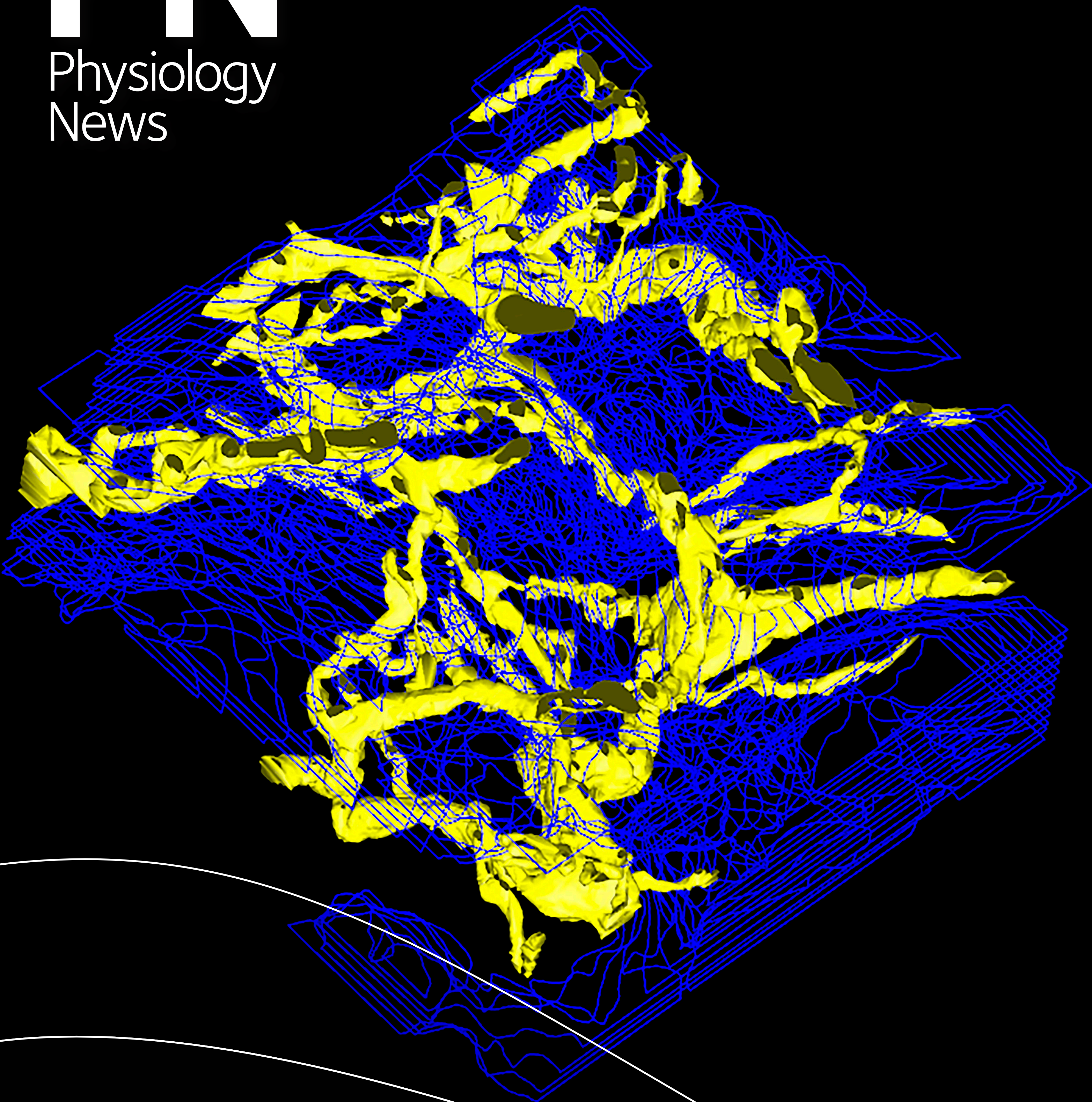
PN
Physiology News

Issue 120/ Winter 2020



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Physiology News

We welcome feedback on our membership magazine, or letters and suggestions for articles for publication, including book reviews, from our members.
Please email Julia Turan at **magazine@physoc.org**.

Physiology News is one of the benefits of membership, along with reduced registration rates for our high-profile events, free online access to our leading journals, *The Journal of Physiology*, *Experimental Physiology* and *Physiological Reports*, and travel grants to attend scientific meetings. Membership offers you access to the largest network of physiologists in Europe.

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Fellow Member	£120 per year
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Cover image: Intimacy between autonomic nerve fibres and sinus node myocytes. 3D reconstruction based on serial block-face scanning electron microscopy of a square of sinus node tissue from the rabbit. Yellow, nerve fibres. Blue, sinus node myocyte clusters. Diagonally, the square is about 100 µm across. From Shu Nakao, Mark Boyett and Ashraf Kitmitto (unpublished).

COVID-19: Lessons Learned from the Frontline

14 - 16 DECEMBER 2020 VIRTUAL CONFERENCE

Bringing together physiologists and critical care specialists, this conference will review the challenges of understanding the pathophysiological changes occurring throughout the body following COVID-19 infection.

Organised by:

Susan Deuchars, University of Leeds, UK

Steve Mathieu, Queen Alexandra Hospital, Portsmouth, UK

Hugh Montgomery, University College London, UK

Mike Tipton, University of Portsmouth, UK

Satellite session

COVID-19 and mental health: Exploring the impact on academics

Register by Monday 7 December 2020 at 23:59 GMT

physoc.org/covidconference

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The Physiological Society

Light at the end of the tunnel

Julia Turan
Managing Editor, *Physiology News*

Keith Siew
Scientific Editor, *Physiology News*

We think all of you will join us in saying thank <insert deity/expletive of your choosing> 2020 is coming to a close!

This year has seemed to last forever, and yet somehow gone by in the blink of an eye. We have all been challenged in ways we never expected – emotionally, physically, and mentally – often finding ourselves questioning our values and re-evaluating our priorities in life. And so, we felt it apt to take this moment to reflect on our time together and shared experiences.

In particular, we extend our deepest condolences and thoughts to our members and their families who have endured great loss. Too many, too soon. We also send our thanks and appreciation to our colleagues, friends and family in hospitals and laboratories across the world who have borne the burden, and sacrificed, to reduce the suffering of others. Please accept our heartfelt gratitude.

There is finally light at the end of the tunnel.

We are now armed with rapid antigen tests, which, while not perfect, allows for large-scale mass testing to root out the scourge of hidden cases. We have antiviral drugs such as remdesivir, which can reduce patient recovery time, and corticosteroids like dexamethasone or monoclonal antibody therapies to reduce mortality in the most severely ill and vulnerable.

Most excitingly, within days of writing this editorial, there have been three COVID-19 vaccine Phase III trials reporting effectiveness of up to 90% or greater, both in the young and old, and with early evidence of reduced transmission and decreased disease severity. We could simply not have wished for more. The ingenuity and collaborations forged between academia and industry have allowed us to achieve what was inconceivable but a year ago. Together we have harnessed the latest in RNA and viral technologies to shorten the timeline to develop, trial and mass manufacture vaccines from years to just a matter of months. A true medical marvel!

And as the holidays come and go, the new year will bring with it another great wave of change. The rollout out of vaccine programmes, formalisation of new relations between the UK and EU, a change of power for our friends across the Atlantic Ocean, and a long and winding road to economic recovery. Within our own Society we say farewell and thanks to our first female president, Bridget Lumb, who has been a champion for positive change and overseen a focus on diversity and inclusivity in the Society, and we welcome our new president David Paterson who takes up this mantle.

We at the *Physiology News* Editorial Board wish to convey our warmest thanks to Sarah Hall, the outgoing Chair of the Education, Public Engagement and Policy Committee (EPEP), for all her support and the copious amount of time dedicated to the magazine over the years. And we welcome our new EPEP Chair, Lucy Green who provides oversight for our activities and we look forward to working with her on the strategic direction of the magazine in the years to come.

We (Julia and Keith) have had the pleasure of working together on the editorial leadership of *Physiology News* for 3 years now, and we are proud of our tireless Editorial Board, who have been bringing their energy and ideas to our meetings with an unfathomable gusto (and we all know how we feel about long Zoom meetings these days, so we really do appreciate it). Especially in these difficult times, we are proud to have maintained the quality and diversity of magazine content that we hope represents the voices of our Physiological Society members, and that is both responsive to current events and is also setting trends in the digital and print communications landscape for learned society magazines.

We look forward to a new year full of exciting potential. We will endeavour to further improve diversity and inclusion among our authorship and continue to innovate and improve the quality of *Physiology News* magazine.

So, for now friends, stay safe and enjoy the holidays. Hopefully with a slow return to normality, before the end of next year we will start to see more bums on seats in our lectures, the return of hustle and bustle around the labs, and dare we say a cheeky pint in Birmingham with far-flung colleagues after a poster session at Physiology 2021.

https://doi.org/10.36866/pn.120.5

Bridget Lumb

President 2018-2020, The Physiological Society

Striving for inclusivity, diversity, equality, and accessibility to keep physiology flourishing

Creativity is indispensable for scientific progress. The more diverse our physiology community, the more creativity we can foster, stemming from everyone's diverse perspectives. Therefore, doing everything we possibly can to make our community as inclusive, diverse, equal, and accessible as possible is paramount for ensuring an engaged membership community and thus for allowing physiology to flourish.

To achieve this, The Society continues to take steps to increase the diversity of our membership and ensure that those diverse voices are heard and reflected in our activities. We are excited to announce the formation of the Diversity and Inclusion Taskforce, which will allow the member voice to better inform our work around inclusion, diversity, equality, and accessibility.

In addition to involving the membership more in our diversity work, we also continue to sponsor conferences for underrepresented communities. This year we were proud to sponsor the STEM Village Symposium, the first global LGBTQ+ STEM conference, organised by STEM Village, the LGBTQ+ STEM community in Scotland.

In order to embed these principles of inclusivity into our membership categories, we have launched new membership categories. Members will have received information about this in their email inbox and can now renew. The changes specifically facilitate inclusivity by allowing physiologists to become and remain members, regardless of whether they are working inside or outside of academia, thus better reflecting their career progression. In addition to increased inclusivity, they will allow us to provide:

- Increased networking and collaborative opportunities for members working in more diverse roles in physiology
- Improved tailoring of the support we offer our members across different categories
- Improved membership journey to encourage the transition of early career researchers to Full Members

The Society's membership fees have remained unchanged since 2016, while our operating costs have continued to increase. Therefore, an introduction of a small increase in fees was considered proportionate at this time. As a charity, all income from membership fees is invested in our membership services and events to ensure we are able to continue to support a diverse range of physiologists in all senses of the word. We want to continue to provide a more comprehensive range of benefits for members and this small increase will help us to do this. More information can be found on the FAQs page on our website. **https://www.physoc.org/join/membership-category-and-fee-changes-frequently-asked-questions/**

By increasing the scope for those working in physiology but outside of research to join The Society, we anticipate we will enhance the value of networking both for career development and forming interdisciplinary research collaborations, and make The Society a more inclusive community of physiologists.

Another initiative in the equality and diversity arena has been The Society's contribution to the inquiry report on equity in STEM education, released by the All-Party Parliamentary Group (APPG) on Diversity and Inclusion in STEM in June of this year. The APPG aimed to include and progress people from underrepresented backgrounds in STEM, and encourage government, parliamentarians, academics, businesses and other stakeholders to work towards a STEM sector that better represents the diverse UK population.

The findings highlight shortcomings across the education system. They include the need for a more joined-up approach by government to tackle the causes of inequity in STEM education and an urgency to take a wider, more holistic view of inequity beyond the lens of gender, economic disadvantage or ethnicity.

From these findings, the APPG has created six key recommendations. They include calling for a minister responsible for addressing inequity within the education system, making STEM education more relevant to young people, and more action to address teacher shortages in STEM subjects. The report is available at **https://www.britishscienceassociation.org/appg**

As a testament to our work to improve membership engagement, I am very pleased to note that we have had over 70 applications for the vacancies across our committees and other member-led groups, a much larger number than in recent years. I think this indicates a higher level of engagement by members who are looking to help shape the future of our community, while networking and developing their own set of soft skills important for any career in physiology.

I think this increased level of engagement is due in part to better communication with the members, stemming from the hard work of our staff, Trustees, committee members, Themes Leads, Society Representatives, Editorial Boards, committees, as well as engagement with our members via the vast array of scientific and professional development webinars that The Society has hosted since the spring. This has been a great opportunity for collaboration across the organisation and I look forward to seeing this continue next year under the leadership of David Paterson, University of Oxford, UK as President and David Attwell, University College London, UK as President-Elect.

After 2 years, this is my final President's View in *Physiology News*. I joined The Society back in 1990 and have been honoured to have become our first female president. While I will no longer be in this role, I will continue to be an active member and I look forward with excitement as we begin our next chapter of increased inclusivity and engagement.

https://doi.org/10.36866/pn.120.6

Dariel Burdass

CEO, The Physiological Society

Adapting our member benefits during a global pandemic

As we draw to the close of 2020 and reflect on what has been a year of unprecedented challenges, it has been heartening and uplifting to see that, as an organisation, we have drawn on The Society's core strengths, namely the knowledge and skills of our members and the professional expertise of our staff. Combining this with our innovative and responsive approach, we have continued to find opportunities for physiology to flourish amid difficult constraints.

In doing this we have continued to put The Society's purpose – *To advance physiology in order to foster the understanding and improvement of life* – at the forefront.

The COVID-19 pandemic, which looks like it is here for the long haul, has significantly impacted the global economy and we recognise that the pre-pandemic environment will be very different from the one our community will be faced with going forward.

We recognise that challenges face all our members, from those embarking on an undergraduate degree through to members working across academia. To gain a more in-depth understanding of these challenges and find out what we can do to help, we have drawn on the feedback from the 2020 member survey, which we thank members for completing. This gave us a better understanding of what the situation is like on the ground in universities and higher education institutions and has helped us better understand some of the difficulties and crucially how we can continue to support our members going forward.

For example, we have already heard from members that the shift to online education has meant an increased amount of time spent preparing resources, which has reduced the amount of time available for research activity. When we asked about the impact of the pandemic on physiological research, of those that responded around 70 percent felt that it had a large impact, around 50 percent were no longer able to conduct their research, and 15 percent had their lab time reduced.

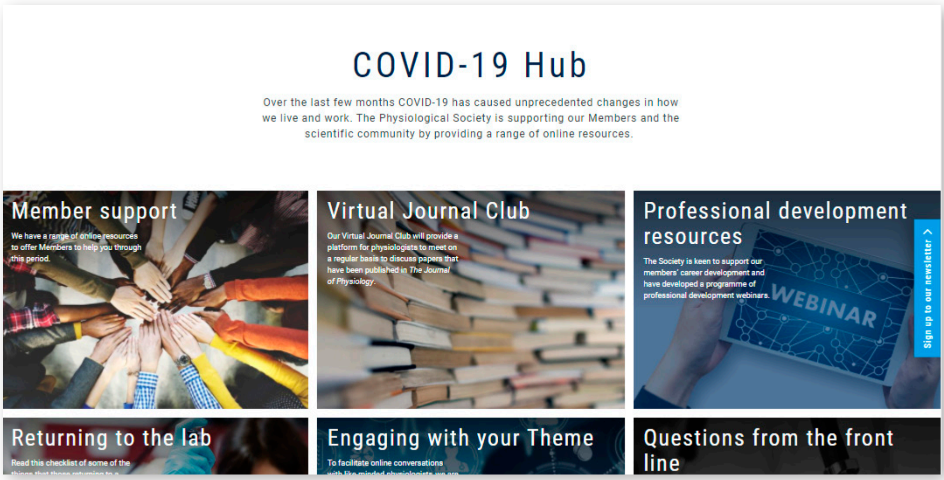
Members were also asked how we could support their teaching, and 75 percent who responded replied they would like The Society to facilitate the sharing of resources. We are already acting on this request by creating a dedicated webpage for members to share their resources and by providing more support for practical teaching.

I think it is important to keep highlighting the range of resources that we have produced, in conjunction with members, which can be found in the COVID-19 hub on our website. These cover the breadth of physiology including the Scientific Theme webinars and *The Journal of Physiology's* Virtual Journal Club through to professional development opportunities too.

With membership at the heart of The Society, it was positive to hear that the value of membership was recognised and the initiatives we have introduced during the pandemic had been well received.

> "With membership at the heart of The Society, it was positive to hear that the value of membership was recognised and the initiatives we have introduced during the pandemic had been well received"

At a time when many of us are having to connect in a virtual world, members have told us that providing opportunities to network with peers is more important than ever. We have some exciting initiatives for 2021 including a new member area on our website with resources and activities that are exclusive to members. Membership is at the heart of The Society and we look forward to working with our members during 2021 to connect them with peers, improve networking opportunities and learn about the latest breakthroughs in physiology.



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Reports of The Society's recent committee meetings

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

The Board

June 2020
The President, Bridget Lumb, introduced the paper entitled *Planning for the Future*, which specified how The Society's strategy and related activities would need to adapt to the post-COVID-19 world. The paper identified new pressures and challenges in higher education as well as positives that could be harnessed. It also noted the success of The Society's COVID-19 hub and its links with clinicians.

The Honorary Treasurer, Frank Sengpiel, informed the Board that the auditors, haysmacintyre, had issued an unqualified opinion without modification. (This means that the audit firm carried out a thorough audit of The Society's internal systems of control and its financial statements and all supporting documents and was able to satisfactorily conclude that the financial statements were free from material misstatement.) The Treasurer commented this was the second year the audit was done in partnership with Js2, The Society's outsourced accountancy firm. It went very smoothly, despite occurring remotely during the lockdown, and the auditors commended the process. The Board approved the Trustee Annual Report.

The Board approved moving the Member Forum & Celebration to a virtual event on the afternoon of 20 November 2020. The event would include an update to members, Trustees standing up and down, a recognition of new Honorary Members and Fellows, and the President's Lecture.

The Chief Executive, Dariel Burdass, spoke to the paper on member engagement and answered questions on the proposal to commission a custom-built platform intended as a forum for members and home to The Society's online resources. She explained that this project would build on the success of the website relaunch and The Society's increased digital content output. The Board approved the cost for the new secure member area of the website.

The Head of Professional Development and Engagement, Chrissy Stokes, presented a paper to the Board on membership categories (a follow-up paper to the membership work presented in 2019). She stated that a second ongoing task-and-finish group had expressed their approval of the proposed membership categories. The group suggested that the categories better track the careers of physiologists by including a specific postgraduate category. Trustees also agreed to change the Undergraduate membership criteria to include Master's students.

Conferences Committee

October 2020
The autumn 2020 meeting of Conferences Committee was held online (which perhaps now goes without saying) on 17 October, chaired by Sue Deuchars, University of Leeds, UK. The Committee welcomed Dayne Beccano-Kelly (University of Oxford, UK) as a new member and Diversity and Inclusion Champion. Dan Brayson and Mat Piasecki were thanked for their valuable contributions during their terms.

The meeting first discussed a particularly significant and topical forthcoming conference, COVID-19: Lessons Learned from the Frontline (14 – 16 December 2020), a virtual conference to be held jointly with the Intensive Care Society. The conference follows on from the COVID Advisory Panel, an online Q&A collaboration between physiologists and clinicians, and pairs speakers from the two communities.

Sarah Bundock, Events and Marketing Manager, reported on the results of a Society survey into attitudes around scientific conferences post COVID-19. The survey aimed to track changes in attitudes with time, and to use the information in planning our meetings programme.

The Scientific Theme Webinars run by The Society have been warmly received by participants. It was agreed that the webinars should always be recorded and uploaded to YouTube as a resource. Following on, there was a consensus that, apart from review lectures, speakers at The Society's events should be strongly encouraged to share novel data, although it would not be mandatory.

The Events Team asked for ideas for enhancing online networking as this was challenging to offer in an online environment.

The meeting reviewed the conferences programme for 2021, which is the following:

- **Future Physiology 2021** (Spring 2021) This will be organised by the new team of Early Career Theme Leads and will most likely be a virtual conference.
- **Physiology 2021** (ICC Birmingham, 12–14 July 2021) Council had agreed that Physiology 2021 should be a hybrid conference (so in-person and online). The programme was warmly noted.
- **Biomedical Basis of Elite Performance 2021** (University of Nottingham, 14–15 September 2021) The venue had confirmed that this could be run as a hybrid meeting.
- **Regeneration Across the Systems: Translational Opportunities for Novel Therapeutic Avenues** (University of Edinburgh, 14–15 December 2021) This meeting was postponed from December 2020. The Events Team has the Edinburgh venue on hold as first option.
- **Processing and Modulation of Sensory Signals: From the Periphery to the Cortex**. This had already been postponed from April 2020 to March 2021 because of the COVID-19 pandemic [Since the Committee met it has again been postponed, to June 2022, to ensure that it can run as a face-to-face conference].

Education, Public Engagement and Policy Committee

September 2020
The Education, Public Engagement and Policy Committee (EPEP) met via video conference on Tuesday 15 September. The meeting was chaired by Sarah Hall, Cardiff University, UK.

The committee recognised the increase in Education and Teaching Theme activity that has provided opportunities for the sharing of

https://doi.org/10.36866/pn.120.8

best practice, and peer support and guidance on topics such as online teaching, since the onset of the pandemic. They discussed ways that The Society can continue to build on this work to support members during these unprecedented times for teaching in higher education.

The committee received an update on policy consultation, responses and projects in 2020. Priority areas for responsive policy were agreed as research and development funding, the medical curriculum and public health.

The committee noted the success of the recent professional development webinar series, as part of the wider response to COVID-19 in supporting the membership over the lockdown period. This series brought together expertise from across the membership, The Society staff and allied organisations to deliver advice and guidance on topics including publishing, media skills and scientific writing. Another series of webinars is being planned for late autumn focusing on topics requested by members.

The committee received a report from *Physiology News* to update on recent activity and plans for the upcoming winter issue on medical technology, devices and biometrics in physiology. They also noted that The Society is in the process of recruiting a Scientific Editor who would start from Spring 2021.

Finance Committee

October 2020
Tom Wilson from haysmacintyre updated the Committee that they intended to issue an unmodified audit opinion and that the remote audit process had gone smoothly. The Committee received and discussed the Trustees' Annual Report (TAR) and accounts for the year ending on 31 December 2019. The TAR's introductory section was amended to reflect COVID-19; however COVID-19 was not expected to make a big impact on The Society's financial position in the short term. The Committee also received and discussed the Q120 Management Accounts narrative and figures. The Committee discussed options for where to move money in the 190 Day account when the notice period expires on 29 October 2020. The Committee also reviewed the investment policy constraints in The Society's Investment Policy Statement (IPS) but made no changes to it.

Newly appointed committee members

Conferences Committee
- Daniel Johnson *Open University, UK*
- Rehan Junejo *Manchester Metropolitan University, UK*
- Ana Cruz *University of Exeter, UK*

Publications Committee
- Markos Klonizakis *Sheffield Hallam University, UK*

Education, Public Engagement, and Policy Committee (EPEP)
- Harry Witchel *Brighton and Sussex Medical School, UK*

Finance Committee
- Kamalan Jeevaratnam *University of Surrey, UK*

Early Career Theme Leads
- Greg Sutton *University of Edinburgh, UK (Cardiac & Vascular Physiology)*
- Ruth Norman *University of Leeds, UK (Education & Teaching)*
- Shelley Harris *University of Southampton, UK (Endocrinology)*
- Jennifer Pearson-Farr *University of Southampton, UK (Epithelia & Membrane Transport)*
- Paul Ansdell *Northumbria University, UK (Human Environmental & Exercise Physiology)*
- Kelly Bowden Davies *Manchester Metropolitan University, UK (Metabolic Physiology)*
- Laura Rich *University of Nottingham, UK (Neuroscience)*

Physiology Feed

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

Measuring earwax cortisol concentration using a non-stressful sampling method

Changes in cortisol levels are associated with several pathologies (e.g., Cushing's syndrome, Addison's disease, depression). Assessing cortisol concentrations accurately is clinically challenging since stressful sampling methods might affect its release. In this pilot study, the investigators compare conventional practices of determining cortisol levels (i.e. via hair, blood, and saliva sampling) with earwax cortisol concentrations obtained through a novel ear-swabbing technique. They demonstrate that the self-sampling of earwax does not elicit a local or a systemic stress response that alters the levels of cortisol. They suggest that this testing device may be cheaper and faster to employ in patients compared to prior procedures, and could reflect more precisely chronic cortisol concentrations.

https://doi.org/10.1016/j.heliyon.2020.e05124

Accelerated ethanol elimination via the lungs

Ethanol toxicity owing to excessive alcohol consumption accounts for over 3 million deaths annually worldwide, thereby constituting a major public health challenge. Although principally metabolised by the liver, ethanol is also cleared via the kidneys and lungs. Given this, the authors of this proof-of-concept pilot study examined whether isocapnic hyperpnea (IH; i.e., the maintenance of high levels of ventilation through deeper and faster breathing) may hasten ethanol removal as it has been shown to do for carbon monoxide clearance. They show that when blood ethanol levels are raised to 0.1%, IH triples the ethanol elimination rate in comparison with regular breathing. These findings support further investigations into the possible use of IH to treat acute severe ethanol poisoning in a clinical setting.

https://doi.org/10.1038/s41598-020-76233-9

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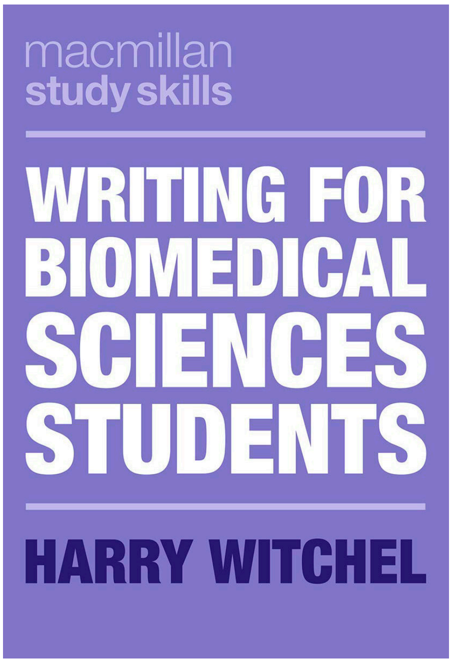
Book Review: *Writing for Biomedical Sciences Students* by Harry Witchel



Harry Witchel, Red Globe Press (2020)
ISBN: 9781352008753

Katherine Rogers
Queen's University Belfast, UK

This book is a comprehensive guide to all aspects of academic writing in the field of biomedical sciences. Although it is identified as being for undergraduate students, while reading it I found that there are many topics that are equally relevant to postgraduate students and even early career researchers. This was due to the inclusion of very useful chapters covering aspects such as writing for poster presentations and talks or presentations, all of which are useful for those preparing their first conference presentation or even for the more experienced biomedical scientist who is looking for hints and tips on how to improve their oral or poster presentations.

The book is broken into four parts that take the reader on a journey of bioscience writing. It begins by covering the basic process of writing in Part 1 and then explores specific forms of writing in Part 2. Parts 3 and 4 discuss more advanced academic writing skills including organising the writing, selecting reference material, online searching and note-taking, using figures and tables, and performing an analytical critique. Part 4 focuses on skills associated with editing, referencing, avoiding plagiarism, proofreading, and editing and responding to feedback. The final chapter provides useful advice on writing for non-native English speakers. Appendices include samples of real essays that provide examples of reflective writing and critical thinking. These are taken from the author's own students and readers will find these examples useful for illustrating much of the key guidance highlighted in the book.

The book is designed as a tool that can be dipped into, with each chapter presented as a separate entity that can be read as a stand-alone section, so there is no need for the reader to have read from the beginning of the book – this layout is always attractive to readers who can use the book as a guide. Nevertheless, in some chapters, reference is made to content in other chapters if the reader needs further information. These reference points are signposted well and do not detract from the content. I found these cross-references very helpful and was able to find the other sections with ease to supplement my reading.

Although other books exist on the market that provide guidance on academic writing for undergraduates, this book stands out for me as it is targeted specifically at the biomedical sciences and hence the advice and guidance it provides is entirely applicable to this group of students. Due to its field specificity, every chapter has something useful to offer and while reading I was confident that the advice was relevant to the writing style expected in the field.

Throughout the book the author has provided the reader with a range of useful hints and tips such as the hourglass model of the IMRaD structure of a bioscience report or the BEER hourglass model for constructing a paragraph. Many of these concepts will not be new to science undergraduates but the clear instruction and explanation may help the reader to use and apply them in a way that is explicit, hopefully resulting in better writing and hence better marks.

A number of short exercises are interspersed through the book and I will certainly use some in my own workshops on assignment preparation for Master's students – this is testament to the benefit this book offers to all levels of students. The book is particularly useful for full-time Master's students who often commence postgraduate studies directly from an undergraduate programme and can find the higher expectations of writing at Master's level quite challenging.

For me, as a lecturer with many years of experience in reading and correcting academic writing, a number of points in the book will help me to give more constructive feedback and advice to students on how to improve their academic writing. Below I have highlighted several "how to" items covered in the book that I will be emphasising to my students:

- Deconstructing an assignment title – identifying logical sections that will help structure the writing.
- Timed essays in exam situations – students have been used to doing these in the past but perhaps it is becoming less common due to changes in assessment strategies brought about by the pandemic.
- Using an outline or plan when writing - something many students do not value enough.
- Applying an approximate word allocation when constructing an outline.
- Tips for using MS Word technology to develop outlines and using that to check for logical progression of the writing – in future, I am going to try to use this facility more in my writing!
- IMRaD – useful for those doing a final-year project or even students on a PhD or Master's by research; I think this chapter is very useful for all students and I intend to direct all my postgraduate students to this chapter in the future.
- Techniques for incorporating critical arguments into biomedical writing – a very important concept that when students grasp it, will enable them to achieve higher marks in their academic writing.
- Revising, editing, and proofreading – students at every level struggle with these aspects of writing, often due to time constraints and over-familiarity with the work.

This book provides something for every biomedical science student at every level, but to get the most out of the book I would strongly recommend it to first-year undergraduates who will reap the benefits of the advice and guidance throughout their years of study.

Policy Focus: Physiological Objectives for Medical Students

Prem Kumar

University of Birmingham, UK

Physiology is the science of life, and I am sure it is self-evident to all members and regular readers of *PN* that in order to understand how and why the body goes wrong in disease, we have first to know how it operates in health.

Working alongside clinical colleagues, I am extremely fortunate to be able to draw connections between my own and other colleagues' research interests and the subjects I teach in order to provide a research-led education to healthcare professionals who will go on to have a direct impact on the treatment and care of patients. This has always been invaluable but never more so than during the past 6 or 7 months, as the COVID-19 pandemic sweeps the world.

Time spent teaching physiology to medical students is becoming increasingly brief as the curriculum becomes ever more crowded. It is therefore timely that The Physiological Society has recognised the need to support those responsible for teaching medical students the fundamental mechanisms of physiology that underpin their careers by providing specifically designed objectives for undergraduates through this document.

The changes introduced by the General Medical Council (GMC) to the assessment of newly qualified doctors from 2023 and its accompanying guidance, *Outcomes for Graduates*, gives The Physiological Society an opportunity to build a dialogue with senior medical stakeholders.

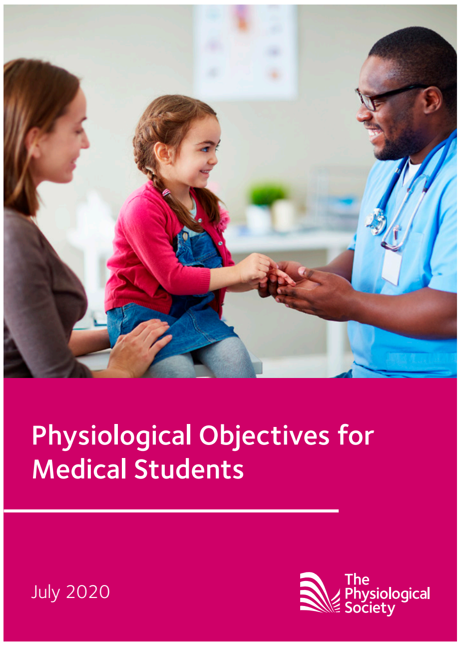
Similarly, The Physiological Society's 2019 policy report *Growing Older, Better* made a series of recommendations on interdisciplinary working including one that specifically related to raising the profile of physiology within medical and nursing curricula.

These developments arise in response to growing concerns from a number of physiologists and medical practitioners that a decline in the *understanding* of physiology, within the commonly adopted, problem-based approach to learning in many medical schools, could lead to unintended gaps in knowledge. These gaps have the potential to lead to a decline in resilience for reacting to unusual or rapidly changing medical circumstances.

This is not a new problem. Indeed, the core group that I chaired were extremely grateful to be able to build on the work of Richard Dyball and colleagues, who instigated an equivalent project on behalf of The Society over 10 years ago. It is a reflection of both the amount of knowledge required and the quality of expertise that exists within physiology that we were able to draw on a wealth of talent from across The Society to review and update that original curriculum.

Whilst our focus was primarily upon providing an essential physiology curriculum for medical students that could be adopted by the GMC, we were also aware that the objectives defined could form a key part of any healthcare-related or science-based undergraduate programme in which there is a requirement for an understanding of how the body works in health and disease. Whilst we have attempted to have a broad, core curriculum, based upon body systems, we may have inadvertently excluded or under-emphasised some key elements and Society members may wish to comment upon that as the document will be revised regularly with the ambition that future editions should become increasingly definitive, without becoming overly specific.

We hope that this piece of work represents the beginning of The Society's engagement



with organisations that represent healthcare professionals to ensure that the skills and insight physiology can offer will make it from the laboratory to the bedside. In a year that has been characterised by the emergence of a novel and deadly virus with symptoms that impact the whole body, the need for medical students to understand the fundamentals of physiology has never been more important.

COVID-19 and Ageing Report Launch

Public health agencies across the UK should launch a *National COVID-19 Resilience Programme* to support older people through the pandemic and to keep them healthy and resilient over the winter. That's the recommendation made in a new report by The Physiological Society and the Centre for Ageing Better launched last month in a Parliamentary and Scientific Committee meeting. The Expert Panel for the project brought together 20 leading scientists and clinicians.

A *National COVID-19 Resilience Programme* would bring together a package of measures to support older people through the lockdown and beyond, keeping them healthy and resilient over the winter, and should include:

- A tailored exercise programme, focused on older people with key COVID-19 risk factors (obesity, type 2 diabetes, cardiovascular disease, and sarcopenia). This can draw on existing programmes such as "Make Movement Your Mission"; (**facebook.com/groups/MakeMovementYourMission**);
- Clear guidance about the importance of a healthy balanced diet containing sufficient levels of protein and appropriate energy content;
- Enhancing mental health by creation of virtual communities to counter social isolation;
- Enlist help of relatives and volunteers to support behaviour change among older people.

Read the report on our website at **physoc.org/policy/covid19resilience/**

https://doi.org/10.36866/pn.120.12

The 2020 member survey results are in!

The Society conducted a survey during June and July of this year, to better understand the impact COVID-19 was having on our members and their work. We were also keen to receive feedback on the member benefits that we had introduced and gather ideas as to how we might build on this support going forward.

Members were invited to share their thoughts on topics such as the impact of the pandemic on physiological research, support from The Society, and willingness to attend in-person scientific conferences.

Approximately 13% of members responded. Over half of these members said they felt supported by The Society during the lockdown period, with the professional development webinar series being the most valued resource. The Scientific Theme webinars and the Future Physiology virtual conference were also well-received by members. At this difficult time, 48% of members valued being part of a community.

Members felt there were some areas where The Society could further enhance support, for example by providing online teaching resources and increasing the number of professional development webinars.

Many members were forced to change their professional focus because of the pandemic: 75% of respondents using the time to write up and publish research, 39% were delivering online teaching, 36% were applying for grants and funding, and 37% preparing for online and blended teaching.

Members were asked their feelings on attending scientific conferences, and when they would feel comfortable returning to in-person meetings. The size of the meeting, and the location, were the factors impacting this decision. While a third of respondents felt they would be comfortable attending small, focused meetings within 3 to 6 months, most felt it was too soon to know if they would be comfortable attending large international conferences within this time period.

When asked their views on the long-term impact of the pandemic on physiology research, 46% said it was too soon the know the long-term impact and 34% felt research was likely to return to pre-lockdown levels. When asked how the pandemic had affected research funding in their institution, over two-thirds confirmed there had been a negative impact.

Overall, the results of the survey suggested that The Society had responded well to ensure members felt supported during this time; 55% said they felt supported during the lockdown. We have already responded to some requests for additional support, such as sharing teaching resources on our website, publishing an Education Special Issue of our member magazine *Physiology News* and running additional professional development webinars, which started on 30 October. We will continue to facilitate a dialogue with, and amongst, the community to ensure our membership offer remains the best it can be during these unprecedented times.

We would like to thank all members who took the time to complete the survey.

An executive summary is available to all members on The Society website; anyone wishing to discuss the survey and the results further, can contact Jen Happe, Membership Engagement Manager at **membership@physoc.org**

https://doi.org/10.36866/pn.120.13

The Journal of Physiology's Virtual Journal Club: A new way to discuss research online

Every first and third Wednesday of the month, since August 2020
Held online

Rosie Hynard

Events and Marketing Officer, The Physiological Society

In August, The Society launched an exciting new initiative, *The Journal of Physiology*'s Virtual Journal Club. Introduced in response to the COVID-19 pandemic, the Virtual Journal Club provides an online platform where researchers can meet on a regular basis from anywhere in the world, to discuss the latest physiology and learn about what is best practice for publication.

Taking place on the first and third Wednesday of every month, each meeting of the Virtual Journal Club is hosted by a different early career physiologist. The hosts are tasked with selecting papers from *The Journal* for discussion, on the condition that they must have been published within 3 months prior to each meeting, ensuring that the focus is always on the latest research. The host is then responsible for forming an expert panel of authors and editors to allow for valuable conversations about both new research and publishing.

The exact structure of each meeting varies but there is always an initial panel discussion followed by an audience Q&A session, giving attendees the chance to comment on the chosen papers and ask for advice about publishing in *The Journal*. Each meeting is followed by a short networking session, giving the host, panellists, and audience members the opportunity to meet and reflect on what was discussed.

The online format of the Virtual Journal Club means that it has a global reach. In the 2 months since its launch, it has already been hosted by researchers based in Australia, Brazil, Ireland, France, and the UK. This international diversity is reflected in the attendees, with one meeting attracting researchers from 16 different countries.

The feedback we have received about the Virtual Journal Club so far has been very positive with all respondents rating it as either "good" or "excellent" and all saying they would recommend it to a colleague, collaborator or peer.

You can find recordings of past meetings of the Virtual Journal Club and details of upcoming meetings on our website: **https://www.physoc.org/covid19/the-journal-of-physiologys-virtual-journal-club/**

> "In the 2 months since its launch, it has already been hosted by researchers based in Australia, Brazil, Ireland, France, and the UK"

Séverine Lamon
Deakin University, Victoria, Australia

In the midst of the COVID-19 pandemic, virtual gatherings have rapidly become our new normal. As scientists, we are naturally resilient and adaptable, and most of us have found a way to embrace some of the opportunities offered by the virtual environment. There are even things that we may never do the same way again. However, the pandemic also made us realise how much we can learn from interacting with each other. Great research ideas and collaborations often stem from informal chats at a conference or discussions around a drink at the end of a university function. Until 2020, it was unknown whether it would be possible to re-create this environment in an online setting, at least to some extent.

The Journal of Physiology's Virtual Journal Club initiative has successfully demonstrated that we may not need to travel halfway across the world to have meaningful interactions with our fellow physiologists. I was invited to host one of the first Virtual Journal Clubs in early August. I am located in Melbourne, Australia. Melbourne's time zone is not easily compatible with the rest of the world's working hours. Regardless, a week to the meeting, we had over 100 attendees from four continents registered and counting.

I enjoyed many aspects of the Virtual Journal Club: the flexible presentation format that allowed me to invite other early career researchers (ECRs) to act as panellists; the diversity of the audience who had from very little to very specific knowledge background; the interest and ease all demonstrated at question time; and the opportunity to invite my mum who had never heard me presenting before!

Another highlight was the virtual networking event that followed. A range of students, ECRs and mid-career researchers (MCRs) came together and shared their scientific stories. Young researchers from Brazil and the US reported waking up at 05.00 or 06.00 because the topic of the webinar was of interest to them. I reconnected with someone from Slovenia, who I had met at a conference years ago. I discussed future collaborations with a fellow muscle physiologist from the UK. All things I would have done at a conference, with zero carbon footprint and the opportunity to sleep in my own bed that night.

Don't get me wrong – we all hope that the world will recover from the pandemic and that we will be able to get together again soon. Some aspects of human interactions cannot be replaced. In the meantime, the Virtual Journal Club initiative led by The Physiological Society is a brilliant demonstration of the capacity of science and scientists to evolve and adapt to our changing environment. I am confident that we will be able to remember and keep some of these COVID-19-driven innovations in the future to further foster the discussions and collaborations that our field greatly needs to progress.

Bryan Saunders
University of São Paulo, Brazil

For those who work in physiology, The Physiological Society is a reference in the area and *The Journal of Physiology* is a holy grail where most aspire to publish their findings. I was more than delighted then, when The Physiological Society invited me to host a session for *The Journal of Physiology*'s new Virtual Journal Club scheme.

https://doi.org/10.36866/pn.120.14

It is quickly becoming a cliché but these virtual web meetings, be it a full conference, webinar, group meeting with students, undergraduate lecture, or journal club meeting, have rapidly become the "new normal". However, for the most part, it is envisaged that these events will return to their normal format once the worst of the pandemic is over and local and international travel is no longer limited. However, *The Journal of Physiology*'s Virtual Journal Club initiative is one that could (and should!) be here to stay.

The open format of the Virtual Journal Club session was refreshing, with The Physiological Society giving the host a flexible reign over the proceedings, which led to several unique sessions. I decided it might be interesting to provide an overview of my reasons for selecting the article to be discussed, before handing over to Rasmus Jensen, the lead author, to present and highlight the key points from his article. The clarity with which Rasmus presented his group's data allowed me to discover new concepts and identify new avenues of research, which I otherwise might not have had without this Virtual Journal Club session. Much can be overlooked as we race through superficial readings of dozens of new articles simply trying to keep pace with the literature, but these Journal Club meetings provide the perfect opportunity to dig a little deeper. *The Journal of Physiology* editor Bettina Mittendorfer also provided some excellent insight into which aspects of the work rendered it of sufficient standard to be accepted in *The Journal*. Again, for those of us who dream of publishing our work in these top-level journals, this kind of information was gold.

The opt-in networking session that followed the more structured Journal Club format was a breath of fresh air, which is welcome for many during these stifling times with so many still cooped up indoors. Like any conversation, it requires input from all those involved but the few who stayed seemed keen and willing to talk science in a far more informal setting. It felt like a post-conference session down the pub, albeit without the alcohol and karaoke, but maybe that's not such a bad thing.

I have thoroughly enjoyed *The Journal of Physiology*'s new Virtual Journal Club scheme and have attended several sessions aside from hosting my own.

You can watch all the sessions of the Virtual Journal Club at **physoc.org/jpjournalclub**

Variability: How to **Deal** with it, **Interpret** it, and **Learn** from it

#Variability2020

Meeting notes

Variability: How to Deal with It, Interpret It, and Learn from It

5 – 6 October 2020
Held online

Rodrigo Fernandez-Gonzalo

Karolinska Institutet, Sweden

In October 2020, The Physiological Society organised, in collaboration with the European Space Agency and sponsored by the Energy Institute, a virtual symposium about individual variability. The event was divided into several themes including individual response to exercise and training, space physiology, and temperature regulation on day one, and clinical and industry settings on day two, to conclude with a specific section about how to deal with individual variability from a statistical perspective.

Physiologists certainly acknowledge that there is variability in the response to an intervention. Yet, not enough attention has been paid to how to approach this issue methodologically, which has led to erroneous claims about individual responsiveness to specific interventions. This is why some of us in the field of physiology were so eager to take part in this symposium. The interest generated through the event exceeded the expectations of many participants and the organisers.

During the different presentations, we could enjoy a wide range of examples on how to address individual variability. These presentations highlighted the pros and cons of different approaches, and the challenges that researchers face. During day one, it became obvious that the work to analyse the individual variability in response to a certain intervention should start during the study design with, for example, the need for a control group or the use of cross-over designs with a control intervention.

On day two, the talk by Lindsay Edwards describing how researchers try to purposely increase variability in different systems biology models to study natural diversity, broke some stereotypes about variability with a clear take-home message: scientists should embrace, rather than avoid, individual variability. After all the talks, some questions remained unanswered, but they were elegantly addressed by the two expert physiology statisticians presenting at the end of day two, Alan M Batterham and Greg Atkinson.

The networking sessions at the end of each day deserve special attention. It was a real pleasure and a good learning experience to discuss specific issues among the attendees, including at least one or two of the speakers in each group. During these sessions, it was clear that there is a need for events like this one, where researchers could get together and, with the help of statisticians, design and analyse their studies using the correct tools to shed light on the variability of the individual response to an intervention.

All in all, I personally enjoyed the workshop, and I look forward to the second edition next year, a feeling that I am sure is shared among the majority of the attendees and speakers. I would like to finish this short reflection by thanking Michael Tipton and Igor Mekjavic, the organisers of the workshop, for their great work. See you at #Variability2021!

https://doi.org/10.36866/pn.120.15

Meeting notes

Physiology of Obesity: Lessons learned from a webinar series

Summer and autumn of 2020
Held online

Jo Edward Lewis

University of Cambridge, UK

Peter Aldiss

University of Copenhagen, Denmark

Peter Aldiss (L) and Jo Edward Lewis (R)

Back in July of this year, we were delighted to chair our first webinar, Circadian Rhythm in Skeletal Muscle: When to Eat and Exercise, as part of the Physiology of Obesity: From Mechanisms to Medicine series, hosted by The Physiological Society.

The webinar series looked to explore the molecular, cellular and neural mechanisms underlying obesity, as well as behavioural aspects, integrating existing knowledge to drive future discovery. It followed successful symposia led by early career researchers (ECRs) at the European Congress on Obesity (in 2018 and 2019), and Experimental Biology (in 2019), cumulating in a 1-day satellite, called Physiology of Obesity and Diabetes (organised together with Lora Heisler, University of Aberdeen, UK and Dan Brayson, University College London, UK), at Physiology 2019.

Our aim throughout has been to run events "for ECRs by ECRs"; invited speakers not only showcased their research but also their career progression, and we aimed to connect the next generation of leaders in the field of obesity research.

Furthermore, ECRs are likely to be disproportionally affected by COVID-19 as they are at a critical juncture in their career; the ability to generate data and publish findings has been hampered, while pressure has not, and this is compounded by short-term contracts. In addition, many institutions have delayed or frozen recruitment, and cancelled fellowships.

In addition, conference organisers and societies have postponed meetings at an unprecedented scale. Whilst we obviously support those decisions, conferences are opportunities to gain recognition for and gather feedback on data, as well as establishing a network of collaborators around the world. This series aimed to be a step towards negating some of these negative impacts.

Here are seven lessons we learned while organising these webinars:

- **The hard work started back in May, 3 months before the first webinar**
  Identifying ECRs at the forefront of obesity research, persuading them to partake during a global pandemic, whilst gauging interest in the series on Twitter and generating a buzz, were the major hurdles when planning a webinar series. Not limiting our focus aided immensely; however, it did mean operating outside our comfort zones, albeit from our favourite armchairs.

- **Remember the "two, perhaps one" rule**
  For every two people who register, perhaps one will attend. Do not be disheartened. Demands on time, unforeseen events, and brain-fog result in 40%-60% of those registering to attend; this is still a win.

- **Your audience is now truly international**
  Remember that running these webinars online also offers an opportunity to engage with an international audience. Attendance is no longer prohibited by registration fees, travel and subsistence. Smaller, more focused meetings can thrive in the online environment.

https://doi.org/10.36866/pn.120.16

“The webinar series looked to explore the molecular, cellular and neural mechanisms underlying obesity, as well as behavioural aspects”

- **Work on the visuals in your slides**
  An appealing slide deck is key for holding viewers’ attention and therefore disseminating research. Whilst in the conference hall, attention can be laser-like, the same is not true when individuals are dialling in via their computer. When it comes to your slides, a greater emphasis on style is required, whilst maintaining substance.
- **Engage with your audience**
  You are live (and being recorded) – so don’t forget you have an audience despite being in your living room with a bored dog looking on. Remember to ask questions and encourage feedback. Furthermore, if you are an attendee, the question and answer (Q&A) session offers you the opportunity to comment on, upvote and provide insight into others’ questions. This is invaluable. The Q&A sessions of our webinars were lively affairs, perhaps even more so than in a traditional conference.
- **Don’t leave anything to chance**
  Have a pre-meeting call to iron out any technical difficulties. Technical faults lurk in every corner, so have a back-up plan for a dodgy connection. Last-minute issues will arise, so know how to restart your router.
- **Remember to consider timezones and timing**
  With registrations and attendees from over 40 countries, consider the timing of your webinars and record them for future availability where possible. Advertised as 1-hour webinars, we kept to this (more or less) and then continued the conversation on social media, to make sure people could keep to their schedules.

Ultimately, this webinar series was fun and rewarding. And its success was entirely dependent upon the speakers and those who did the work behind the scenes. Special thanks go to those speakers, and to Caitlin Oates, Events and Marketing Officer at The Society.

Meeting notes

R Jean Banister Prize Lecture: Mind Affects Matter – Brainstem Circuits Linking Stress, Physiology, and Behaviour

17 November 2020
Held online

Marie Holt

Florida State University, US

It is an amazing honour to be chosen as the 2019 R Jean Banister Prize Lecture recipient. The previous awardees are incredible early career researchers and come from a strikingly wide range of scientific backgrounds, a testament to the broad spectrum of physiology supported and celebrated by The Society. On top of that, I am sure it would not have escaped R Jean Banister’s notice – she was a staunch champion of women’s education – that the previous recipients of this prize have all been women.

When I was 17, I did a project for school on the God Helmet – a device that purportedly elicits mystical experiences through stimulating the brain with a weak magnetic field. While the scientific validity of those studies may be questionable, my new-found passion for neuroscience was not! A decade later, I completed my PhD in Neuroscience from University College London (UCL) under the guidance of Stefan Trapp. My research at UCL revealed how a group of neurons in the brainstem, the GLP-1 neurons, control food consumption under certain physiological conditions, including stress. This was ground-breaking work and started my interest in exploring how physiology affects behaviour and vice versa.

Over 500 million people in the world live with anxiety or depression, a number which has increased dramatically during the COVID-19 pandemic. These disorders are triggered and exacerbated by continuous stress and carry with them a swarm of comorbidities. In spite of this huge societal burden, we have few effective therapies and a very limited understanding of the brain circuits involved.

At its core, stress is of course beneficial: it prepares the body for potential threats and ensures rapid return to ‘normal’ physiology. However, repeated and unrelenting stress can induce an anxiety state, characterised by behavioural inhibition, vigilance, and sympathetic arousal.

In the R Jean Banister Prize Lecture, I argue that these stress-related behavioural and physiological changes are driven by GLP-1 neurons in the lower brainstem. I present evidence that GLP-1 neurons have the ability to suppress appetite, but mainly in response to stress.

I also share our recent findings that GLP-1 neurons mediate anxiogenic effects of stressful stimuli and have the ability to increase heart rate, most likely by increasing the activity of the sympathetic nervous system. These effects – behavioural inhibition and sympathetic arousal – are the hallmarks of anxiety, supporting the idea that GLP-1 neurons play a crucial role in orchestrating the brain’s responses to stress. It is my hope that my findings, by contributing to our understanding of brain responses to stress, will ultimately help the millions of people world-wide living with anxiety disorders and their comorbidities.

“I am indebted to The Society for giving me the opportunity to share these findings with a broad audience”

I am indebted to The Society for giving me the opportunity to share these findings with a broad audience and I am determined to pay it forward through research, mentorship, and service. I read somewhere that Daphne Park, who knew Jean Banister well, said of her at her retirement ceremony, “She has absolute integrity and she is a perfectionist; she is also an optimist.”

As a scientist, these are truly characteristics to live up to and it is my hope that someone will say the same about me at my retirement party. Until then, I will continue to conduct research with the hope that my contribution will help us understand the brain just a little better.

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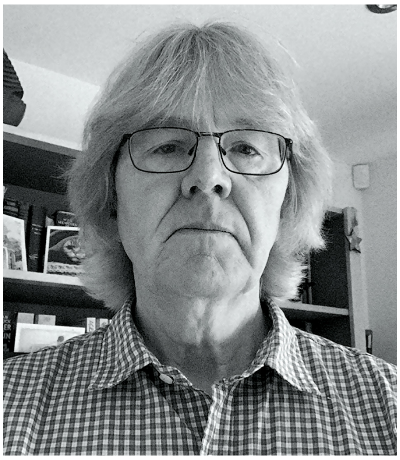
DOI: 10.36866/pn.120.18

Are you ruled by your head or your heart?

Neurogenic versus myogenic debate on the origin of the heartbeat



Mark Boyett

University of Copenhagen, Denmark

Alicia D'Souza

University of Manchester, UK

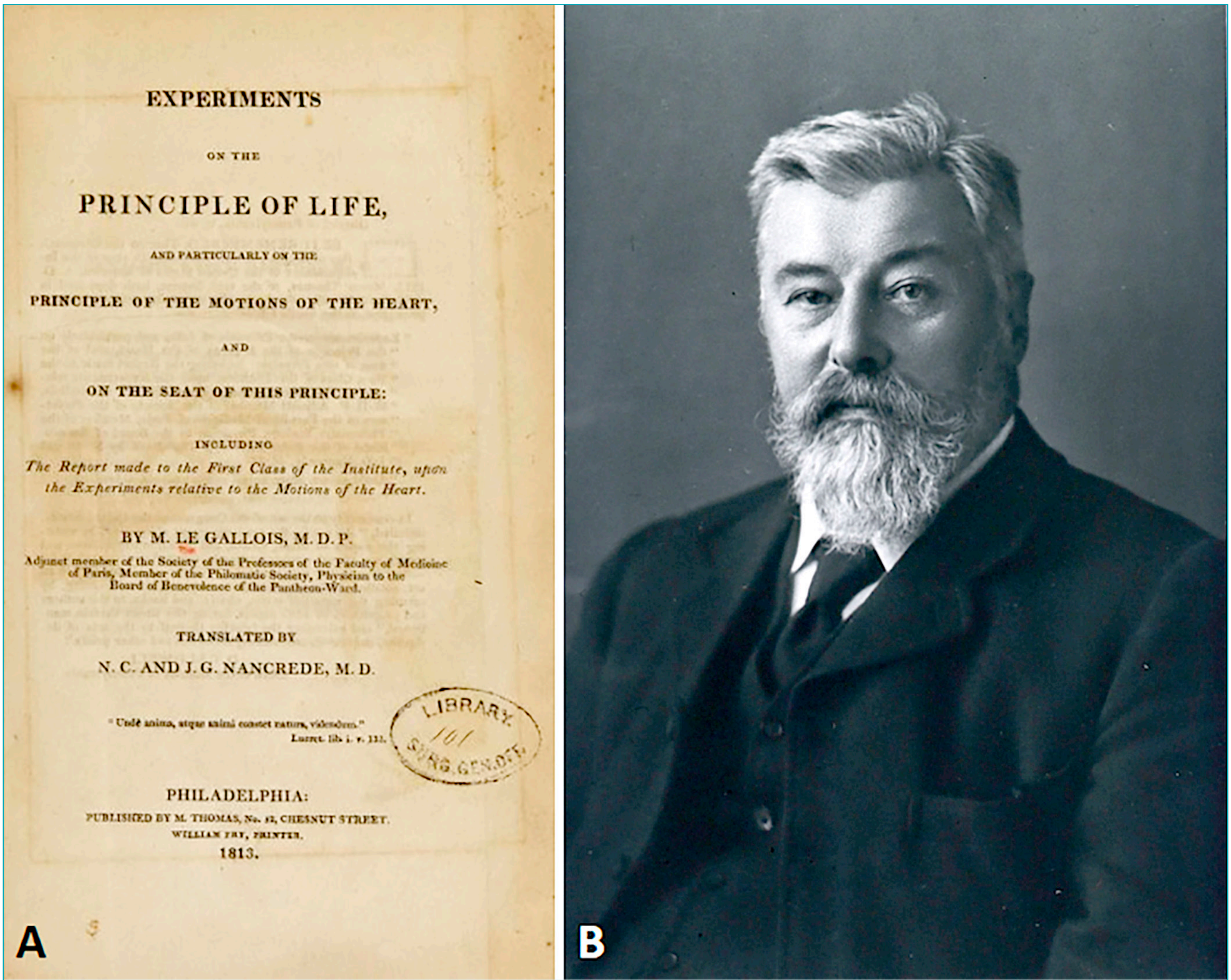
"One of the most remarkable phenomena of nature is the incessant rhythmic action of the heart" (Fye, 1987). For around 1,000 years, there was a debate about whether the heartbeat is neurogenic or myogenic in origin, i.e. whether the contraction of the heart is initiated by motor nerve activity (like that of skeletal muscle) or whether the contraction is initiated within the muscle of the heart itself. The original debate only reached a conclusion in the 19th century, but there is now a new, related neurogenic versus myogenic debate.

The original neurogenic versus myogenic debate on the origin of the heartbeat

Galen was a physician, surgeon and philosopher in the Roman Empire and, when he observed that the heart continued to beat after it had been excised, he concluded that, "The pulsative faculty of the heart has its source in its own substance" (Fye, 1987). This is the essence of the myogenic theory of the origin of the heartbeat and can be considered the original thesis. In the 19th century, the French physiologist and physician César Julien Jean Legallois observed that the mammalian heart stopped beating when the spinal cord was abruptly crushed and he concluded that the heartbeat is neurogenic in origin (the antithesis) (Legallois, 1812); Fig.1A shows the title page of the English translation of Legallois's publication. As the understanding of the autonomic nervous system grew and the intracardiac ganglia were discovered, ideas evolved and the German physiologists Eduard and Ernst Weber concluded that the sympathetic nerves acting via the intracardiac ganglia were the motor nerves of the heart – the proposed involvement of the ganglia could explain why the isolated heart carries on beating after the autonomic nerves innervating the heart are sectioned (Fye, 1987).

However, Walter Holbrook Gaskell, working in Trinity College Cambridge, went on to disprove the neurogenic theory and prove the myogenic theory of the heartbeat. In 1880 he wrote that most physiologists attributed the heartbeat to "the action of certain ganglion cells situated in the heart itself, while the cardiac muscular tissue is credited with the purely subordinate role of responding to the impulses generated in these nerve cells" (Gaskell, 1880). Gaskell's central observation was that the apex of the tortoise heart, although devoid of ganglion cells, has the ability to beat rhythmically like other parts of the heart (Gaskell, 1883). Furthermore, he showed that the conduction of the impulse through the muscle of the heart "does not depend upon the nerve trunks between sinus and ventricle." He showed that, "if the auricular muscle be carefully separated from the ventricle and along each side of the inter-auricular basal wall, so that the ventricle is connected with the sinus and auricle only by the band of tissue which contains the large nerves and coronary veins, then the sequence between auricle and ventricle is entirely lost" (Gaskell, 1882). Instead he showed that the

https://doi.org/10.36866/pn.120.18


EXPERIMENTS

ON THE

PRINCIPLE OF LIFE,

AND PARTICULARLY ON THE

PRINCIPLE OF THE MOTIONS OF THE HEART,

AND

ON THE SEAT OF THIS PRINCIPLE:

INCLUDING

The Report made to the First Class of the Institute, upon the Experiments relative to the Motions of the Heart.

BY M. LE GALLOIS, M. D. P.

Adjunct member of the Society of the Professors of the Faculty of Medicine of Paris, Member of the Philomatic Society, Physician to the Board of Benevolence of the Pantheon-Ward.

TRANSLATED BY

N. C. AND J. G. NANCREDE, M. D.

"Undè anima, atque animi constet natura, videndum."
Lucret. lib. i. v. 132.

PHILADELPHIA:

PUBLISHED BY M. THOMAS, No. [illegible], CHESNUT STREET.
WILLIAM FRY, PRINTER.
1813.

Figure 1. **A.** Title page of the publication from César Julien Jean Legallois that first established the neurogenic theory of the origin of the heartbeat. **B.** Walter Holbrook Gaskell, who finally proved the myogenic origin of the heartbeat.

impulse is able to conduct through the muscle of the heart (Gaskell, 1882).

Today we know that cardiomyocytes are electrically and mechanically coupled together, allowing the impulse or action potential to propagate from cell to cell throughout the heart such that the heart functionally behaves like a single cell or syncytium. In this way, the original neurogenic versus myogenic debate was settled in the 19th century. Many more scientists were involved in the debate than the ones mentioned here, and an excellent account of the debate and its eventual resolution has been written by Wallace Bruce Fye (1987) and it is from this account that most of the details given here have been taken.

The Professor of Genetics at Harvard Medical School, David Reich, recently wrote, "An important strand in continental European philosophy beginning in the eighteenth century was that the march of ideas proceeds in a "dialectic": a clash of opposed perspectives that leads to a synthesis. The dialectic begins with a "thesis", followed by an "antithesis". Progress is achieved through a resolution, or "synthesis," which transcends the two-sided debate that engendered it" (Reich, 2018). The original neurogenic versus myogenic debate fits this pattern. What about the "synthesis" following the debate? Of course, we now know that the heartbeat is initiated by pacemaker activity in the heart itself and the sinus node is the heart's natural pacemaker in keeping with the myogenic theory. However, we now also know that the heartbeat of some lower invertebrates such as decapod crustaceans and hirudinid leeches is neurogenic (Calabrese *et al.*, 2016) and of course we know that in myogenic hearts the rate of the heartbeat initiated in the sinus node is regulated by the autonomic nervous system.

The 21st century debate

There is now a new dialectic, a new neurogenic versus myogenic debate, which has parallels with the 19th century debate. Of course, we all know that the heart rate is controlled by the autonomic nervous system – if we begin to run, the heart rate immediately increases and if we immerse our face in cold water the heart rate immediately decreases (the "diving reflex"). However, the heart rate varies *chronically* in other circumstances and this is the focus of the debate.

It is well known that athletes have a low resting heart rate – elite cyclists have been documented to have a resting heart rate of around 30 beats/min (D'Souza *et al.*, 2015). For many decades in the 20th and 21st centuries, this has been commonly attributed to the autonomic nervous system and, in particular, to high vagal tone and this view is still widespread. An advocate of this neurogenic theory was the eminent British physiologist John H Coote (Al-Ani *et al.*, 1996). It is also well known that the resting heart rate varies in a circadian manner from day to night and the resting heart rate is low

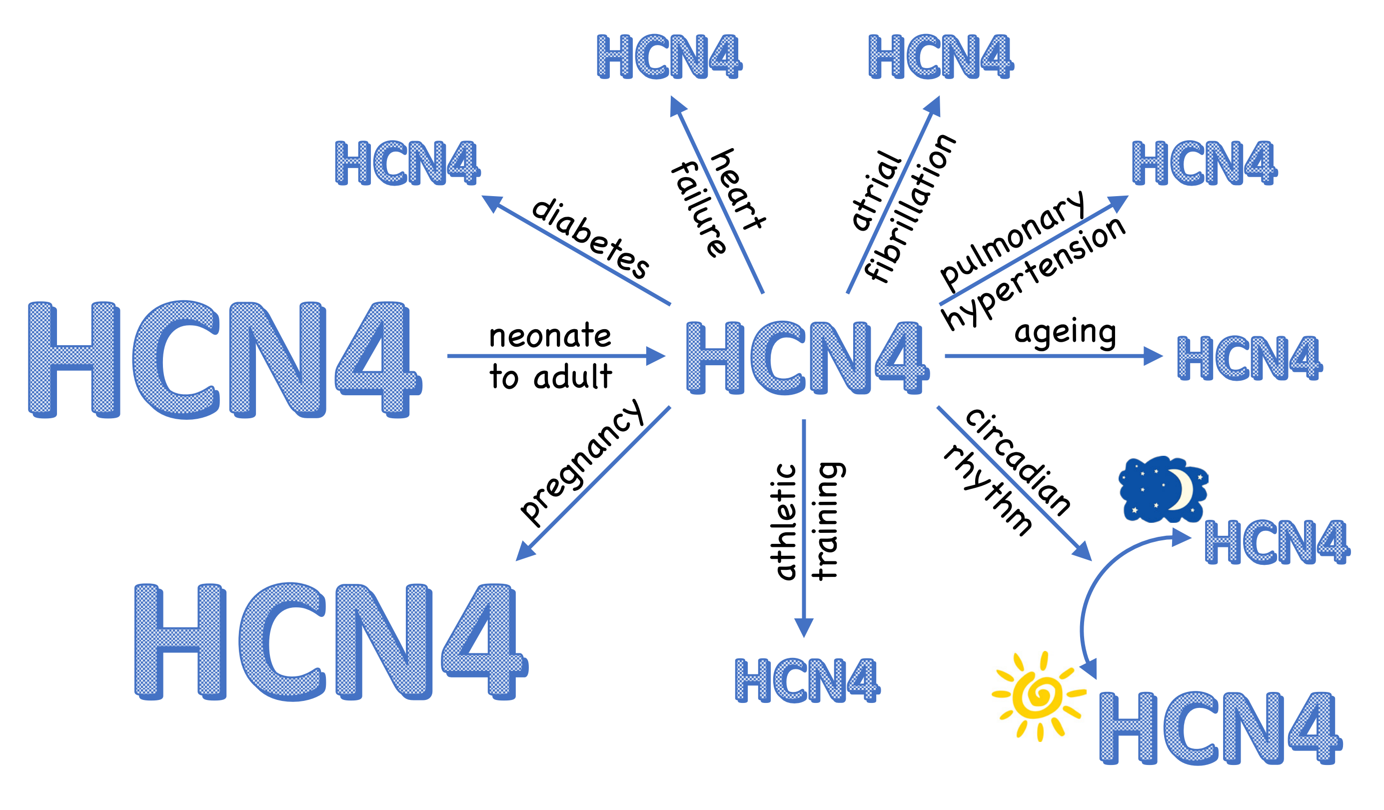


Figure 2. Control of pacemaking according to the myogenic theory. Evidence shows that in the sinus node HCN4 is under transcriptional control and expression of HCN4 varies under many different conditions. Here, the size of the HCN4 text is a qualitative indicator of the expression level. The schematic diagram shows HCN4 expression varying in different physiological states (during neonatal development, during pregnancy, and following athletic training) as well as disease states. Recent evidence also shows expression of HCN4 varying between day and night.

at night. This is especially true in athletes whose heart rate is already low, and athletes have "nocturnal pauses" at night – the longest nocturnal pause documented in the literature is 15 seconds in a veteran athlete (Northcote *et al.*, 1989). 15 seconds is a long time to wait for your next heartbeat! The circadian rhythm in the resting heart rate is again attributed to the autonomic nervous system and, in particular, to high vagal tone at night. As an example, a recent advocate of the neurogenic theory as applied to the circadian rhythm in the resting heart rate is the chronobiologist David Bechtold (West *et al.*, 2017).

The neurogenic theory in the 21st century debate can therefore be considered the "thesis" in the current dialectic. Over about a decade, we have developed the "antithesis", a voyage we have found fraught with controversy. Our involvement began with an investigation of heart rate variability, which is widely used as a surrogate measure of autonomic nerve activity (sympathetic and parasympathetic) to the heart – on the day of writing this article, a PubMed search using the term 'heart rate variability' returned 26,075 papers demonstrating the popularity of the technique. We showed that heart rate variability is primarily affected by the heart rate and to conclude anything about a factor independent of heart rate is difficult or impossible (Monfredi *et al.*, 2014).

We debated the use of heart rate variability as a measure of autonomic tone in the pages of *The Journal of Physiology* (Boyett *et al.*, 2019; Malik *et al.*, 2019). Heart rate variability measurement has been the principal technique used to support the neurogenic theory of both the low resting heart rate in athletes and the circadian rhythm in the resting heart rate (Aubert *et al.*, 2003; Sammito *et al.*, 2016). If heart rate variability cannot be used as a measure of autonomic tone to the heart, we have to take a fresh look at the mechanisms responsible for the heart rate in athletes and the circadian rhythm in the resting heart rate. However, a second line of evidence for the neurogenic theory comes from the effects of pharmacological autonomic blockade, but this too is unconvincing because whilst some authors report that the change in heart rate is abolished (consistent with the neurogenic theory), others report it is not (Boyett *et al.*, 2013; Black *et al.*, 2019)!

Therefore, it is still necessary to take a fresh look at athletes and the circadian rhythm. We first investigated the resting bradycardia (decrease in resting heart rate) in exercise-trained rodents (D'Souza *et al.*, 2014; D'Souza *et al.*, 2017). We showed that there is a remodelling of various ion channels in the sinus node following exercise training. In particular, there is a downregulation of the important pacemaker HCN (hyperpolarisation-activated cyclic nucleotide-gated) channels, or humorously named "funny" channels, as well as the corresponding ionic ("funny") current. By blocking the HCN channels using ivabradine we were able to abolish the difference in resting heart rate between exercise-trained and sedentary mice and we obtained data consistent with this from human athletes. The neurogenic theory of the resting bradycardia in athletes as put forward by John Coote and the myogenic theory as put forward by us was again debated in the pages of *The Journal of Physiology* (Coote & White, 2015; D'Souza *et al.*, 2015). Next, we have taken a fresh look at the circadian rhythm in heart rate (unpublished data). In the mouse, we have shown that there is an intrinsic circadian rhythm in sinus node pacemaking, for example as observed in the isolated sinus node. Using RNA-seq, we have investigated the transcriptome of the sinus node over 24 hours and of 16,387 transcripts we observed a significant circadian rhythm in 44% of them

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“By blocking the HCN channels using ivabradine we were able to abolish the difference in resting heart rate between exercise-trained and sedentary mice and we obtained data consistent with this from human athletes”

(7,134 transcripts). The circadian rhythm is all pervasive and was observed in all cellular systems we looked at. For example, there is a functioning circadian clock as well as a prominent circadian rhythm in the pacemaker HCN channels, and once again by blocking the HCN channels using ivabradine we were able to abolish the difference in resting heart rate between day and night (D'Souza *et al.* 2020).

The neurogenic theory only addresses the resting bradycardia in athletes and the circadian rhythm in the resting heart rate and it does not address chronic changes in heart rate in other conditions. Such changes are widespread: the heart rate of the newborn is high and it drops as we approach adulthood. As we age, there is a decrease in the intrinsic heart rate set by the sinus node (but not the normal heart rate set by the interaction of the sinus node and autonomic nervous system). There is a 25% increase in the heart rate in the pregnant female. There is a decrease in the heart rate (or intrinsic heart rate at least) in various disease states: heart failure, pulmonary hypertension, diabetes and atrial fibrillation. In all of these cases, there are appropriate changes in the expression of HCN channels (and/or the density of the funny current) that can explain the change in heart rate (Fig. 2). Therefore, the changes in funny current and/or HCN channels in athletes and during the circadian rhythm are not unique.

It is too early for there to be a resolution of the 21st century neurogenic versus myogenic debate concerning the heartbeat. Of course, it is also too early for there to be a “synthesis”. We privately discuss whether the circadian rhythm in the resting heart rate involves the autonomic nervous system as well as intrinsic mechanisms in the sinus node. However, the role of the autonomic nervous system may be different from the traditional one and the autonomic nervous system may be controlling gene transcription – there is early evidence for this line of reasoning (Tong *et al.*, 2013). Although our questioning of the long-standing view of the role of the autonomic nervous system in the resting bradycardia of athletes and the circadian rhythm in the resting heart rate has proved to be very unpopular (as we know from vehement opposition during peer review!), we realise “the march of ideas proceeds in a ‘dialectic’” and are therefore encouraged in persisting in our efforts!

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Seventy Years On

Charles Lovatt Evans retired at University College London

Otto Hutter

Emeritus Regius Professor,
University of Glasgow, UK

With sadness, we note that Otto Hutter died very soon after writing this article. He will be remembered with an obituary in the next issue of the magazine.

Note: The digital PDF of this article has been modified from the print version. Further details to follow in next print issue.

It was at University College London that Otto Hutter started his own long and distinguished academic career, studying in the Physiology Department, then headed by Charles Lovatt Evans. In 1949, Otto was able to attend the retirement festivities for Lovatt Evans described in this charming article. The signatures on Otto's copy of the dinner menu, illustrated here, feature many Physiological Society greats.

The retirement in June 1949 of Sir Charles Lovatt Evans (1884 – 1968) from the Jodrell Chair of Physiology at University College London was the end of an era. At the dinner in Sir Charles' honour, the menu cards were circulated to be signed by the guests, who then gathered for a group photograph at the physiology building. As Sharpey Scholar, I attended these festivities; and I have kept the signed menu card and the group photograph ever since, for I count Lovatt Evans as one of my benefactors.

On leaving school in 1942, I was a laboratory assistant at the Wellcome Physiological Research Laboratories in Beckenham, Kent. At first, I was engaged in the biological assay of insulin, then essential work in wartime as it was in peace. Encouraged by the senior staff, university lecturers who had been recruited for war work, I began to study physiology part-time. The 1941 edition of Starling's *Principles of Physiology*, kept up to date by Lovatt Evans, became my principal text.

By the end of the war, I had completed the first 2 years of a BSc course at the then Chelsea Polytechnic. Our lecturer there was a youthful R A Gregory, who came up twice a week from Leatherhead, to where the University College London (UCL) Medical School had been evacuated. He delivered memorable lectures, especially those on gastric secretion, having just returned from B P Babkin's laboratory in Montreal.

To fulfil my ambition to become a physiologist, I then needed to take a BSc Honours course; but such courses had been suspended during the war. So, after Victory over Japan (VJ) Day in 1945, I wrote to Sir Charles to ask when the honours course at UCL would be reinstated and to plead for admission. Graciously Sir Charles granted me an interview.

I arrived early one Monday morning in October 1945 and waited in the corridor joining the physiology and pharmacology staircases for Sir Charles to arrive from Porton Down [the Government research establishment]. The Admiralty then still occupied the rest of the Physiology Department. Only the rooms along that corridor had been released. After a while, a gentleman attired with a beige mackintosh topped with a Homburg hat came up the pharmacology staircase. He ushered me into his temporary office, put me at ease and kindly heard me out. Throughout he treated me, a mere youngster laboratory technician, with, to me, astonishing courtesy, as if I were a colleague. Much later, I learned that Sir Charles himself had an unconventional education and that he also sat for a London university degree in physiology as an external student.

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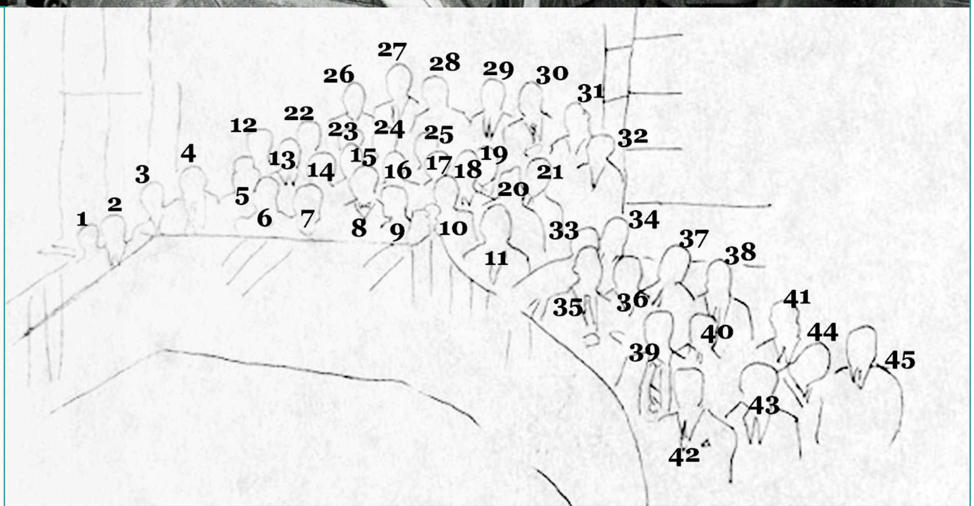
University College London, Steps of the Physiology building 1 July 1949.



In those days, the second MB (Bachelor of Medicine) course lasted five terms, and the intercalated BSc course four terms. So the first post-war BSc course did not start until April 1946. It was a small class consisting of two medical students of distinction, namely David Fryer, who sadly was later killed in an accident while serving in the RAF, June Hill, who became Mrs Douglas Wilkie, and me. Our teachers were Leonard Bayliss, Bernard Katz, F G Young for biochemistry and G P Wells for comparative physiology. But mostly we were guided to read and learn by ourselves. Under (Chief Technician) Charlie Evans' watchful eye, we worked our way through Sherrington's *Practical Physiology* (*Mammalian Physiology: A Course Of Practical Exercises*, 1919). An amplifier built by Bayliss in a National Milk tin and an oscilloscope purchased from an army surplus store allowed us to record action potentials.

A university studentship fell to me on the basis of the examination results. And as the first post-war science student with any extra laboratory experience, Sir Charles kept me back as demonstrator. After a year, he appointed me Sharpey Scholar, a post he himself held under E H Starling. As to how to start research, Sir Charles advised me first to repeat some interesting, published work: I was sure to find some discrepancy, requiring further investigation.

The Wellcome Laboratories in Beckenham, besides their research function, were also a production site: stables in the extensive grounds housed old army horses used for

Key *(Bold = signatures identified from signed menu)*

1. **GF Bonsard**
2. **Olof Lippold** (1923 – 2016)
3. **Lawrence E Mount**
4. LE? Cowan
5. *Unknown*
6. *Unknown*
7. **Marion Grace Palmer Eggleton** (1905 – 1970)
8. **Sir Charles Arthur Lovatt Evans** FRS (1884 – 1968)
9. Lady Laura Lovatt Evans
10. **Ruth Verney?**
11. **Katherine H Coward** (1885 – 1978)
12. ? Mendez
13. Detlev Wulf Bronk (1897 – 1975)
14. **Archibald Vivian Hill** CH FRS (1886 – 1977)
15. **Leonard Ernest Bayliss** FRSE (1900 – 1964)
16. **James Yule Bogue**
17. *Unknown*
18. **Michael De Burgh Daly** (1922 – 2002)
19. *Unknown*
20. **Sir Alan Sterling Parkes** FRS (1900 – 1990)
21. **Alfred Schweitzer** (d 1952)
22. **Sir Jack Cecil Drummond** FRS (1891 – 1952)
23. Margaret Kerney?
24. **Sir Frank George Young** FRS (1908 – 1988)
25. **Robert James Brocklehurst** (1899 – 1995)
26. *Unknown*
27. *Unknown*
28. *Unknown*
29. Roderick Alfred Gregory CBE FRS (1913 – 1990)
30. *Unknown*
31. **Sir John Henry Gaddum** FRS FRSE (1900 – 1965)
32. David Henry Smyth FRS (1908 – 1979)
33. **Heinz Otto Schild** (1908 – 1984)
34. Hermann Karl Felix (Hugh) Blaschko FRS (1900 – 1993)
35. **Otto Hutter** (1924 – 2020)
36. **Ernest Basil Verney** (1894 – 1967)
37. **Frank Winton** (1894 – 1985)
38. *Unknown*
39. **Robert Douglas M Harkness** (d 2006)
40. *Unknown*
41. *Unknown*
42. **Charlie Evans**
43. **Harold E Lewis** (d 1972)
44. *Unknown*
45. Hugh Davson (1909 – 1996)

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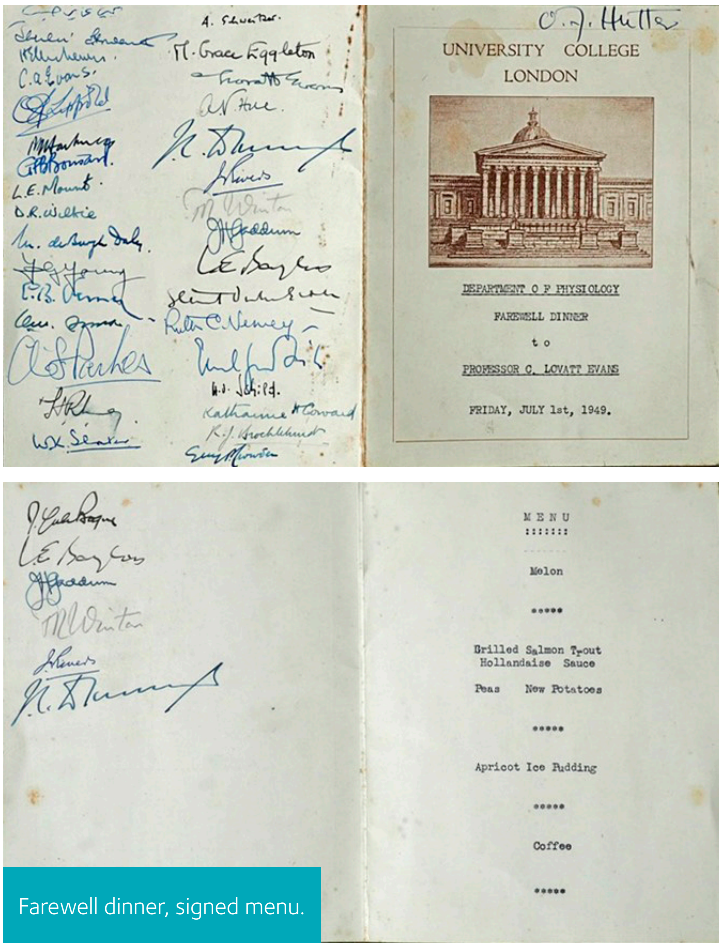
the production of tetanus anti-toxin. This had aroused my curiosity about the action of tetanus toxin. In particular, a paper by A M Harvey (1939) caught my attention. In it he claimed that tetanus toxin had a peripheral excitatory action that could be revealed by suitably timed injection of the toxin into a muscle before its motor nerve was severed.

If this were so, I thought, it should be possible to record spontaneous end-plate potentials from an excised muscle showing tetanus of peripheral origin. So bearing in mind Sir Charles' advice, I started to repeat A M Harvey's procedure. But try as I might, I could not repeat his observations. In my hands, a toxin-injected muscle never displayed tetanus once the motor nerve was cut (Hutter, 1950).

In the course of these experiments, a cat nipped the forefinger of my left hand. Weeks later a tiny irritating blister appeared, then my trochlear gland became enlarged and then that adenopathy engulfed also my axillary gland. I was eventually cured by massive doses of potassium iodide, prescribed by Professor Max Rosenheim, later President of the Royal College of Physicians. I was still under treatment at UCH when I slipped out to join the tribute to Sir Charles.



Farewell dinner, signed menu.

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Putting Charles Lovatt Evans into context

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Many readers of Otto's delightful piece will, regrettably, hardly know the name of Lovatt Evans and little of his work. His current absence from Wikipedia hardly helps modern readers (a prompt perhaps to any willing Wikipedia writer?).

Sir Charles Arthur Lovatt Evans was born in 1884 in Birmingham. His unusual education and early career was gained in part as a technician and then as a lecturer at two colleges in Birmingham. Offered a scholarship by Ernest Starling, he worked at UCL from 1910. Medical training followed and then war work, together with Starling, on the challenges posed by gas warfare. He investigated the effects of arsine, phosgene, hydrocyanic acid, and mustard gas, as well as respirator efficacy. His rise in physiology was meteoric. In 1918, he was made professor at the University of Leeds, but 1 year later moved to London at the National Institute for Medical Research, Hampstead; from there he went to the Chair of Physiology at St Bartholomew's Hospital (1922) and last to the Jodrell Chair of Physiology in UCL (1926).

His predecessors, Starling and AV Hill, were still at UCL and he collaborated with both. With Starling, he investigated the metabolism of the heart and lungs and the role of lactic acid in muscle metabolism. He published on cardiac, voluntary, and smooth muscle in relation to lactic acid and heat production. This work developed the "heart oxygenator" preparation, insights that laid the foundations for open-chest surgery. After retirement in 1949 he researched anticholinesterases, analysing how they affected respiration by bronchoconstriction, neuromuscular block, and central respiratory failure. He showed that sweating in the horse is controlled by circulating adrenaline rather than by nerves. His last published paper was on the toxicity of hydrogen sulphide, work done at the age of 83.

Lovatt Evans was among the first physiologists to recognise the importance of the then new subject of biochemistry, being a founder member of the Biochemical Society. Another major contribution was in editing and writing highly respected and influential textbooks (e.g. 14 editions 1930–58 of Starling's *Principles of Human Physiology*, and authoring 4 editions of *Recent Advances in Physiology*). He was universally regarded as an inspirational leader with the prized ability to help people find their own way largely independently. He made major managerial contributions to the work of the Medical Research Council and in re-establishing UCL after World War 2. Knighted in 1951, Lovatt Evans died in 1968.

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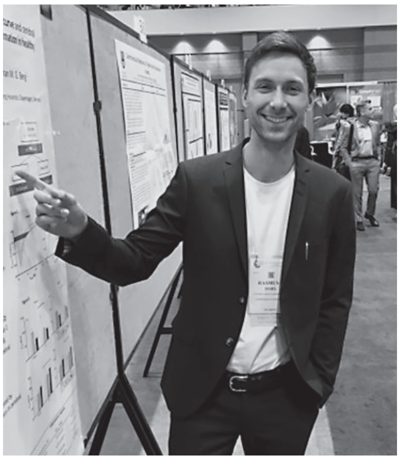
Trigonometry of the ECG

A formula for the mean electrical axis of the heart



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Electrocardiography is a method used to measure the electrical activity of the heart in order to detect cardiac disease. The cardiac conduction system synchronises the pumping action of the heart, and during cardiac contraction a spike in the electrical current represented by the QRS complex on the electrocardiogram is observed due to depolarisation of cardiomyocytes. The direction of this net current is termed the "mean electrical axis of the heart", which is a mandatory topic in almost any undergraduate course on cardiac electrophysiology, and which may be used clinically to detect hypertrophy, cardiac conduction disturbances, and the origin of arrhythmias.

As with many other physiological concepts that are strictly mathematical, the mean electrical axis of the heart is a somewhat divisive topic among undergraduate students. Some find it intuitive while others do not. Thus, when teaching this topic, a firm outline of the underlying trigonometric principles may either be an eye-opener ("ah, now I get it, it's all just about triangles!") or cause even more confusion ("you have completely lost me now – what do triangles have to do with anything?"). In any event, the mean electrical axis of the heart is indeed all about triangles, and in the present paper, we use the underlying trigonometric principles to derive a general equation that permits the determination of the mean electrical axis of the heart from any two limb leads in a quick and easy manner. Although this approach will not be suitable for all students, it may unveil the wonders of cardiac electrophysiology to those who find mathematics intuitive.

What is "the mean electrical axis of the heart"?

The concept of a mean electrical axis of the QRS complex in the ECG was first introduced by Willem Einthoven in 1913 (Einthoven *et al.*, 1913), and to this day it remains a clinically important aspect of ECG diagnostics. It represents the average direction of the ventricular depolarisation wave in the frontal plane, that is, the total vector of all the depolarisations that occur throughout the ventricles during the cardiac cycle. It is represented graphically in a triaxial system, the so-called "circle of axes" (Fig. 1).

According to the concept of a mean electrical axis of the heart, the centre of the heart is assumed to be located at the centre of the "circle of axes", the triangles formed by the bipolar (I, II, and III) and augmented unipolar (aVL, aVR, and aVF) limb leads are assumed to be equilateral, and the thorax is assumed to be a homogeneous conductor. In the "circle of axes" the equilateral triangle of the bipolar leads is visualised by the vector sum of lead

“Good teaching is all about knowing your audience, and a strictly mathematically based approach like this one is probably not suitable for most physiology lecture settings”

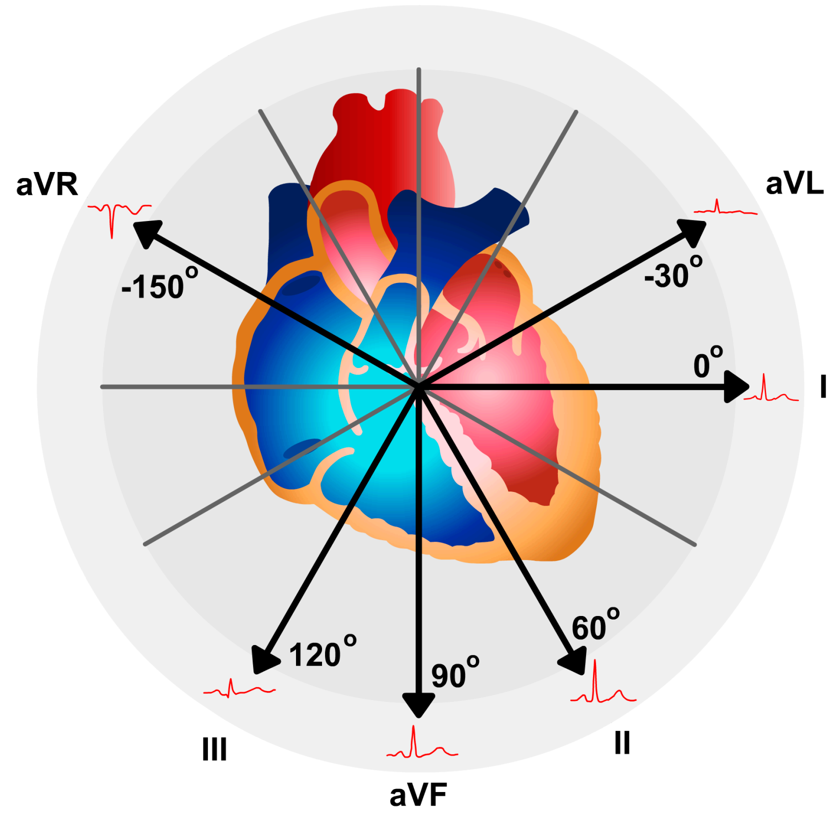

Figure 1. **The circle of axes.** The electrical axis of the heart may be visualised on a Cartesian coordinate system in the frontal plane. A horizontal line from the centre towards the left arm is defined as 0˚, and any rotation clockwise represents a positive angle, while a counter-clockwise rotation represents a negative angle. The bipolar (I, II, III) and augmented unipolar (aVF, aVR, aVL) limb leads are shown as position vectors with a well-defined angle to the *x*-axis.

I and lead III, which is equal to lead II. The equilateral triangle of the augmented unipolar leads is constructed by connecting the head of vectors in the “circle of axes” (Fig. 1).

Obviously, none of these assumptions are entirely valid *in vivo*, but the mean electrical axis nonetheless provides information on the state of intraventricular conduction, as well as left vs. right ventricular muscle mass. The electrical axis of the heart is normally between -30˚ and +90˚, and may vary by up to 35˚ during normal breathing due to the associated movements of the heart (Moody *et al.*, 1985). An electrical axis between -30˚ and -90˚ is coined left axis deviation, while right axis deviation is defined as an electrical axis between +90˚ and +180˚. During normal sinus rhythm without bundle-branch block, left axis deviation may notably be caused by left anterior fascicular block, left ventricular hypertrophy and/or fibrosis, while left posterior fascicular block and right ventricular hypertrophy may cause right axis deviation. Fascicular blocks occur when electrical activity of either the anterior or posterior fascicle of the left bundle branch is delayed or blocked. Furthermore, assessment of the mean electrical axis may be an aid for identifying the origin of some arrhythmias, notably so-called broad complex tachycardias.

The “circle of axes” vs. the “Novosel formula”

The abovementioned “circle of axes” is typically used to graphically derive the mean electrical axis of the heart by plotting the net voltage of the QRS complex in two bipolar limb leads (Carter, 1919). A line that is perpendicular to the respective lead axis is drawn through each mark, and the centre of the circle of axes (tail of vector) is connected to the intersection point between these two lines (head of vector) to form the cardiac vector. The mean electrical axis is then measured as the angle of this position vector (Fig. 2).

The underlying trigonometric principles also permit an alternative equation-based approach, so that the mean electrical axis may be determined from any two limb leads, including both the bipolar and augmented unipolar limb leads. The derivation of a general equation for the mean electrical axis is available as an online supplement to this article. Several specific formulas may be derived from this, and the combination of lead I (V_I) and aVF (V_{aVF}) yields the following formula:

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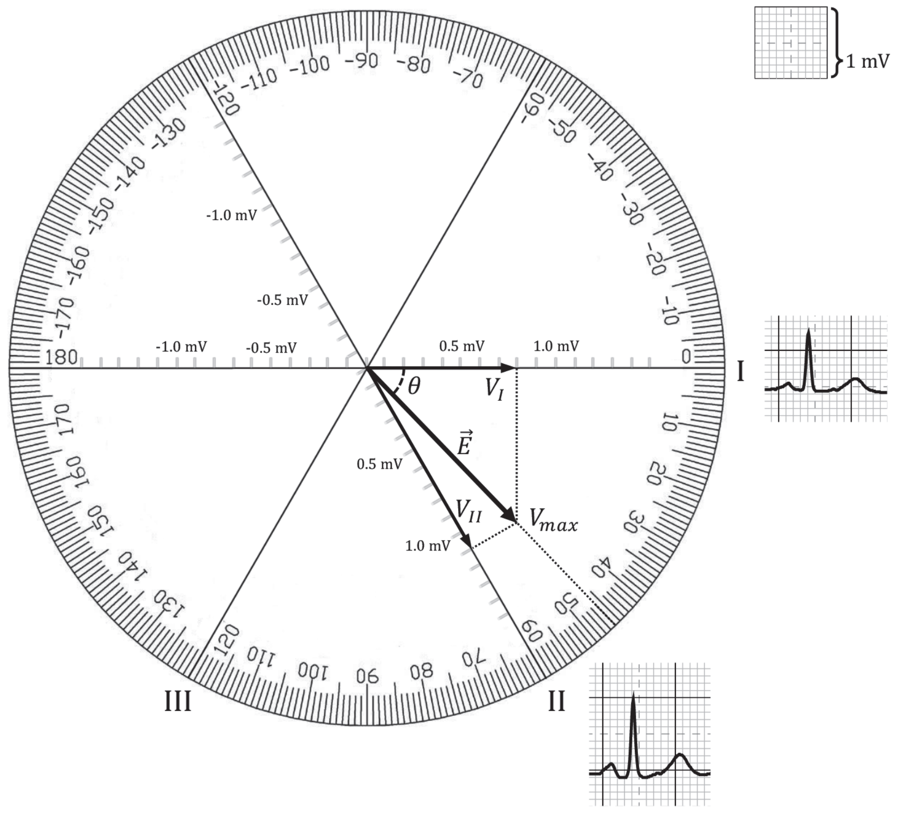

Figure 2. **The graphical method for determining the mean electrical axis of the heart**. The mean electrical axis of the heart, θ, can be determined graphically using the "circle of axes". The cardiac vector, $\vec{E}$, is reconstructed from the net QRS voltage in two bipolar limb leads, here leads I and II. The length of the projection of the cardiac vector onto leads I and II equals the net QRS voltage. Here, the net QRS voltage is 0.8 mV in lead I and 1.2 mV in lead II, so that θ = 49˚. This ECG with normal axis is shown in Fig. 3.

$$\theta = \arctan\left(\frac{2 \cdot V_{aVF}}{\sqrt{3} \cdot V_I}\right)$$

where θ is the mean electrical axis of the heart. Incidentally, this specific equation has previously been derived on an entirely different basis (Novosel *et al.*, 1999), and we therefore designate it the 'Novosel formula'. In Fig. 3 this formula is used to derive the mean eletrical axis in three ECGs with normal axis, left axis deviation and right axis deviation.

Conclusion

Good teaching is all about knowing your audience, and a strictly mathematically based approach like this one is probably not suitable for most physiology lecture settings. Outside lectures, it may nonetheless be used as an extracurricular tool to unveil the wonders of cardiac electrophysiology to interested students that find mathematics intuitive. Furthermore, the 'Novosel formula' presented here provides a much easier and quicker means for determining the mean electrical axis of the heart than the "circle of axes" and may thus be of use in the clinical setting.

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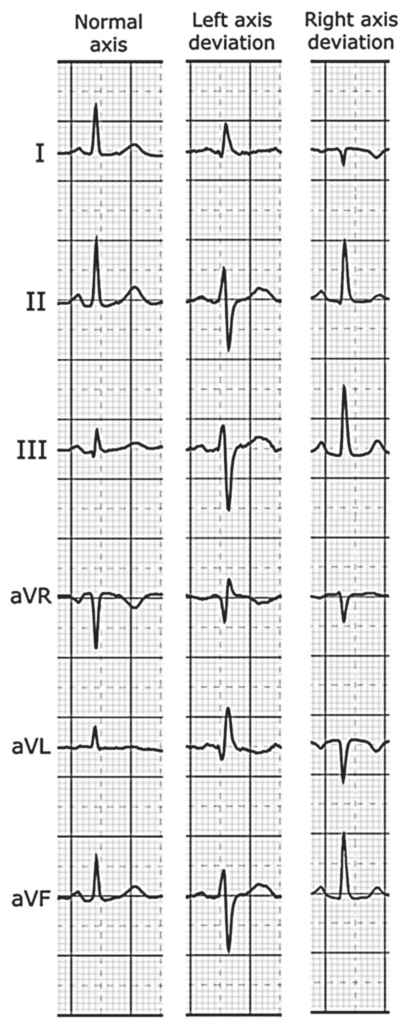

Figure 3. **The mathematical method for determining the mean electrical axis of the heart.** Examples of ECGs with normal electrical axis, left axis deviation, and right axis deviation. The mean electrical axis can be calculated by the Novosel formula using the net QRS voltages in leads I and aVF. For the ECG with left axis deviation, we find V_I = 0.5 mV – 0.1 mV = 0.4 mV and V_{aVF} = 0.4 mV – 1.0 mV = –0.6 mV. By insertion into the formula we get: tan(θ) = –1.73. This equation has two solutions in the interval from 0˚ to 360˚, which are θ_1 = –60˚ and θ_2 = 120˚. The mean eletrical axis always has the same sign as the net QRS voltage in aVF, thus the result is θ = –60˚. The same method can be used to calculate the normal axis (V_I = 0.8 mV, V_{aVF} = 0.8 mV, θ = 49˚) and right axis deviation (V_I = –0.3 mV, V_{aVF} = 1.1 mV, θ = 103˚).

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Family ties in Star Wars

Is Force-sensitivity a matter of non-Mendelian inheritance?

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With *Star Wars Episode IX: The Rise of Skywalker* (2019), the main storyline of the most influential space opera in contemporary pop culture has come to an apparent end. Over the past 40 years, Star Wars has touched on themes relating to family, religion, and politics. These themes are closely intermingled in the saga, and a critical reassessment of the films unveils some rather unexpected plot twists. For readers that are unacquainted with the saga, the following probably won't make much sense, but I must warn you that it will contain numerous spoilers.

In *Star Wars Episode IX*, we learn that Rey, the main protagonist of the sequel trilogy (2015 – 2019), despite growing up as an orphan scavenger on the desert planet Jakku, is in fact the granddaughter of Sheev Palpatine, the most influential political figure in Galactic history. Just like Palpatine – and members of the Skywalker family – Rey exhibits notable so-called Force-sensitivity. Indeed, the numerous plot lines of the saga invariably centre on the mystical and ubiquitous energy field, laconically designated "the Force," which forms the basis of the belief system of the monastic Jedi and Sith Orders. As Jedi Master Obi-Wan Kenobi expresses in *Star Wars Episode IV: A New Hope* (1977), it "surrounds us and penetrates us; it binds the galaxy together." It thus appears to be a composite of what a physicist here on Earth would call the four fundamental interactions, that is, gravity, weak and strong nuclear forces, and electromagnetism. In any event and somewhat different from conventional views here on Earth, Jedi and Sith cosmology consider the Force a product of living organisms themselves, and to complicate matters further, they believe that Force-sensitivity is caused by midi-chlorians, which are endosymbiotic lifeforms that reside inside living cells, quite similar to mitochondria and chloroplasts. Accordingly, Force-sensitivity is an inheritable trait, and the Star Wars saga is thus not only about family, but more specifically about genetics.

The prevailing view is currently that Rey inherited her Force-sensitivity from her father, that is, Palpatine's son, who Palpatine must have conceived at the height of his rule of the Galactic Empire, although he does seem very career focused throughout the Star Wars saga without any apparent aspirations of settling down with a family. It is nonetheless highly unlikely, or at least inconsistent, that Rey inherited such a trait from her father, unless the cellular biology of the *Homo sapiens*-like beings in the Star Wars Galaxy are entirely different from here on Earth. Given that Force-sensitivity depends on the organelle-like and thus extranuclear midi-chlorians, Force-sensitivity must exhibit *maternal* inheritance, because the midi-chlorians that are present in the zygote at fertilisation mainly originate from the oocyte!

From the above, it should be clear that while Anakin Skywalker/Darth Vader inherited his Force-sensitivity from his mother (who

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Figure 1. **Skywalker-Naberrie-Palpatine family tree.** Gold halo: documented Force-sensitivity. A particularly mysterious "unknown" is the mother of Sheev Palpatine Sr. The age gap between her and Sheev Palpatine Sr. must be somewhat disturbing, but in the post-Game of Thrones era I guess anything goes. But who of all the people in the Star Wars saga has the charisma of an Empress and would likely be able to soften Palpatine's heart? It must be someone with a serious weakness for bad boys, and after having watched *Solo: A Star Wars Story* (2018), I suspect that the resurrected Darth Maul, Palpatine's buddy and former apprentice, somehow played the role as a matchmaker. Illustration by Chi-Han Henry Ma.

exhibited clear signs of this, i.e. by performing a virgin birth!), none of his children inherited it from him. They must have inherited it from their mother, Padmé Amidala (born Naberrie), who indeed possesses exceptional skills way beyond those of a common child prodigy. Accordingly, she manages to become a democratically elected queen of her home planet Naboo at 14 years of age, and Jedi Master Yoda specifically acknowledges her Force-sensitivity in the script of *Star Wars Episode II: Attack of the Clones* (2002), with the remark "With you, the Force is strong", although this line did not make it into the final film. Even though the importance of the Naberries is, at least ostensibly, somewhat neglected in the saga, they may nonetheless be the most Force-sensitive family in the whole Star Wars Galaxy.

"Even though the importance of the Naberries is, at least ostensibly, somewhat neglected in the saga, they may nonetheless be the most Force-sensitive family in the whole Star Wars Galaxy"

So, how do the Naberries fit into Rey's origin story? It so happens that Padmé's sister Sola had two daughters Pooja and Ryoo who were present at Padmé's funeral in *Star Wars Episode III: Revenge of the Sith* (2005), and it would make perfect sense if one of them were Rey's grandmother! Indeed, I have found nothing within the narrative of the now 11 films of the Star Wars saga to falsify this claim.

I can see a yet untold love story unfold from ashes of the Galactic Empire during the dramatic finale at the end of *Star Wars Episode VI: Return of the Jedi* (1983) where the party-craving Galactic citizens lose all inhibitions and cause utter turmoil throughout the Galaxy. A Romeo and Juliet-like story about two young people from Naboo who fall in love despite their irreconcilable Naberrie and Palpatine lineages, and who choose to abandon their noble heritage to settle down as junk traders on a distant desert planet. Like in so many of the other Star Wars films, there is a tragic twist, as they ultimately fail to escape the ghosts from the past (i.e. Sheev Palpatine's). I would tentatively title this film *Jobal and Sheev: A Star Wars (Love) Story*; Jobal, because it is custom among Naberries to name their first-born daughters after the mother's maternal grandmother; Sheev because I think Palpatine is the kind of person that would name his son after himself. This would make Rey (who should have been named Sola, but that would have given it all away) the great grandniece of Padmé, and the first cousin twice removed of Luke and Leia (Fig. 1).

I contend that the above demonstrates the true depths of Luke's famous line: "The Force is strong in my family," in *Star Wars Episode VI*, as he is most probably, but perhaps unknowingly, specifically referring to the non-Mendelian inheritance pattern of this trait. So, perhaps *Star Wars Episode IX: The Naberrie Legacy* would have been a more suitable title for the saga's final instalment.

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Physiological Reports

Knockout of MD1 contributes to sympathetic hyperactivity and exacerbates ventricular arrhythmias following heart failure with preserved ejection fraction via NLRP3 inflammasome activation

Yang H et al. (April 2020)
https://doi.org/10.1113/EP088390

Ventricular arrhythmia (VA) is a principal source of sudden cardiac death (SCD), and SCD is a common cause of mortality in patients with heart failure with preserved ejection fraction (HFpEF). Sympathetic hyperactivation elicits VA, and myeloid differentiation 1 (MD1) – a component of the NLRP3 inflammasome – contributes to obesity-mediated VA. However, whether MD1 interacts with sympathetic nerves in VA during HFpEF is unknown. To address this, the investigators model HFpEF via uninephrectomy (the surgical removal of one kidney) in wild-type and MD1 knockout ($MD1^{-/-}$) mice. Wild-type animals with HFpEF exhibit cardiac hypertrophy, greater susceptibility to VA, sympathetic hyperactivity, and NLRP3 inflammasome stimulation. Moreover, these pathological alterations are worsened in $MD1^{-/-}$ mice. The authors suggest that the loss of MD1 exacerbates sympathetic hyperactivation and VA via NLRP3 inflammasome activation, contributing to the HFpEF phenotype. Therefore, stimulation and inhibition of MD1 and NLRP3, respectively, may mitigate the risk of VA in HFpEF patients.

Experimental Physiology

Sexually dimorphic production of interleukin-6 in respiratory disease

Reddy KD et al. (May 2020)
https://doi.org/10.14814/phy2.14459

Sex differences are increasingly recognised as determinants of susceptibility and severity in a multitude of pathologies (e.g. cardiovascular and respiratory diseases). These disparities are often ascribed to variations in sex hormones, although these cannot completely answer for sex differences observed in respiratory illness. Genetic evidence implicates sexual dimorphism – the distinct characteristics of the sexes beyond the variance of sexual organs – in playing a role. Given this, the authors investigate whether the production of the pro-inflammatory cytokines interleukin (IL)-6 and C-X-C motif ligand 8 (CXCL8) differ between pulmonary fibroblasts derived from male and female respiratory disease patients when stimulated by tumour necrosis factor-alpha (TNF-α), a strong initiator of lung inflammation. This study shows that, when treated with TNF-α *in vitro*, female-derived fibroblasts generate twice as much IL-6 compared with cells originating from male subjects. There are no differences in CXCL8 production. Such findings corroborate clinical observations of sexual dimorphism in respiratory disease.

The Journal of Physiology

Augmentation of endothelium-dependent vasodilatory signalling improves functional sympatholysis in contracting muscle of older adults

Hearon Jr CM et al. (April 2020)
https://doi.org/10.1113/JP279462

Functional sympatholysis is the capability of contracting skeletal muscle to offset vasoconstriction following sympathetic alpha-adrenergic activation. This property is essential for upholding blood flow during exercise but deteriorates with age, thereby worsening oxygen delivery and fostering endothelial dysfunction. This investigation demonstrates that triggering endothelium- dependent vasodilation in 16 "older" healthy individuals (8 male, 8 female; age: 68 ± 7 years) subjected to moderate (handgrip) exercise enhances sympatholysis. Using Doppler ultrasound to measure forearm blood flow, the authors show that intra-arterial infusion of the alpha agonist phenylephrine induces vasoconstriction at rest, an effect that is not ameliorated after moderate exercise (thus confirming that sympatholysis is impaired in this group). However, administration of acetylcholine or adenosine triphosphate (both endothelium-dependent vasodilators) during moderate exercise mitigates phenylephrine-induced vasoconstriction. These results indicate that sympatholysis can be elicited pharmacologically in older adults, pointing towards prospective therapeutics to bolster blood flow and oxygen delivery in this patient population.

Placental fatty acid transport across late gestation in a baboon model of intrauterine growth restriction

Chassen SS et al. (April 2020)
https://doi.org/10.1113/JP279398

Intrauterine growth restriction (IUGR – the failure of a foetus to attain its genetic growth potential) is associated with greater perinatal morbidity and postnatal disease risk (e.g. neurological disorders and cardiovascular disease). During IUGR, alterations occur in the transport of amino acids, folate, and ions across the placenta; yet, knowledge of the role of fatty acids (FAs – which are vital for proper fetal growth and brain development) in IUGR is limited. Employing an IUGR model in baboons – where pregnant animals are fed either a control or maternal nutrient restriction (MNR) diet – the authors examine the changes in placental levels of FA transport proteins (FATPs) and FA binding proteins (FABPs). They reveal that, in late gestation, the expression of placental FATP2, FABP1, and FABP5 are elevated following MNR, while fetal FA plasma concentrations are unaltered. Such findings shed light on the adaptive response of the placenta to preserve FA transfer during MNR.

Congratulating our 2020 Honorary Members

Following their formal announcement at the 2020 Member Forum, the Board is delighted to announce the 2020 Honorary Members of The Society.

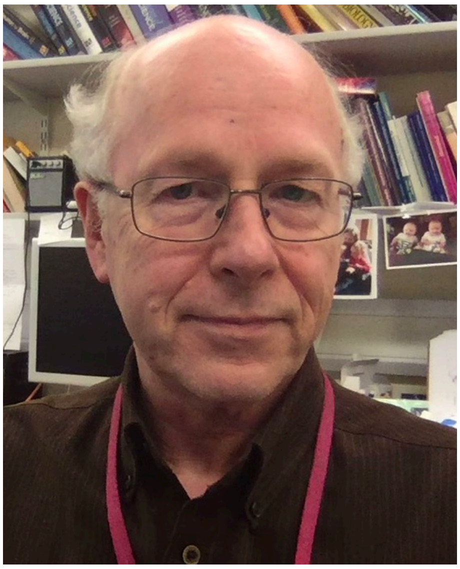
Peter Ratcliffe

Peter J Ratcliffe, MD is a physician scientist who trained as a nephrologist, before founding the hypoxia biology laboratory at Oxford. His laboratory elucidated mechanisms by which human and animal cells sense oxygen levels and transduce these signals to direct adaptive changes in gene expression.

Ratcliffe received his degrees from the University of Cambridge and medical training at St Bartholomew's Hospital, London and the University of Oxford. He is a Fellow of the Royal Society and a recipient of several international awards for his laboratory's work on oxygen sensing, including the Louis-Jeantet Prize for Medicine, the Canada Gairdner International Award and the Lasker Award for Basic Biomedical Research. He was knighted for his services to medicine in 2014 and won the Nobel Prize in Physiology or Medicine in 2019. In 2012 he gave The Physiological Society's Annual Review Prize Lecture, in Edinburgh, with a lecture entitled "Oxygen sensing in animals".

He holds appointments as Director of Clinical Research at the Francis Crick Institute and Director of the Target Discovery Institute at the University of Oxford and is a member of the Ludwig Institute for Cancer Research.

Richard Ribchester



My formal introduction to The Physiological Society was in June 1976, at the Centenary Meeting in Cambridge: my oral communication was scheduled as the opener, C1. Since I was only a second-year PhD student at the time (under John Harris's supervision at the muscular dystrophy labs in Newcastle) and the audience was peppered with many distinguished physiologists, this caused me quite some trepidation.

I obtained my PhD in 1977. After postdoctoral fellowships in the Department of Physiology at the University of Colorado School of Medicine, under Bill Betz's mentorship, and the Physiology Institute in Oslo, guided by Jan Jansen, I was appointed to a Lectureship in Physiology at the University of Edinburgh in 1980, where I have remained through my entire career, focusing my research (and teaching) on the physiology of neuromuscular junctions in health and disease.

I was elected to Ordinary Membership of The Society in 1983 and to the Editorial Board of *The Journal of Physiology* in 1986. I was one of the three appointed Distributing Editors from 1988 to 1991. In 1988, I wrote to the Treasurer of the Society (Julian Jack) suggesting that The Society might use some of its funds to support research seminar programmes in all UK Physiology Departments.

This idea was enthusiastically received by the Committee and I am pleased to see that the seminar support programme still continues to benefit the dissemination and discussion of physiology in this fashion. I served on the Committee myself from 1994-98. The University of Edinburgh awarded me a DSc in 2005 for my contributions to research on development and plasticity of neuromuscular innervation and I was promoted to a Personal Chair in Cellular Neuroscience the same year.

Over the period of 2006 – 2009, I worked closely with local philanthropists Donald and Euan MacDonald, and with the University, leading to the establishment of the Euan MacDonald Centre for motor neurone disease research, for which I acted as Director until a clinician-scientist was identified and appointed. The Centre now comprises over 200 researchers and its diverse basic, translational and clinical work is recognised internationally. I was elected as a Fellow Member of The Physiological Society in 2017. I feel indeed honoured by my election now as an Honorary Member. I am looking forward to continuing research as an experimental physiologist during my impending retirement, and to attendance and contribution to Society meetings, hopefully for many years to come.

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David Eisner

David Eisner's scientific career has focused on calcium signalling in the heart and the link to both normal and abnormal electrical activity and contraction. Following undergraduate studies in Cambridge, and a PhD under the supervision of Denis Noble at the University of Oxford, he held faculty positions at University College London and the University of Liverpool before moving to the University of Manchester in 1999.

He joined The Physiological Society in 1980 and has served it in various roles including Chair of The Editorial Board of *The Journal of Physiology*, and from 2016-2018, as President. He has also had a keen interest in the international role of The Society. He held the post of International Secretary, was chair of the Scientific Programme Committee for the International Union of Physiological Sciences meeting, held in Birmingham in 2013, and chaired the Organising Committee for Europhysiology 2018.

Patrick Vallance

Sir Patrick Vallance FRS FMedSci FRCP is Government Chief Scientific Adviser (GCSA) and Head of the Government Science and Engineering (GSE) profession. His personal research was in the area of diseases of blood vessels and endothelial biology.

Patrick was President, R&D at GlaxoSmithKline (GSK) from 2012 until 2017. Prior to this, he was Senior Vice President, Medicines Discovery and Development. He joined the company in May 2006 as Head of Drug Discovery. He was a member of the GSK Board and the Corporate Executive Team. During his period as head of R&D, over 14 new medicines were approved for use worldwide, for diseases ranging from cancer to asthma and HIV.

Prior to joining GSK, he was a clinical academic, Professor of Medicine and led the Division of Medicine at UCL. He has over 20 years' experience of basic and clinical research and was a consultant physician in the NHS. His research spanned from work on medicinal chemistry and structural biology, through to cellular work, studies in humans and use of large electronic health record databases.

He was elected to the Academy of Medical Sciences in 1999 and to the Royal Society in 2017. He was on the Board of the UK Office for Strategic Coordination of Health Research (OSCHR) from 2009 to 2016. He is an Honorary Fellow at UCL and holds honorary degrees from Imperial College London, the University of Glasgow, the University of York and St George's, University of London. He was a non-executive director and board member for UK Biobank and a non-executive board member for Genome Research Limited but stepped down in taking up the GCSA role.

(Source: https://www.gov.uk/government/people/patrick-vallance)

Obituary: Ronan O'Regan 1937 – 2020

Ronan O'Regan

I first encountered Ronnie in 1983. He was a lecturer in physiology, and I was a second-year medical student. I recall he wore a white laboratory coat over his jacket as a protection against chalk dust and probably to facilitate nipping to and from theatre and the laboratory. Ronnie loved electrophysiology and was an experimental physiologist *par excellence*.

Although I had many great teachers at University College Dublin (UCD) Medical School it was obvious to me and many others that Ronnie was not just transmitting new knowledge but actively mining for it. I still remember one of his off-hand asides when he was describing the pulse waveform as it progressed down ever-narrowing vessels of the circulation. "There are a number of mathematical models that describe the effect of wave reflection and you could study them, but you would be wasting your time."

Needless to say, this news was gratefully received by students, but Ronnie had also sown a seed of doubt on the relationship between mathematical models and reality. According to the late Professor Caoimhin Breathnach, a colleague of Ronnie's, the last cognitive gain of the adolescent mind is a sense of profound doubt.

Near the end of that academic year of 1983, interested students were invited to visit the various laboratories of physiology to witness ongoing research *in situ*. Ronnie's laboratory was dominated by an enormous walk-in Faraday cage built to minimise electrical interference. On the wall was a beautiful illustration of the extracranial circulation. In the centre, Ronnie had just completed a successful single nerve fibre recording and bristling action potentials were booming from an audio amplifier. Cardiovascular and respiratory signals were dancing across a paper recorder and to complete the scene Ronnie was sitting back enjoying a celebratory cigar.

I was astonished at the tiny femoral artery that he had cannulated, the perfect union of engineering, physics and biology brought to the service of physiology. It was at that moment I experienced the beauty of the action potential and realised that I was to become a truant of medicine.

And I was not alone in this truancy; Ronnie had also greatly influenced other medical students, Paul McLoughlin, in particular, who currently occupies the Chair of Physiology at UCD, and Philip Nolan who is the President of the University of Maynooth. In Ronnie's retirement he and I met frequently, and he would always enquire about Paul and Philip. He was so delighted in their success. Of course, his greatest source of delight and pride was very evident whenever he updated me on his accomplished children, Ruth and Anthony. Other protégés of Ronnie include Aidan Bradford of the Royal College of Surgeons of Ireland and Ken O'Halloran, who holds the Chair of Physiology in University College Cork.

Within the membership of The Physiological Society, the O'Regan name was a passport to instant camaraderie. In England the mere mention of my roots brought an instant smile and a stream of anecdotes regarding Ronnie.

His main research interest focused on the carotid body, a tiny organ that has a wet weight of only a few milligrams, but a mighty significance in oxygen sensing. The slender nerve fascicles he peeled were tens of microns in diameter and yet he managed to simultaneously measure blood flow and single axon activity from this wonder of nature. Only last month I reviewed a paper on the state of the art of carotid body research and his famous experiments from the 1970s are still cited. Until some novel imaging method is feasible, few relish the prospect of trying to revisit his technically demanding experiments. Later in his career he studied water receptors on the tongue of a frog and carbon dioxide receptors of the larynx with Philip Nolan. The latter experiments revealed a sophisticated and beautiful metering system of the breath.

Ronnie exhibited the admirable qualities of loyalty, humility and industry. He made manifest an impossible admixture of lone scientist and sociable companion. When he was younger, he engaged in heated, passionate, and constructive controversies about the carotid body, but when he was older, he laughed at how pointless that acrimony was. As the old adage goes, "knowledge passes, wisdom lingers."

"Within the membership of The Physiological Society, the O'Regan name was a passport to instant camaraderie"

One of the highlights of completing a BSc in Physiology was the final year *viva voce* with the Professor of Physiology and external examiner. During one apocryphal episode an examiner was chosen who happened to enjoy cigars as much as Ronnie did. When the last student of the day was called to the professor's office the smoke plumes were so thick that he had difficulty locating his seat. And, although he could hear his interrogators' voices, he couldn't see them through the smoky miasma.

There will be no more rendezvous with Ronnie. But I am blessed to have been taught by him, to have worked with him and to have counted him as a friend. He is survived by his wife Deidre, and his children, Ruth and Anthony.

Written by James Jones, University College Dublin, Ireland.

https://doi.org/10.36866/pn.119.34

Obituary: Geoffrey Burnstock 1929 – 2020


Geoffrey Burnstock

Geoffrey Burnstock discovered that adenosine 5′-triphophate (ATP) is released from cells and functions as a chemical transmitter. Geoff died in Melbourne, on 3 June 2020, aged 91.

Geoff hailed from a working-class background in East London. He lived through the Blitz, studied at Greenford County Grammar school, and after national service enrolled at Kings Technical College to get more A levels. His BSc was from King's College London in 1953, where he began in theology and switched to zoology.

For his PhD [in JZ Young's department at University College London (UCL)], Geoff developed a novel method for observing intestinal movements of freely moving brown trout.[1] As a postdoc, first with Wilhelm Feldberg at Mill Hill and then in Edith Bülbring's group at Oxford, he and Ralf Straub developed the sucrose-gap method to record the membrane potential of smooth muscle: this early work was mostly published in *The Journal of Physiology*.

At Oxford, he met and worked with visitors from Melbourne, Mollie Holman and Mike Rand. Geoff was taken by the informality and irreverence of the Aussie approach to science when compared to the stuffiness of the British and particularly Oxbridge "establishment". He also married Nomi Hirschfeld at this time, whose family was from New Zealand. In 1959 he accepted a position as Senior Lecturer in the Department of Zoology of the University of Melbourne.

In 1960, Burnstock and Holman first recorded *excitatory* postsynaptic potentials in the vas deferens, and they concluded that these were not mediated by the sympathetic transmitter noradrenaline.[2] Within a few years, Burnstock proposed that ATP was the extracellular transmitter. He later used selective desensitisation to show conclusively that the excitatory neurotransmitter in the vas deferens was ATP, as well as in the bladder and certain blood vessels.

Six years later, with Max Bennett and Mollie Holman, Burnstock reported that *inhibitory* chemical transmission from parasympathetic (now termed enteric) nerves within the wall of the intestine was also unaffected by substances known to block cholinergic and adrenergic junctions (non-adrenergic, non-cholinergic or NANC transmission).[3] In 1970 Burnstock proposed that ATP was also this inhibitory transmitter.

His experiments soon resulted in the extension of the hypothesis to many other tissues, and in 1972 he introduced the notion of "purinergic nerves", meaning nerves that release ATP to do "the work" of transmission. By 1985, Burnstock had distinguished between cell surface receptors for adenosine (P1 receptors; now they are termed A1, A2A, A2B and A3 receptors) and receptors for ATP (P2 receptors). Good antagonists were not available, and Burnstock used the classical criteria of rank order of agonist potency and selective desensitisation, to distinguish P2X and P2Y receptors.

There was great dubiety throughout this period that ATP could serve as a transmitter between cells, given the many roles in intracellular energy metabolism and phosphorylation that were being worked out for it within the cell. Geoff weathered this scepticism, even the ridicule, with a thick skin and a broad smile. When he returned to the UK in 1975 to become JZ Young's successor as head of UCL's Department of Anatomy and Embryology there were more than a few feathers ruffled by his Antipodean approach to research – "don't just think about it, do it".

It was fitting indeed that Burnstock and Holman's 1960 paper led to the use of RNA from the vas deferens to isolate and express the first P2X receptor cDNA. This unequivocal demonstration that P2X receptors were indeed ion channels activated by extracellular ATP scattered the doubters to far winds.

Prompted by Burnstock, John Wood at UCL soon thereafter cloned a P2X3 receptor cDNA, finding that it was an ATP-gated ion channel expressed only by a subset of sensory neurons.[4] It has since become clear that ATP, released from primary sensory cells, can act as an afferent transmitter to activate P2X receptors on sensory nerves: examples are found in the chemoreceptors of the carotid body, in some taste buds, and in the bladder urothelium. Advised by Burnstock, Roche and later Afferent Pharmaceuticals (acquired later by Merck) developed a selective P2X3 receptor antagonist that is now in clinical use for idiopathic chronic cough (gefapixant).

On the P2Y side, Burnstock collaborated with Eric Barnard (who had been with him as a PhD student at UCL) and others to clone the first metabotropic P2Y receptor, showing that it was a G-protein coupled receptor.[5] His discovery of 30 years before on the inhibition of intestinal smooth muscle is now seen to involve activation of the P2Y1 receptor. Gus Born had shown in the 1960s that ATP (and ADP) were potent inhibitors of platelet aggregation: this turns out to involve the P2Y12 receptor. Blockade of this receptor by clopidogrel, marketed since 1997, now saves thousands of lives each year.

Burnstock's *oeuvre* is profuse and encyclopaedic of colleagues and collaborators. He was both champion and cheerleader, inspiring generations of others to embrace and pursue purinergic signalling. He founded professional societies and journals devoted to the study of purinergic transmission. His widespread recognition includes the Outstanding Contribution award of the British Neuroscience Association, election to the national scientific academies of Australia and the United Kingdom, the Royal Medal of the Royal Society, the Copernicus Medal, the Erasmus Medal of Academia Europeae, and Honorary doctorates from Frankfurt and Leipzig.

In 1929, ATP was discovered (by Cyrus Fiske and Yellapragrada Subbarow, and by Karl Lohmann) and the first effects of extracellular purines were reported when Szent-Györgyi described the action of adenosine on the mammalian heart. Geoff Burnstock was born that year. His long life married geniality with defiance, wisdom with plain-speaking. His legacy is an entire subfield of physiology that continues to thrive and intrigue.

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Written by Alan North, Emeritus Professor, University of Manchester, and Past-President of The Physiological Society.

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