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Welcome to the Autumn 2023 edition of Physiology News

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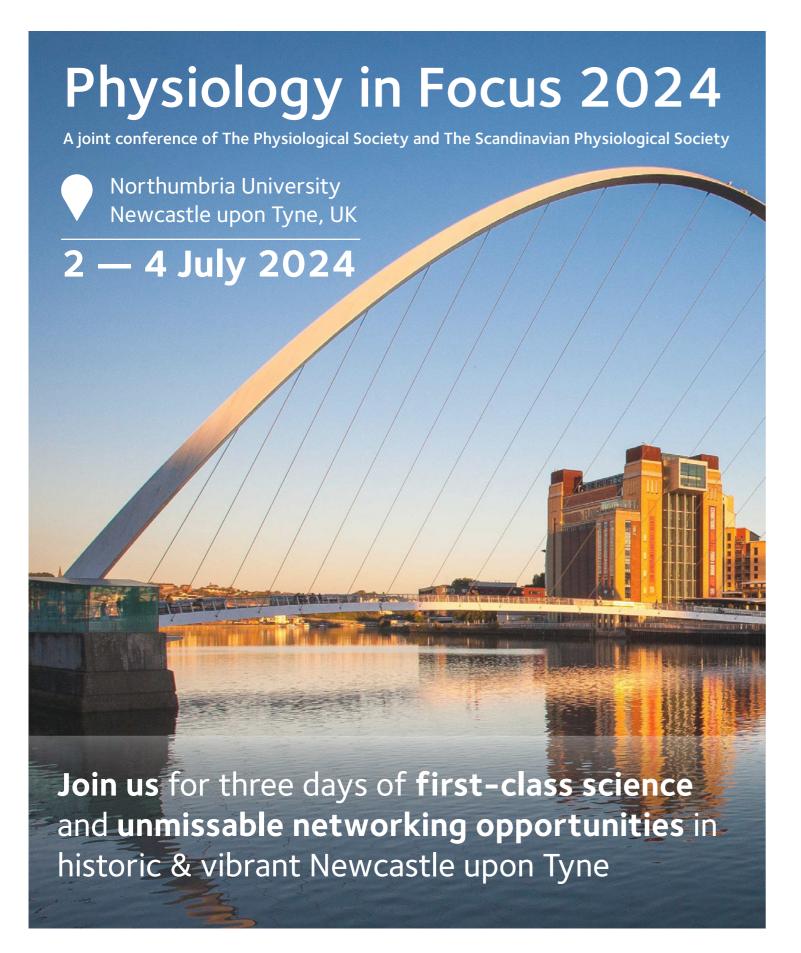
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SAVE THE DATE

physoc.org/physiologyinfocus2024

Having heart: Bringing communities together to spark new ideas

Dr Keith Siew

Scientific Editor, Physiology News

Alanna Orpen

Media and Communications Officer, The Physiological Society

As this issue goes to print, leading researchers in the field of cardiac arrhythmia and disease will be gathering in Liverpool to discuss cutting edge research at our Cross-Talk of Cells in the Heart: Novel Mechanisms of Disease and Arrhythmias meeting. Following tightly on its tail, will be Regenerating the Cardiovascular System: Mending Broken Hearts and Beyond meeting. What better way to kick off the new academic year than gathering with your community; the lecture theatres filled with the humming excitement of new ideas being formed, a time of sharing and discovering research, along with the promise of great ventures that could arise from new collaborations.

A new academic year is also a time of change, and we are delighted that Professor Kim E. Barrett has returned as Editor-in-Chief of *The Journal of Physiology (p*10). *The Journal* is a leader in the discipline, and as an important hub for authors to convey their research to the wider community Professor Barrett is committed to building on outgoing Editor-in-Chief, Professor Peter Kohl's successful series of Special Issues to cater for specialised communities of physiologists.

This appointment coincides with the dedicated efforts of our three journals' Editorial Boards who want to ensure that research submitted to one of The Society publications finds the right home. They have improved the referral and transfer process from both *The Journal of Physiology* and *Experimental Physiology*, so that the work is shared with the most interested audience (p11).

There is also exciting news at *Physiological Reports*, which has introduced a new article type to the journal's repertoire. Professor Jo Adams, Editor–In–Chief of *Physiological Reports*, tells us about this new article type (p11) which will be for showcasing developed or improved physiological methods to benefit the physiological community (p11).

The dissemination of research, both to the academic community and the public, is fundamental to making progress and improving lives. The national press, including the BBC, recently reported the pioneering research about the long-term impact of multiple concussions on the brain health of rugby players. The study, published in Experimental Physiology, shed light on the effect of the persistent symptoms of concussions leading to cognitive impairment in rugby players later in life, which could increase their vulnerability to dementia even in their retirement. The findings could lead to targeted interventions to improve brain blood flow and cognitive function and to better protect players throughout their careers. We recommend reading the summary of this research in our Journal Insights on p13. Among this great collection of journal research highlights, you will also find out more about the influence of exercise on the human gut microbiome (p14).

Outreach is also instrumental in inspiring younger generations and raising awareness of physiology. We learn more about the fascinating project of our Fellowship Award winner, Dr Mark Dallas on p38. Dr Dallas shares how he engaged students with his outreach efforts to reset their perception of physiology as a career opportunity and explains the importance of this for maintaining excellence in physiological research.

Turning to our feature articles, Dr Tess Flood and Professor Kirsty Elliott-Sale have written a wonderful feature (*p*17) on the impact of ovarian hormones on athletic performance.

It serves as a stark reminder of how little sport and exercise science research has been conducted on women, as Dr Flood and Professor Elliott-Sale emphasise how the lack of research limits our current knowledge and understanding about sportswomen and athletic performance.

Continuing on the theme of exercise, a fundamental principle in human physiology around cardiac output during exertion is questioned on p16. Professor Eric J. Stöhr discusses a new perspective on how the cardiovascular system could be controlled and if this alternative theory is true, could offer the potential for new concepts in cardiovascular physiology.

For our second feature, we encounter the world of wonder with Dr Svetlana Mastitskaya, who explains how insights from neuroscience provide deeper understanding of the connection between the brain and the heart, particularly the protective role of the vagus nerve in rescuing the heart.

For those curious of what is to come in The Society's events diary, we hope you enjoy our sneak previews of our Neurophysiological Bases of Human Movement meeting on p30, and our celebratory Member Forum, Award Ceremony and President's Lecture. We are very excited to share with you that Sir Jeremy Farrar, OBE FRCP FRS FMedSci will be giving the President's Lecture this year. You can read more about this on p31.

On this celebratory note, we end this issue with a tale of adventures in physiology experienced by Professor Jim Parratt (p40). Professor Parratt shares the collaborations and opportunities taken through his 60 years of membership with The Society. Then on p42, we hope you are moved by the remarkable work of dedicated member Ann Silver, her character and impact shine through in the obituary written by Professor Tilli Tansey.

We hope that you enjoy this issue!

https://doi.org/10.36866/pn.131.5

The dawn of a new academic year:

Continuing to raise the status of physiology



Professor David Attwell
President,
The Physiological Society

Meetings and online events

Three days of exciting physiology with nearly 500 registered attendees from 190 universities, in a beautiful spa town, with great restaurants in which to eat and discuss science: Physiology 2023 hit all the right notes as the first major conference of my period as President. I thoroughly enjoyed it, including presenting my own abstract (on increasing cerebral blood flow in Alzheimer's disease) with mercifully fewer savage comments from the audience than when I gave similar presentations as a PhD student!

The format of the meetings we put on has been much debated by the Conferences Committee and Council in the last year, with an increasing number of attendees now being attracted to briefer (two days), more specialised meetings. I attended one of these recently, the Vascular Sandpit meeting, which had the unusual format of trying to bring researchers together to write more competitive grant applications and (more ambitiously!) bridging the basic research/clinical research divide. Despite cultural differences on that last point being much in attendance, it was impressive that a large number of potential grant consortia were formed at the meeting. Other twoday meetings coming up include: Cross-Talk of Cells in the Heart: Novel Mechanisms of Disease and Arrhythmias in Liverpool in September; Regenerating the Cardiovascular System: Mending Broken Hearts and Beyond in Oxford in September; an online meeting on Drowning Prevention and Treatment in October; and The Neurophysiological Basis of Human Movement at King's College London in December.

While the format of these specialised two-day meetings seems to be a winner with attendees, the question of how to organise our main meeting of the year, covering all of physiology, has been dominated by the realisation that most conference centres are now too expensive for us to hire and they also do not attract as many participants as they used to do. Accordingly, decisions have been taken to make most of our future main meetings jointly organised with other

societies, and also to try to make them cost neutral. The first such meeting will be Physiology in Focus 2024 in July next year, with the Scandinavian Physiological Society in Newcastle, and this will be followed by a joint meeting (IUPS 2025) with IUPS and Europhysiology to be held in Frankfurt.

Add to all these meetings a host of online lectures, and the President's Lecture and Awards Ceremony at the Royal Society on 1 December, and it is clear that our members have a large number of exciting opportunities to engage with and to meet each other at. The President's Lecture this year is being given by Sir Jeremy Farrar, formerly head of the Wellcome Trust and now Chief Scientist at the World Health Organization*. Jeremy has been awarded the Order of Ho Chi Minh (for services to tropical disease research in Vietnam), and I look forward to hearing how his work in that environment led to him becoming the head of one of the wealthiest and most influential science-supporting agencies in the world.

Journal news

Two aspects of journal funding play a role in determining the health of our finances: the income from the journals, and the cost of running them. Historically, income from The Journal of Physiology has kept the Society's finances strong, but the move towards Open Access publishing will reduce the income we receive per published article. This will almost certainly mean that we will need to publish more papers (ideally without sacrificing quality) and perhaps start a new journal to provide an extra revenue stream. For money-saving reasons, but also to reduce travel in order to produce less of the global heating we have seen in so many catastrophic fires this year, we will also need to make more Editorial Board (and other Committee) meetings online rather than in person. On the topic of the Editorial Board of The Journal of Physiology, I'm delighted to welcome back Kim Barrett as Editor-in-Chief, after a productive period with Peter

Policy

We continue to try to raise the status of physiology, by fixing blue plagues on university buildings to celebrate pioneering physiologists. The last six months have seen a plaque erected in Glasgow to commemorate Sir John Boyd Orr - a nutritionist and Nobel Peace Prize winner (the man who gave us free school milk until Mrs Thatcher took it away again), and in King's College London to commemorate Ernest Starling - discoverer of the first hormone (secretin), as well of how fluids move across capillary walls and how the force of contraction of the heart is regulated by its filling. On the more political front, the Policy Team presented reports to the Oireachtas on Future funding

for basic research in Ireland, and to the UK Parliament on the conditions needed for Artificial Intelligence to meaningfully and safely contribute to healthcare (in brief, it is important to understand how the data processing leads to the conclusions used to infer information about patients' conditions). As physiology grows in less well-developed countries, it is also important that we lend a hand to help the scientists there set up their own meetings. In this context we have awarded a small amount of money to help support the first meeting of the East African Society of Physiological Sciences. and I (together with several IUPS scientists) am serving on the organising committee, to try to ensure that the conference proceeds smoothly.

As the new academic year approaches, I hope you will come back to physiology feeling refreshed, and willing to try out some of the large range of activities that we have organised for you.

*Institutional affiliation is provided for identification purpose only and does not constitute institutional endorsement. Any views and opinions expressed are personal and belong solely to the individual and do not represent any people, institutions or organisations that the individual may be associated with in a personal or professional capacity unless explicitly stated.



Members only

THE PRESIDENT'S LECTURE

With guest speaker Sir Jeremy Farrar

The Royal Society, London, UK | Online 1 December 2023 | 18:00 – 19:45

SAVE THE DATE for the most prestigious event in The Society's calendar; our 2023 President's Lecture and Awards Ceremony.



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Policy Focus
Policy Focus

From Black Box to Trusted Healthcare Tools: Physiology's Role in Unlocking the Potential of AI for Health

Shania Pande

Policy Officer, The Physiological Society



Physiological knowledge is essential to lifting the lid on this 'black box' to improve AI algorithms. Physiology can provide insight into the underlying biological processes and mechanisms that drive various health conditions.

The potential for AI in healthcare

The UK health system is under ever-increasing pressure due to public health challenges such as a growing and ageing population coupled with an overburdened NHS. The Office for National Statistics estimates that by 2045 4.3% of the country's population (3.1 million people) will be aged 85 years and over. This significant demographic shift means that we must ensure the health system is fit for the future by rapidly diagnosing disease and preventing ill health.

Artificial intelligence (AI) and machinelearning technologies are already being used to improve health outcomes. For example, data from patient-monitoring devices collecting physiological measurements such as heart rate, blood pressure and oxygen saturation are being used to personalise care; similarly, data on sleep quality can be used to suggest behavioural changes.

The UK's political leadership has also recognised that AI technologies present opportunities to support the NHS, with the Government announcing that they will host a summit in the autumn to consider the risks of AI and how they can be mitigated, as well as discuss a global coordinated approach with other countries.

However, work in AI tends to happen in silos. Since healthcare is a vast field, encompassing numerous specialties and sub-specialties, AI developers tend to focus on specific areas of expertise, leading to the creation of specialised tools that only address specific

medical conditions or processes. There is a need for cross-disciplinary collaboration to enhance our understanding of, and trust in, the results generated by Al technology, which is often seen as a 'black box'.



Physiology and AI

Physiological knowledge is essential to lifting the lid on this 'black box' to improve AI algorithms. Physiology can provide insight into the underlying biological processes and mechanisms that drive various health conditions. This domain knowledge can help inform the development of AI algorithms and ensure that they accurately model the plausible physiological processes and reduce risk of identifying confounding factors. Further, physiologists can interpret and contextualise the data used to train AI models, ensuring that they contain plausible measurements and are representative against known standards for the target end users.

To this end, The Society recently launched our report "From 'Black Box" to Trusted Healthcare Tools' in Parliament. The report found that

limited inclusion of physiological evidence in the development of AI tools can lead to reduced trust, challenges with applicability and, at worst, to the identification of spurious correlations without sufficient physiological plausibility.

The event, kindly hosted by Viscount Stansgate, brought together physiologists, doctors, healthcare professionals and as well as representatives from industry. The panel featured AI, healthcare, and policy experts. We heard speeches from Stephen Metcalfe MP (Chair of the All-Party Parliamentary Group on AI); Dr Richard Siow from King's College London and The Physiological Society; Svitlana Surodina, also from King's College London; Michael Ball from the Medical Research Council: and Katrina Pavne from The Alan Turing Institute. The discussion that followed highlighted the need for physiologists to work alongside AI experts to develop AI tools that accurately model plausible physiological processes and reduce the risk of identifying confounding factors.

Al summit on physiological plausibility

As such, The Physiological Society is committed to collaborating with all stakeholders involved in designing, regulating, and implementing AI tools in healthcare.

By the end of 2023, The Society commits to:

 support the development and adoption of principles and success criteria that describe physiologically plausible technological applications to clarify Al's "black box".



- initiate a forum to facilitate regular discussions between physiologists and other key stakeholders to achieve a shared understanding of physiological plausibility and the opportunities and risks associated with AI tools in healthcare.
- begin to outline and deliver a training programme for physiologists, developers and data scientists to establish a shared language and understanding for building physiologically plausible technology by design.

In the coming months, The Society will be working closely with members and experts at the AI and health nexus to take forward the recommendations from the report and develop a set of principles and success criteria that describe physiologically plausible technological applications. If you are interested in being involved in these next steps please email us at policy@physoc.org.

Further information about this report and our policy work can be found at physoc.org/policy.

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Burdass, Chief Executive, The Physiological Society; Dr Richard Siow, King's College London.

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News and Views

News and Views

The Society welcomes returning Editor-in-Chief of The Journal of Physiology

One of the things that make *The Journal of Physiology* so special is its breadth of coverage; it touches all topics of contemporary physiology and neuroscience.

The Society is pleased to announce Professor Kim E. Barrett as returning Editor-in-Chief of *The Journal of Physiology. The Journal* is the leading general research journal in the discipline, with the highest number of citations of any physiology journal. As The Physiological Society's oldest journal, it has a distinguished history of publishing research that significantly advances our knowledge of how the body functions in health and disease.

Professor Kim Barrett is Vice Dean for Research and Distinguished Professor of Physiology and Membrane Biology at the University of California Davis (UC Davis) School of Medicine, USA, positions she has held since 2021. A native of the United Kingdom, Professor Barrett completed her doctoral training at University College London before moving to the United States for postdoctoral work at the National Institutes of Health. In 1985, she was recruited to the University of California San Diego, where she rose through the ranks in the Department of Medicine to attain the title of Distinguished Professor of Medicine. She also served as Vice Chair for Research in the Department of Medicine and was Dean of the Graduate Division for the campus as a whole from 2006 to 2016. Immediately prior to joining UC Davis, she was also the rotating Director of the Division of Graduate Education at the National Science Foundation in Alexandria, VA.

In terms of scientific focus, Professor Barrett's research has centred on the physiology and pathophysiology of the gastrointestinal epithelium throughout her career, with research findings that are applicable to the understanding

and treatment of infectious diarrhoeal disorders and inflammatory bowel diseases. She has published almost 300 original research papers, review articles and book chapters, and a number of widely used physiology textbooks. She has received several honours for her career contributions, including the Distinguished Achievement Award in Basic Science from the American Gastroenterological Association (AGA) and election as an Honorary Fellow of The Physiological Society (UK and Ireland). She is also Past-President of the American Physiological Society and the former Editor-in-Chief of *The Journal of Physiology*, and serves currently on the AGA Governing Board as Councilor-at-Large.

During her term as Editor-in-Chief at *The Journal of Physiology*, Professor Barrett is committed to building on *The Journal's* position as a gathering place for international physiologists across the world by introducing new regional Editors, as well as by building on outgoing Editor-in-Chief, Professor Peter Kohl's very successful series of Special Issues to cater for specialised communities of physiologists.

Speaking about why she thinks *The Journal of Physiology* is unique, she said:

"One of the things that make *The Journal of Physiology* so special is its breadth of coverage; it touches all topics of contemporary physiology and neuroscience. Furthermore, as the most highly cited physiology journal in the world, with an incredibly storied history – from Nobel laureates to early career researchers – it is an important hub for authors to convey their research to the wider community.



Finding the best home for your research: Manuscript transfers for Society journals

How our updated referral and transfer policy for articles benefits authors and the dissemination of your research

Lucinda Periac-Arnold

Head of Publishing

At the Society, we are proud of our three journals leading the discipline, promoting best practice and pushing the boundaries of scientific endeavour. These are *The Journal of Physiology, Experimental Physiology* and *Physiological Reports*. The varied purposes and scopes of each of these journals ensures we cater to the particular focus and breadth of physiologists' research and that the work is shared with the most interested audience.



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 publishes work highlighting novel insights into fundamental homeostatic and adaptive responses in health, and articles that further our knowledge of pathophysiological mechanisms in diseases. Translation and integration research is a key focus

Physiological Reports is a joint publication of the American Physiological Society and The Physiological Society, published by Wiley. It showcases original research in all areas of basic, translational and clinical physiology and allied disciplines. Both Experimental Physiology and Physiological Reports are open access journals and so article publication fees will apply. Find out if your institution is covered by one of Wiley's many Transformative Agreements at https://www.wiley.com/enus/network/publishing/research-publishing/editors/enabling-open-access-through-transformational-agreements.

Updated referral and transfer policy

We like to have our journals working together as a family. This is why our three journals' Editorial Boards are firmly committed to working together to ensure that research submitted to a Physiological Society publication finds the right home. We have now improved the functionality of the transfer process from both *The Journal of Physiology* and *Experimental Physiology*, allowing authors given a referral decision to transfer both their manuscript, and any related peer review comments, to the

recommended destination journal. Editors will recommend the destination title based on their assessment of the manuscript, meaning a recommendation to either transfer to Experimental Physiology or Physiological Reports. This has resulted in an expedited peer review process following rejection and will enable authors to disseminate their research in as timely a manner as possible. We have further enabled efficient transfer through the introduction of free format original submission, so there is no need to edit manuscripts to fit the destination titles formatting and referencing requirements until a revised manuscript is submitted.

For more information on how this transfer process works, visit our Peer Review Process and Guidance page at https://jp.msubmit.net/cgi-bin/main.plex?form_type=display_rev_instructions&dm.

The Publications Team will be happy to answer any questions you have about this process. Please contact us at jphysiol@physoc.org.



The Editors of *Physiological Reports* are delighted to announce a new, separate manuscript type "Methods Article". Methods manuscripts should describe new or improved methods for the recording, collection, or quantification, and/or analysis of data relevant to understanding how a physiological system works. The articles may also provide resources, protocols, tools, simulations or computational models that will be useful to the research community.

"This is a great addition to *Physiological Reports*" repertoire of article types. I invite authors who have developed or improved physiological methods to submit their manuscripts, so that they can be shared, discussed and utilised by the physiological community. Where applicable, Methods articles are included in transitional APC agreements. Potential authors can find out more online."

Professor Jo Adams, Editor-in-Chief of *Physiological Reports*



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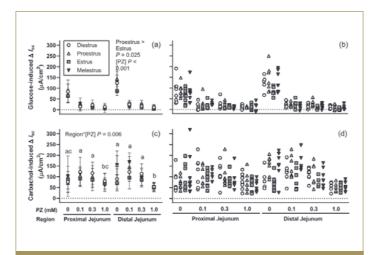
Experimental Physiology

Open Acces

Active glucose transport varies by small intestinal region and oestrous cycle stage in mice

Overduin TS et al. (Feb 2023) https://doi.org/10.1113/EP091040

Food intake and blood glucose levels following test meals in women change across different phases of the menstrual cycle, with a peak in the luteal phase. These changes are thought to be related to circulating sex hormone levels. However, it has not been shown whether the active absorption of glucose by the sodium-glucose transporter (SGLT) 1 changes in different phases of the oestrus cycle. In this study, the regional and cyclical differences of SGLT1-mediated glucose absorption were investigated in female C57Bl/6JSAH mice. Glucose transport was highest in the distal jejunum. Using the jejunum, the oestrus cycle-specific phases of glucose absorption by SGLT1 were then investigated. In prooestrus (late follicular phase), SGLT1-mediated glucose transport was found to be higher than in oestrus (early luteal phase). These



Glucose transport in the distal jejunum was higher in during the pro-oestrus phase compared to oestrus phase

results provide a partial explanation for the increased blood glucose responses observed, which may be due to more glucose transport. While specific hormone levels were not measured, this study may be important for people with dysregulated hormone levels, such as in polycystic ovarian syndrome, where insulin resistance and obesity are often comorbidities, or in pregnancy and lactation, where changes in food intake and hormone levels are sustained for a longer period of time

CALL FOR PAPERS Cardiac muscle, skeletal muscle and tendon plasticity in disuse and inactivity Scan the QR code for more info bit.ly/JPCallForPapers SPECIAL ISSUE Submission deadline 30 November 2023 The Journal of Physiology

The Journal of **Physiology**

A systematic review of computational models for the design of spinal cord stimulation therapies: from neural circuits to patient-specific simulations

Liang L et al. (Nov 2022) https://doi.org/10.1113/JP282884

A mathematical model describing action potential generation published by Hodgkin and Huxley in 1952 underpinned development of computer modelling for electrophysiological applications. One such application is spinal cord stimulation (SCS), which is primarily used to treat chronic pain and restore movement. Simulations have been used to influence SCS clinically by contributing to lead design, stimulation configurations, waveform design and programming protocols. As models for SCS have evolved, they have increased in number and complexity; it is important to establish if this complexity is necessary for increased accuracy and clinical efficacy.

Accordingly, articles were identified following a systematic literature search. Models of neurostimulation rely on both electrophysiological principles as well as anatomically based, three-dimensional volume conductor models to estimate effects on neural membrane voltage. Therefore, the 87 papers identified for use included volume conductor models of the spinal cord and a computational model to simulate SCS-generated fields.

Reasons for increased complexity include a shift from two-dimensional to three-dimensional models, alongside the inclusion of more anatomical components. Additionally, recent use of medical imaging increases complexity, as well as allowing for use in patient-specific models. These changes demonstrate an improvement in translational and mechanistic studies. However, whilst recent studies increasingly use quantitative validation, metrics are inconsistent across the research, which hinders identification of clinically meaningful benchmarks.

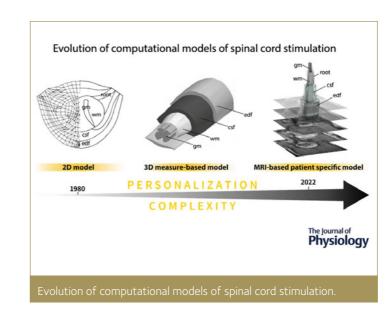
Experimental Physiology

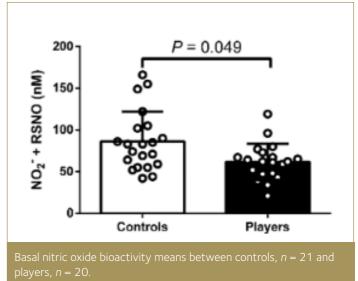
Open Access

Lower systemic nitric oxide bioactivity, cerebral hypoperfusion and accelerated cognitive decline in formerly concussed retired rugby union players

Owens TS et al. (July 2023) https://doi.org/10.1113/EP091195

Rugby union is a sport enjoyed by many; however, it is characterised by high incidents of contact-related injuries, the most concerning of all being concussions. Players that are concussed, are at greater risk of mild-cognitive impairment and chronic traumatic encephalopathy, which can lead to severe disabilities later in life. There are two proposed reasons for the above pathophysiology; firstly, the blunt forces experienced during repeated contact events promote mitochondrial dysfunction and elevate free radicals that scavenge nitric oxide (NO) molecules and secondly, the same mechanical forces can compromise structural integrity of neuronal networks. To investigate this, the study recruited 22 retired rugby players (regional and international level, aged 64 ± 5 years) who had incurred at least 3 concussions over their playing careers and cross-sectionally compared them against 22 agefitness-and-education matched control participants who had never been diagnosed with concussion or participated in contact sports. The researchers found that the retired players suffered significantly from concussion-related symptoms, namely headache and pressure build-up in the cervical and cranial regions, which was accompanied by psychological issues of increased anxiety, lack of concentration and emotional stability, memory loss and difficulty in falling asleep. More importantly, NO, a key player in maintaining cardiovascular homeostasis, was found to be less systemically available compared to the control group. Additionally, the lower bioavailability of NO was accompanied by lower middle-cerebral artery velocity and cerebral oxygen delivery at rest and during hyper/hypocapnia. The study confirms a potential mechanism for cognitive decline in rugby players and calls for further longitudinal research along with development of methods for assessing neurovascular damage. To conclude, concussion is "NO" joke and must be a key agenda at the organisational level of the sport.





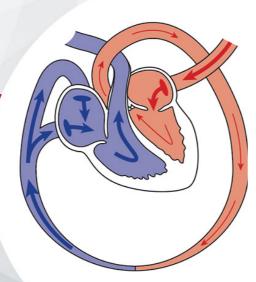
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Experimental Physiology

Call for papers

Submit by 30 November 2023

The unspecific control of cardiac output during exercise and in (patho-)physiology

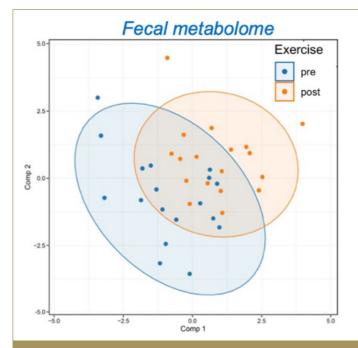




Exercise training modifies xenometabolites in gut and circulation of lean and obese adults

Kasperek MC et al. (March 2023) http://doi.org/10.14814/phy2.15638

The human gut microbiome—an adaptable ecosystem of microorganisms—may influence host physiology through the microbial production and modification of metabolites (xenometabolites). The interplay between the microbiota and the human body/host remains to be fully understood. This study explored the influence of 6 weeks of moderate-to-vigorous intensity aerobic exercise training (60%-75% heart rate reserve, 30-60 min, 3 times a week) on the faecal and serum xenometabolome in sedentary, lean (n = 15) and obese (n = 9)adults. Multiple faecal and serum xenometabolites (obtained pre and post the 6-week intervention) responded to exercise training, with the most prominent changes within aromatic amino acid metabolic pathways. Faecal and serum aromatic amino acid derivatives were associated with body composition, and markers of insulin sensitivity and cardiorespiratory fitness. Two serum aromatic microbial-derived amino acid metabolites that were upregulated in response to exercise share metabolic pathways within the microbiota and were associated with body composition and markers of insulin sensitivity pre- and post-intervention. This study demonstrates that microbial- and host-derived metabolites respond to aerobic exercise training, and



Metabolic profiles of feces collected before— (Pre- blue) and after— (Post- orange) a 6- week aerobic exercise intervention. Residuals from linear mixed models accounting for obesity status, sex, and study cohort were used in PLS- DA models. Axes indicate values for PLS- DA scores (i.e. sample projections). Metabolites were selected for inclusion if Variable Importance in Projection (VIP) value was >1. All model development, feature selection, and visualizations were conducted on training data (n = 18).

that body composition is an important factor that influences these responses. This study reinforces the view that host metabolic health influences gut microbiota population and function.

Experimental Physiology

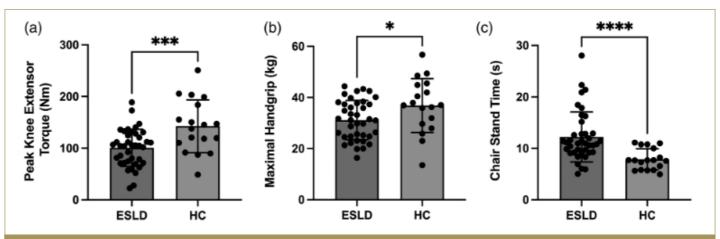
Open Access

Impaired lower limb muscle mass, quality and function in end stage liver disease: A cross-sectional study

Quinlan J et al. (May 2023) https://doi.org/10.1113/EP091157

Patients with end-stage liver disease (ESLD) commonly experience decreased muscle mass (sarcopenia), which impairs their quality of life and reduces their survival even after liver transplantation. In this article, authors used ultrasonography, magnetic resonance imaging, anatomical measurements and physiological tests to calculate multiple indices that evaluate mass, quality and function of the quadriceps muscle in 39 patients with ESLD and 18 age- and sex-matched healthy control subjects. They also did L3 skeletal

muscle index (SMI) and mid-arm muscle circumference (MAMC), which are the conventionally used tests to assess sarcopenia. Results showed significantly reduced mass and volume of the quadriceps muscle, with increased quadriceps intermuscular adipose tissue. Physiological assessment by the handgrip strength, peak knee extensor isokinetic torque, and chair rise time revealed significantly reduced muscle strength in ESLD. However, the conventional L3 SMI and MAMC showed no significant change in ESDL patients versus control subjects. The conclusion was that assessment of sarcopenia in ESLD should focus on testing the mass, quality and function of the quadriceps muscle rather than doing the conventional tests, which assess other muscles. Early identification of sarcopenia in these patients allows timely intervention to try to improve their quality of life and reduce mortality.



Differences in physical function (a,b) and performance (c) between patients with end-stage liver disease (ESLD) and healthy age-matched control participants (HC). Data are expressed as grouped mean average with individual data points. Significance between groups identified as *P < 0.05, ***P < 0.001, ****P < 0.0001.

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Your Heart May Not "Know"...



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I have been told many times that cardiac output increases during exercise proportionately to the workload. Most readers of this short article, I assume, have probably also heard or read similar statements. Such statements reflect the fundamental principle in human physiology that any increase in physical work and energetic demand must be matched by a greater oxygen consumption. The Fick principle beautifully highlights that this greater oxygen consumption can be achieved in two ways: by enhanced convective delivery of blood flow (i.e. cardiac output) and/ or by increased diffusive delivery of blood flow (i.e. local extraction of oxygen from the blood). Importantly, the heart itself has two components to control its overall output. The portion that can be termed the mechanical part, which is reflected by stroke volume (SV), and the component that can be referred to as being autonomic, which can be measured as heart rate (HR).

Like any healthy relationship, these two should talk to each other to agree on the joint outcome because a lower SV should be accompanied by a higher HR and vice versa, to result in the same cardiac output for a specific energetic demand. Only... SV and HR often seem to behave more like the cranky couple in your favourite Netflix drama – they do not seem to communicate well at all. To verify this scientifically, SV and HR need to be investigated during submaximal

conditions when there is enough of a reserve for either contributor to make up for the shortcomings in the other. And indeed, several studies suggest that SV and HR do not adjust according to each other and do not produce a specific cardiac output (Stöhr, 2022). One such study, carried out by a talented Masters student during an Erasmus exchange programme, shall be briefly described here (van Mil et al., 2016):

Think of yourself as lying down on a comfortable bed in a laboratory. Then, your arms will be wrapped in a water-perfused suit and heated up. As expected, the blood flow in your arms will increase, but elsewhere in your body blood flow will remain normal. The increased blood flow in your arms will be matched by an increased HR while SV remains the same as before heating, reflecting the "hyperadrenergic state" referred to by Lowring Rowell (Rowell, 1990). Now comes the trick with which the heart will be challenged to make a crucial decision. Around your upper arms, blood pressure cuffs will be inflated to mean arterial pressure, reducing the blood flow in the arms back to the normal baseline condition. But they are still hot and HR is still up accordingly! Will the heart now produce the cardiac output for the hot condition (as it should), or will it not? The answer is, it will not, because SV will reduce during arm cuffing. These data suggest that the heart does not control its output according to the demand. Future studies should replicate this work under locally increased metabolic demand.

Although the results from the example may be surprising and perhaps even disconcerting, such observations give rise to exciting speculation. For example, it is possible that all the different components of the cardiovascular system are controlled separately, and that there is less "coupling" across the entire system than previously assumed. Or, there may be an as of yet undiscovered principle that explains the function of the heart and arteries in a new way, which does not rely on the assumption that the function of the heart is to provide the specific output according to the prevailing (energetic) demand. If this is true and the heart does not know how much blood flow our body needs, then the field will be wide open for radical new concepts in cardiovascular physiology.

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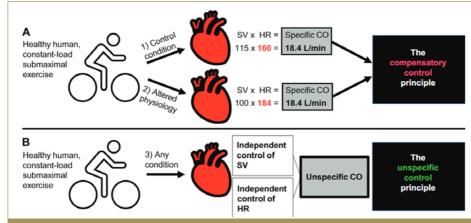


Figure 1. The "compensatory control" and the "unspecific control" principles. In the schematic, it is assumed that exercise in 1, 2, and 3 is performed at the same absolute, submaximal workload. A shows the current thinking termed compensatory control principle, while B shows alternative evidence in favour of the unspecified control principle.

Ovarian hormones, the menstrual cycle, and athletic performance

The impact of ovarian hormones on athletic performance



cis-gendered sportswomen not taking hormonal contraceptives. The cycle is regulated by the hypothalamic-pituitary-ovarian axis and is characterised by large fluctuations in the key ovarian hormones oestrogen and progesterone. These fluctuations are predictable and can be used to create distinct phases of the cycle that make up the eumenorrheic hormonal profile.

The eumenorrheic menstrual cycle is an important biological rhythm in

Phases of the menstrual cycle

A eumenorrheic menstrual cycle has a cycle length of of between 21 and 25 days. Historically, the menstrual cycle was broken down into two main phases – follicular and luteal – that were split by ovulation. Currently the menstrual cycle is divided into four phases, which have distinct hormonal concentrations (Fig.1, Phases 1 – 4).

Physiology of the menstrual cycle

The menstrual cycle is a reproductive cycle; at the beginning follicle stimulating hormone and luteinising hormone stimulate follicle maturation and oestrogen production. The increase in oestrogen – via positive feedback – causes a surge in luteinising hormone, which triggers ovulation and the release of a mature egg. A corpus luteum forms, which secretes large quantities of oestrogen and



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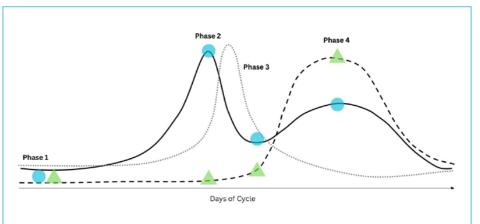


Figure 1. Phases of the eumenorrheic menstrual cycle. Redrawn from Elliott-Sale et al. (2021). The solid line is oestrogen, the dotted line is luteinising hormone, and the dashed line is progesterone. The circles indicate mean oestrogen concentration, and the triangles indicate mean progesterone concentrations.

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These statistics highlight how little research is conducted on women and, as such, how limited our knowledge and understanding are about sportswomen and athletic performance.

progesterone and subsequently increases cervical mucus. If fertilisation does not occur the corpus luteum regresses, ovarian hormone levels decrease, the egg passes through the uterus, and the endometrium lining sheds, and the next cycle begins.

Menstrual cycle dysfunction

Menstrual dysfunction can occur due to numerous reasons (i.e. illness or disease, low energy availability, first two years of menses, before menopause) (Elliott-Sale et al., 2021) and can result in the conditions shown in Fig.2. Amenorrhea or the loss of menstruation is the most publicised [by the media] type of dysfunction; however, subclinical dysfunction can also occur and include luteal phase deficiency (LPD, suppressed progesterone at Phase 4) and anovulatory cycles (no ovulation, suppressed oestrogen and luteinising hormone surge) (Allaway et al., 2016). Clinical dysfunction such as oligomenorrhea (inconsistent intermenstrual intervals and hormonal characteristics) and amenorrhea (loss of menstruation) are much easier to detect as they result in noticeable changes in a women's cyclic pattern (Allaway et al., 2016).

It is worth stating that, outside of menstrual dysfunction, the menstrual cycle can also be perturbed by pregnancy, menopause, and hormonal contraceptives; please note that this list is not exhaustive. Although these profiles are outside of the scope of this article, in brief they represent elevated (i.e. pregnancy), depressed (menopause)

and exogenous (hormonal contraceptives) hormonal profiles.

Quantity of research

To date 6% of the research in sport and exercise science has been conducted exclusively on women. Within this 6%, 20% of the research has focused on sexspecific topics such as the menstrual cycle or hormonal contraceptives. Women account for approximately 34% of the participants studied between 2014 and 2020 when mixed-sex studies are included (Cowley et al., 2021). In the most recent review of the effect of menstrual cycle on exercise performance, 78 studies were included with a total of 1193 participants (McNulty et al., 2020). However, in a review of the biomechanical surrogates for anterior cruciate ligament (ACL) risk and ovarian hormones, only 7 studies were included in the review totalling 194 participants (Dos'Santos et al., 2023). In addition, no studies assessing the menstrual cycle focus on elite women populations; instead, research is conducted in amateur and sub-elite populations assuming a linear relationship with elite women (Burden et al., 2021). These statistics highlight how little research is conducted on women and, as such, how limited our knowledge and understanding are about sportswomen and athletic performance. In the following sections, we have provided some examples of the outcome measures being investigated in relation to ovarian hormone profile; however, we acknowledge that this list is not

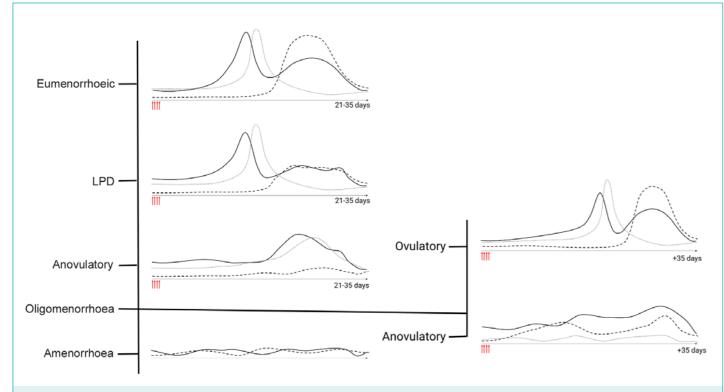


Figure 2. Hormonal profiles at the different stages of menstrual dysfunction. Redrawn from Allaway et al., (2016). LPD = luteal phase deficiency. Note. This is a graphical representation of data from Allaway et al. (2016) and not measured data.

Perception and symptoms

From a sample of 1,086 non-hormonal contraceptive-using athletes across 57 sports, approximately 78% of them [self] reported experiencing menstrual cycle symptoms (Ekenros et al., 2022). The most common symptoms were breast tenderness, bloating, irritability, fatigue, loss of energy, and tearfulness. Often, these symptoms were perceived to impact women's athletic performance; women on average perceived a negative impact on aspects of physical performance during the early follicular phase (during menses) and the late luteal phase (in the days prior to menses) compared to the ovulatory phase (mid-cycle) of the menstrual cycle (Ekenros et al., 2022).

Athletic performance

In a recent meta-analysis, performance was trivially reduced in Phase 1 compared with the other phases of the cycle (McNulty et al., 2020); however, this response was highly variable between studies. This metaanalysis included studies using laboratorybased assessments of endurance and acute strength performance. As such, the authors concluded that at present an individualised approach should be adopted until a sufficient high-quality dataset is available. The impact of "trivial effects" in elite sportswomen is unknown; it could be suggested that the impact will be of greater relevance to elite sportswomen where the margins in performance are smaller or conversely the impact could be of less relevance to elite sportswomen as they can be more resilient to adverse conditions and the size of the effect could be lost amongst other competitive factors. In all cases, an individualised approach is recommended for women, where the menstrual cycle is tracked and any alterations to training are tailored to and informed by the individual athlete and/ or their data.

Strength adaptations

Acute and chronic strength changes have been suggested to occur across the menstrual cycle. A recent umbrella review paper (Colenso-Semple et al., 2023) examined and critically evaluated the reviews on menstrual cycle and strength outcomes (acute and chronic). The study showed largely inconsistent evidence of differences in strength and hypertrophy outcomes with changes in ovarian hormones. Therefore, the authors concluded that, at the present time, it is highly premature to conclude that shortterm fluctuations in ovarian hormones over a menstrual cycle influence acute strength or longer-term adaptations to resistance training. It was also suggested that "phasebased" training models are not an evidencebased approach.

Substrate utilisation

There is currently conflicting evidence on whether changes in oestrogen through the menstrual cycle impact substrate utilisation (i.e. carbohydrate and fat utilisation during exercise) (Boisseau and Isacco, 2022). While some studies have shown that increased oestrogen at Phase 2/4 promoted greater fat oxidation rates, others have not replicated these findings. This could have occurred due to differences in energy demands between studies (e.g. increased energy demand, increased endogenous glucose production). It is also postulated that inter-individual differences in magnitude of change in oestrogen could have influenced the impact on substrate utilisation (Oosthuyse et al., 2022). In the studies demonstrating an effect, it was hypothesised that increases in oestrogen concentrations promoted greater muscle glycogen synthase activity that led to greater glycogen storage and sparing during exercise and a reliance on fat utilisation.

ACL injury

Sportswomen are ~3.5 times more likely to suffer an ACL injury than men [depending on sport] (Dos'Santos et al., 2023). While ACL injuries are multi-factorial, it has been suggested that changes in ovarian hormone concentration throughout the menstrual cycle could potentially increase the susceptibility to ACL injury. However, at the current time research is inconclusive whether increased oestrogen levels predispose eumenorrheic sportswomen to greater ACL injury risk. Whilst some research has shown greater knee laxity in Phase 2 associated with increased oestrogen concentrations, evidence hasn't linked this to ACL injury (Moriceau et al., 2022). It has been suggested that increased oestrogen (Phase 2) may influence soft tissue compliance, collagen formation, properties, and integrity of ligaments, knee laxity and neuromuscular function (Dos'Santos et al., 2023). In addition, a review examining biomechanical and neuromuscular injury risk surrogates showed no evidence to suggest elevated risk across the menstrual cycle (Dos'Santos et al., 2023).

Quality of the research

As well as a lack of research in sportswomen, the quality of research assessing ovarian hormones and athletic performance is poor. In McNulty $et\ al.$, (2020) 78 papers were included in the meta-analysis; of these, 8% were rated high, 24% medium, 42% low, and 26% very low quality. In this paper considerations were taken of the methods used to identify and verify the menstrual cycle phase (and subsequent change in ovarian hormones) in the included studies. In Dos'Santos $et\ al.$ (2023), all studies in the review were rated as low (n = 3/7) and very

In all cases, an individualised approach is recommended for women, where the menstrual cycle is tracked and any alterations to training are tailored to and informed by the individual athlete and/ or their data.

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Issue	Implication for findings
Combining women taking hormonal contraceptives with eumenorrheic women and discussing menstrual cycle phase.	Eumenorrheic women and women taking hormonal contraceptives have different hormonal profiles. Hormonal contraceptives remove the cyclic fluctuations of ovarian hormones and therefore women taking hormonal contraceptives do not have menstrual cycle phases.
Not reporting testing days clearly (using unclear/inconsistent terminology).	Considerable changes occur in the hormonal profile within phases of the cycle (i.e. follicular phase or luteal phase vs. Phase 1-4).
Not considering variation in cycle length within and between women.	Testing on a particular day of the cycle (i.e. day 20) may have a different hormonal profile both within and between women.
Not using ovulation tests to ensure ovulatory profile.	Research may be including women who have an anovulatory profile and who therefore have different concentrations of ovarian hormones at specific phases.
Not measuring hormone concentrations to ensure exclusion of LPD cycles.	Research may be including women who may have an LPD profile and who therefore have different concentrations of ovarian hormones at specific phases.
Not measuring hormone concentrations to verify hormones to ensure correct phase.	By not measuring hormones researchers cannot attribute findings to increases in concentrations of ovarian hormones that may not be occurring (i.e. Phase 2- impossible to know if oestrogen has peaked without measuring).

Table 1: Methodological issues highlighted by McNulty et al., (2020) and implications on findings

low quality (n = 4/7) using the methodology from McNulty *et al.*, (2020). Table 1 highlights some of the methodological issues highlighted by these reviews.

Research containing these methodological issues could, for example, be including women who experience menstrual dysfunction (anovulatory or LPD) with eumenorrheic women. Therefore, these papers are not assessing the same fluctuation in ovarian hormones that are seen in an eumenorrheic profile; Fig.3 presents a graphical representation of this. Verifying ovarian hormone profiles in women is key to the trustworthiness of the result of the study (McNulty et al., 2020).

In 2021, methodological recommendations for testing women across the menstrual cycle were developed (Elliott-Sale *et al.*, 2021). This paper provided a consensus on the hormonal profiles of interest and the *a priori* guidelines for eligible data. Fig.4 summarises the recommendations for research designs

assessing the impact of ovarian hormones on athletic performance (Elliott-Sale *et al.*, 2021).

Summary and take-home messages

Before any conclusions are drawn about the impact of ovarian hormone concentrations and the menstrual cycle on athletic performance, more high-quality research is needed on these topics in both amateur and elite populations. By including recent recommendations into future research, robust guidance will be able to be created for sportswomen. At the moment evidence suggests an individualised approach, which is tailored to and informed by the athlete's experiences. At the current time it is highly premature to make firm conclusions on the impact of ovarian hormones and the menstrual cycle on athletic performance based on the available research evidence

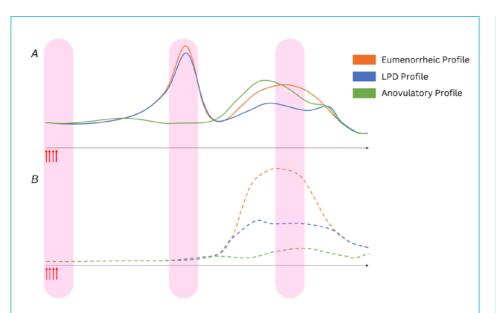


Figure 3. Potential differences in hormonal profiles between eumenorrheic and LPD and anovulatory hormone profiles in a study investigating athletic performance across Phases 1, 2, and 4 (highlighted with the pink boxes). Graph A shows a graphical representation of oestrogen within an eumenorrheic, LPD and anovulatory profile. Graph B shows a graphical representation of progesterone concentrations within an eumenorrheic, LPD and anovulatory profile. Redrawn from Allaway et al. (2016). LPD = luteal phase deficiency. Note. This is a graphical representation of data from Allaway et al. 2016 and not measured data.

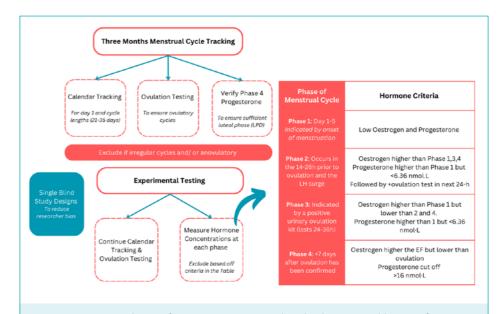


Figure 4. Recommendations for assessing menstrual cycle phases on athletic performance. Taken from Elliott-Sale *et al.*, (2021). LPD = luteal phase deficiency.

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Rescuing the Heart: Insights from Neuroscience

The central role of the vagus nerve



Dr Svetlana Mastitskaya

British Heart Foundation Intermediate Basic Science Research Fellow at University College London, London, With a PhD in cardiac regeneration and several years of research in the field of cardiovascular neuroscience, I've always been fascinated by bidirectional interactions between the brain and the heart, and how these interactions are coordinated by the vagus nerve. My research is focused on neural and humoral (bloodborne) mechanisms of coronary blood flow regulation in health and disease. I'm curious as to how these mechanisms can be manipulated to improve cardiovascular health.

The wonders of the wanderer

The vagus nerve, also known as the wanderer due to its extensive distribution and complex path, plays a vital role in regulating various bodily functions. As the main peripheral nerve of the parasympathetic branch of the autonomic nervous system, it controls heart rate, blood pressure, digestion, respiration, and immunity. Vagus nerve stimulation is used for drug-resistant depression and epilepsy (Nemeroff et al., 2006; Fisher et al., 2021) and has potential for treatment of hypertension, heart failure, and cardiac arrhythmias (Capilupi et al., 2020). Through my research, I have demonstrated the crucial importance of the vagus nerve in protecting the heart during a heart attack, preserving cardiac function in heart failure and improving exercise capacity (Mastitskaya et al., 2012; Machhada et al., 2020).

In heart failure, the autonomic balance is shifted towards upregulation of the sympathetic nervous system to compensate for the reduced functional capacity of the damaged heart and maintain an adequate blood supply to the body. However, these alterations become detrimental in the long term, overriding vagal activity and promoting maladaptive cardiac remodelling.

Vagus nerve stimulation is known to reduce the heart rate, reduce susceptibility of the myocardium to malignant arrhythmias and oppose the effects of sympathetic system overactivation in general, which improves survival. If the vagus nerve is stimulated acutely during a heart attack, it dramatically reduces the infarct size (death of the heart tissue due to inadequate blood supply) (Calvillo *et al.*, 2011). The question is, how does it work?

Time is muscle; muscle is life

Time is critical in a heart attack. Within 80-90 minutes of halted blood supply, the heart muscle starts dying, and after six hours most of the affected heart tissue is irreparably harmed. Promptly removing the blockage in the culprit artery is vital to prevent cardiac tissue death. However, in as many as 40% of cases, reopening the artery does not fully restore blood flow on the microvascular level, leading to the detrimental "no-reflow" phenomenon (Soeda et al., 2017). No-reflow heavily contributes to the poor healing of the infarct, which can lead to heart failure, malignant arrhythmias and even cardiac rupture. Fortunately, vagus nerve stimulation limits infarct size and prevents noreflow, offering potential solutions (Mastitskaya et al., 2012; Uitterdijk et al., 2015).

Brain-gut-heart axis

The vagus nerve's influence extends to the abdomen, where approximately 90% of its efferent fibres (carrying impulses away from the central nervous system) are found, regulating digestive tract motility and the production of gut hormones that are essential for energy homeostasis. Among these hormones, glucagon-like peptide-1 (GLP-1) exhibits substantial positive effects on the cardiovascular system, including vasodilation, reduced blood pressure, improved myocardial blood flow, and cardiomyocyte survival.

Stimulation of the vagus nerve can thus indirectly protect the heart during an acute heart attack due to an increased release of GLP-1 from the gut (Basalay et al., 2016; Mastitskaya et al., 2016). In emergency scenarios where direct vagus nerve stimulation is impractical, downstream activation of GLP-1 receptors can trigger a protective pathway for the heart.

A tight squeeze: pericytes and cardiac health

The intricate capillary network within the myocardium plays a pivotal role in meeting the heart's ever-changing metabolic demands. Capillaries consist of endothelial cells forming the capillary tube, surrounded by pericytes. Pericytes are contractile cells extending their processes around and along the capillaries. They play key roles in maintaining vascular integrity and mediating regeneration of both the vasculature and cardiac tissue.

Pericytes express receptors to various vasoactive substances, hormones and neurotransmitters and thus can regulate the capillary blood flow in response to metabolic and neural stimuli (O'Farrell and Attwell, 2014). In ischaemia (decreased blood flow and oxygen to the heart muscle), pericytes contract and constrict the underlying capillaries. If the ischaemia is prolonged (as in a heart attack) pericytes may die in rigor, and the capillaries remain permanently constricted (O'Farrell et al., 2017). Notably, pericyte contraction during ischaemia can be reversed using pericyte-relaxing agents such as adenosine and GLP-1, offering a potential avenue for preventing the noreflow phenomenon and improving the outcomes of heart attack by targeting the microvasculature.

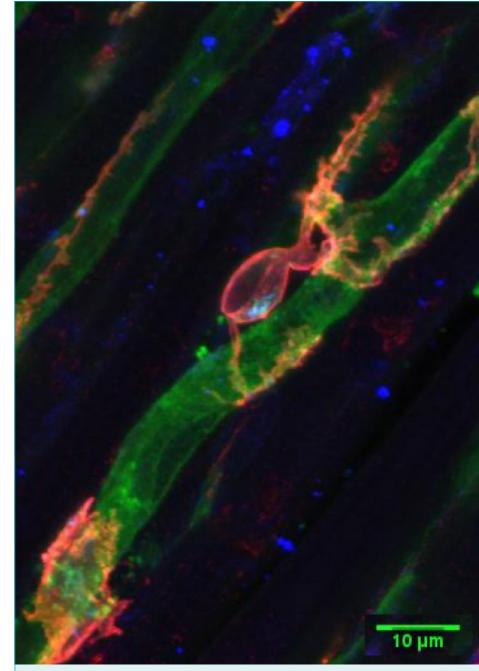


Figure 1. Cardiac pericyte (labelled for the proteoglycan NG2, red, and PDGFRb, blue) with processes around a coronary capillary (labelled for isolectin B4, green). Image taken by Ferqus O'Farrell (O'Farrell and Attwell, 2014).

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The vagus nerve, also known as the wanderer due to its extensive distribution and complex path, plays a vital role in regulating various bodily functions.

Fine-tuning cardiac health through modulation of cardiac pericyte function and selective stimulation of the vagus nerve

Investigating the regulation of coronary blood flow through autonomic control of cardiac pericyte function is the main focus of my research. However, I have several ongoing projects where I'm delving into preventing pericyte constriction during ischaemia, elucidating the role of cardiac pericytes in diabetic cardiomyopathy and Alzheimer's disease-related cardiac complications, and modulating cardiac pericyte function to enhance exercise capacity.

I use pharmacological and optogenetic (a technique to control the activity of

approaches to modulate the activity of the autonomic nervous system and understand how the vagus nerve affects the function of cardiac pericytes. I am also developing technologies that specifically target the fibres within the vagus nerve to improve heart health. Continuing to explore the connection between the brain and the heart can help us understand what goes wrong to better protect hearts from breaking.

neurons using light and genetic engineering)

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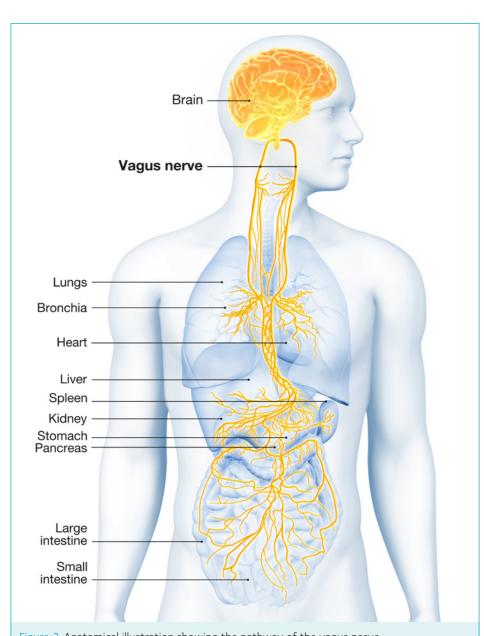


Figure 2. Anatomical illustration showing the pathway of the vagus nerve.



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Events Events

Meeting Report

Physiology 2023

10 – 12 July 2023, Harrogate Convention Centre, UK

This was my first year attending a Society meeting, and I got to present my work on the impact of bed rest and a mixed-exercise countermeasure on muscle atrophy and muscle proteomics in adults. I was both honoured and pleasantly surprised to receive the Physiological Reports Early Career Abstract Prize, considering my prior emphasis on clinical work. Looking back, this recognition is reflective of the conference's overall essence, which was a perfect blend of fundamental and translational research.



Our community of physiologists were greeted with a warm (albeit slightly wet) Yorkshire welcome to this year's Annual Conference in July.

However, the weather did not dampen the mood, with Physiology 2023 providing a programme packed with the latest physiological research and a return to face-to-face networking and discussion following an online Physiology 2021.

Across the three days, physiologists enjoyed and engaged with a variety of content, both scientific and career-enhancing.

Our 18 symposia spanned a range of topics from "Skeletal Muscle Atrophy in Response to Disuse" through to "Retinal Signalling and Myopia" as well as two education themed symposia, "Diversifying Physiology Teaching" and "Technology in Teaching Physiology". Inspiring talks were given by world experts in the form of our Prize Lectures as well as by researchers and educators at all career stages showcasing their work in either one of the 12

oral communication sessions or two poster sessions. These vibrant sessions highlighted the importance of physiology as a discipline and how physiology can change the world.

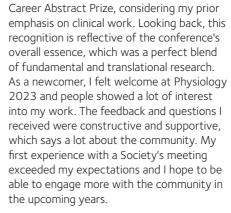
New to Physiology 2023 were our Training Hub sessions which provided physiologists with guidance and expertise on topics to help enhance their career. Participants were able to learn about intellectual property within a research context, discuss strategies to help improve the human physiology research funding landscape, gain insight into the process of publishing a paper and how to successfully implement the use of invertebrates and immature non-human vertebrates in practical education.

It was a pleasure to be back meeting and engaging with our members and the wider physiology community at Physiology 2023 and we would like to thank everyone who participated. We look forward to seeing you at Physiology in Focus 2024 with The Scandinavian Physiological Society.





This was my first year attending a Society meeting, and I got to present my work on the impact of bed rest and a mixed-exercise countermeasure on muscle atrophy and muscle proteomics in adults. I was both honoured and pleasantly surprised to receive the Physiological Reports Early



welcome at Physiology
2023 and people showed
a lot of interest into my
work. The feedback and
questions I received were
constructive and
supportive, which says a
lot about the community.
My first experience with a
Society's meeting
exceeded my
expectations and I hope
to be able to engage more
with the community in
the upcoming years.

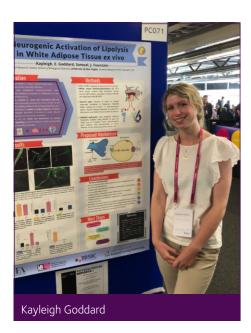
As a newcomer. I felt





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Events





Kayleigh Goddard

University of East Anglia, UK

I attended the Training Hub session 'Applying the 3Rs to education: switching from rodents to invertebrates' as I am always keen to learn more about options for other non-mammal models for scientific research. My PhD uses a substantial amount of murine-based animal work, which can be guite difficult. I took a lot from the session, particularly the concepts around insects as reductive models for more basic physiological and scientific questions that wouldn't necessarily need a mammalian study to prove. The idea that we can utilise non-mammals for educational purposes, with the same level of physiological-based hypothesis is an attractive alternative, particularly with ethical and religious considerations.



Organising a symposium at Physiology 2023 was easy, fun and rewarding. The guidance and support from the Society's staff was comprehensive, continuous and prompt from the moment the symposium proposal was accepted until it's conclusion in Harrogate. The great thing is that it is only the beginning with speakers able to convert their presentations into Symposium Reviews for Experimental Physiology, new collaborations starting and existing ones strengthened. It was also a great way to connect with and give back to the Society.

Our symposium organisers share their thoughts



"Organising a symposium at Physiology 2023 was easy, fun and rewarding. The guidance and support from the Society's staff were comprehensive, continuous and prompt from the moment the symposium proposal was accepted until its conclusion in Harrogate. The great thing is that it is only the beginning with speakers able to convert their presentations into Symposium Reviews for Experimental Physiology, new collaborations starting and existing ones strengthened. It was also a great way to connect with and give back to The Society."

Dr Toby Mundel, Brock University, Ontario, Canada



"Organising a symposium for Physiology 2023 enabled us to bring together physiologists with expertise in application of optical devices and engineers with expertise in optical device development. The experience of hosting this multi-disciplinary symposium was excellent from start to finish. The benefits have extended beyond the symposium in the connections we have made with the expert speakers and keen audience members."

Dr Siana Jones, University College London, UK and Dr Gemma Bale, University of Cambridge, UK



I attended the Training Hub session 'Applying the 3Rs to education: switching from rodents to invertebrates' as I am always keen to learn more about options for other non-mammal models for scientific research. My PhD uses a substantial amount of murine-based animal work, which can be quite difficult. I took a lot from the session, particularly the concepts around insects as reductive models for more basic physiological and scientific questions that wouldn't necessarily need a mammalian study to prove.

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Events

Meeting Preview

Neurophysiological Bases of Human Movement

12 - 13 December 2023, King's College London, UK

Dr Irene Di Giulio Dr Ricci Hannah Dr Marco Davare

King's College London, UK



We are delighted to invite you to our meeting Neurophysiological Bases of Human Movement, taking place at King's College London on 12 and 13 December 2023.

The meeting will bring together researchers in this field, foster productive exchanges about recent advancements and topical issues. Moreover, the event is designed to provide a vibrant platform, actively engaging and promoting early career researchers.

To this end, we are grateful to have a fantastic line-up of invited speakers. Their talks will be structured around four main themes spanning the two days:

- Cortical mechanisms and behavioural aspects underpinning skilled sensorimotor control
- Advanced methods for probing sensorimotor circuits
- Variability in neurophysiology: its representation and relevance
- Development and recovery of sensorimotor function

In the spirit of active engagement, the afternoon of the second day will feature three point-counterpoint sessions. These sessions will be guided by six academics within the field and will centre around three highly pertinent issues: "One vs. many participants" to discuss

the relevance of extensive, longitudinal data from a small sample or large cohort studies; "Real world vs. laboratory experiments" to debate the merits of testing participants outside or inside the laboratories in terms of controlling factors and data quality; and "Micro (neuron) vs. macro (behaviour) in neurophysiology" to discuss the role of the two approaches in neurophysiology.

Following this, all interested attendees will have the opportunity to join a round-table discussion aimed at reaching a consensus on these topics. These discussions are geared towards fostering collaboration and initiating joint publications in The Society journals.

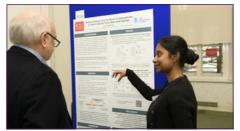
The programme has been developed to provide ample time for attendees to present their work, either as a short oral communication or a poster. Our aim is to ensure that everyone feels included, plays an active role in discussions and enjoys the meeting.

For those attending their first meeting, this promises to be a valuable scientific experience. It is a great opportunity to connect with fellow scientists and forge new collaborations. The Society has some great tips on attending your first meeting (www.physoc.org/our-events/advice-for-attending-your-first-meeting)

We look forward to seeing you all in December. Register now at physoc.org/ events/neurophysiological-bases-of-humanmovement/#Registration Meeting Preview

Member Forum, Award Ceremony and President's Lecture

Join us on 1 December 2023 at the Royal Society in London or online for a celebration of physiology, physiologists and The Society with our Member Forum, Award Ceremony and President's Lecture







Member Forum

Our Member Forum will provide you with an opportunity to hear about our recent activities and exciting plans for the future as we embark on the second year of our new strategy. There will be a chance to meet new Trustees of The Society and thank demitting Trustees, and opportunities throughout to ask questions.

Members can attend the Member Forum at the Royal Society in London either in person or online. For those able to attend in person, there will be a chance to catch up with colleagues and friends over refreshments before the event during the networking and poster session. On display will be our 2023 Rob Clarke Award posters, recognising excellence in undergraduate physiology projects.

Award Ceremony and President's Lecture

The Physiological Society

Following the Member Forum is the most prestigious event in The Society's calendar – our 2023 President's Lecture and Awards Ceremony. This is a fantastic opportunity to celebrate the triumphs of our community during the Award Ceremony, as well as hear from a notable speaker in our President's Lecture. This year, we are delighted to announce that Sir Jeremy Farrar, OBE FRCP FRS FMedSci will be giving the President's Lecture.

Sir Jeremy is a medical researcher who has served as Chief Scientist at the World Health Organization since 2023*. He was previously the director of the Wellcome Trust from 2013 to 2023 and a professor of tropical medicine at the University of Oxford.

Timings

Registration, networking and Rob Clarke Award poster presentations:

14:30 - 15:30 GMT

Member Forum: **15:30 - 17:00 GMT**

Networking drinks reception: 17:00 – 18:00 GMT

Award Ceremony: 18:00 – 18:45 GMT

President's Lecture: 18:45 – 19:45 GMT



*Institutional affiliation is provided for identification purpose only and does not constitute institutional endorsement. Any views and opinions expressed are personal and belong solely to the individual and do not represent any people, institutions or organisations that the individual may be associated with in a personal or professional capacity unless explicitly stated.

Key dates

Abstract submission closes: **30 September 2023**

Early bird registration deadline: **24 October 2023**

Conference Attendance Award deadline:

31 October 2023

Registration deadline: **28 November 2023**

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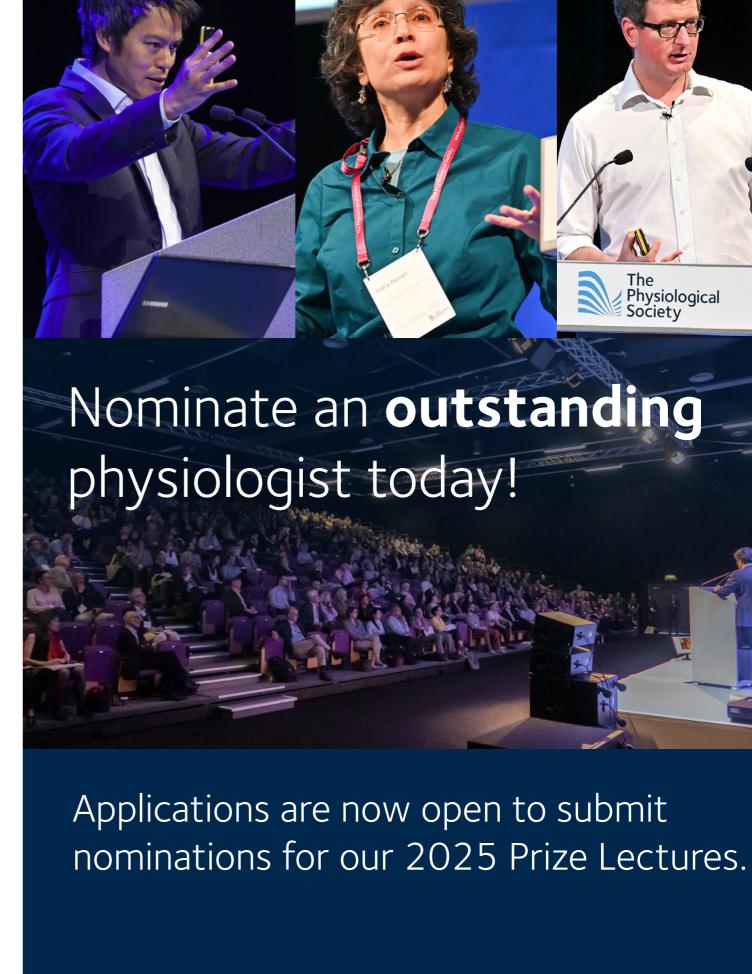
"The programme of live workshops and webinars are great for learning skills and building my networks."

Kiu Sum

"The resource library is full of information and videos that I can access from anywhere at any time to develop my career."

Josh Osofa





Submit by 30 November 2023: physoc.org/prizelectures

Congratulations to our Research and Knowledge Exchange Award winners!

The Society is delighted to announce the four winners of the Research and Knowledge Exchange Award, designed to support members wishing to conduct pilot studies, develop a new technique or to finalise a project, as well as supporting activities to promote knowledge transfer and impact.



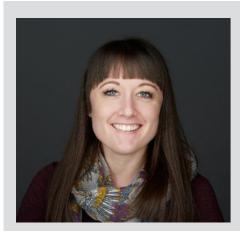
Dr Joshua Tremblay
Cardiff Metropolitan University, UK

Project title:

Investigating how urbanisation impacts cardiovascular health in the Tarahumara Health Project

Project aims: The aim of this proposal is to examine nail samples for chronic measures of stress (cortisol, cortisone, dehydroepiandrosterone) and sex hormone (testosterone, progesterone) levels. These will provide novel, mechanistic insight on how urbanisation alters the trajectory of cardiovascular ageing, the role of stress and sex hormones, and complements our comprehensive dataset. We are applying for this funding to finalise this project.

"This support from The Physiological Society helps to finalise a project that sets the trajectory of my research programme. Critically, this funding bridges my postdoctoral training and my first academic position"



Dr Faye McLeod
Newcastle University, UK

Project title:

Monitoring neurotransmitter release in a preclinical human model of monogenic epilepsy

Project aims: I hypothesise that loss of STXBP1 will reduce synaptic vesicle recycling at the presynapse in subplate neurons, causing secondary, "emergent" effects upon the developmental programme in human neuronal networks. To investigate this, my aims are to:

- Learn a new optical imaging technique to accurately monitor presynaptic neurotransmitter release.
- Assess the impact that loss of STXBP1
 has on presynaptic signalling in human
 brain slice cultures, and the subsequent
 development of the cultures.

"I'm excited about receiving this award because the techniques I am developing offer so much potential for translation, from understanding how some faulty genes may cause epilepsy, to testing novel therapies on developing human neurons. I hope that my research can really make a difference! This Award will consolidate new academic collaborations and provide a springboard for future grant applications, which are crucial to the continuation of my career as a principal investigator in the field of epilepsy."



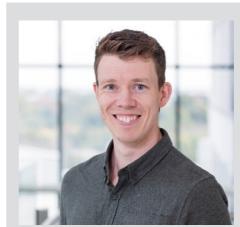
Dr Sadaf Ashraf
University of Kent, UK

Project title:

Generating a novel 3D in vitro synovial model to study osteoarthritis-producing signals

Project aims: Changes in the synovial microenvironment due to chronic lowgrade inflammation can contribute to the initiating and progression of osteoarthritis (OA). To test this hypothesis, I aim to (i) develop a reproducible preclinical multicellular in vitro 3D model of the synovium that mirrors the complexity of the synovial tissue microenvironment to act as a synovial analogue and (ii) assess the functional validity of this synovial analogue in response to inflammatory and pain mediators involved in OA. This is with the ultimate goal of identifying the signals responsible for disease progression and targets for therapy.

"I am extremely excited to be awarded The Research and Knowledge Exchange Award, which will enable me to generate a clinically relevant in vitro 3D synovial model to investigate early tissue changes in arthritis. As an early career researcher this award will enable me to gather data that are essential for securing further research funds and expanding my collaborative networks. In addition, this project has direct healthcare and patient benefit (drug testing, identifying novel therapeutic targets, understanding disease mechanisms and bridging the gap between preclinical and clinical models)"



Dr Christopher Shannon
University College Dublin, Ireland

Project title:

Role of the mitochondrial pyruvate carrier in diet-induced adipose remodelling

Project aims: Aim 1: Investigate whether the mitochondrial pyruvate carrier (MPC) regulates de novo lipogenesis in white adipose tissue (WAT)? Silencing adipocyte MPC blocks *de novo* lipogenesis (DNL) from carbohydrates in cultured adipocytes and in isolated WAT explants from male and female mice. Aim 2: Investigate whether the MPC influences adipose amino acid metabolism.

"I'm very grateful to The Physiological Society for the opportunity to explore novel metabolic aspects of adipose dysfunction. The award will help me to develop my independent research identity, strengthen important international collaborations and will hopefully act as a springboard for future funding success!"

Find out more about our grants and awards: physoc.org/grants-and-prizes

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Membership

Q&A with a Fellowship Award winner: Dr Marlou Dirks



Dr Marlou Dirks
Sir Henry Wellcome Postdoctoral
Fellow, University of Exeter, UK

Q. What initially led you into academia?

A. My fascination with muscle physiology originated in 2007, when I had my leg cast for 7 weeks after a basketball injury. At the time I had to pick a dissertation topic for my BSc Nutrition and Health at Wageningen University (Netherlands). After being left with a very thin leg once the cast was removed, I decided to write a thesis about muscle disuse atrophy. Shortly after that I met Professor Luc van Loon at Maastricht University, whom I had approached for an MSc project, and he suggested to come over for a year to work on a study with spinal cord-injured individuals. Ever since stepping into the lab I knew I wanted to do a PhD, and I was delighted that several years later the opportunity came up. I find the fact that we can lose muscle mass so rapidly incredibly fascinating. As an example, a healthy individual who remains bed-rested for a week loses close to 1.5 kg of lean tissue, while it takes at least 8-10 weeks of progressive resistance training to gain a similar amount of muscle. Gaining insight into why we lose muscle during physical inactivity and how we can prevent this muscle loss is, to date, still the focus of my academic career.

Q. How did you hear about membership of The Physiological Society, how long have you been a member and what do you value most about your membership?

A. When I started as a postdoctoral fellow at the University of Exeter in 2016, my colleagues told me about the opportunities that membership of The Physiological Society would provide, and I signed up. There are various benefits of my membership that I value, including hearing about and taking part in the various meetings and workshops that are organised, the opportunities to apply for fellowships, and the support The Physiological Society provides to Society Representatives to organise institutional seminars or conferences. The Society contributes to physiology research, education and dissemination in many ways, and I appreciate that they are always open to input and suggestions.

Q. You were funded by The Physiological Society to conduct a project on the role of dietary branched-chain amino acid ingestion and omittance on skeletal muscle protein synthesis and insulin sensitivity. Why is this an important research question to investigate?

A. Despite a strong focus on the potential beneficial effects of branched-chain amino acids (BCAAs) on skeletal muscle mass in the field of muscle amino acid metabolism, their role in the stimulation of postprandial muscle protein synthesis remains to be elucidated. Importantly, the potentially anabolic effect of BCAAs may be overridden by their potential involvement in the development of muscle insulin resistance. In my Physiological Society Accelerator Fellowship, I am investigating whether BCAAs are required to stimulate muscle protein synthesis, and simultaneously examine the effect of dietary BCAA omittance on muscle insulin sensitivity. This will advance the field of physiology by providing insight into the mechanisms that underlie muscle mass maintenance and metabolic health. and specifically the role of BCAA therein. Moreover, I envisage that the data generated via this Accelerator Fellowship will act as the foundation for further work in insulin resistant populations, e.g. individuals with type 2 diabetes (in whom BCAA omittance or restriction might be a potential interventional strategy to attenuate muscle loss and improve metabolic health) or ICU patients (who have large quantities of exogenous amino acids coming from muscle protein breakdown, accompanied by the rapid development of severe insulin resistance).

Q. You are now roughly halfway through your project; how has the support helped your project move forward?

A. The funding by The Physiological Society has enabled the start of a new research line on the role of BCAAs in skeletal muscle protein turnover and metabolic health. Practically, this support has helped me in taking up a part-time position at Wageningen University in the Netherlands, in addition

Gaining insight into why we lose muscle during physical inactivity and how we can prevent this muscle loss is, to date, still the focus of my academic career.



Experimental setup of the forearm balance technique, which we use to measure if the forearm muscles are in a state of taking up or releasing nutrients such as glucose, amino acids, and fatty acids. By combining this with intravenous infusion of stable isotope amino acids we can measure the uptake and release of amino acids into/from muscle.

to my position at the University of Exeter. Importantly, the Society's support has provided me with opportunities to expand my research team via the appointment of a PhD student and a research nurse, and new collaborations to establish the required mass spectrometry analyses. Although most progress at this stage has taken place behind the scenes, I am very pleased that the expansion of my research team will ensure that the study will start shortly, with the next generation of scientists benefiting from training on this project.

Q. How do you think receiving support from The Society has helped with your career development?

A. Being able to expand my research team has been a tremendous step for my career. Importantly, the PhD student starting on the project will provide me with the opportunity to take on the role of primary supervisor for the first time. Although I have had the opportunity to co-supervise several PhD students in the past, being able to take on the role of primary supervisor will be very important for my career development.

my research team has been a tremendous step for my career.
Importantly, the PhD student starting on the project will provide me with the opportunity to take on the role of primary supervisor for the first time."

"Being able to expand

Moreover, the 4 years of funding for the PhD student will enable them to follow up the results from this project with future work on skeletal muscle BCAA metabolism. As such, the support via the Accelerator Fellowship has not only supported me by providing funding for the first study of a new research line, but also follow-up work to develop this further. I am very grateful for the support from The Physiological Society and the opportunities it has provided, and am looking forward to being able to share the results from this support in the years to come!

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Q&A with a Fellowship Award winner: Dr Mark Dallas



Dr Mark Dallas

Associate Professor in Cellular

Neuroscience, University of Reading,
UK



Q. What led you into academia?

A. My undergraduate degree in Anatomy and Physiology opened the world of physiological research to me and from there I was intrigued to know more about getting involved and my career options. After graduating I took the plunge to continue my journey in academia with a PhD in neuroscience. My PhD studies provided me with a first-hand experience of scientific research and I had an excellent supervisory team that inspired me to be an active part of the wider scientific community. This experience really shaped my desire to continue in neuroscience research, but also highlighted the fragile nature of career progression in academia. I have been lucky in my career progression, and that is down to an unhealthy work-life balance, but also connections I have made in the wider scientific community supporting me along the way

Q. How did you hear about membership of The Physiological Society, how long have you been a member and what do you value most about your membership?

A. I joined The Physiological Society when doing my PhD at the University of Leeds and it was my supervisors who highlighted the importance of being a member of a learned society to develop as a scientist. Membership of The Society has supported me at distinct points along my career timeline. I have valued

the access to different funding streams. For example, my Fellowship Award offered me the opportunity to develop some Outreach resources, which I am enthusiastic about but have routinely struggled to find funding to support my creative ideas.

Q. You were funded by The Physiological Society to conduct an outreach project that would increase awareness, curiosity, and subject engagement with physiology. Why do you think it is important to raise awareness of physiology in schoolchildren?

A. My Fellowship seeks to expose schoolchildren to the wonders of physiology, and in particular the brain. We are creating a range of resources to support engagement in physiological research, and we hope to share these with teachers and members of The Physiological Society soon. With all the pressures in the educational system it is hard to find time and the right material to inspire school students that physiology is interesting and can offer career prospects for their futures. Too often it is a career in medicine that grabs the attention of students, but rarely does the contribution of physiology get a mention so my Outreach efforts aim to reset students' perception of physiology as a career opportunity through engaging them with innovative research. This is vital if we are to maintain excellence in physiological research and continue the work of The Physiological Society.

Q. You are now roughly halfway through your project; how has the support helped your project move forward?

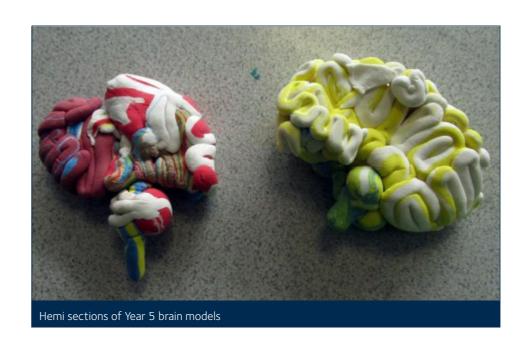
A. The support I received has been instrumental in me taking these ideas and bringing them together in a coherent programme of work. It has also allowed me space in my calendar to build towards something. The support has therefore given me time to develop ideas and collaborate with others to make resources and materials that teachers and other members of The Society can use.

Already we have been into primary school classrooms to deliver some workshops where the children get a chance to build a brain. This was exciting, and challenging as well, as it was slightly different to delivering lectures. Dr Lizzie Burns, an artist, whom I have been collaborating with has been able to help me visualise things in a creative and engaging way, which I could not have imagined. It was great to see the children engaging in the session and asking loads of questions, not only about the brain but about my job as a scientist. These are sessions I now look forward to rather than just seeing them as a process about ticking an outreach box for promotion.

Q. How do you think receiving Society support has helped with your career development?

A. Outreach is often overlooked. There is a constant demand to submit research grants, and this is viewed by institutes through the lens of the financial reward and often Outreach awards are of a lesser amount. I would argue that making an impact with any Outreach event can be as reputational-building for an institute and funders as a research grant award. This Fellowship therefore provided me with external recognition that was valued by my institute, and I wish to build on this and help shape Outreach/Public Engagement activities within my institute and share my passion with other researchers who are keen to try but are unsure of first steps. The Physiological Society award has therefore added to my external esteem in Public Engagement, which has helped me to develop my career in this area and is which is now being recognised at an institutional level. This will therefore help with any promotional application down the line, and build my evidence base to support my Public Engagement narrative.

"... my Outreach efforts aim to reset students' perception of physiology as a career opportunity through engaging them with innovative research. This is vital if we are to maintain excellence in physiological research."



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Adventures in physiology – celebrating 60 years of membership



Professor Emeritus Jim Parratt

Alumnus of University College London, London, UK Adventures in Physiology is the title of a book by Sir Henry Dale published 70 years ago in 1953 and later reprinted (Dale, 1965). It is a collection of his research papers, some as far back as 1902, including many first published in The Journal of Physiology. As a first-year research student, I was fortunate to be introduced to the great man at a meeting of The Physiological Society. My hand was then not washed for several days!

This year I celebrate two special events: my 90th birthday and, perhaps even more significant, 60 years as a member of The Physiological Society. These milestones and the 70th anniversary of Dale's book made me think about my own paths in science.

My journey with The Society began in the mid-50s when I first attended their meetings and which coincided with my first publications in *The Journal* about my research on mast cell mediators. One of my papers on the anaphylactoid reaction (Parratt and West, 1957) became a stimulus for much later studies, in collaboration with a group in Strasbourg led by Professor Jean-Claude Stoclet and supported by a grant from the Commission of European Communities, on the role of nitric oxide in shock induced by bacterial endotoxin and sepsis. We first presented our results at The Society meeting in Oxford in 1989 (Fleming *et al.*, 1990).

The 1950s and 60s were dominated by the discovery of drugs that prevent the effects of endogenous substances, such as histamine and the catecholamines, on receptors. Intrigued, I wrote to the Rhône-Poulenc organisation in France requesting some of their compounds that antagonised the effects of histamine. I received a positive response from the lead



pharmacologist, Dr Parot. These were the days when histamine was assayed on the guinea-pig ileum, the contractions being recorded by a lever on a smoked drum, a piece of physiological equipment now found in museums. When I first met another renowned physiologist, Wilhelm Feldberg (a one-time collaborator of Dale) he too was using this technique, gently tapping the work bench to return the lever to the baseline. Only after this was successful were we introduced!

I was elected a member of The Physiological Society in 1963, by which time I was teaching physiology to medical students in Nigeria. University College Ibadan was Nigeria's first university, founded in 1948 in collaboration with the University of London. I remained there for almost 10 years. These adventurous years





included independence (1960), the military coups (my family reasonably safe behind military guards at the entrance to the university complex) and the "evacuation" of students and staff who had come from what was then Eastern Nigeria. As a family we left Ibadan a few months before the start of the civil war.

With only about 30 or 40 students to teach there was ample time for research, well-funded by the West Africa Medical Research Council. It was in Ibadan that I began a life-long interest in the regulation of coronary blood flow. I think I might be the only one who has studied this in a hyena and a baboon, "gifted" to us by the university zoo because of bad behaviour — theirs not ours! It is difficult to publish with results from just one animal.

It was difficult at that time to return to a university department in the UK from as far away as Nigeria but an airmail letter out of the blue brought me to Glasgow, where a new department had been formed at the University of Strathclyde, the origins of which go back over two centuries to Anderson's University and Medical School; the original Chair of Physiology was created in 1799.

My first opportunity to work in a European laboratory came as a post-doctoral fellow with Wilhelm Lochner at the Physiologisches Institut in Düsseldorf, one of two German laboratories working at that time on coronary blood flow control. At that time, the most significant

publications in this area were in German, then considered perhaps the most important language for scientific publications. For example, British pharmacologist Sir John Henry Gaddum's classic monograph *Vasodilator substances of the tissues* was first published in German in 1936. Only 50 years later did the Cambridge University Press publish an English edition (Gaddum, 1986). It was hearing a lecture by Gaddum that inspired me to attempt a life in basic medical research.

A longer-lasting adventure in physiology began when I was invited to speak at a meeting of the Polish Physiological Society in the early 1970s. This stimulated frequent visits during the communist period to Poland, Czechoslovakia, Hungary and East Germany (DDR). Working, and then living, in Eastern Europe through the 70s to the 90s became the most stimulating and exciting period of my life in medical science. This was at a time when only a few British scientists collaborated with scientists working in the "Eastern bloc". These visits were not without risk, both to them and to myself (Parratt, 2021).

Many younger colleagues from Eastern
Europe came to work with me in Glasgow at
the University of Strathclyde. Then in 1990,
the EU funded the European Network on the
Protection of the Heart, which I chaired. This
linked departments in Germany, France, Holland,
Spain and Scotland with those in the former
DDR, the Czech Republic, Slovakia, Poland and

Hungary. The final meeting in London in 1998 corresponded with my official retirement.

Following my retirement, I was awarded an Emeritus Fellowship from the Leverhulme Trust and later, a Szent-Győrgyii Fellowship from the Hungarian State Government. This enabled me to continue to live and work in Hungary. It was from there that I published my final paper (2005), which was concerned with the protective effects of exercise on the heart, almost 50 years after my first publication in *The Journal of Physiology*.

I believe the current tendency is for postgraduate studies to be undertaken at various eminent universities in the USA, where the language is quite like our own. This is often followed on return to the UK by rapid promotion into the "profusion of Professors"!

I hope these experiences will be an inspiration to early career researchers. I would like to make a plea that younger physiologists continue to examine the possibilities of "looking east" rather than west. This despite the disastrous effects of Brexit on such collaborations. You will be rewarded not only with good science, and great friendships, but with all the other benefits that European culture brings.



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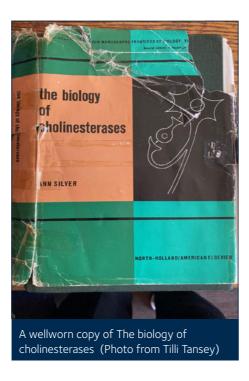
Obituary: Ann Silver (1929–2023) Member 1963; Honorary Member 1990



Ann Silver. Photo from http://www. histmodbiomed.org/taxonomy/term/ ann-silver.html

When The Physiological Society held several scientific meetings each year, Ann Silver was always in a lecture theatre during Communications, always clutching piles of pre-circulated abstracts. Every abstract had to be approved for publication by the Membership and had already been scrutinised by Ann on behalf of The Society. If necessary, she would query statistics, style, and clarity; resolve ambiguities; and seek confirmation that experiments complied with UK legal and ethical requirements and were thus publishable in The Journal of Physiology. During refreshment breaks she would chase up recalcitrant authors for their corrections and signed copyright forms. Back in Cambridge after the meeting she would work with the Publications Office to publish the meeting's *Proceedings*. She then started examining submissions for the next Society meeting. In between she reviewed, edited, proofread and contributed substantially to practically everything published by The Society.

Ann Silver was born into a military family in India, a circumstance that bizarrely led to her never having a birth certificate, and when renewing her passport in 1977 she had to unearth several family birth and marriage certificates to prove she was a British citizen. After erratic schooling, disrupted by the Second World War and ill health, she attended the University of Edinburgh and graduated in Physiology in 1953. Heavily influenced there by Catherine Hebb, to whom the anachronistic word "neuroscientist" would now be applied. Ann started a PhD on nerve function in hens, using both histology and neurophysiology to investigate the effects of organophosphorus compounds, identified as anti-acetylcholinesterase agents during the war, and then suspected of causing demyelination. Her first PhD year in Edinburgh was taken up with building the requisite electronic apparatus, nicknamed "Henrietta", and then she and Henrietta joined Hebb who had moved to the Agricultural Research Council (ARC)'s Institute of Animal Physiology at Babraham, where Ann remained for the rest of her active lab career working on nerve function. Her work contributed to the debates, still current in the 1950s, about the role of acetylcholine in neurotransmission, and to the later "cholinergic hypothesis" of Alzheimer's Disease. Inter alia, she studied: axonal transport of acetylcholinesterase; iontophoresis of acetylcholine (with Kris



Krvnević in Babraham and in Montreal): carotid body function (with Tim Biscoe in Babraham); and blood pressure regulation (with Wilhelm Feldberg and Pedro Guertzenstein at Mill Hill). Much of her detailed researches were assembled in a notable monograph, of a type unimaginable today, The Biology of Cholinesterases (Elsevier North Holland, 1974). Written in the evenings and weekends, so as not to interfere with her ARC "day job", it was frequently known as The Bible, as in the lab where I did my PhD. One reviewer noted: "Silver carefully separates facts from ideas, and her analysis is critical but not destructive... so clearly written it is a pleasure to read" (Collier (1976), The Quarterly Review of Biology 51, 142). Such clear writing was always Ann's specific objective, and indeed, the repetitive, stultifying nature of the Minutes of one Meetings Secretary of The Physiological Society in particular drove her to versify "whilst never a sin, to use 'begin'; it's always an offence, to use 'commence'".

From the 1970s onwards Ann became heavily involved in addressing legislative proposals to ban or further regulate animal experimentation amid increasing anti-vivisectionist activity. Within The Physiological Society, elected to the Committee (analogous to today's Council) in 1978, she served most significantly with Cec



David Miller, Jonny Goodchild, Ann Silver, Richard Boyd, Tilli Tansey; History & Archives Committee, Hodgkin Huxley House April 2013 (Photo from Jonny Goodchild)

Kidd, Bernard Ginsborg and Jim Pascoe as the Legislative Sub-committee; at Babraham she became the Institute's Information Officer dealing with such matters. The Sub-committee's work, involving regular meetings and detailed briefings with legislators in both Houses of Parliament (for all of which Ann was obliged to take annual leave by the ARC) and frequent liaison with other national and international scientific societies and the press was onerous, and at times personally risky. The ultimate passing of the Animals (Scientific Procedures) Act 1986 was regarded as a workable and successful outcome.

In 1985, ARC cutbacks resulted in Ann's redundancy, her status as a single woman, without a family to support allegedly influencing her fate, and she never again held a formal position. Invited by Robert Comline to work in the Cambridge Physiological Laboratory, she assisted departmental editorial work and gave courses to Part 2 and PhD students on scientific writing. Jonny Goodchild, then of The Society's editorial staff, remembers visiting her there in later years:

Ann worked in a dingy little office, more like a store room, on the ground floor in the 'Physiological Laboratory', which she shared with Horace Barlow, though he had stopped coming in. I went round a few

times for one reason or another. When I was made redundant and became a freelance copyeditor, we were down in her office and Ann said she wanted to give me a present. She suggested Hart's Rules, but I already had a copy so she gave me the Oxford Dictionary for Writers & Editors, which I consult for unusual terms, particularly to check whether to use italics.

After leaving Babraham, Ann became even more heavily involved in The Physiological Society affairs, principally in editorial roles on the Quarterly Journal of Experimental Physiology (now Experimental Physiology), on a newly inaugurated Editorial Committee, acting as formal Ethics Editor for both The Society's principal journals and increasingly working with The Society's publications staff and publishers in a variety of official and non-official roles, as Carol Huxley recalls:

I first met Ann in 1987 at my interview for a copyediting job with the Publications Office, then in the Cambridge University Press Printing House. ...Before the interview, I had to complete an English test, devised by Ann. It was a physiology-themed piece of text including all the most common grammatical and spelling errors and some of the more widely known and frequently misspelled physiological terms. The errors were liberally sprinkled through the text and one had to be careful to catch them all. That was my



Ann Silver, Cec Kidd and Tilli Tansey in Ann's flat before Robert Comline's funeral, 2003. (Photo taken by Tony Angel, from Tilli Tansey)



Jonny Goodchild and Ann Silver, Publications Office BBQ, September 2012 (Photo from Jonny Goodchild)

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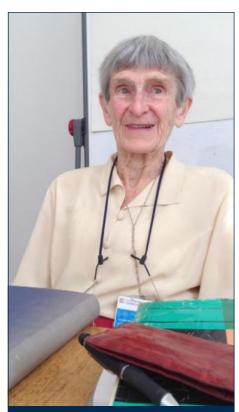


Photo from http://www.histmodbiomed. org/taxonomy/term/ann-silver.html

introduction to Ann's facility for writing correct, well–expressed English and her eagle eye for spotting mistakes. Later, after joining the publications team, I often administered the test to applicants for vacant positions. It was a very useful "sieve" for short–listing candidates.

Ann remained a helpful consultant to the Publications Office long after her retirement from the Press Secretary role. She was always ready to answer questions such as the correct way to index "Michael de Burgh Daly" or track down missing author details, by consulting her copiously annotated master copy of The Grey Book. Thornier questions might require some investigation, but she always provided clear reasoned responses that could be incorporated into the journals' house style quide for future reference.

Her longevity and many senior roles meant that she had an almost unique perspective on, and memory of, The Society. As The Society's former Honorary Archivist (1986–2022) I can attest to how helpful she was, in planning Special Interest Group meetings, finding speakers, and she also alerted me to numerous sources and contacts, including an amusing file of complaints and enquiries that she started in the Publications Office, entitled "the Lunatic Fringe". Former Secretary Tony Angel agrees:

She undertook many roles in The Physiological Society with her usual competence, integrity, and zeal. She was a friend who helped me when I was Meetings Secretary and Committee Secretary, and she had an impish sense of humour... I will sorely miss her'

Ann Watson of the Publications Office exemplifies that humour:

Ann had been out collecting for charity and had a door opened wide to her by a completely naked man! ('I think he may have been expecting someone else', she said, quite deadpan).

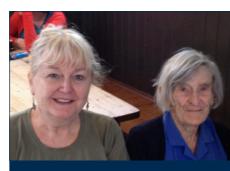
'Oh no!' I said, 'Did you scream and run awav?'

'No' said Ann, 'I said "I'm collecting for Mencap, would you like to contribute?"'

'Yes, of course, wait here' said the man, who closed the door and returned wearing a dressing gown and holding a £5 note.

Structural changes in The Society from the early 2000s onwards, the increasing influence of professional staff and the concomitant decline in roles and responsibilities of Members distressed her, as did changes in the numbers and nature of scientific meetings, but she never allowed these to influence her loyalty to the subject nor to The Society. Her honesty was much appreciated, even by those she disagreed with, as David Eisner, a former Society President acknowledges:

I particularly valued her integrity and straightforward approach to life. There was never any doubt that she was always motivated by wanting to do the best for others. When I was President of The Physiological Society, I could always rely on her to be frank when she disapproved of something that we were doing!



Tilli Tansey and Ann Silver, Cambridge 29.08.19 (Photo from Tilli Tansey)

This view is emphasised by Dafydd Walters, former Chairman of The Society's Executive Committee:

I liked her very much – an intelligent person who always expressed herself clearly and would give accurate information about people and projects... A great supporter of The Society, but never blindly!

Written by Professor Tilli Tansey,

Emeritus Professor of Medical History & Pharmacology, William Harvey Research Institute, Barts & The London School of Medicine and Dentistry, Queen Mary University of London

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Ann Silver at IUPS Kyoto 2009 (Photo given to Tilli Tansey by Ann Silver).





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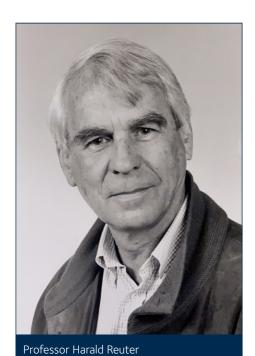
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Commemorating the life and work of Professor Harald Reuter (1934 – 2022)



On 22 February 2022, the eminent physiologist and pharmacologist Professor Harald Reuter died in Bern, Switzerland at 87 years of age. Through his pioneering investigations on voltage-gated cardiac calcium (Ca²+) channels and on regulation of intracellular Ca²+ concentrations, Reuter became one of the founding fathers of research on Ca²+-mediated signal transduction. His work also provided the basis for understanding the cardiac actions of the autonomic nervous system and sympathetic neurotransmitters, and it helped explain the mechanisms of action of cardiac glycosides and Ca²+-antagonist drugs.

Reuter was born in Düsseldorf, Germany in 1934 as the son of an attorney. After earning a medical degree, he joined the Pharmacological Institute at the University of Mainz where he completed his doctoral thesis in 1960 and obtained his habilitation in 1965.

During a research stay in 1966 at the Institute of Physiology at the University of Bern, Switzerland, he collaborated with Silvio Weidmann, a pioneer of electrophysiological investigations in mammalian Purkinje cells. They were the first to demonstrate the presence of a voltage-gated Ca²⁺ inward current that supported the plateau phase of the cardiac action potential (Reuter, 1967). Following this, Reuter then worked with GW Beeler as an assistant professor at the Mayo Clinic in Rochester, Minnesota, to achieve a quantitative analysis of these Ca²⁺ currents and their role in activating myocardial muscle contraction.

In parallel with his work on voltage-gated Ca²⁺ movements into myocardial cells, Reuter began working with Norbert Seitz to study Ca²⁺ outward movements in an uphill flux against the ion's electrochemical gradient. They discovered that this transport was mainly achieved via a Na⁺/Ca²⁺ exchange, using the inwardly directed electrochemical gradient for Na⁺ to expel Ca²⁺ in the opposite direction and thus maintain a low intracellular Ca²⁺ concentration. After finishing a manuscript describing this work (Reuter and Seitz, 1968), Reuter learned that Blaustein and Baker in the group of Allan Hodgkin at the University of Cambridge had simultaneously studied a similar exchange system in squid axons. When Reuter and Blaustein met at an international Congress in 1968 they started a long-lasting friendship that subsequently led to a successful collaboration.

In 1969 Reuter accepted the offer for a tenured position as Professor of Pharmacology at the University of Bern, Switzerland. At the time, the Pharmacological Institute was headed by Walter Wilbrandt, a pioneer in the quantitative analysis of membrane transport processes, whose work and thinking impressed Reuter deeply. In 1972, Reuter succeeded Wilbrandt as head of the institute. During his entire academic career until his retirement in 1999, Reuter remained loyal to the University of Bern even though he received several offers for attractive positions at universities in Germany and the United States.

Originally a German citizen, Reuter took up Swiss citizenship in 1987. He maintained an extended network and continuous scientific exchange with leading research groups in England and the US. For example, he enjoyed several sabbatical visits to Yale and Stanford. At the same time, his own laboratory in Bern attracted both young and established researchers from Switzerland and abroad.

In 1977, Reuter and Beeler used their earlier investigations and developed them with other evidence to formulate a broadly accepted mathematical model integrating all known ion currents that contribute to the myocardial action potential. The experimental basis of this project required tissue samples from calf and sheep hearts freshly obtained from the local slaughterhouse. This was quite popular with other members of his group, not only for the fascinating science but also for the delicious ragout prepared from calf hearts by Reuter's wife Liselotte.

The complex structure of the multicellular preparations used in these electrophysiological experiments made it very difficult to separate unequivocally membrane Ca²⁺currents from other overlapping membrane currents. To circumvent these difficulties, the novel patch clamp technique developed by Erwin Neher and Bert Sakman offered an elegant way to allow a detailed kinetic analysis of single myocardial ion channels. To adapt this method to cultured cardiac muscle cells. Reuter convinced Neher to join him, along with two other eminent colleagues with strong biophysical interests, David Colguhoun (London) and Chuck Stevens (Yale), for an intensive "Summer Camp" in Bern.

As a byproduct of the exchange of experimental know-how, the group discovered that intracellular Ca²⁺ activated

a previously unknown membrane channel mediating a voltage-independent inward movement of cations. Reuter dubbed it the CNRS channel, an acronym derived from authors' last names, thus rivalling the famous French research organisation with the same four-letter acronym. A few months later, Reuter, Stevens, Richard Tsien and Gary Yellen published a detailed kinetic analysis of single cardiac Ca²⁺ channels (Reuter *et al.*, 1982). Soon thereafter, Reuter leveraged patch clamp methods to study effects of adrenaline on single Ca²⁺ channels.

Later, other research groups showed that in addition to the L-type Ca²⁺ channels dominating in myocardial cells, various excitable tissues contained other types of voltage-gated Ca²⁺ channels with different kinetic, pharmacological, and molecular properties. Beyond electrophysiology, Reuter never hesitated to adopt novel methodological approaches, like confocal or fluorescence microscopy or molecular biology, in order to gain deeper insights into the effects of drugs or neurotransmitters on cellular Ca²⁺ handling in excitable tissues.

Reuter was a passionate and exceptionally skilled experimenter with a strong commitment to hands-on experimental work. Consequently, for most of the original papers he published during his scientific career, he himself contributed an important part of the experimental results.

Reuter gained many awards and honours for his scientific achievements. These included the Marcel-Benoist Prize, Switzerland's most prestigious Science Award, the Schmiedeberg award of the German Pharmacological Society, the K.S. Cole award of the US Biophysical Society, honorary memberships of the Belgian Royal Academy of Medicine and of The Physiological Society, London. He was a chosen member of several scientific academies, among them the German National Academy Leopoldina and the National Academy of Sciences USA. As chair of the Committee for Human Rights of the Swiss Academies and of the International Network of Academies and Scholarly Societies he was a committed advocate of scientists in precarious working and living conditions.

Reuter was a very good and mindful teacher and mentor. He supported his co-workers generously while leaving them much freedom to pursue their own projects. He almost never lost his temper, but would feel physically ill if someone cast doubt on his careful experimental work or his scientific integrity.

Privately, he was an impressive personality, inquisitive and multi-talented, blessed with a dry yet warm sense of humour. For many years he played the violin and enjoyed skiing in the Swiss mountains. He collected works of fine art, cultivated acquaintances with contemporary painters and enjoyed a long-standing friendship with an eminent Swiss gallerist. During trips to Japan, Reuter and his wife Liselotte met several well-known ceramicists and brought back a small but beautiful collection of Japanese ceramics.

He was happily married to Liselotte, a doctor and fellow student, for more than 50 years. The pair complemented each other perfectly. They were proud of their three children and eight grandchildren. They enjoyed a large circle of friends and generously shared their lovely home and hospitality. Each year all members of the institute were invited to a festive summer party in their house and garden overlooking a lake close to the city of Bern.

The death of Liselotte from cancer in 2015 affected him deeply and cast a shadow over his last years. Reuter's passing marks the loss of an unforgettable personality, a dear friend, great scientist and teacher.

Written by Professor Richard W.Tsien and Professor Emeritus Hartmut Porzig.

Professor Richard W. Tsien

Druckenmiller Professor of Neuroscience, Department of Neuroscience and Physiology, New York University.

Professor Emeritus Hartmut PorzigDepartment of Pharmacology, University of

Bern, Switzerland

Richard W. Tsien was a close scientific colleague and friend of Harald Reuter. Hartmut Porzig was a senior research fellow and long-time co-worker of Harald Reuter at the Department of Pharmacology, University of Bern, Switzerland.

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