (BBB) physiology. As my research career progressed, I became more focused on the effects of hypoxia/ischæmia on transport processes at CPs and BBB. Exploring cell-to-cell signalling in the brain during hhypoxia/ischæmia and the role of these processes in tissue adaptation to reduced partial pressure of oxygen. I am currently focused on investigating the effects of type 1 respiratory failure, induced hypoxæmia on cell-to-cell paracrine signalling in the brain. I have been a member of The Physiological Society for just over 20 years. During that time, I have tutored medical students on physiology of all body systems, especially neurosciences and respiratory physiology and I have supervised many graduate theses in neurophysiology. My general interest in scientific journalism led to nine years working as an Associate Editor for the journal *Fluids and Barriers of the CNS*. I have always found that *Physiology News* provides a diverse output of news and research in physiology. My hope is that as a member of the Editorial Board of *Physiology News* I can become more involved with The Society and that I can continue to promote science, physiology, and an evidence-based view of the world to inspire younger generations of physiologists.

Kevin John

University of Canberra, Australia

It was my passion for biology and sport in school that led me to complete an undergraduate degree in sport and exercise science from Swansea University. Following this, I successfully gained a Master's by Research in exercise physiology under the guidance of Dr Mark Waldron. My Master's thesis aimed at developing a mobile passive heating strategy to supplement training and enhance endurance performance. At present, I am a scholarship-funded PhD student in the Environmental Physiology Research Laboratory led by Professor Julien Périard at the University of Canberra Research Institute for Sport and Exercise. My research aims to better understand how heat acclimatisation develops in woman and how it influences performance. I have recently become a member of The Physiological Society as I was highly inspired by The Society's commitment to making physiology accessible to everyone and raising awareness regarding the impact of physiological research on the betterment of life. Furthermore, The Society organises excellent educational events that are highly beneficial for early career researchers. As such, by joining the *Physiology News* Editorial Board I intend to contribute towards the magazine's quest for effective scientific communication of physiology research and The Society's activities.

Matthew Hardy

University of Bradford, UK

I am an Assistant Professor in Human Biology at the University of Bradford. Whilst my research background is in cellular cardiology and electrophysiology, recent years have seen me transition to a more teaching-focused role. My interests lie not only in the delivery of biology, physiology and pharmacology education, but also in how we can scaffold student progress by embedding academic skills into bioscience programmes. My focus in these areas is influenced by past experiences working as an Academic Skills Advisor in the Leeds University Library; here I discovered that student achievement can be dramatically enhanced by a relatively small input into their skill development, for example writing and other communication skills. I am very excited to become a part of the Editorial Board of *Physiology News* and hope that my interests in writing, communication and physiology will enable me to make some positive contributions.

https://doi.org/10.36866/pn.129.39

Physiology Friday 2022 festivities at Newcastle University

Every year, we celebrate Physiology Friday and call on our members to hold exciting outreach activities to help showcase the amazing world of human and animal bodies. Here, member Dr Harley Stevenson-Cocks from Newcastle University, UK reports on the university's Physiology Friday 2022 celebration and their ongoing engagement activity centred on the question "What is Physiology?". The project is growing a video collection of interesting perspectives from physiologists and the general public sharing their thoughts in response to the question.

Dr Harley Stevenson-Cocks

Biomedical, Nutritional and Sport Sciences at Newcastle University, UK

The cities of Newcastle and Durham were joined by the love of science as part of Physiology Friday 2022 events organised by Newcastle University physiology students and staff. The centrepiece of the day was a public lecture given by Dr Graham Burns, Consultant Respiratory Physician at the Royal Victoria Infirmary in Newcastle, entitled "Coming up for Air", which focused on how we breathe, in particular what drives us to take our next breath. Graham gave a fascinating lecture on lung physiology and pathophysiology to an engaged audience, and was kept busy well after the lecture with questions from the public.

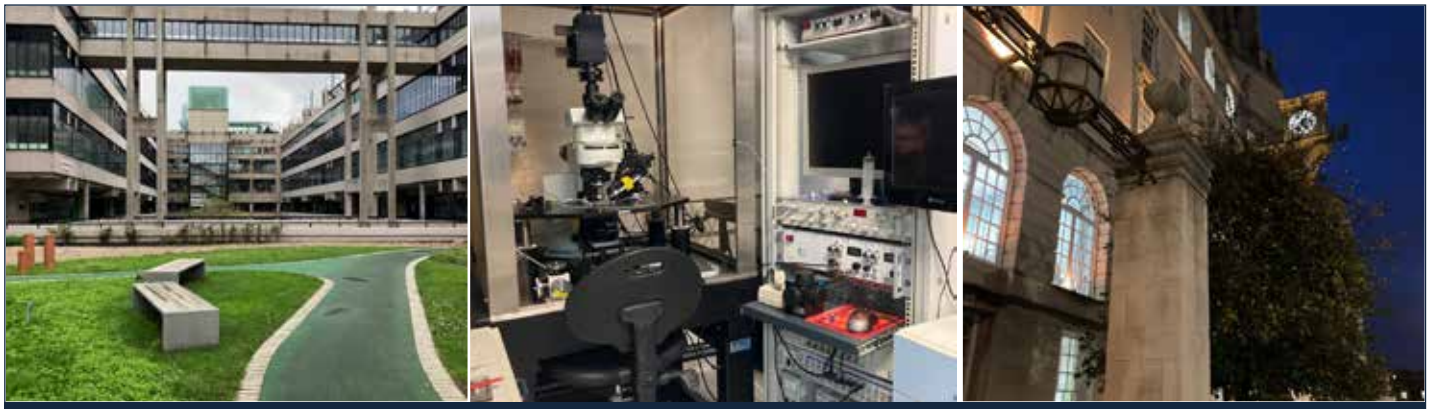
Either side of his talk, physiology students and staff from Newcastle University ran a series of interactive sessions for the public, centred on various aspects of physiology including neuroscience and cardiology.

Continuing from the success of inaugural events of Physiology Friday 2021, our students also led two external engagement activities. First, students ran an ECG workshop at Durham Sixth Form Centre, answering many questions and inspiring enthusiasm for physiology among A-Level students.

Second, our students were tasked to record interviews with academics from other universities about their thoughts on "What is Physiology?". This year, we were fortunate enough to be able to send two of our students, Rebecca and Joe, to the University of Leeds, UK, to conduct some in-person interviews with staff there. While rail strikes scuppered our plans to do the same at the University of Manchester, UK, we were thankful our students were still able to interview some Manchester-based staff remotely via Zoom instead. With thanks to Charlotte, Al, Matthew, Ruth and Sue (Leeds), and Tristan, Liz and Donald (Manchester) for speaking with our students and for some excellent interviews!

We have a growing online repository of our Physiology Friday, and related, engagement activities where you can check out our latest interviews, lectures and associated events (https://doi.org/10.25405/data.ncl.c.5725439). We are keen to encourage contribution to the "What is Physiology?" conversation so please do consider contributing your thoughts on all things physiology by scanning the QR code if you'd like to register your interest to be our next interviewee.

Sixth-form pupils from Durham enjoying our students' ECG workshop on Physiology Friday



A selection of pictures from Rebecca and Joe's trip to the University of Leeds. Left: The Faculty of Biological Sciences and sustainable gardens; Middle: a glimpse into the Cellular Cardiology lab; Right: Leeds City Council's golden clock.

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In memory of Professor Hisako Ikeda-Wolstencroft

31 July 1928 to 22 December 2021

In these pages, we celebrate the life and work of Professor Hisako Ikeda-Wolstencroft, a valued member of The Society and a world leader in the field of vision research. In her memory, Professor Ikeda-Wolstencroft's family made the founding donation to The Society's new Unlocking Futures Fund with the aim of unlocking the potential of a future leader of physiology.

We begin with an account by Dr Jon Robbins, a family friend and former colleague, who shares life in the lab with Professor Ikeda-Wolstencroft, a role model for both work and family life.

Dr Jon Robbin

King's College London, UK

Hisako, 1993.

Hisako left Japan in 1955/56 with an MA and a young daughter, Utako. She was first employed at the Institute of Psychiatry, London as a Research Assistant where she achieved a PhD by 1960. She obtained a fellowship at the Institute of Ophthalmology, London and was promoted to lecturer of Ophthalmology in 1966. She then moved to the Royal College of Surgeons London as a senior lecturer in Ophthalmology.

Her final move was to St Thomas' Hospital Medical School as a Senior Lecturer in Physiology. She was head of the Vision Research Unit at the Rayne Institute at St Thomas' Hospital by 1974. In 1982, Hisako was made Professor of Visual Physiology, which at the time would mean she was one of the very few non-white female professors in the country. More recent data from a colleague in the Wellcome Trust estimated that in 2017 there were only 54 non-white female professors in the UK.

Hisako's scientific publications range from the effects of ethanol on the function of the eye (1963) through to the effects of Parkinson's disease on retinal function (1994) and much in between. She published over 110 papers in her career, she has an H-index over 28, and 2380 citations in total, though she is still cited around 25 times a year (Scopus, Nov 2022). Hisako's work has led to real-world impacts, from advising on the use of sodium streetlights, the treatment of amblyopia and squinting, the early identification of retinal dysfunction in Parkinson's patients, to the development of a novel animal model for multiple sclerosis. Her work was "bench to bedside" before the term was coined. Simultaneously running vision electrodiagnostic clinics for private and NHS patients and performing basic electrophysiological research of the visual system, each of her activities informed the other.

In 1982 I joined her laboratory as a Research Assistant and part-time PhD student, having graduated from UCL. Hisako set the benchmark for work rate; she would be the first to arrive in the morning and the last to leave. A week consisted of a whole-day clinic on Monday, experimental set-up on Tuesday, followed by a forty-eight-hour experiment on Wednesday and Thursday. Fridays were filled with grant and paper writing, as well as teaching medical students. There was usually an emergency request for further electrodiagnostic tests at least once a week!

Hisako sat on her bed in her office. She had a bed for when she worked too late to go home.

This is not to say Hisako did not enjoy life; her weekends were spent with her family in her much-loved cottage in Kent. She would host parties both in Kent and her flat in London. An enduring memory is on a trip to a scientific meeting in Florida, where she was keen to see the swamp alligators close up in a canoe; she had little fear!

We gave Hisako a Festschrift in 1993 at St Thomas' Hospital (Robbins 1995, ISBN978-1-4757-9364-2) and she was made Emeritus Professor of Visual Physiology and entered into the 11th edition of Marquis' "Who's Who in the World". However, in her retirement she did not slow down; she embarked on degrees in History of Art, Philosophy and English Literature.

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To Grandma, thank you for being my inspiration

John Nicholson

In this poignant tribute to Professor Ikeda-Wolstencroft by her grandson, John Nicholson, he shares the story of his grandmother, a woman who followed her dream and challenged prejudices. Through kindness and generosity, she encouraged others to discover and pursue their own interests to carve out their own paths.

Professor Hisako Wolstencroft was just Grandma to us. We knew she did an important job but didn't really know what it was. We knew she worked hard, but she never took her professional life home with her when she was with us. All we saw was an incredibly loving, caring and fun Grandma who'd spoil us rotten, but impressed values upon us that have stayed with us since our childhood.

The biggest of which was the importance of education. Grandma was born in Japan in the 1920s, and both her parents were academics. Her father Kiguma taught English; her mother Chizu taught maths. It was extremely rare in Japanese culture for a woman to study for a degree and work as a teacher in Japan back then. I'm certain that's where Grandma's passion for education came from, as well as her daring attitude to break convention and stereotype. By the time us grandchildren came along, she was succeeding in a career that would have been considered impossible a few years earlier, and absolutely impossible for her in Japan. Grandma had seen what her education and upbringing had given her, and wanted the same for us.

Grandma would never push us into any particular subject or area though. She was a scientist with a daughter who played the flute for a living, and she placed just as much importance on the arts as she did academia. All she wanted for us was to learn, to find something we had a passion for, and to pursue that passion wholeheartedly. So when we announced we had a new-found enthusiasm for something – cricket, astrology, sports journalism – she'd furnish us with the equipment or books or space to do those things. It was incredibly generous, but the thing we took from that generosity wasn't really the material gift, but the emotional support that was always there, unstinting and unapologetically biased towards her grandchildren.

Grandma looked after us almost every weekend while our parents played in concerts, driving us to the cottage she'd bought with her second husband John in the Kentish countryside. It could have been a relaxing haven away from busy London life, but Grandma didn't see it that way. She would pretty much never stop, and her energy was infectious. I think she saw sleep as a waste of time, and she'd always be up first and wanting us to wake so we could seize the day. She didn't like us watching TV and getting "square eyes", so there'd always be something to do – shopping, gardening, drawing, she'd play football with us and swim with us. It ensured time with Grandma was never dull; we were never killing time and were always doing something productive.

As a migrant from a strange country, and as a woman working in a male-dominated profession, Grandma also knew how harmful and hurtful prejudice was. She placed a great importance on being polite, fair and well mannered. She loved being with people, hearing their stories and learning from their experiences. Grandma was extremely popular and had friends from all over the world, which I think tells you how kind and generous she was with everyone. She treated everyone the same. Well, almost everyone.

There's no doubt that Grandma reserved special affection for us grandchildren. We were showered in her love, her passion and wisdom, and we're very grateful for that. As an adult now with a family of my own, I can honestly say Grandma is my inspiration, the person I admire most out of everyone I've come across and been influenced by. Her story of following a dream, refusing to be blocked by society's expectations, and above all being a kind, supportive and loving person is one I will tell to my children and will encourage them to tell to theirs. And if I can be even half the grandparent she was to us, then I'll have done very, very well.

The Unlocking Futures Fund

Physiology was Professor Ikeda-Wolstencroft's passion. Exploring the frontiers of visual pathways and neurobiology to improve understanding of how to diagnose and treat eye disorders was her dedication to serving society.

Our Unlocking Futures Fund has been started in memory of Professor Ikeda-Wolstencroft. It is open to postdoctoral researchers who require additional support to help them achieve their full potential.

Applications are now open
Unlocking Futures Fund is open to postdoctoral researchers who require additional support to help them achieve their full potential.

The grant has two deadlines:
31 March 2023
15 September 2023
Each applicant can apply for up to £2,500.

Find out more and apply at
physoc.org/grants-and-prizes/grants/unlocking-futures-fund/

Donate to the fund
The Unlocking Futures Fund supports members facing barriers to career progression. The fund is currently open to donations. If you would like to help physiologists achieve their full potential please consider donating here at
physoc.org/grants-and-prizes/grants/unlocking-futures-fund/unlocking-futures-fund-donate/

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Gerald Francis Yeo: mapping the brain

Professor Mark Cunningham

Head of the Discipline of Physiology, School of Medicine, Trinity College Dublin, the University of Dublin, Ireland

"With the exception of geography, there is no science which has been so susceptible to the rhetorical appeal of cartography as the science of medicine"

Douwe Draaisma (2009)

Last June, The Physiological Society unveiled a blue plaque to celebrate the legacy of Irish physiologist Gerald Francis Yeo (1845 - 1909). Yeo was one of 19 physiologists who gathered at the house of John Burdon in March 1876 to form The Physiological Society for "promoting the advancement of physiology and facilitating the intercourse between physiologists". Yeo was the Secretary of The Society until 1889 and campaigned for the value of *in vivo* research in response to Victorian anti-vivisection campaigns. Professor Mark Cunningham shares the legacy of Yeo's life and work.

Gerald Francis Yeo was born in 1845 in Howth, County Dublin. The Yeo family arrived in Ireland from southwest England in the late 18th century. Yeo's father, Henry was a Justice of the Peace and had been the Registrar of the Court of the Exchequer. Yeo was sent north to the Royal School Dungannon, County Tyrone and from there, he entered Trinity College Dublin (TCD) and graduated in Natural Sciences (1867) and an M.B./B.Ch. (1867). Yeo gained valuable research experience during time spent in Paris, Vienna, Leipzig and Berlin. During his time on the continent, Yeo would have interacted with figures such as Carl Ludwig and Friedrich Goltz. Yeo recognises Ludwig as his master in terms of his training as an experimentalist (Royal College of Surgeons) and stated that "I am proud to call him (Goltz) my friend." (Yeo, 1882)

Back in Dublin, Yeo demonstrated anatomy in the School of Physic (Medicine) at TCD and was appointed as the Lecturer in Physiology at the Carmichael College of Medicine. The Carmichael had been previously known as the School of Medicine of the Richmond Hospital. Alongside his teaching activities, Yeo was active in research. In his monograph on the history of medicine in TCD (Coakley, 2014), Coakley discusses a decline in the Irish School of Medicine, a failure to match developments in biomedicine taking place in countries such as Germany and France being the main cause. Yeo was pushing against this downturn. He published numerous papers in the Proceedings of Pathological Society Dublin and the Irish Hospital Gazette. Yeo's scientific output at this time included studies on the brain. In 1874, he published a paper in the Proceedings of the Pathological Society (Dublin), describing a particular type of cerebral tumour (Yeo, 1874).

In 1875 Yeo was appointed Professor of Physiology at King's College London, following in the footsteps of his compatriot and fellow alumnus – Robert Bentley Todd. He was also appointed assistant surgeon at King's College Hospital. King's was an exciting environment with Lister, Watson Cheyne and Ferrier active in the faculty. Yeo collaborated with Watson Cheyne who was then a strong advocate of Lister's antiseptic methods. In 1879, the British Medical Journal reported the proceedings of the Pathological Society of London and described a presentation by Watson Cheyne in which the surgical contributions of Yeo in studies examining the presence of micrococci in wounds treated using Lister's antiseptic method were acknowledged.

Yeo's colleague David Ferrier had spent the preceding decade at the West Riding Lunatic Asylum working on experiments that would culminate in his book "The Functions of the Brain." In 1872, Ferrier had been invited by Crichton-Browne to investigate the findings of Gustav Fritsch and Eduard Hitzig. Using direct current stimulation, they demonstrated cerebral localisation. Fritsch and Hitzig's work had not been universally accepted and further work was required. Ferrier used both "Faradic" stimulation and surgical ablation in a variety of species to address this. However, the ablation studies were limited as with the absence of aseptic condition, the animals failed to survive much beyond the surgery. Yeo's surgical skills coupled with his experience with antiseptic techniques provided Ferrier with an ideal collaborator. Additionally, Yeo and Ferrier would use primates rather than dogs. Their scientific opponent was Friedrich Goltz, who refuted the localisation theory and based his objections on studies in dogs.

Photograph: Carte-de-visite of Gerald Francis Yeo by Barraud and Jerrard. In the New York Academy of Medicine, Carte de Visite Collection

The denouement took place at the Physiological Section of the International Medical Congress in London in 1881. At the Royal Institute, Goltz discussed a dog with a large area of the cortex removed and how this produced no effect. Goltz argued that this demonstrated the functions of the brain were not localised. Ferrier and Yeo countered that a localised paralysis in their monkey due to the removal of the putative motor area supported localisation (Klein and Langley, 1884).

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Professor David Paterson and Professor Michael Gill (School of Medicine, Trinity College Dublin, Ireland) at the blue plaque unveiling in Dublin to celebrate Gerald Francis Yeo

In his presentation at the physiology section, Ferrier highlighted the contributions of Yeo, stating that:

"*....I have had opportunities of observing animals operated upon by my colleague, Professor Gerald Yeo, in an investigation into the application of the principles of antiseptic surgery to lesions of the brain and its coverings.*"

Yeo recognised the importance of his contributions, stating:

"Those who have experience of the aseptic method of operation will excuse my presumption in saying that I think absolute localization of the cortical lesion have not been arrived at with at all the same exactness in any set of experiments undertaken without its aid."

Yeo also played an important role in the scientific relationship - that of the sceptic. This is captured by Yeo's comments:

"I commenced this series of experiments with distinct misgivings as to the existence of local cortical centres, in Ferrier's sense, so that I may say I was rather prejudiced against, than in favour of, his views."

Perhaps Yeo's initial view of the experiments may have been prejudiced by his friendship with Goltz. Indeed, Yeo took a conciliatory position stating:

"These very remarkable negative results obtained by my friend, Professor Goltz, in the case of dogs, cannot be said to be an adequate argument against the positive results arrived at in our experiments upon monkeys; while, on the other hand, our positive results seem to curtail in an absolute manner the very extensive generalizations Professor Goltz wishes to draw from his experiments."

The discussion was closed with a decision to form a committee that would examine the brains of both animals. The committee was to assess the extent of the lesion given the conflicting results presented. That afternoon a delegation visited Yeo's laboratory at King's to view the animals that had been described in detail during the morning's section meeting. Goltz's dog showed an absence of sensory or motor deprivation – the animal responded in a normal manner, running around and reacting to its environment. In contrast, one of the monkeys, which had undergone ablation of the motor area of the left hemisphere, presented with unilateral paralysis of the right arm and leg. Charcot is reported to have exclaimed, "C'est un malade!". Yeo and Ferrier had recapitulated in the laboratory a condition frequently observed in hospital wards or neurology clinics. The examination of the brains of the animals by the committee supported Yeo and Ferrier's demonstration of cerebral localisation.

Yeo had contributed to determining that sensory and motor functions were located in the cerebral cortex. His work with Ferrier, like that of Hughlings Jackson and Todd, applied to the neurophysiological origin of epileptic seizures. The use of Yeo and Ferrier's "functional maps" of the brain, alongside antiseptic surgery, led to the first successful operations to remove a brain tumour.

The events that followed further emphasise Yeo's crucial role. The emergence of experimental animal studies produced a significant anti-vivisection movement in English society. This movement was led by Francis Power Cobbe, who had established the world's first anti-vivisection organisation in 1875. Cobbe was influential in the decision made by England to pass the world's first animal protection law (Cruelty to Animals Act of 1876). The high-profile nature of the 1881 International Medical Congress (and an endorsement of a statement supporting animal experimentation by delegates) meant that the anti-vivisection community were actively targeting experimental physiologists. When news reached Cobbe that Ferrier did not have a licence from the Home Office for the studies he had presented, the scene was set for another showdown. A summons was issued against Ferrier. However, the cross-examination at Bow Street magistrates revealed that Yeo had conducted the experiments per the Act. He had used anaesthetic, had a licence for the operation and a certificate for keeping the animals alive for the duration of the studies. The summons was dismissed.

Yeo's interactions with Cobbe did not cease here. They participated in a series of vociferous printed debates published in Victorian periodicals (Cobbe, 1882; Yeo,1882). This war of words focused on the moral qualities of the two protagonists rather than the issue of vivisection. The Physiological Society was founded with the aim of the advancement and protection of physiology. With his experience and a track record in public defence of the topic, Yeo made important contributions in advocating scientific research using animals. He was part of a Physiological Society committee that raised the issue of the refusal of certificates from the Home Office and the prevention of experiments taking place due to notification that licences or certificates would not be issued. Ferrier's trial had elicited donations to assist with any associated legal costs. The British Medical Association subsequently covered the costs and the monies raised were used to establish a Science Defence Association. Yeo was tasked by the Physiological Society with the administration of the subscribers and donations. With the Association for the Advancement of Medicine by Research (AAMR), Yeo was appointed to promote research in physiology and "remove existing practical difficulties associated with the 1876 Act." Yeo also took on responsibilities of engagement and communication with the medical media and was specifically tasked

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"Trinity College Dublin is proud to have been the launching pad for the impressive scientific career of Gerald Francis Yeo. His enthusiasm for experimental science and his dedication to the discipline of physiology made great inroads into our understanding of how the brain works." Professor Michael Gill, who unveiled the blue plaque at Tercentenary Hall at Trinity College Dublin, Ireland, where Yeo first graduated in Natural Sciences in 1866.

with looking after communication via *The Lancet*. However, Yeo's interactions with the Home Office were not positive. In 1884, he reported to The Society that his work had been obstructed by the Home Office (Sharpey-Schafer, 1927) and in 1884 Yeo was denied a certificate (Lushington, 1884).

Yeo was one of the original founding members of The Society and the first meeting at 49 Queen Anne Street was adjourned to be resumed at his house, 37 Dorset Street. He served as Secretary to The Society from 1876 until 1889. Sharpey-Schafer describes Yeo as "typically Irish....but impetuous, and unyielding in argument, steadfastly declining to be 'convinced against his will'." There is evidence to support this statement. Sharpey-Schafer (Sharpey-Schafer, 1927) reported that at a Society dinner, Professor Preyer, who had an interest in hypnotism, found his attempts on Yeo "only served to exhaust the hypnotiser". Yeo was also a major force, alongside Kronecker and Foster, in establishing the international physiological congresses. Yeo served as the honorary secretary for the first congress, which was held in Berne in 1889 (Franklin, 1938).

The last words should be left to George Romanes, who in reviewing a book written by Yeo, praised the author as 'something more' than a man of science and a logician....a man of large and generous heart, of finely strung feelings, and a lover of animals as well as a "lover of men"' (Romanes, 1883).

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Obituary: Dr Philippe Ascher (1936-2022)

Dr Philippe Ascher

The death of Philippe Ascher on 3 October 2022 leaves a gaping hole in the neuroscience community.

Philippe Ascher's father was a medical doctor who had emigrated to France from his native Hungary. Following his father's example, Philippe was tempted by medicine, but eventually he opted for scientific research. He studied biology at Ecole Normale Supérieure (ENS) in Paris. He then began a PhD thesis under the guidance of Pierre Buser, performing electrophysiological recordings in cats, but soon felt frustrated by what he felt as a lack of access to cellular mechanisms in this type of research. He became interested in the research conducted at Institut Marey, then directed by Alfred Fessard, on the simpler nervous system of the sea mollusc *Aplysia*. There, he met his future wife, JacSue Kehoe, as well as his life-long friend Hersch ("Coco") Gerschenfeld.

In May 1968, the entire teaching/research system in France was turned on its head. Philippe and his new friends clashed with some of the hierarchy at Institut Marey and for a while, Philippe's prospects appeared rather gloomy. Fortunately, in 1970, the director of the ENS offered Philippe space in a new building to host research laboratories in biology. This unexpected opportunity gave Philippe a chance to make his dreams come true. Around the nucleus formed by Kehoe, Gerschenfeld and himself, he quickly gathered a series of talented young scientists. Together, they formed a unique structure of very small teams united by a spirit of solidarity and by friendly scientific discussions (often occurring in corridors). This laboratory became a beacon of cellular neuroscience.

Philippe's academic models were Steve Kuffler's Neurobiology Department in Harvard and the Biophysics Department at UCL. He liked the "do it yourself" style of British neuroscience at the time. He greatly admired Bernard Katz, and like Katz, failed to see the advantage of increasing his team beyond two or even three, even when he was overburdened with administrative duties.

In the 1970s, Philippe's research focused on cholinergic synapses in *Aplysia*. He found that certain drugs such as tubocurarine, long considered as a pure receptor antagonist of acetylcholine receptors, acted by blocking the channel associated with the receptor. Together with Humphrey Rang, he extended this mechanism of action to describe several blockers of the mammalian autonomic nervous system.

In the 1980s, Philippe turned his attention to NMDA receptors (NMDARs). With Linda Nowak and others, he found that extracellular Mg^{2+} ions antagonise the action of glutamate on these receptors by a familiar mechanism: channel block. Mg^{2+} ions act at negative, but not at positive potentials, as the electric field drives the ions into their blocking site. They also found that NMDAR channels are highly permeant for Ca^{2+} ions. These findings attracted much attention as they contributed to understanding the unique role of NMDARs in certain forms of long-term potentiation (LTP). During LTP induction, a flux of Ca^{2+} ions through NMDAR channels results from the concerted activation of the presynaptic neuron (inducing glutamate release) and of the postsynaptic neuron (releasing Mg^{2+} block).

In equally important work from the same period, Jon Johnson and Philippe discovered that activation of NMDARs requires the binding of glycine in addition to that of glutamate. This unexpected finding originated in a seemingly trivial observation: an odd time course of the response of NMDARs obtained with a "U-tube" application (where the NMDA-containing solution was kept separate from the bath). This anomaly was eventually explained by the presence of a contaminant (glycine) in the bath solution, but not inside the U-tube.

In 2001, Philippe moved to University of Paris Saints Pères school of medicine as an emeritus professor. This allowed him to focus on his own research. Together with Mariano Casado and others at ENS, he uncovered an unexpected dependence of cerebellar long-term depression (LTD) on presynaptic NMDARs, mirroring the role of postsynaptic NMDARs in LTP. In more recent years, with Boris Lamotte d'Incamps, he studied mixed glutamatergic and cholinergic transmission at synapses made by motoneuron collaterals on Renshaw cells. Philippe was performing experiments up to the week preceding his death.

During his career, Philippe exerted a considerable influence on the organisation of research and biology teaching in France. The French university system lacks MD-PhD programmes but Philippe worked hard during the last two decades of his life to encourage MDs to obtain a basic science PhD. He obtained funds for two national programmes along these lines as well as teaching in them. His joy was to spend one or two full-time weeks with medical and pharmacy students as part of a crash course on basic science, often arguing long into the night. His effect was not only to spread his encyclopædic knowledge of biology and of medicine, but also to engage many students and to guide them at the start of their professional careers.

Philippe Ascher was an idealist who had high aspirations for scientific research. He knew how to communicate his enthusiasm for research and how to convince young researchers that success does not necessitate many collaborators, a large budget, or ethical compromise. The entire neuroscience community will miss him greatly.

Written by Professor Alain Marty
Saint Pères Paris Institute for the Neurosciences (SPPIN), Paris, France

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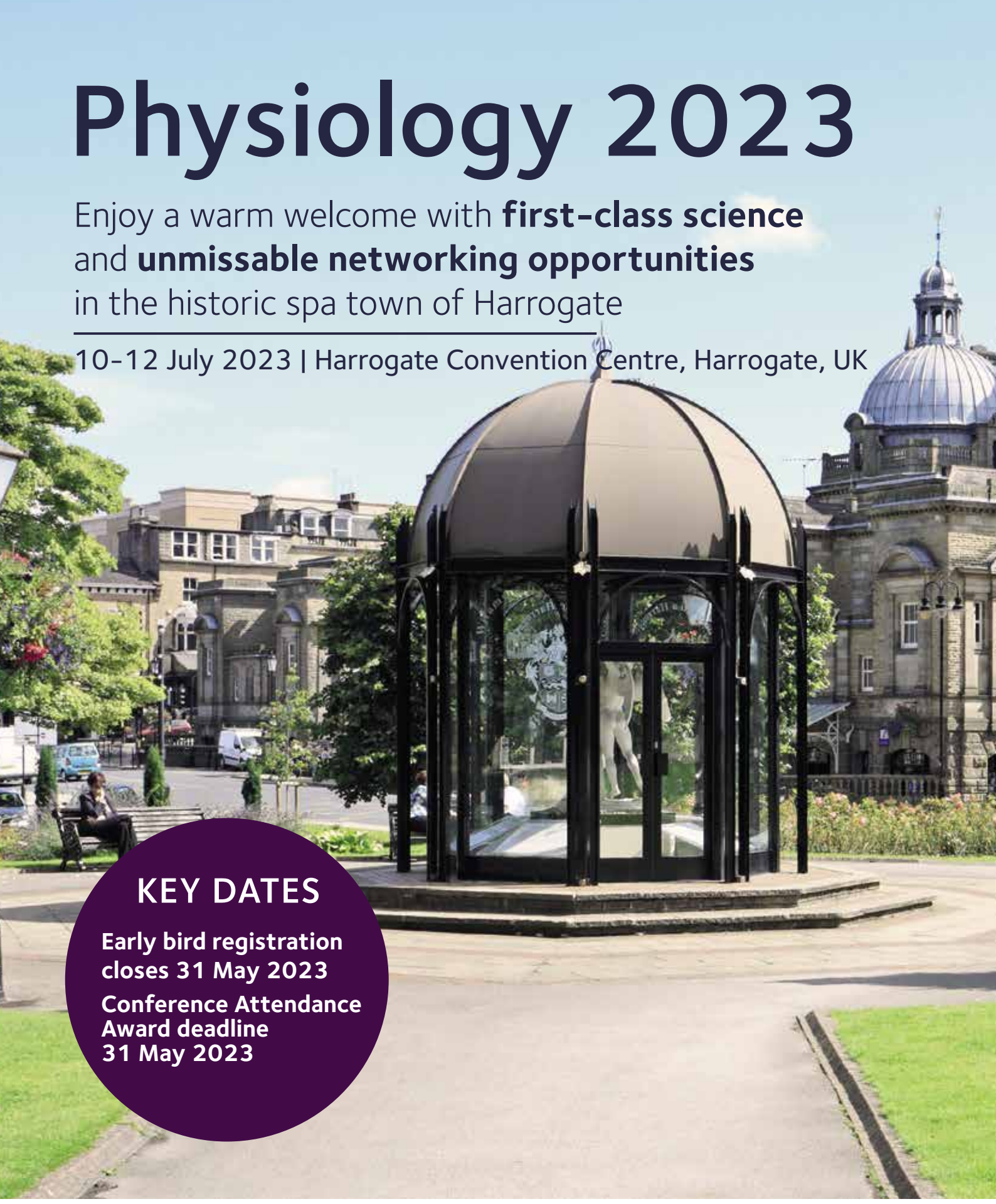

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