PN
Physiology News
Issue 116 / Autumn 2019

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Welcome to the Autumn 2019 edition of *Physiology News*

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Cover image: Artist's impression of the BodyApp – an augmented reality app to visualise metabolism for use in teaching . Image by Kalyan Veera, Medical Illustration, University of Aberdeen.

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The Physiological Society

Keeping the EDI conversation going

Keith Siew
Scientific Editor

Julia Turan
Managing Editor

We must first start this issue by once again thanking our authors for their informative and emotive contributions to *Physiology News* 115 – Diversity Special Issue. In the combined years of our Editorial Board, none can remember a topic eliciting so much audience engagement. The dozens of anecdotes from colleagues recounted to the editorial board, the emails and letters of thanks and personal stories sent to the editors, the hundreds of reactions on social media and many long overdue conversations... the response has been overwhelming.

In particular, we were moved to see the expressions of sheer delight by many online who were seeing themselves and their stories represented in this way for the first time. We were also encouraged by letters to the editor which continue important conversations on the need to increase ethnic diversity in academia (Jeff Allen, p.11) or how best to present your science for a colour blind audience (Nick Birch, p.10), something which we noted a number of delegates enacted last minute on the trains and flights to Physiology 2019 (p.22) to improve the accessibility of their work. Other correspondents have raised some EDI (equality, diversity and inclusion) issues which were not addressed in *PN* 115 but are worthy of further discussion, namely the influence of educational socio-economic background on access to opportunities (Michael Taggart, p.10), cultural diversity in the laboratory (Sara AlMarabeh, p.42) or diversity of thought in health education of the public (Christine Wilcox-Baker, p.44). It is clear that there is appetite for EDI content and we're glad to be part of that greater conversation going forward, and the *PN* microsite now more explicitly states our contributor guidelines on diversity and accessibility which we welcome feedback on to improve further (**physoc.org/explore-physiology/contribute/**).

As mentioned above, the greatest desire of any communicator, or indeed educator, is to facilitate the greatest amount of audience engagement and responsiveness. In this issue, we have two education-themed articles focusing on just that. The cover story of this issue embraces the fact that many students today have a smartphone or tablet to hand, and rather than try to fight that, instead redeploys them in a ground-breaking way to help students grasp molecular physiology concepts in the classroom via augmented reality. The app projects digital objects into the 3D space when viewed through the smart device (John Barrow, p.28). The second article explores what happens when you take the oldest teaching method of them all, the lecture, and turn it completely on its head in an institute with over 800 years of teaching experience (Matthew Mason & Angela Gayton, p.31).

With the launch of the new Themes we've decided to restart our Theme Lead reports segment starting with the new independent Metabolic Physiology Theme (which was formerly paired with Endocrinology). The report from Andrew Murray and Paul Meakin (p.40) highlights what an exciting time it is for metabolic research with many old concepts being brought back to the drawing board now that it is known that many metabolites are not mere substrates but cellular mediators of metabolic function or can interact with a number of receptors. Textbooks are now being updated to reflect this thinking (Andrew Murray, p.19) and a greater appreciation is given to the role of the gut microbiome in nutrition, metabolic signalling and the potential for novel therapeutic approaches (Katerina Petropoulou, p.46).

Additionally the overlap of metabolic research with other disciplines is perhaps most evident in the study of the pathophysiology of its disorders, as discussed in one of our feature articles exploring the impact of metabolic syndrome on the microcirculation (Marcus Machado, Aline Vieira & Eduardo Tibiriçá, p.37), or the crossover with exercise which is now more often seen as a remedy that should be prescribed clinically as much as any drug, as suggested by our authors or indeed likely many of those interviewed in the sport and exercise science (SES) case studies (p.7), which is also highlighted in this issue's President's View (Bridget Lumb, p.6).

Last but by no means least, we want to take the time to encourage readers to enjoy our feature article on non-synaptic neural communication by electric fields (i.e. ephaptic coupling), an exciting study that shows openness to new ways of thinking (Dominique Durand, p.34). In line with this ethos, as *PN* moves to become a truly dual format publication we must consider how to best utilise the new mediums and tools available to us. To that end, *PN* is now featuring short author videos for selected articles, a number of which have already been released for *PN* 115. We must also reflect on how our materials are used and the *PN* team is exploring options to fully digitise the *PN* back catalogue, move future content to a Creative Commons license and obtain DOIs for every article for citability. So watch this space!

The impact of Sport and Exercise Science

Bridget Lumb

President, The Physiological Society

"As The Physiological Society's membership continues to grow and expand, Sport and Exercise scientists will play an important role as we seek to reflect the impact of their physiological research"

Those of you who were in Aberdeen in July would surely agree that Physiology 2019 was a fantastic showcase for the quality and breadth of physiology being undertaken by the membership and its colleagues. I was asked in an interview to identify my highlight of the meeting. For me it was not a single lecture or event, rather the opportunities to network and the enthusiasm that was evident in the "buzz" throughout the meeting. Plenary and keynote lectures covered diverse aspects of physiology. It was a pleasure to welcome Kevin Fong OBE, to give The Paton Prize Lecture on "Life, death and the limits of the human body". We were extremely fortunate to have the opportunity to build on this relationship and work alongside Kevin as part of the programme for Extreme Physiology, which was hosted in Portsmouth in September this year.

Physiology 2019 presented The Society with the opportunity to discuss its recent publication *Sport & Exercise Science Education: Impact on the UK Economy*, which was a joint project with GuildHE, the UK's registered body for smaller and specialist universities and colleges. The report, and the case studies it contained, acted as a springboard to discuss successful grant applications and how to demonstrate real-world impact with representatives from BBSRC and the Wellcome Trust. As an example of the all-encompassing nature of the report, the session included a presentation from Abertay University about how the impact of their research was enhanced by working closely with communities in Dundee, which is home to some of the most deprived communities in Scotland and the UK as a whole.

In May, it was an enormous pleasure to welcome over 100 attendees to the launch of the report in Parliament. Those in attendance included Members of Parliament, their staff and representatives from universities and colleges. We were also enormously grateful to Gordon Marsden MP, Shadow Minister for Higher and Further Education, for hosting us in Parliament. The findings from the report are clear; as well as being academically rigorous, Sport and Exercise Science (SES) courses provide enormous contributions to the UK economy – to the tune of almost £4 billion every year, supporting almost 150,000 jobs. As The Physiological Society's membership continues to grow and expand, Sport and Exercise scientists will play an important role as we seek to reflect the impact of their physiological research.

In addition, it is important to reflect on the benefits of SES for those that study and research in the field. Every £1 that a student invests in their SES education yields £5.50 in higher future wages and SES graduates will earn on average £667,000 more across their working lives compared to those that do not attend university. This is a significant boost and demonstrates that employers value the skills that SES graduates leave university with, whether they decide to stay in research or enter the job market.

Our continued improved scientific understanding of how the body works is on display every time an athlete pushes themselves that little bit further, or runs that little bit faster. However, the report also makes quite clear that the impact of this research extends far beyond elite athletes. Obesity, diabetes, cancer, depression are all areas that are just as applicable to the general population and are areas in which SES research is playing a pivotal role in improving health for everyone. Our report also estimates that SES students from the 2016/17 academic year alone will save the taxpayer £267 million in costs associated with poorer health, crime and unemployment benefits. Thus, the value of SES education goes well beyond the value to the individual. As The Physiological Society, we must do more to share these insights within our universities and with the public as a whole. With this in mind, I would encourage you to read the excellent case studies (as well as Chris Gaffney's contribution in our Spring 2018 edition of *Physiology News*, "The genesis of a new Sports and Exercise Science degree") that have been provided by colleagues from up and down the country at different stages in their careers and share them as widely as possible! For more case studies, read on and also please read the full report, which can be downloaded on our website at **physoc.org/sportscience**

Image courtesy of Hartpury University

Sport and Exercise Science (SES) case studies

While Sport and Exercise Science Education: Impact on the UK Economy focuses on the financial impact of SES courses, it builds on research generously provided by institutions representing over 250,000 students from across the UK. The report features case studies demonstrating the wider benefits for students, graduates, the national economy and wider society. Below are some of these contributions.

Jo Bowtell
University of Exeter, UK

The Bioactives and Exercise research group (BioActivEx) led by Jo Bowtell at the University of Exeter is focused on investigating the effects of bioactives and exercise on musculoskeletal, cognitive, vascular and metabolic ageing, and exercise performance. A combination of whole-body, cellular and molecular techniques are employed to perform hypothesis-driven research. We are currently conducting a project led by Mary O'Leary, in which we are investigating the effects of phytoestrogen-rich shatavari root on bone and muscle metabolism in post-menopausal women. This project has been funded by Pukka Herbs, an organic herbal beverage and supplement company. Vivien Rolfe, Head of Herbal Research a Pukka Herbs has said "We are very excited about the Exeter University research partnership as it will provide a comprehensive exploration of shatavari's effects. Working with the team at Exeter allows us to conduct outstanding research, and we aim to grow this more deeply through internships and Pukka scholarships". Through our partnerships with Pukka and others, BioActivEx will continue to generate and evaluate evidence-based bioactive interventions to support longevity, exercise performance and quality of life.

Camila Rodrigues
BSc Sport and Exercise Science
University of Sunderland 2018 graduate

My research investigated the feasibility of getting inactive, overweight, sedentary individuals active using a 12-week personalised exercise programme in a fun and enjoyable social environment. The programme gradually progressed from an hour of low-intensity twice weekly to moderate- and vigorous-intensity exercise. Pre and post measures of sedentary behaviour, moderate to vigorous physical activity (MVPA), mental well-being and depression were measured. Results showed the positive impact of personalised exercise on health with a reduction in sedentary behaviour, body mass index and depression score, and an increase in MVPA, mental well-being and perceived fitness.

Exercise physiology not only informed the programme design (frequency, intensity, mode and duration) and rate of progression but allowed me to accommodate individual needs based on age, sex, body size, body composition and medical history. It allowed me to explain what was happening inside the body; beneficial metabolic, cardiorespiratory and musculoskeletal changes and why we sometimes ache a little after exercise! Exercise physiology opened up many interesting conversations including the importance of fluid intake and nutrition, energy balance and the dangers of overtraining, and adaptations to potentially hostile environments (cold, heat and high altitude).

Lydia Simpson
Bangor University, UK

Understanding the complex and integrative nature of how the body responds to exercise is vitally important in not only optimising sporting performance but also improving health and managing disease. Research in this discipline is fundamental to global health, as physical inactivity is fast becoming one of the biggest problems facing western society. A sport and exercise science degree is often considered a poor man's medicine degree; but, exercise is medicine. My research focuses on how the sympathetic "fight or flight" nervous system is activated during exposure to low oxygen availability, which can be experienced at high altitude or in disease. More specifically, I determine how this affects blood pressure control and what enables high-altitude populations to thrive under these conditions.

Image courtesy of Liverpool John Moores

Christopher Jones
Swansea University, UK

The Swansea University LookAhead project is funded by Sports & Wellbeing Analytics (SWA) and uses the PROTECHT system to objectively monitor head impacts in contact sports. The research project's initial focus was validating the PROTECHT system. After the system had been completely validated, the focus has progressed to monitoring head impacts in a number of sports such as professional men's rugby union, women's rugby, American football and field and ice hockey. Through the system it is possible to start to characterise and quantify the head impact demands of these sports, and subsequently look to improve the performance and welfare of an individual or team.

Mike Tipton
University of Portsmouth, UK

The University of Portsmouth research in cold water immersion physiology is the foundation of the search, rescue and treatment of a large number of organisations worldwide. For example, research led by Mike Tipton, Heather Massey, Clare Eglin, and Martin Barwood (now Leeds Trinity University) has played a key role in the development of new approaches to drowning prevention and water safety education. Drowning is a significant risk for sportspeople engaged in sports on and near water, and a leading cause of accidental death in the UK, particularly in young people, causing approximately 400 deaths per year. Aside from the human cost, drowning and related incidents cost over £63 million per year, costs that can be prevented by safety measures and education. To that end, Portsmouth's research has underpinned the Royal National Lifeboat Institution's "Respect the Water" National Water Safety Campaign, informing its "know about Cold Shock" and "Float First" approach to cold-water survival. This campaign has been cited by a number of drowning-incident survivors, without solicitation, as the reason they survived an immersion.

Image courtesy of Bangor University

John Saxton
Northumbria University, UK

Research at Northumbria University led by Professor John Saxton, in collaboration with clinical colleagues based in Newcastle, Norwich, and Sheffield, is investigating the important role that structured exercise programmes can play in improving the quality and duration of cancer survivorship. Cancers of the breast, prostate, and colon are amongst the most common in western societies and although survival rates are increasing, the physiological impact of these cancers and their treatments is long-lasting. Current research is focused on (i) the role of exercise training, in conjunction with dietary advice, in reversing adverse body composition changes in hormone-positive breast cancer patients, (ii) exercise interventions for ameliorating the side-effects of prostate cancer and its treatments, and (iii) how exercise programmes prior to surgery can be used to improve fitness and treatment outcomes in colorectal cancer patients. Macmillan Cancer Support predicts that support for people with cancer beyond their initial treatment will cost the NHS at least £1.4 billion every year by 2020. This research is closely aligned with NHS treatment pathways and is helping to build a solid evidence base to support the use of exercise in the clinical and self-management of people living with and beyond cancer.

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Making colour blindness more visible

Nick Birch
Emeritus Professor of Biomedical Science,
Academic Consultancy Services Ltd

I was delighted to see Christopher Torrens' article in *Physiology News* (issue 115) which was both scientifically informative and also touched on the problems which affect those of us who are part of the 8% of the male population who have colour blindness or deficiency.

I am in my seventies and long retired from university but I have to say that my colour-blindness affected my career because it steered me away from areas which were colour-sensitive. My reduced colour vision only became evident when in the Sea Scouts I was unable to recognise the colours of some flags. At A-level in the early '60s it was not really recognised in school and so I had no assistance in my examinations. However, by the time I reached my degree finals I had been able to obtain a certificate based on an Ishihara test to say that I was colour deficient and this resulted in having examiner behind me during chemistry practical titrations saying "one more drop, one more drop". Unfortunately, there is no way in which an examiner can help in histology practicals when you are told to: "counter stain to a rose colour". As a consequence I have steered clear of microscopes ever since.

I am glad that he has highlighted the most irritating question which one can ask someone with colour anomalies. Even after 30 years of marriage my wife still asks me about colours of flowers in the garden and what I see. In fact my colour discrimination for some of the reds is very precise because I am lacking the longer end of the spectrum. I see some reds as black and indeed there was a particular colour of Austin A40, probably in the 1970s, which I had always believed was black and I was quite shocked when someone described it as red. I still have, however, problems with car park ticket machines which say: "press the green button" to receive the ticket when there are three faded buttons of, to me, indistinguishable colour.

The issue with which I have most difficulty these days is graph charts presented in the media to indicate changes in time, for example, unemployment or the price of oil, when various different colours are used for different features and many of these are indistinguishable as far as I am concerned. In the mid-1990s I was so frustrated by the quality of slides which were appearing at scientific conferences (for example, a numerical table of the analysis of 23 amino acids in six individual subjects) that I developed what I called "The Rule of Sixes" [1, 2, 3]. This was designed to define the minimum screen size, limit the number of items on a slide and to define the size and thickness of typefaces employed. I also included as one of the six rules the idea that, with some poetic licence, 6% of the audience were likely to be colour deficient and therefore to make sure that slides predominated in the yellow-blue axis where there were likely to be fewer problems. This work was rapidly overtaken because of the change from photographic slides to computer projections which followed soon after. The principles in relation to content and clarity, however, still apply.

Many thanks to Christopher Torrens for highlighting this problem. I think it is important to keep on banging the drum for the one in 12 men who are not greatly visible but whose presence needs to be more widely recognised. I am glad to see that scientific journals are beginning to recognise the issues which he highlighted and I hope that others will follow.

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Educational privilege vs equal opportunities

Michael Taggart
Newcastle University, UK

Many congratulations on an interesting and informative recent Diversity Special Issue of *Physiology News* (*PN* 115). The range of circumstances highlighted really does send out an important message to us all (e.g. it alerted me to change the colouring in my slides for a pending presentation). If I may, I'd like to draw attention to one issue not mentioned – the influence of educational privilege.

At the time of writing (26 July) the UK has a newly-appointed Prime Minister. He is the 28th (out of 78) to have attended Oxford University and the 20th to have been schooled at Eton College. Of his cabinet members 64% were privately educated (more if you include selective education) and 45% attended Oxbridge. Moreover, the Diversity Special Issue of *Physiology News* arrived in my pigeon hole at the same time as a publication by the Sutton Trust and Social Mobility Commission of their report on "Elitist Britain 2019 – The educational backgrounds of Britain's leading people" [1].

This report highlights how educational privilege – in essence assessed as the lift-up to life opportunities offered by private/selective schooling and/or attendance at Oxbridge universities – permeates all aspects of our professional structures. It makes for stark reading. Yet, there seems to be resistance to the idea of fully examining the extent to which any such privilege might influence matters in the broad higher education arena. Of the many Equality, Diversity and Inclusion (EDI) initiatives at universities and research institutes, has any acknowledged this topic as a potential obstacle to meeting EDI aspirations of staff?

In the Diversity Special Issue of *Physiology News*, there was only a brief nod to this when Chi Onwurah MP suggested that "socio-economic status" should be considered as a component of diversity. Perhaps the reticence is because it's undoubtedly a complex matter, even an uncomfortable one, to consider. Maybe, to many fair-minded individuals, it's thought to be an unnecessary query to pose. However, the foregoing suggests it is important to engage with this issue and gather evidence because EDI is not, I suggest, just about widening access. It is also about assessing if there are equal opportunities for successful participation in all aspects of our social and professional environments, including occupying the major decision-making roles. Indeed, a relevant recommendation from the Sutton Trust and Social Mobility Commission report is as follows:

"Data on the socio-economic background of employees should be collected and monitored by employers in the same way as gender or ethnicity. In order to combat inequalities in the workplace, employers and government need to have better data to identify where the barriers lie. There should be a particular focus on how class background interacts with level of seniority in an organisation."

So, my gentle suggestion to organisations controlling agendas for research, teaching and learning in the higher education setting – the UK and devolved governments, UKRI and associated Research Councils, universities, independent research charities (e.g. member organisations of the Association of Medical Research Charities), "independent" research institutions, and, yes, learned societies like The Physiological Society – is to survey whether there has been privileged access to the decision-making roles. Do people from backgrounds of private/selective schooling

and/or Oxbridge attendance disproportionately occupy the roles of major influence such as Vice-Chancellors, Presidents, Chief Executives, Deans, Head of Departments or Chairs (or members) of grant review/policy/strategy/promotion panels? There may be some interesting findings that imbue confidence, concern or curiosity. As Bridget Lumb wrote in her President's View in *Physiology News* 115: "Recognising one's own … unconscious bias is a good first step to making positive change."

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[1] Sutton Trust and Social Mobility Commission (2019). *Elitist Britain.* [Online] Available at: www.suttontrust.com/wp-content/uploads/2019/06/Elitist-Britain-2019.pdf

Cultural change is coming

Jeff Allen
Cardiff University, UK

What a fantastic issue – the Diversity Special Issue – congratulations on this achievement! I was lifted on seeing the cover and then reading your publication. I found the articles by Kayisha Payne (p.15), Chi Onwurah (p.17) and Olusoga Sofola (p.42) particularly thought-provoking. For our Physiological Society to be publicly recognising the diversity of our membership and highlighting diversity in physiology has made a significant positive impact on me, and I am sure also to the broad spectrum of those involved in physiology and STEM. Looking through your pages brought me to reminisce on my physiology-laden path through higher education.

I am black-British; my Jamaican parents came to the UK in the 1950s and I was born in London in 1959. Britain is more culturally diverse now, but back then, when I was growing up in the 1960s and 1970s, there were very few black scientists. I was motivated to pursue the sciences, supported by the notion that in science people succeed on research and discoveries. I was so naive.

Having graduated from the University of East Anglia in Norwich following a third year project with Eduardo Rojas on frog skeletal muscle fibres, Peter Baker welcomed me to King's College London and the laboratories at the Marine Biological Association in Plymouth for my PhD on the squid giant axon. Through those early years, whether in the lab or at meetings, there were scant "home-grown" black faces. This remains very much still the case for my age group, for whom evidence highlights black academics are paid less (promoted less), and universities have found it very challenging to address this for their staff, highlighted in studies by the Equality Challenge Unit and The Leadership Foundation. However, universities recognise there is more potential for driving change through our new scientists and physiologists, by better supporting more applications and a rise in Black, Asian and minority ethnic BAME undergraduates. Cultural change doesn't happen overnight, but the trend is positive and The Physiological Society is helping to lead the way by openly discussing issues and supporting ideas.

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Arthur John Buller (1923–2019)

By Bruce Matthews, Nigel Buller, John Nicholls, Tim Biscoe, Tony Ridge, and Kuda Ranatunga

Arthur Buller died on 9 May 2019 at the age of 95 years. He was brought up in a military family and attended the Duke of York's Royal Military School in Dover. He first became attracted to a career in medicine while visiting his father in the hospital at the age of 12 and was fascinated by a ward-round he witnessed that was being conducted by a neurosurgeon. His aim of studying medicine was made difficult by his school not providing courses in chemistry or biology, and to gain entry to medical school he had to study on his own and take additional courses. He was admitted to the second MB course at St. Thomas's Hospital at the age of 17 and qualified when he was 20. At that age he could not work as a doctor because he was too young to sign a death certificate. Before starting his House appointments, in an important step in determining his future career, he became a Demonstrator in Physiology at St. Thomas's.

After 10 years in clinical departments, he returned to physiology at Thomas's, worked with Katz on muscle spindle discharge at University College, and in 1958 went to spend a very formative year with Jack Eccles in Canberra, during which they discovered that the contraction speed of skeletal muscle twitch fibres was determined by their nerve supply. Arthur was invited by Jack to pursue the mechanism of this effect, which he did with his research group over several years. Arthur and his colleagues made major contributions to the experimental evidence that showed that it was the pattern of impulse discharge in the motor nerve fibres rather than a chemical, trophic effect provided by the nerves, that determined the contraction speed of the twitch fibres.

Soon after Arthur returned from Australia, he was appointed as a Reader in Physiology at King's College, London and then, in 1965, as Professor and Head of the Physiology Department in Bristol. With excellent accommodation in a nearly new building, he quickly recruited additional staff and established a department with an outstanding record in both teaching and research. He led the department by example, and was extremely kind and caring to the staff; for example, on one occasion he took new equipment from his own laboratory and gave it to a new lecturer who had arrived with only an old and obsolete set of instruments. Also, with his wife Joan, he hosted the wedding reception of a Sri Lankan PhD student. Many who worked with him will be very grateful for the inspiration and guidance he provided for their research and teaching.

Arthur made very significant contributions to the MRC. He became a member of the Neurosciences and Mental Health Board from the time it was formed in 1972 and was Chairman from 1975 to 1977. He was then appointed Chief Scientist at the Department of Health and Social Security from 1978 to 1981, a post in which (amongst many other undertakings) he worked very hard to ensure that, after government cuts in the level of funding, some of the support for medical research was restored back to the MRC from the Department of Health. This was obviously the least enjoyable part of his career.

In Bristol he was Dean of Medicine from 1976 to 1978, and returned briefly to the Physiology Department in 1981 after his spell at the DHSS. He took early retirement in 1982 but continued to support the work of medical charities, particularly those concerned with muscular dystrophy. Also, in retirement, he maintained his life-long fascination with physics and mathematics, and obtained an Open University degree in mathematics.

Three interviews with Arthur that were made in 1995 by Max Blythe on behalf of the Royal College of Physicians are available at the Oxford Brookes University website under Radar Collections/Archives/Buller.

Open access: Widening access to the scholarly literature increases the literature's value to society

Simon Rallison

Director of Scientific Programmes, The Physiological Society

Since the first commercial Open Access journals were launched in the late 1990s, there has been a steady migration from subscription to Open Access.

Plan S, driven by Science Europe, was launched in September 2018. Fourteen national research-funding bodies across Europe (with UK Research and Innovation by far the largest) set out conditions for publication of the research they paid for. Plan S will have serious implications for our publications and in January 2019 The Society responded to the Plan S consultation.

What is Plan S?

Plan S is an initiative aimed at accelerating the transition of the journals market from subscription to Open Access (OA). It sets out conditions for the publication of the research paid for by a group of funders. The stated principles of Plan S begin:

"With effect from 2021, all scholarly publications on the results from research funded by public or private grants provided by national, regional and international research councils and funding bodies, must be published in Open Access Journals, on Open Access Platforms, or made immediately available through Open Access Repositories without embargo."

Isn't Open Access expanding anyway?

Open Access has been viable since the mid-1990s and has grown steadily since then. In 2018 19% of articles were published as Gold OA (OA immediately on publication), either in fully OA journals or in "hybrid" journals, former subscription journals that publish OA papers alongside articles still only available to subscribers. However, the transition has been slower than many people had hoped.

Who's behind Plan S?

Plan S was launched by cOAlition S, a group of 16 research-funding bodies across Europe, including UKRI. The number of funders signed up to it has since grown to 21, including the Wellcome Trust and the Gates Foundation. The Swedish Riksbankens Jubileumsfond signed up but later dropped out.

Will researchers still be able to publish in the journals they want to?

Not necessarily. It depends on the OA policy of the journals and on where your funding comes from. To publish research funded by cOAlition S members, journals must comply with Plan S.

Controversially, in the longer term cOAlition S will not permit publication in 'hybrid' journals, even though an individual paper could still be OA. The exception to that rule is where the journal's subscription content is made immediately available, without embargo (and under a Creative Commons licence permitting re-use as well as access), in an OA repository. The jury is still out on whether libraries will continue to subscribe to journals if their content is simultaneously made freely available elsewhere. This and other business models for a transition to Plan-S-compliant OA are outlined in this discussion paper from the consultancy Information Power. A later blog piece from Information Power focuses on the implications and options for learned societies.

Although funders like the British Heart Foundation and the National Institute of Health have not joined cOAlition S, Research England (the former HEFCE) is part of UKRI, so to be included in REF submissions, articles will presumably have to be published in journals that comply with Plan S. As things stand, Plan S would dramatically restrict where researchers funded by cOAlition S could publish their work (70% of journals as currently published would be ruled out, including *Nature*, *Science* and *Cell*). The funders will monitor compliance and sanction non-compliant grant-holders.

When does Plan S take effect?

Plan S takes effect on 1 January 2021: "As a minimum requirement, cOAlition S members must apply the Plan S principles at the latest in calls published, or application deadlines, after 1 January 2021. cOAlition S encourages its members… to implement Plan S on all grants awarded from January 2021."

What has the response to Plan S been?

Since Plan S was announced last autumn, three major information-gathering and consultation exercises have been carried out (although remarkably little has been heard from the researchers themselves). As a result of pushback in these and other discussions, some of the more contentious requirements of Plan S were relaxed in a revised implementation plan and some unintended consequences avoided. It is clear that cOAlition S are willing to listen, up to a point. The start for compliance was put back from January 2020 to January 2021 and the deadline for total compliance from the end of 2023 to the end of 2024. As a further concession, between those dates, hybrid journals will be considered Plan-S-compliant if they are on a transitional pathway to complete OA as part of a transformational arrangement.

Where do The Society's journals fit into all this?

The Journal of Physiology (*JP*) and *Experimental Physiology* (*EP*), both of which are hybrid journals (*Physiological Reports* was born fully OA), would as currently published eventually be non-compliant. However the revision of Plan S at least recognises the particular difficulties faced by international journals (not all countries have money for Article Processing Charges), the importance and economics of selectivity (much time and money are invested in the peer review of papers that *JP* and *EP* eventually reject) and the different levels of service to authors that journals offer (*JP* and *EP* provide a first-rate service, with corresponding costs).

Happily *JP* and *EP* do already have at least one foot on a Plan-S-compliant transitional path to OA through agreements negotiated by Wiley, our publishing partner, with consortia of libraries and funders in Germany and the US. The deals are "publish and read", meaning that technically the institutions are paying to publish in the journals rather than for access to them (although the payment also covers access to Wiley's subscription content).

As an incidental positive outcome, cOAlition S's recognition of the unique role of societies has helped focus attention on the central part that society-owned journals play in their respective disciplines.

What does it mean for The Society and its Members?

Plan S acknowledges the key role played by academic societies in their respective disciplines: "The coalition members view Learned Societies as an essential component of the scholarly infrastructure". It commits to support societies in the transition of their journals to OA, although without much detail about what form that support will take.

Because the surplus from its journals allows The Society to pursue its charitable activities, the impact of Plan S on journal economics is hugely significant to us. There is already enough money in the academic library system to allow a transition to OA if the flow of funds is redirected. The Wiley deals show that an orderly migration is achievable, even if some details have yet to be worked out.

There are unanswered questions too for the Members as scientists. Most consequentially, would collaboration on research become less attractive if researchers outside Europe would then be prevented from publishing in some of the leading journals? Despite that, 67% of respondents to the Wiley annual membership survey (across many societies) wanted societies to provide more OA publishing.

What is The Society doing?

The Society will continue to stay abreast of developments, to analyse their impact (Plan S is a standing item on the Council meeting agenda) and to keep the membership informed. It will also ensure that the journals themselves are positioned for a successful transition to OA. Our firm belief is that service to authors and quality of content will continue to be the keys to success.

As Plan S enters its second phase, we would encourage our Members to talk to their research funders about the implications of Plan S, highlighting the importance of society journals for both authors and readers. Plenty has been written about Plan S and its potential impact, from a range of viewpoints. A good starting point and place to keep up with developments is cOAlition S's own website **www.coalition-s.org/**

Shortly before *Physiology News* went to press, the consultancy Information Press released its report "Society Publishers Accelerating Open Access and Plan S" (SPA OPS). The report was commissioned by the Wellcome Trust, UKRI and ALPSP (a trade body for journal-owning societies and publishers), and helpfully maps out alternative routes from subscription to Open Access and provides toolkits for societies and publishers to use. It is available for download at **wellcome.figshare.com/articles/Society_Publishers_Accelerating_Open_Access_and_Plan_S_-_Final_Project_Report/9805007.**

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

First signs that human ageing can be reversed

The Thymus Regeneration, Immunorestoration and Insulin Mitigation (TRIIM) trial tested nine white men between 51 and 65 years of age using a cocktail of recombinant human growth hormone and two diabetic medications, dehydroepiandrosterone (DHEA) and metformin, to prevent or slow signs of immunosenescence in ageing humans. Unexpectedly the researchers not only found evidence of the participants' immune system rejuvenating, but had also reduced their biological age (as measured by epigenetic markers) by an average of 2.5 years after 12 months of treatment and improved risk indices for many age-related diseases, with effects persisting six months after stopping the trial.

DOI: 10.1111/acel.13028

Cellular communication via small parcels

Communication between cell populations is generally thought to occur through paracrine or endocrine chemical messengers or neuronal action potentials. However the emerging field of exosomes (a type of tiny extracellular vesicles containing RNAs and proteins) show that these can be secreted by one cell population and taken up into the cells of another. Recent research has demonstrated that skeletal muscle cells can secrete microRNA-enriched exosomes which can improve the function of endothelial cells and promote angiogenesis through a vascular endothelial growth factor independent signalling, as exemplified by promoting proliferation, migration and tube formation in human umbilical vein endothelial cells.

DOI: 10.1113/EP087396

Our lizard legacy

Using whole-mount immunostained 3D imaging, a team of evolutionary biologists have discovered the presence of previously undescribed limb muscles in early-stage human embryos. During normal human embryonic development several of these atavistic muscles - normally found in our ancestors but not normally present in adulthood - grow in the hands and feet but later disappear before birth of the foetus. Notably these muscles can be found in the more dexterous digits of reptiles, and may be some 250-million-year-old remnants from when mammals began evolving from mammal-like reptiles.

DOI: 10.1242/dev.180349

Q&A with the Head of Parliamentary Office of Science and Technology (POST) Grant Hill-Cawthorne

Grant Hill-Cawthorne

Head of POST

The Parliamentary Office of Science and Technology (POST) is the UK Parliament's in-house research and science advice unit that bridges research and policy. POST serves both the House of Commons and the House of Lords as a joint establishment, through output that is apolitical and of widely acclaimed value to Parliamentarians of all parties. As part of POST's 30 year anniversary celebrations, The Physiological Society met with its Head, Grant Hill-Cawthorne, to learn more about POST, its role, its plans for the next 30 years and how members of The Physiological Society can contribute to a more evidence-informed policy.

Can you explain POST's origins and why it was felt to be necessary by its founders?

POST was established in April 1989 following a delegation of MPs to the US Congress' equivalent Office of Technology Assessment (OTA) which had been established in 1972 to provide technical assessments to Members of Congress. By the middle of the 1980s, Parliament was facing a number of new, emerging issues related to science from topics as varied as the first computer viruses, the ethics of human embryology science and bovine spongiform encephalopathy (BSE). With so many new areas of science that required political attention, POST was established to provide politicians with insight into short- and long-term impacts of changing technology from political, economic, social, technological, legal and ethical perspectives. We were founded by the Parliamentary & Scientific Committee and started with a £100,000 charitable donation from organisations like the Leverhulme Trust and Wellcome Trust and were adopted by both Houses of Parliament in 1992 and made a permanent parliamentary institution by 2001. In 2013, with funding from the Economic and Social Research Council, we added social sciences to our remit.

Can you give a sense of the kind of advice and expertise you offer members and what formats this can take?

I think the main role of POST is to horizon scan for members, giving them a sense of the kind of issues in science and technology that there is little or no academic research into but that will present challenges for policymakers in 5-10 years' time. A good example of this would be something like microplastics. POST wrote a briefing on this three years ago as an emerging issue and then as political pressure grew, the Common's Environmental Audit Committee picked this as an inquiry topic leading to a Government ban on microplastics based on the inquiry's findings. So we tend to be at the very start of scientific policymaking but this does mean that not all the issues we identify will be picked up as political hot topics.

Can you explain the difference between your work and that of the select committees? Is there ever any overlap?

I think the difference between POST and the Commons Science and Technology Committee, for example, is that we are more proactive in identifying medium- to long-term challenges as opposed to the Committee which scrutinises Government responses to current or existing challenges. This is obviously not always clear cut but the role of Parliament is to scrutinise Government policy and legislation, so it is right that members fulfil this role. We are there to ensure that through our horizon-scanning work; "POSTnotes" (briefings on the latest scientific research); liaising with our academic and society stakeholders, members have the best tools to conduct their oversight.

What are the issues that members most often ask for advice or clarity on?

Again, this is not clear cut but in order to understand where we add the most value to the work of members, you have to look at their competing priorities and responsibilities. MPs have to balance the needs of constituents, their party and their committee roles. Often, the Commons or Lords libraries will deal with matters related to constituency queries (such as unemployment figures, existing legislation, policy history for debates, etc.). Similarly, the parties have established mechanisms that help members develop policy positions which reflect manifesto pledges in areas they may not be that familiar with. Where we tend to provide the most value is helping members think about their committee responsibilities or prepare for a Private Members' Bill (a piece of legislation brought to the Commons or Lords without Government support) or a member's role on a specific bill committee. Members want help to ensure that they understand future challenges so they can plan their bill's wording accordingly or ask a witness specific questions during a committee. The debate around 5G rollout is a good example of where we have provided this information.

POST also develops"POSTnotes" which are there to help members think about future challenges presented by scientific and technological innovation. We also host public and private events to enable members to ask questions of experts. To give members a better understanding of some of the ethical and legal questions posed by the emergence of biometric authentication for example, we organised a panel session so that members could quiz officials from the Home Office and the Government Office for Science about its use and implementation.

Are there any examples of where POST's work has helped to make a positive contribution to science policy?

It is hard to show direct correlation but the role of POST is to spark an idea. I have already mentioned the work of the EAC committee on microplastics but I would also point to the current Women & Equalities Committee's inquiry into "Health and Social Care and LGBT

"Health and Social Care and LGBT communities" is one of POST's current enquiries.

"We are always looking to expand our network of academics that we reach out to for advice and counsel on new and emerging areas of science policy. "

communities". POST did some initial research tracking the poorer health outcomes of LGBT communities compared to the general population as a result of a disproportionate burden of certain conditions among the LGBT community but also how they are treated within the healthcare system. We also provided close support for the Forensic Linguistics (Standards) Bill 2015-16, which was inspired by a POSTnote on forensic language analysis.

How can members of The Physiological Society best support you in making sure members (of Parliament) have access to the most up-to-date scientific evidence? How can early career researchers with an interest in science policy get involved with POST?

Members of The Physiological Society can most definitely make a positive contribution to the work of POST. We are always looking to expand our network of academics that we reach out to for advice and counsel on new and emerging areas of science policy. As a first step, I would encourage your members to follow POST (**@post_uk** and **@UKParl_Research**) and our Knowledge Exchange Unit on Twitter and join our mailing list. We also share upcoming topics for POSTnotes, for which we are always looking for new contributors.

In terms of the best ways of communicating your science to parliamentarians, I would encourage people to engage with just some of the 550+ All-Party Parliamentary Groups – they are excellent fora for getting your messages to interested parliamentarians in a non-partisan manner. Finally, part of my role at POST is acting on the Lords Liaison Committee's recommendation that more is done to promote the diversity of committee witnesses and, within that, boost the number of academics that give evidence to committees. For some committees, academics make up only 2% of witnesses called to give evidence and this leads to a perception that peer-reviewed evidence holds no more weight than evidence which is published with less scrutiny and analysis.

On the topic of witness diversity, I should be clear that while the Liaison Committee focused particularly on gender equality, we are using a broader definition. In short, if you are an expert in a specific field and could add value to the evidence provided for a committee's inquiry, you don't have to be a world-renowned professor – we still want to hear from you!

How can someone with a science background transition into a role like those at POST? Do you look for people with a general science background, a balance of specialisms of a combination of the two? And how did you come to be involved with POST?

We tend to look for people with a background in methodological techniques, the sort of thing you would see covered as part of an MRes, MPhil or PhD so that you can prove an ability to use and appraise research effectively. Beyond that, we have four different categories we use to organise our work and teams: Biological Sciences and Health; Physical Sciences and ICT; Environment and Energy; Social Sciences. I imagine the work of The Physiological Society's members will have application across a few of these fields so physiologists will be well placed to adapt their knowledge into areas of science they may not necessarily be experts in. A background in science communication, writing for non-scientific audiences is also important because your work will be shared with members who may have no scientific background whatsoever. I originally trained as a medic before working as a Clinical Adviser to NICE. I then went back into academia and worked in Saudi Arabia and Australia before coming back to the UK to take up my role with POST.

What does the next 30 years look like for POST? Have you noticed the topics that you cover have changed or is changing?

As part of our "POST at 30" strategy, we have set the objective of being at the forefront of using evidence to inform policy and legislative changes. The Government Office for Science and the network of Chief Scientific Advisers should be applauded for the work that they do at a governmental level but often Parliamentary work is not at the same level because of a lack of time, resources and differing pulls on members' time. We are working hard to ensure that all of our work in Parliament is underpinned by the best available research evidence. At the same time, we want to increase POST's international focus, making it a role model for those countries that are looking to establish similar organisations for their democratic institutions, just as the now defunct OTA was for POST in the early 80s. With POST taking over the presidency of the European Parliamentary Technology Assessment network (EPTA) next year, we have a great platform to do this. Beyond Europe, we have recently been working with colleagues in Colombia and Argentina, which gives an indication of the global legacy that POST's work can have.

Outstanding physiologists awarded 2019 Honorary memberships

Following their formal announcement at the 2019 Annual General Meeting, Council is delighted to congratulate the 2019 Honorary Members of The Society.

John Barton Furness

The award of Honorary membership was given to John Barton Furness in recognition of his work as a leading expert on digestive and autonomic nervous system research, which has been instrumental in leading to the modern understanding of the functioning of the enteric nervous system, the intrinsic nervous system of the digestive tract. He is known for developing the chemical coding hypothesis that states that neurons that project to specific targets and have specific functions can be uniquely identified by their chemistries. This has led to an unravelling of nerve circuits in both the periphery and in the central nervous system. He was also responsible for the identification of intrinsic sensory neurons of the digestive tract.

Furness undertook his early studies and PhD at the University of Melbourne and postdoctoral studies at the Physiology Department, University of Birmingham, and the Institute of Animal Physiology in Cambridge. He is currently Professor in the Florey Institute of Neuroscience and Mental Health and in the Department of Anatomy and Neuroscience at the University of Melbourne. Prior to this he spent 15 years at Flinders University in Adelaide. In addition to his academic roles, he has extensive interactions with the pharmaceutical and devices industries, including the conduct of clinical trials.

In addition to The Physiological Society's recognition Professor Furness is also recipient of a number of prestigious awards such as the Australian Neuroscience Society Distinguished Achievement Award, the Australian Government Award for Service to Australia, the Centenary Medal, the Gold Medal, L'accademia delle Scienze Dell'Istituto di Bologna, for service to scientific development in Italy, and the Davenport Award of the American Physiological Society.

He is also a Fellow of the Australian Academy of Science, Fellow of the Australian Academy of Health and Medical Sciences, Honorary Life Member of the Australian Neuroscience Society, for distinguished neuroscientists who have rendered notable service to the society, and the Honorary Vice-President of the International Society for Autonomic Neuroscience. He holds Fellowships of the Academy of Science of Bologna (L'accademia delle Scienze dell'Istituto di Bologna) and the American Gastroenterological Association

Professor Furness has published 15 papers in *The Journal of Physiology* and has been a regular reviewer for the Journal. He has also published in the American Journal of Physiology and numerous others.

Fiona Broughton Pipkin

The award of Honorary membership was given to Broughton Pipkin in recognition of her ground-breaking studies into the pathophysiology of pregnancy with special reference to pre-eclampsia and the renin-angiotensin-system (RAS). Her most readily identifiable contribution to improving the quality of life was probably the first demonstration of the deleterious effects of angiotensin-converting enzyme inhibitors on the fetus which led rapidly to their classification as being strongly contra-indicated in pregnancy.

Broughton Pipkin read Natural Sciences at Somerville College, University of Oxford (1972 MA) and completed her DPhil in 1973 at the Nuffield Institute for Medical Research, University of Oxford. She has been, and continues to be a big supporter of The Physiological Society (Committee member 1998 – 2001; Chairman, Animal Legislation and Welfare sub-committee 1998 – 2001) and has contributed throughout with numerous publications in The Society's journals, first presenting her work at The Physiological Society meeting in June 1970.

Broughton Pipkin has held several senior roles within the University of Nottingham including becoming the 1st female Vice Dean of the Faculty of Medicine (1991–1994). She has also been President of, and held numerous committee roles within, several other learned societies, including Presidencies of the International Society for the Study of Hypertension in Pregnancy (1998 – 2000), the Royal College of Obstetrics & Gynaecology's Blair Bell Research Society (1993 – 1999), the European Society for Developmental Pharmacology (President, 1992 –1994) and the Neonatal Society (1994 –1997).

She has sat on several Editorial Boards in addition to her own >200 peer-reviewed publications in high-impact journals, including *Nature* and *Nature Genetics*, as well as many physiology journals. She continues to publish, with three publications already in 2019 and several in preparation.

For over 30 years, Broughton Pipkin lectured in maternal and fetal physiology and was a personal tutor and postgraduate advisor to medical, BMedSci, Masters and PhD students and has successfully supervised 33 PhD/DM students to completion, many of whom have gone on to senior academic positions, including President of the Royal College of Obstetrics and Gynaecology. Although she now has Emeritus status, she remains very much research active and continues to mentor and guide junior staff in all aspects of physiology and academic life.

In addition to The Physiological Society's recognition, Broughton Pipkin has also been awarded many other prestigious accolades such as Fellowship *ad eundem* of the Royal College of Obstetrics & Gynaecology and

awards from the ISSHP as "Pioneer of perinatal physiology and pathophysiology of pre-eclampsia" and the Chesley Award in recognition of her sustained and substantial contribution to research in pre-eclampsia and for encouraging the work of others.

Tasuku Honjo

The award of Honorary membership was given to Tasuku Honjo in recognition of his discovery of a cancer therapy by inhibition of negative immune regulation for which he was jointly awarded the 2018 Nobel Prize in Physiology or Medicine. Honjo delivered his Nobel Lecture on 7 December 2018 at Aula Medica, Karolinska Institutet in Stockholm.

Honjo studied medicine at Kyoto University and received his PhD there in 1975. During the 1970s he also worked in the United States at the Carnegie Institution of Washington in Washington, DC, Department of Embryology, Baltimore and at the National Institutes of Health in Bethesda, Maryland, with which he also was later associated as a visiting research fellow. In Japan, he has worked at the University of Tokyo, Osaka University and is currently Distinguished Professor of Kyoto University Institute for Advanced Study and concurrently Professor of Department of Immunology and Genomic Medicine, Kyoto University, and also Chairman of the Board of Directors, Foundation for Biomedical Research and Innovation.

In addition to The Physiological Society's recognition Honjo has received many awards, including the Imperial Prize, the Japan Academy Prize, the Robert Koch Prize, the Order of Culture, the Tang Prize, the Kyoto Prize, the Keio Medical Science Prize and Japan Bioindustry Award. He was honoured by the Japanese Government as a person of cultural merits in 2000 and elected as a foreign associate of the National Academy of Sciences, as a member of Leopoldina, the German Academy of Natural Scientists and also as a member of Japan Academy.

Congratulations to physiologists in the Queen's birthday honours

Graham Collingridge, Professor of Neuroscience in Bristol's School of Physiology, Pharmacology & Neuroscience has been awarded a CBE for his services to neuroscience research. His research has advanced our understanding of the cellular basis of memory and learning, by looking at how synaptic plasticity affects brain function.

Kevin Fong, UCLH's consultant anaesthetist and Honorary Senior Lecturer in Physiology received the OBE for services to healthcare and medicine. He has a degree in astrophysics, a master's degree in astronautics and space engineering and has contributed to several reviews of UK space policy. As a science broadcaster for the BBC, Kevin engages audiences in many of the scientific, technological and ethical challenges that face modern medicine.

Growing Older, Better

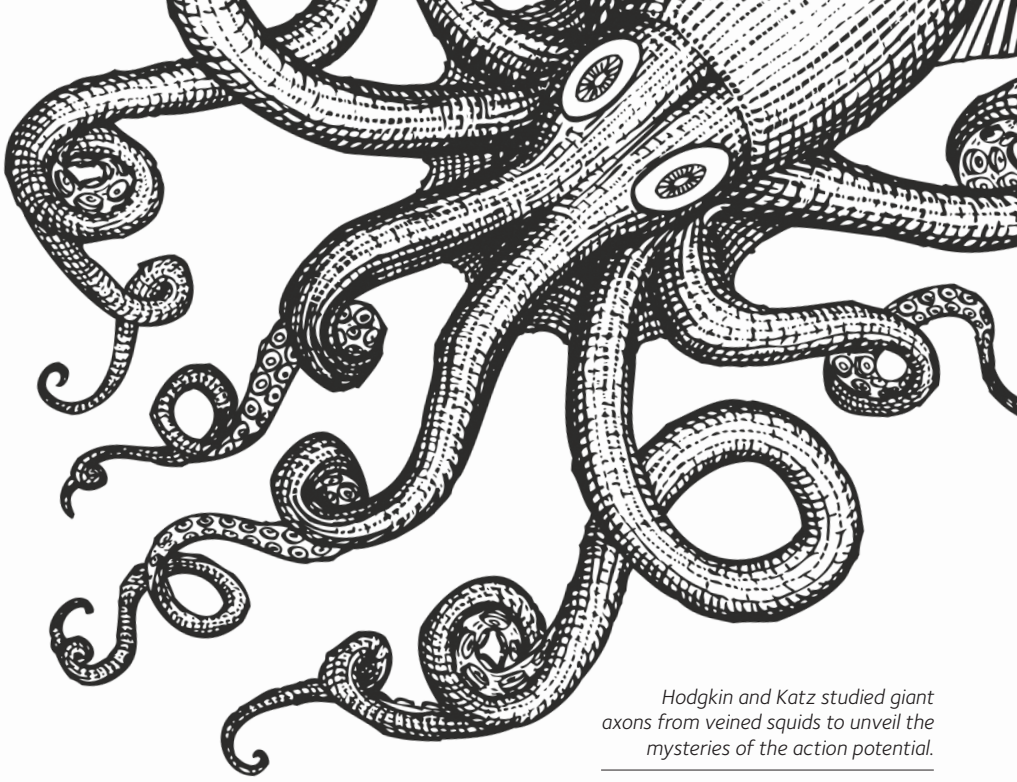
The Physiological Society has identified healthy ageing as an area of public policy which would benefit from increased involvement from The Society and its Members' research. We have convened an Expert Group, chaired by Paul Greenhaff, and including experts within The Society on ageing, world-leading epidemiologists, BBSRC, Dunhill Medical Trust, the Academy of Medical Sciences' FORUM team and Alzheimer's Research UK. For the past 12 months we have worked with over 60 expert stakeholders from a variety of different backgrounds including researchers, funders, charitable organisations, public health bodies and government. Our aim is to identify ways in which The Society and its Members can support the Government's Healthy Ageing Grand Challenge target of an average of "five healthier, more independent years by 2035."

The final report *Growing Older, Better: Ensuring a physiology-based response to healthy ageing* covers four main themes: the variety of physiological research currently being undertaken into ageing, the funding landscape for physiology, the importance of interdisciplinary working to improve our understanding of healthy ageing and how to best integrate current physiological understanding into public health guidance. The report has been designed to be relevant to a number of different audiences, with a particular focus on funders and policymakers.

While the report is being launched formally on Tuesday, 15 October, 19:00 – 22:00 in the Houses of Parliament, the report will be available on our website **physoc.org/healthyaging**.

Where it all began

A look back at papers from our journal archives that went on to become classics.



Hodgkin and Katz studied giant axons from veined squids to unveil the mysteries of the action potential.

50 years ago: The number and volume of preceding breaths does not determine breath-hold time

Godfrey S, Campbell EJ (1969). Mechanical and chemical control of breath-holding. *Quarterly Journal of Experimental Physiology and Cognate Medical Sciences* **54**(2), 117–128.

In this study, the renowned respiratory physiologists Simon Godfrey and Moran Campbell conducted a series of experiments in nine healthy male volunteers, which included themselves. They found that when a standardized breath-hold was interrupted by a rebreathing period, the duration of a subsequent breath-hold did not depend on the number of intervening breaths (one to five). Their findings highlighted alveolar carbon dioxide tension as a critical factor, which increased linearly at a rate of 0.8 kPa min^{-1} during breath-hold until reaching a threshold value of approximately 10.0 kPa at which point rebreathing was triggered. So, when reaching the surface during free diving, one breath is as good as five before descending for another dive!

70 years ago: Experiments in squids reveal that action potentials are all about sodium

Hodgkin AL, Katz B (1949). The effect of sodium ions on the electrical activity of the giant axon of the squid. *Journal of Physiology* **108**(1), 37–77.

In a series of experiments conducted at the Marine Biological Association Laboratory in Plymouth, Alan Lloyd Hodgkin (1914 – 1998) and Bernard Katz (1911 – 2003) immersed giant axons obtained from the hindmost stellar nerve of the veined squid (*Loligo forbesi*) in seawater and added different hypertonic and dextrose-containing solutions to manipulate extracellular ionic concentrations while measuring the membrane potential using microelectrodes. Based on their findings, they inferred that the resting membrane potential results from a high resting membrane permeability to K^+, and that depolarisation during an action potential results from a transient rise in membrane Na^+ permeability. Hodgkin and Katz both later won the Nobel Prize in Physiology or Medicine for their contributions to neurophysiology.

100 years ago: The birth of capillary physiology as a distinct scientific field

A Krogh (1919):

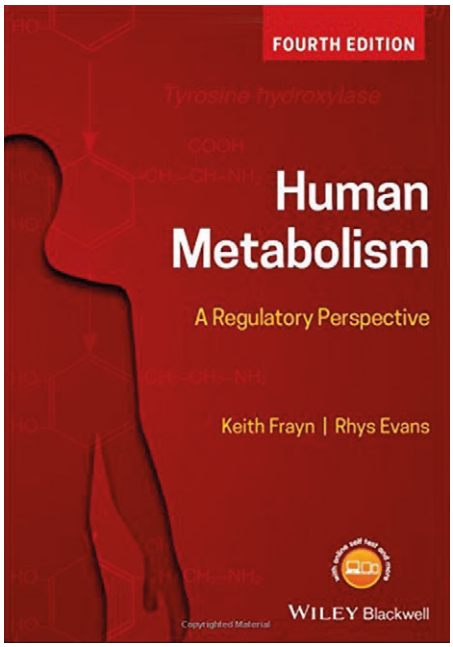
- The rate of diffusion of gases through animal tissues, with some remarks on the coefficient of invasion. *The Journal of Physiology* **52**(6), 391–408.
- The number and distribution of capillaries in muscles with calculations of the oxygen pressure head necessary for supplying the tissue. *The Journal of Physiology* **52**(6), 409–415.
- The supply of oxygen to the tissues and the regulation of the capillary circulation. *The Journal of Physiology* **52**(6), 457–474.

The Danish Professor of zoophysiology August Krogh (1874 – 1949) certainly had a nose for the sensational, which he already demonstrated in 1910 when he published seven back-to-back papers in Skandinavisches Archiv für Physiologie (now Acta Physiologica) in which he systematically deconstructed the oxygen secretion theory of pulmonary gas exchange proposed by his mentor Christian Bohr (1855 – 1911). After that, Krogh's attention turned towards gas exchange in tissue capillaries, which were considered passive tubes whose calibre was determined chiefly by their internal pressure. Because it had been documented that tissue oxygen tension was near zero under resting conditions, and because an increase in blood flow through already open capillaries could not explain how the oxygen supply was maintained under working conditions, Krogh questioned this. He thus constructed equipment to determine the diffusion constant of oxygen in tissues, and made determinations on skeletal muscle and connective tissue from frogs. He furthermore determined the capillary density in skeletal muscle in numerous species, and found that it varied according to the size and metabolism of the animal. Knowing the diffusion constant, and with the help of an equation provided by the mathematician and traffic engineer AK Erlang (1878 – 1929), Krogh then estimated the oxygen tension in the tissues, and concluded that only a fraction of the capillaries had to be open to achieve an oxygen tension near zero under resting conditions. One day, when Krogh sat in the university library, it struck him that this was consistent with a concept which he designated "capillary recruitment". He then arranged a series of experiments on frogs and guinea pigs in which he directly visualised the capillary circulation by microscopy. He showed that while most of the skeletal muscle capillaries are closed for the passage of blood under resting conditions, tetanic stimulation, gentle massage, or spontaneous contraction causes the capillaries to be recruited in a reversible fashion, so that the metabolic demands of the tissue are met. With his habit for the sensational, Krogh subsequently submitted all this work as three papers for publication in the May 1919 issue of *The Journal of Physiology*. The following year, Krogh was awarded the Nobel Prize in Physiology or Medicine for his discovery of the capillary motor regulating mechanism.

Human Metabolism: A Regulatory Perspective

By Keith Frayn and Rhys Evans

Andrew Murray
University of Cambridge, UK



Keith Frayn, Rhys Evans
Wiley-Blackwell; 4th edition (2019)
ISBN: 978-1-119-33143-8

"Frayn and Evans have done a marvellous job of updating this textbook to reflect recent developments in metabolic research"

Readers familiar with previous editions of Keith Frayn's textbook, formerly published as *Metabolic Regulation: A Human Perspective*, might spot two changes when picking up this newly–revised Fourth Edition. Rhys Evans, a cardiothoracic intensivist and metabolic biochemist, has been brought on board as a co-author whilst the title has been enigmatically tweaked. The latter change reflects the inclusion of significant additional material pertaining to integrative aspects of human metabolism, but perhaps also signals the authors' intent to reach a broader audience of medical, nursing, sports science and nutrition students, in addition to biochemists and physiologists.

In its previous incarnations, this book was a fine companion to the more traditional biochemistry textbooks, eschewing detailed descriptions of metabolic pathways and instead favouring lively and lucid discussion of the regulatory and integrative aspects of human metabolism. The text benefitted from Frayn's personable tone and careful use of illustrative examples; an explanation of the comparative storage properties of fats and carbohydrates was, for instance, accompanied by a memorable photograph of 1 kg of potatoes sitting alongside 90 g of olive oil (each representing 3.3 MJ of energy). The result was a highly accessible and very readable text, which became a mainstay on the reading lists of many of us who teach metabolic physiology. The substantial revisions in this new edition lend it the feel of a weightier, more stand-alone volume. Overviews of key pathways of carbohydrate, lipid and protein metabolism have been drafted in, but have helpfully been treated with the same clear and concise tone, with key messages emphasised and the occasional judicious use of analogy, e.g. parallels are drawn between soap manufacture and mobilisation of lipid reserves.

At the core of this book, tissue specificity is highlighted through an analytical, organ by organ account of metabolic function in liver, heart, brain and skeletal muscle, as well as endothelium, enterocytes and immune cells. The revised section on adipose tissue reflects recent research on the importance of brown adipose tissue in humans and factors driving the browning of adipocytes in white adipose tissue. As in previous editions, digestion is dealt with in a separate chapter, and here the authors include up-to-date material on the emerging importance of the human gut microbiome to nutrient acquisition, metabolic signalling and possibly body weight regulation. This section is cross-referenced to a new discussion highlighting the function of metabolites as signalling molecules. A careful line is drawn between these actions and the classic picture of endocrine mechanisms, whilst recognising that the distinction is not as clear as we might once have thought. These, and other hot topics in metabolic research, are handled well throughout; the authors presenting balanced evidence from more controversial areas whilst showing the field to be dynamic, and inspiring prospective researchers amongst the readership.

As with previous editions, the book concludes with a series of chapters covering integrative aspects of metabolic physiology and pathology. Alongside the challenges of exercise and fasting, a new section deals with the metabolic demands of human pregnancy, considering maternal, fetal and placental metabolism and the complex regulatory interplay entailed. This often overlooked area is an exciting yet challenging area of research, with significant implications for lifelong health and is a welcome inclusion here. Similarly, the consideration of metabolic dysregulation in cancer, sepsis and trauma, sits well alongside updated accounts of atherosclerosis and the more classical metabolic diseases of diabetes and obesity. This section will no doubt appeal to medical students, but also rounds off the narrative arc from molecules to whole body, giving this new edition a truly comprehensive feel.

Frayn and Evans have done a marvellous job of updating this textbook to reflect recent developments in metabolic research whilst retaining the core material that made previous editions such a valuable resource. Alongside some of the more cosmetic changes (a two-column format and full-colour illustrations), substantial updates to the content of *Human Metabolism: A Regulatory Perspective* have broadened its scope to thoroughly cover the basics of metabolic regulation whilst expanding discussion of integrative metabolic physiology and pathology. Happily, the text has lost none of its celebrated readability, and so I now have the relatively simple task of updating my reading list for this coming year's lectures to recommend this terrific new edition.

Meeting preview

Future Physiology 2019: Uniting early career researchers

17 – 18 December 2019,
Liverpool John Moores University,
Liverpool, UK

physoc.org/events/future-physiology-2019/

Katie Hesketh & Mark Viggars

Liverpool John Moores University,
Liverpool, UK

Whilst modern medicine has gifted us with an increase in lifespan, physiologists must strive to help meet this with an increased health span. As researchers, our minds are often constrained to our own specific niches: fixated on certain genes, signalling pathways and cell types. However, humans are complex organisms where ageing and age-related disease is often multifactorial. Developing physiologists who can collaborate and translate basic science to clinicians and policymakers to prevent, treat and intervene will be key to achieve extended health span.

Future Physiology 2019, our two-day early career conference in December, will have an overarching theme of "Translating Cellular Mechanisms into Lifelong Health Strategies" where we will aim to bridge the gap between identifying novel mechanisms behind ageing and age-related disease and designing interventions or therapeutics to delay or combat them. The conference, held at Liverpool John Moores University, will be split into four sessions over two days, including eight keynote sessions from international speakers, as well as invited oral presentations and poster sessions from early career researchers.

We will hear insights from our keynote speakers into their successes and failures in their careers and how to manage them effectively. We hope that Future Physiology 2019 will bring early career researchers with backgrounds in basic and applied sciences together to share their work, develop each other's thinking processes and inform each other's future practice.

The first day will begin with a session titled "Lifecourse Epidemiology, Genetics and Epigenetics" and will include a keynote from stem cell biologist Claire Stewart (Liverpool John Moores University, Liverpool, UK), the current Chair of the British Society for Research on Ageing. Claire's talk on what ageing is, contemporary issues in an ageing society and ageing research will be followed by Robert Seaborne (Blizard Institute, Queen Mary University of London) who will discuss how exercise and nutrient stress alter the DNA methylome and the functional consequences this hypo/hyper methylation has on gene expression.

The afternoon will be focused on "Novel Mechanisms Behind Lifelong Health" starting with a keynote from Karyn Esser (University of Florida), expert on circadian rhythm in skeletal muscle. Karyn's work on mutant mice with molecular clock defects has shown that these "clock" genes are key for skeletal muscle structure and function. Karyn Esser will discuss how her lab is using mouse and human models to design lifestyle interventions to enhance molecular clock function for muscle and whole-body homeostasis and health in ageing. Natalie Pollock will follow this session with a talk on sarcopenic motor end plate disruption

and how consequently, this generates reactive oxygen species and mitochondrial dysfunction.

Whilst some crossover is expected to occur between both days, the second day will look in finer detail at translational research, starting with a morning session on "Diet, Obesity and Disease" starting with a keynote from Anton Roks (Erasmus University Medical Centre) on how a low-calorie diet prevents endothelial and smooth muscle genome instability in a mouse model of vascular ageing and how this may translate to humans. This will be followed by Lasse Gliemann (University of Copenhagen) and a talk on reduced vascular function in ageing and how high-intensity aerobic training can help prevent progression and reverse functional decline in different populations.

The final session of the meeting will be aimed around "Exercise and Lifestyle Interventions for Lifelong Health" starting with a keynote from Mats Nilsson (McMaster University) on how lifelong endurance exercise can protect against progressive systemic "inflammaging", is protective against multiple cancer types, extends lifespan in mice and how we can promote this in society. Finally the conference will conclude with Charlotte Edwardson, on the role of physical activity and sedentary behaviour in the prevention and management of chronic diseases.

Join us for these professional developmental sessions:

- Making presentations memorable
- Publishing for the first time
- Lifelong Health Stations-Practical Session
- Postdoc challenges

"We hope that Future Physiology 2019 will bring early career researchers with backgrounds in basic and applied sciences together to share their work, develop each other's thinking processes and inform each other's future practice"

Key information

Abstract submission opens:
1 September

Abstract submission closes:
30 September

Abstract decisions released:
25 October 2019

Travel Grant deadline:
31 October 2019

Early bird registration deadline:
31 October 2019

Online registration deadline:
2 December 2019

Meeting notes

Physiology 2019: Bringing together our vibrant community of physiologists

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

Susan Deuchars
Chair of Conferences Committee,
The Physiological Society
& University of Leeds, UK

It may not have been the warmest of venues if you just consider the temperature but Aberdeen certainly gave physiologists the warmest of welcomes and this is what our Annual Conference is all about! Physiology 2019 was our first "solo" Annual Conference for a number of years and it lived up to a long-standing reputation for presenting the best of physiological research whilst enabling open and wide-ranging discussion on the findings. Stephen Traynelis, one of the distinguished scientists who delivered an inspirational prize lecture, really summed up the ethos of the conference by stating that "findings from one system can translate across the boundaries". His comment and others from the conference show how much all of us value this sharing of ideas across disciplines as it is critical for research to reach its full potential. It was lovely to hear this sentiment echoed not only by senior researchers but also by physiologists at earlier stages of their career. One PhD student who works in cardiovascular science stated how much she had enjoyed Stephen's talk on glutamate receptors because she could consider how it could also apply to her work.

With this in mind, there was the potential for all attendees to showcase their research, regardless of their career stage, and with 126 oral communications, we had talks from incredibly composed undergraduate students, PhD students and postdoctoral researchers as well as senior academics. Symposia, all of which had both established and early career scientists speaking with excellent gender balance, ranged in subject from "The cardiovascular implications of air pollution" through to "Nuclear receptors and transcriptional regulation in metabolism and endocrinology." It was especially pleasing to see such good attendance at the teaching symposia, emphasising how highly physiologists rate the education of future scientists.

A packed programme of workshops at lunchtimes provided opportunities for people to learn about the use and abuse of statistics or the importance of transparency about animal research. For scientists at all points in their career, there were also very well-attended workshops on publishing, grant applications, and CVs, and the feedback has been very positive. There is a great focus at The Society to ensure inclusion of all physiologists and this was highlighted with the first workshop on "LGBT and The Society: Promoting Inclusivity" where a key message was the importance of LGBT allies in ensuring that all our activities are inclusive. Our Equality and Diversity Champions are always happy to learn about future events or support that will encourage attendance and openness at meetings.

Physiology 2019 also saw the introduction of Satellite Symposia and these were very well received, from the science to the social activities. Finally, we could not have a conference in Aberdeen without a ceilidh following the Society dinner. The energetic, if not always step-perfect dancing really allowed people to get rid of energy after a day of scientific discussion, although I defy anyone to try and talk physiology whilst also stripping the willow! Thank you to the local organising committee, especially Guy Bewick and Derek Scott, for their real commitment to boosting the success of this conference, it certainly paid off.

Dariel Burdass
Chief Executive, The Physiological Society

One of the best things about working at The Physiological Society is the opportunity to meet and engage with our Members and I was delighted to be able to do this at our Annual Conference in Aberdeen this year. It was a privilege to be able to hear a range of inspiring and cutting-edge research from our keynote speakers, listen to an impressive range of talks from across our Themes and discuss posters. I was also impressed by the range of professional development opportunities on offer for all stages of physiologists. This was my first Annual Conference and what I most appreciated was the enthusiasm, sense of purpose and inclusiveness – I was proud to be part of this vibrant community that will ensure physiology is flourishing.

Guy Bewick & Derek Scott
Local Organising Committee
University of Aberdeen, UK

Over 850 delegates from all over the world came to Physiology 2019, eager for the "Scottish experience" along with their guaranteed three days of world-class science. Any trepidation in organising such a big meeting was unfounded, as the Events team made it so easy. They did all the "heavy lifting" – advertising, booking venues and accommodation, inviting speakers, organising payments, timetabling the science and the social programme: they handled it all with calm efficiency and fantastic good humour. Keen to incorporate suggestions for creating "local flavour" (whisky tasting, walking tour of Aberdeen, bagpiper welcome and ceilidh dance, to name a few), their wealth of experience also means they have an instinct for what works best (e.g. where and when volunteers are most useful). A highlight for us was the strong involvement from the local universities and colleagues keen to showcase the strength of physiology research and teaching in Aberdeen, from the Principal & Vice Chancellor George Boyne, our Head of School Siladitya Bhattacharya and Heads of the Institutes to the army of undergraduates and early career researcher (ECR) volunteers who contributed hugely to the success and smooth running of the event. Another highlight was the number and variety of Satellite Symposia, many over-subscribed, adding diversity and vitality to the meeting build up. The number of local symposium organisers was another highlight, fantastic opportunities to showcase the breadth of local science.

More generally, we enjoyed the truly world-class and high-profile scientists delivering the prize lectures, particularly the truly stunning Paton Prize Lecture by Kevin Fong, Sylvia Arber's beautifully clear exposition at the Annual Prize Lecture of her ground-breaking work on motor control, Lora Heisler's Annual Public Lecture reminding us all to exercise more and eat less, and the celebrated textbook author Dee Silverthorn's wonderfully whole-hearted commitment to the meeting – not only in the tremendously popular teaching symposium but also at the ceilidh at the Beach Ballroom after the conference dinner.

Finally, some advice for anyone tempted to host future events – start early (we began with Physiology Friday 2017), get local buy-in from your department (let them know it is happening, email deadlines). We ran a "best local abstract" competition to sponsor attendance. Use social media and wider community promotion groups (e.g. tourist information), local press and your public engagement office. Then, post your activities on social media accounts both personal and university. And, most especially, involve the undergraduate and ECR community – who for us were outstanding in their enthusiasm and commitment – from UG membership recruitment campaigns through public engagement and manning the registration desk, to befriending first-time attendees. We, the local organising committee, all had a brilliant time. Thanks to all involved at every level, whether organising or attending. Would we do it again? In a heartbeat. The Society Council and staff made it all so easy – so a very special and final thank you to them.

"Would we do it again? In a heartbeat. The Society Council and staff made it all so easy"

Katarina Miteva
University of Leeds, UK

As a former University of Aberdeen student, I remember once someone told me that Aberdeen is like Marmite – you either love it or hate it - mainly because of the consistent grey colour scheme and unpredictable weather. In my case, Aberdeen will always feel like a warm hug and a home. That's why I was very excited to return to Granite City to attend and present my research at Physiology 2019.

Physiology 2019 was the first time I attended an Annual Conference organised by The Physiological Society. From the Satellite Symposia to the Prize Lectures, I was very impressed by the diversity and quality of research presented. I really enjoyed the inspirational Paton Prize Lecture delivered by Kevin Fong, OBE, on the extreme limits of human physiology and of course, my personal favourite – the Hodgkin-Huxley-Katz Prize Lecture delivered by Stephen Traynelis who presented his exceptional new data which truly pushes the boundaries of what we know about ion channels. The AECC main area was a perfect fit for the dynamic poster sessions and fostered several successful networking encounters (and whisky tasting!). What made my experience in Aberdeen even more amazing was the fact that I was awarded the Vascular and Smooth Muscle Physiology Prize for the Early Career Competition. I would like to thank the judges and The Physiological Society for the award as well as for supporting my attendance with a travel grant.

Morag Mansley
The University of Edinburgh, UK
Epithelia and Membrane Transport Theme Lead & Satellite Symposium Organiser

& Mike Althaus
Newcastle University, UK
Epithelia and Membrane Transport Theme Lead

As Theme Leads for Epithelia and Membrane Transport (EMT), we both thoroughly enjoyed Physiology 2019 in Aberdeen. Over the three-day meeting we had fantastic oral communications, symposia and poster sessions covering a wide range of research into cellular and epithelial transport systems.

On Monday morning, our first session of oral communications provided some fascinating research into the role of membrane potentials in axial regeneration in planaria flatworms, the therapeutic value of gene editing in cystic fibrosis, as well as the regulation of pancreatic stellate cell proliferation by calcium transport. The afternoon symposium, "A nasty case of the vapours – E-cigarettes friend or foe?" organised by Deborah Baines, St. George's University of London, was highly topical and we heard from four researchers who presented their novel findings into the pathophysiological effects of vaping. We arranged an informal dinner with Scottish tapas where scientific (as well as some non-scientific discussions) between students, early career researchers and senior scientists continued late into the evening. The opportunity for more informal networking was a genuine highlight and promoted our network of Epithelia and Membrane Transport physiologists.

Tuesday got off to a great start with the Joan Mott Prize Lecture "Mind the gap: connexions and cell communication in the kidney" by Claire Hills, University of Lincoln. This was a fantastic lecture highlighting the critical role of gap junction signalling in the progression of diabetic nephropathy and how this might be targeted therapeutically in the future. Following on from this was our second session of oral communications where we heard about circadian rhythms of sodium transport within the kidney, modulating mucosal pH in the lung as a possible therapy in cystic fibrosis, as well as novel functions of the delta subunit of the epithelial sodium channel. The following Hodgkin-Huxley-Katz Prize Lecture "Allosteric regulation of glutamate receptors" by Stephen Traynelis, Emory University gave deep and fascinating insight into the structural basis and regulation of glutamate receptor ion channel function. In the afternoon, the symposium "Lung epithelial stem cells in human lung homeostasis and disease" chaired by James Garnett, Newcastle University highlighted an exciting new field in lung epithelial biology, with speakers addressing the role of epithelial stem cells in lung development and epithelial cell differentiation.

Wednesday morning began with our final session of oral communications, with the hardy but slightly weary delegates in attendance following the excellent conference dinner and ceilidh on Tuesday evening at the Beach Ballroom. We heard about the role of the farnesoid receptor X both as a target for intestinal disease as well as its ability to regulate cystic fibrosis transmembrane conductance, and the role of haem oxygenase and carbon monoxide as regulators of ion transport and cytokine release within the airways. Our final symposium was the excellent "Milestone achievements in anion transporter research" organised by Ursula Seidler, Hannover Medical School and Vinciane Saint-Criq, Newcastle University. We heard some great talks covering the structural basis of ion permeation in anion channels up to the physiological regulation of various anion channels across a wide range of cells and systems.

We would like to extend our thanks to all of the EMT delegates who attended Physiology 2019 and made it such a vibrant meeting. We are already looking forward to Europhysiology in Berlin next year!

Laura Rich
University of Nottingham, UK

Physiology 2019 is the best conference I have attended in my career so far. Throughout the conference I enjoyed being exposed to a wide range of research, which encouraged me to think about my own work from different angles. I certainly came away with plenty of notes. A particular highlight was the first day poster session. The opportunity to visit other posters can be limited when presenting your own, so I was looking forward to speaking to other researchers about their work. This was an insightful experience, allowing the opportunity to not only hear about some fascinating science, but also to pick up tips on ways of presenting posters, a useful opportunity for any student. I was then fortunate to have a very positive poster session on the second day; interesting discussions with lots of people have really increased my confidence in my work.

After encouragement from my supervisor I decided to attend the conference dinner and I'm so glad I did. I ended up at a really welcoming and interesting table where we embraced Scotland throughout all three courses of the meal, topped off with a ceilidh. Thank you to everyone for putting up with my terrible coordination! The growing importance of social media in science communication prompted me to embrace Twitter, starting at Physiology 2019. The ongoing enthusiasm portrayed in many tweets enhanced the conference experience. In particular, the reactions on social media to the session promoting inclusivity in STEM were encouraging - a topic explored in the recent Diversity Special Issue of *Physiology News*. I came away feeling inspired and fortunate to be part of such a welcoming Society, so I think all that is left to say is thank you to all the organisers. I can't wait for the next conference.

Susan Currie & Margaret Cunningham
Satellite Symposium organisers,
University of Strathclyde, Glasgow, UK

It was a pleasure to organise the Satellite Symposium "Cellular mechanisms of anti-cancer induced cardiotoxicity" as part of the recent meeting in Aberdeen. The team from The Physiological Society provided ongoing highly professional support which ensured the whole process ran very smoothly. The invited speakers came from across Europe and all delivered excellent presentations that highlighted not only recent research achievements, but also different challenges for the growing field of cardio-oncology. Having this focused forum that brought together basic science and medicine was invaluable and we enjoyed sharing our research and gaining insight into the different approaches across laboratories. There was plenty of time for discussion during the poster session that followed and the whisky tasting that rounded off the evening. Everyone thoroughly enjoyed that – especially with the contributions from local distilleries!

As a result of this symposium, we intend to keep the momentum going and aim to build a European network in the area of anti-cancer cardiotoxicity. We hope to start by organising another meeting next year and to build our collaborative links with both the participants and delegates we've already met and those we have yet to meet. A big thank you to The Physiological Society for providing us with the opportunity to hold this symposium.

"Physiology 2019 is the best conference I have attended in my career so far"

Caitlin Daniels
Sutton Grammar School, UK

I've always had a keen interest in science and biology, but I had never really been aware of the field of physiology until my mum introduced me to it last year. I was immediately intrigued because it combines all of the best bits of biology, chemistry, and physics. I was excited to learn about the new and exciting examples of research and the idea of travelling for a conference sounded incredibly grown up and official – and I was not disappointed. I had an amazing few days and learned so much from all of the talks I attended, in particular the symposia entitled "Pain: Nociception to perception" and "A nasty case of the vapours: E-cigarette friend or foe", which even I, although limited to my A Level knowledge, could see were wonderful examples of how physiology ranges from the very small, single-cell level, right up to the global scale; studying the impact of the smallest particles through to the impact of social attitudes towards science.

It was such a warm, friendly environment; scientists are definitely not the cold, calculating types sometimes portrayed in the media. Everyone was so friendly and the sense of community was almost overwhelming. I hope to have made some good, long-lasting connections. Finally, it was refreshing to see the range of people represented at this event – from different backgrounds, generations and countries – all brought together by a common interest. I also really enjoyed seeing how many female scientists were talking and displaying their research, especially in higher-level positions, clearly having succeeded in their chosen field. It has given me a lot more confidence in my potential career path, knowing that it is possible to go as far as you want. All in all, it was an eye-opening and enjoyable way to spend a week, especially making fools of ourselves attempting to dance at the cèilidh. I would highly recommend to anyone interested in physiology, to come along next time if possible. It is totally worth it.

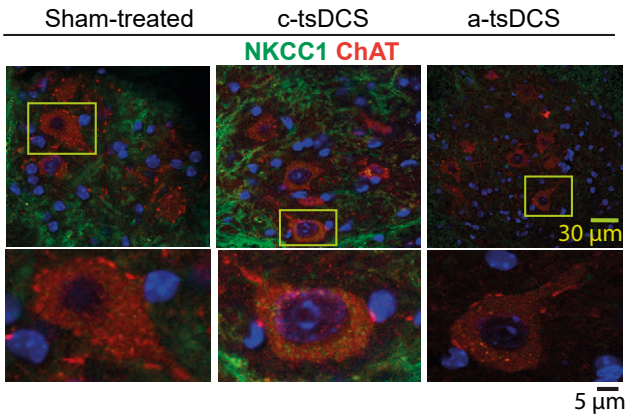
Europhysiology 2020 in Berlin next year!
europhysiology2020.org/

The Journal of Physiology

Repeated anodal trans-spinal direct current stimulation results in long-term reduction of spasticity in mice with spinal cord injury

Mekhael W et al. (14 April 2019)
DOI: 10.1113/JP276952

Spinal cord transection results in paralysis and loss of sensation, but also leads to spasticity in about one third of sufferers, where involuntary muscle contraction results from muscle stretching. It was previously reported that in a mouse model, sciatic-to-spinal trans-spinal subthreshold direct current stimulation, termed cathodal-tsDCS (c-tsDCS), resulted in a significant decrease in muscle tone. Thus the aim of this study was to determine whether c-tsDCS could decrease muscle tone associated with spinal cord injury (SCI). Mice were subjected to experimental SCI followed by a period of c-tsDCS. The main results were that some of the pathological consequences of SCI could be attenuated by the therapy, resulting in decreased spasticity and improved locomotor skills. An intriguing feature is that the mechanism underlying this improvement may be related to the NKCC1 co-transporter, which is up-regulated following SCI, but following c-tsDCS its expression is decreased.

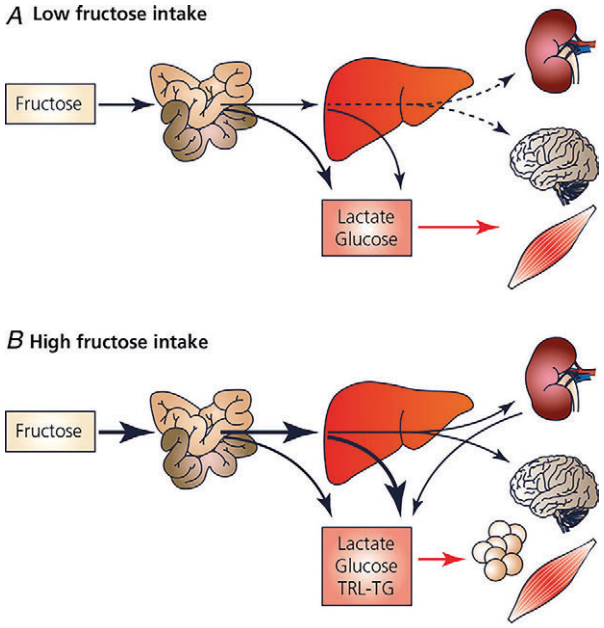


NKCC1 and phospho-NKCC1 expression following one stimulation session in intact mice. Confocal images of spinal motor neurons stained for NKCC1 (green) and ChAT (red). Motor neurons showed an increase and decrease in NKCC1 after cathodal and a-tsDCS respectively.

Health outcomes of a high fructose intake: the importance of physical activity

Tappy L and Rossett R (15 July 2019)
DOI: 10.1113/JP278246

The potentially damaging effects of a diet high in fructose has been a concern to public health for the past 30 years, given that fructose can account for 10% of energy intake in affluent countries. Consumption of high levels of fructose is considered to contribute to fatty liver disease, obesity, insulin resistance and diabetes. However athletes undertaking extreme sustained exercise, such as the three week long Tour de France, consume enormous amounts of fructose without any ill effects. This inconsistency can be resolved if one considers not just the amount of fructose ingested by individuals but the individual's level of physical activity. In the proposed model, fructose only has pathological effects when it is ingested at levels that exceeds the liver's ability to convert and release it as glucose and lactate. Under conditions of low physical activity this released glucose and lactate prevents any further conversion of fructose, which is instead stored as liver glycogen and lipid. The authors propose that an appreciation of the lifestyle of our ancestors can clarify this discrepancy. The physical nature of the work carried out by agricultural workers during harvesting in summer and autumn made fructose an ideal energy source, which coincided with the availability of fructose-rich fruit. In addition, fructose served as an excellent source of stored energy in anticipation of decreased caloric availability during winter.



Rodent studies indicate that with small oral loads (A), almost all ingested fructose is taken up in small bowel enterocytes to be released into the blood as glucose, lactate and various other metabolites. Under such conditions, portal fructose concentration, and hepatic and systemic fructose metabolism are very low. With larger fructose loads (B), intestinal fructose uptake is most likely saturated, and fructose is delivered into the hepatic portal blood, from which it is largely extracted by the liver. Under such conditions, both the gut and the liver release fructose carbons as glucose, lactate and triglyceride-rich lipoproteins into the systemic circulation. A portion (ca 15% of a 30 g fructose load), however, escapes gut and hepatic uptake and reaches the systemic circulation. In humans, the maximal fructose load being taken up by the gut, and the relation between total fructose intake and systemic fructose appearance, remain still unknown. TRL-TG: triglycerides in triglyceride-rich lipoproteins.

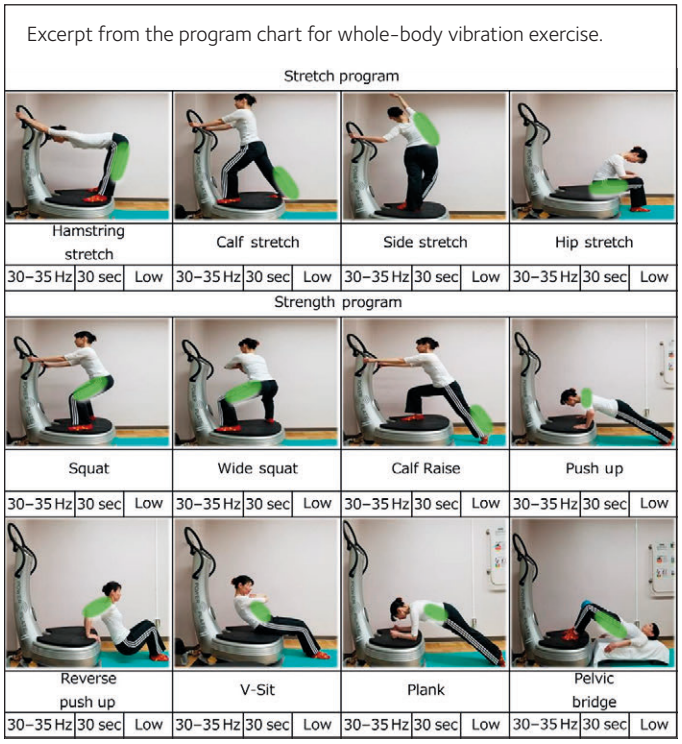
Physiological Reports

Whole-body vibration for patients with nonalcoholic fatty liver disease: a 6-month prospective study

Oh S et al. (13 May 2019)
DOI: 10.14814/phy2.14062

Physical exercise provides benefits for management of nonalcoholic fatty liver disease (NAFLD) but maintaining exercise can be difficult. Whole-body vibration (WBV) which can passively effect dynamic changes in muscle fiber length while the patient sits or stands on a platform may represent an alternative for those who have difficulty performing exercise. In this study of 42 NAFLD patients, 25 participated in WBV (twice per week for 6 months – see Fig. 1 for WBV exercise program chart) while the other 17 received routine counselling on diet and physical activity. After 6 months, WBV had mildly improved BMI, skeletal muscle mass and various metabolic parameters compared to pre-intervention and compared to the non-WBV group. Furthermore, WBV decreased hepatic stiffness and markers of inflammation. The authors conclude that WBV may provide benefits for NAFLD patients who have trouble exercising.

Excerpt from the program chart for whole-body vibration exercise.



Comparison of surgical versus diet-induced weight loss on appetite regulation and metabolic health outcomes

Halliday TM et al. (29 March 2019)
DOI: 10.14814/phy2.14048

Unlike diet-induced weight loss, bariatric surgery has been associated with changes in food preferences away from high-calorie choices and may also "reset" appetite–related hormonal responses. Such "resetting" may increase adherence to weight loss management protocols. Herein, the authors compared the influence of 10kg weight loss by two different methods (Roux-en-Y Gastric Bypass [RYGB] vs. very low calorie diet [VLCD]–induced weight loss) on changes in appetite regulation and biomarkers of metabolic health. The VLCD consisted of the same calorie content and macronutrients provided to the RYGB group post-surgery. The authors found that weight loss was achieved more quickly in the RYGB group (n=6) compared to the VLCD group (n=17). Moreover, RYGB induced changes in appetite-related indices (including ghrelin, hunger, free fatty acids) that may be more favorable for sustained weight loss while VLCD induced changes that may promote weight regain.

Experimental Physiology

The LunHab project: Muscle and bone alterations in male participants following a 10-day lunar habitat simulation

McDonnell AC et al. (31 July 2019)
DOI: 10.1113/EP087482

In response to prolonged periods of inactivity and unloading there is musculoskeletal atrophy. As such, spending time in microgravity may not be of immediate detriment, but problems may arise on return to the Earth's gravity. Space exploration is further complicated by the fact that this would take place in hypobaric hypoxia. This study investigated the impact of hypobaric hypoxia on inactivity-induced musculoskeletal atrophy. Volunteers underwent three, ten-day interventions of i) hypoxic confinement, ii) hypoxic bed rest and iii) normoxic bed rest with muscle strength and bone composition being measured before and after. Ten days of bed rest led to a reduction in muscle volume and muscle strength but with no effect on bone or markers of bone turnover. The impact of bed rest was similar in both hypoxic and normoxic conditions. This study shows that even ten days of bed rest leads to changes in muscle mass and function but it is not altered by hypoxia.

Association of postprandial triglyceride responses with insulin resistanwce among rotational night shift healthcare workers

Kiranmala K et al. (30 May 2019)
DOI: 10.1113/EP087514

Shift work and disturbed circadian rhythms are associated with changes in metabolism and higher risks of cardiometabolic disease. This paper looked at the postprandial triglyceride metabolism and how it varied between healthy healthcare workers who did or did not work night shifts. Participants were fasted and given a standardised oral fat meal. Responses to the challenge were largely similar between the groups but only the shift workers demonstrated a positive correlation between fasting insulin and the homeostatic model assessment of insulin resistance (HOMA-IR) with the postprandial triglycerides, whether comparing the area under the curve or the peak triglyceride. These initial findings suggest that shift work might be associated with insulin resistance, which in turn results in altered triglyceride metabolism.

Visualising cell biology: We've an app for that!

How I am incorporating molecular visualisation into my teaching

John Barrow

University of Aberdeen, UK

Physiology depends on interactions between molecules. With the advent of modern visualisation methods, John Barrow, recipient of the David Jordan Teaching Award, discusses some of the ways that these often abstract molecular processes can be viewed to enhance the student learning experience. The David Jordan Teaching Award enables you to carry out a piece of educational research or to develop an educational resource that is relevant to physiology.

Visualisation for learning

Physiology depends on interactions between molecules. Histones wrap around DNA to package genes into the nucleus, and myosin and actin filaments slide past each other to make muscles contract. Biology is inherently dynamic, and yet most teaching materials (e.g. textbooks, lecture slides, etc.) show static representations of physiological processes. For those students who can think visually, this kind of static imagery can work as they are able to imagine what these processes would look like. However, for many it equates to a set of abstract ideas (e.g. "molecule A is converted into molecule B", or "molecule X interacts with receptor Y") that make the biology challenging to visualise and understand. With the advent of modern visualisation methods there is an opportunity to develop immersive and engaging material for students that will address some of the challenges they face when it comes to their learning. Indeed, if a student can engage with visual representations, then they would have the ability to think visually about dynamic processes (Herráez and Costa, 2013).

Changing with the times

My teaching is largely based on metabolism and biochemical pathways. When I studied biochemistry as an undergraduate my lecturers took a rote learning approach. Fast forward a number of years, and when I had the opportunity to teach the same subject I jumped at the chance, but I was keen to do it differently. My main goal was to make it more accessible for all of our life sciences students, as many of them encounter biochemistry and molecular biology in their foundation years but will not go on to study the subjects at an advanced level.

When I started teaching biochemistry it was my first teaching role, so I adopted lectures from a retiring academic and initially didn't change them very much. After a couple of years of teaching the material in much the same way as I had been taught, I began looking into ways of making the material more engaging and stimulating for students, as well as finding ways of making the concepts as digestible as possible. I began the process of switching from a rote teaching style by incorporating more visual components into my classes. This initially involved adding in videos of metabolic processes so that students could see them in action. From class feedback and talking directly with students, it was clear that these helped some students to understand the processes that had been

Figure 1. A frame from a video showing the metabolism AR app in action. You can see the human model, the digestive system and a reconstruction of blood vessels and cells, all appearing when your device is directed at the AR marker (square piece of paper on the desk).

presented statically in my lectures and their textbooks. But for me this was not enough as the imagery being shown was still a two-dimensional approach as it was being projected onto the lecture theatre wall. I wanted something that allowed students to fully interact with how the processes were actually working in their cells and bodies.

My initial foray into making classes more interactive was the use of 3D-printed protein models. My intention was to show the regions on the proteins that were important to their function, but this wasn't viewed favourably by students. They really liked the idea of seeing the proteins, but because the protein models are made from hard plastic it is difficult to convey the dynamic nature of the processes being taught. This is where digital visualisation comes in, as it offers a highly visual approach, but also provides interactivity to get students fully engaged in their studies.

Augmenting reality

There are several modern approaches to visualisation including virtual reality (VR) and augmented reality (AR). VR can be defined as a fully visualised world that a user can interact with via a headset. AR can be defined as digital visualisations being overlaid on the physical world around the user that usually require a mobile device such as a tablet or smartphone (for a really good guide see Garcia-Bonete *et al.*, 2019).

Both VR and AR have their pros and cons. VR allows for a fully immersive user experience via a headset, but it is usually a single user experience as others around that individual are not viewing the experience in the same way. AR allows users to see the processes on a device but not in a fully immersive way, which then allows for more interactivity between users. Because of this, I decided to use AR as it allows students to interact and see the visualisations, but also provides them the opportunity to work together in class.

How do you make visualisations?

Prior to receiving the David Jordan Teaching Award, I had created an AR app that shows insulin signalling and glucose absorption for high school pupils. To create this three-stage process showing food digestion, insulin release, and insulin action on muscle, the production of nine different models was required, with most of them being created from scratch and others being purchased from various asset repositories. These models were a human figure (1), a chocolate bar (2), hollow tubes to represent the gut (3) and blood vessels (4), pancreatic (5) and muscle cells (6), food particles (7), and finally glucose (8) and insulin (9) molecules. Once the models have been created, they then need to go through a process of refinement to make them as simplistic as possible without removing too much detail. 3D models are made from a wireframe of polygons, so a curved surface on a model is actually made up of many smaller flat-surfaced polygons joined together in a mesh. The more complex the mesh (i.e. the more polygons), the more challenging it is for a device to display, so to make a model that will be visible and animate smoothly on as many devices as possible requires the polygon number to be as low as possible. This creates a challenge, as reducing polygons makes a model less refined (akin to high-resolution graphics becoming more pixelated), so a lot of time and effort are put into minimising the polygon count whilst keeping the model true to form. Once all of the models have been created and refined, they are then given a surface. Surfaces are created to give each model specific surface colours or patterns, as well as allowing the models to be shaded to give them a more realistic appearance. Surfaced and shaded models are then imported into a game engine to allow the creation of animations and visual effects. Game engines are often used as they allow 3D models to be manipulated and animated with relative ease. For this particular application, the game engine allowed the models to be given textures that gave detail rather than the wireframe providing the details - this process makes the models more compatible with mobile devices that have limited processing and graphical capabilities. Following texturisation of the models, they are then animated using the mechanics of the game engine to code the movement for each model where required.

Figure 2. The metabolism AR app is accompanied by a leaflet that highlights how the process of food digestion, glucose absorption and glucose uptake into cells occurs. The edge of the leaflet shows the AR markers that trigger the visualisations for each part of the process.

> "With the advent of modern visualisation methods there is an opportunity to develop immersive and engaging material for students that will address some of the challenges they face when it comes to their learning"

Challenges of working with digital creators

Making augmented reality content has given me some interesting challenges that have been an unexpected surprise. Most of these challenges centred on trying to explain and describe the processes and how they should be visualised. Working with game design experts can be tricky at times as they are incredibly capable when it comes to creating content, but their understanding of the underlying biology is often basic, as the last time they studied biology was in secondary school. Having individuals who are skilled in visualisation methods but also have a solid grounding in the subject matter would streamline the production of high-quality visualisations. Perhaps the addition of coding and computer-aided design, or creative arts in science curricula is something that could work for some individuals wishing to pursue careers in this area, but that is a different story for another day. In practice, the collaboration of game designers, digital artists and me as the scientist worked because we had a process of careful iterations and beta-testing at each stage of the design process. Once each model, animation or design phase was complete, they were tested and approved, then we moved onto the next one in a highly detailed and structured way.

Applications of visualisation

As described here, there are many applications for visualisation in education settings, but the potential to use this type of technology in other areas is huge. Being able to visualise patient data, from brain scans to doppler ultrasound, could allow patients to see the issues they are facing and allow clinicians to easily explain the problems they are hoping to treat. Other areas where visualisation can be of benefit is in allowing patients to experience procedures they may face – a good example of this is the use of virtual reality apps for children who are undergoing stressful or invasive therapies. These technologies are also being used to help individuals deal with situations, such as those with autism, so that they can begin to train themselves to deal with situations in a safe environment that can simulate real world environments. There are also benefits for scientific research, such as the recent virtual reality tumour visualisations that allow scientists to immersively visualise tumours to gain a greater understanding of the structure and cell types found within the tumour (Walsh, 2018).

For me, being able to use this technology to convey the fundamental principles of processes such as receptor function, enzyme activity, protein–DNA interactions and protein–protein interactions will hopefully prove a positive experience for my students. The app I am currently developing with the David Jordan Teaching Award will highlight the dynamic nature of glycolysis and how this pathway is the gateway to the majority of metabolism. I would encourage any member of the society with an interest in teaching to apply for an award as it really can be transformative to your teaching and the experience of your students, so watch this space for updates!

Acknowledgements

I would like to thank The Physiological Society for their generous support through the David Jordan Teaching Award, which has allowed me to take my ideas for visualisation much further. The work highlighted in this article has been a collaborative project with Imagin3D (imagin3d.co.uk).

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Flipping physiology: Can we teach physiology in a different way?

A traditionalist tries out some new tricks

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Angela M Gayton

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Matt Mason has had a central role in teaching physiology to undergraduates in Cambridge for over 15 years. The article is written in the first person, from his perspective. Angela Gayton, formerly of the Faculty of Education in Cambridge, is now a lecturer in Applied Linguistics and Education at the University of Glasgow. She is supporting Matt's investigation of students' reactions to the teaching approach discussed here.

Traditional lectures worked for me when I was an undergraduate. Like most academics reading this article, I did well at university and progressed within that system. I now put a lot of effort into producing similar lectures, and generally get very good feedback. However, when discussing physiological topics with my students afterwards, and when marking their essays, I am often concerned to note a misunderstanding of concepts which I was sure I had explained very clearly.

This must be a common experience for lecturers. When Harvard physicist Eric Mazur found that his students struggled to apply the concepts he had taught to new scenarios, he began using "flipped-classroom" approaches, which resulted in marked improvement (Mazur, 2009). In traditional teaching, the lecturer presents information which is dutifully noted by the students, who may or may not explore this further outside of the lecture theatre. This can too easily degenerate into rote learning, and only superficial understanding. The idea behind flipped-classroom teaching is that the core material is presented *outside* the lecture theatre for the students to assimilate on their own: the lecture session is then used to explore and strengthen understanding through questions and challenges, often performed in groups (Advance HE, 2017). This has been found to augment peer interaction and improve student motivation (Zainuddin and Perera, 2019). Flipped-classroom methods have been used in physiology teaching elsewhere (Street *et al.*, 2015; Entezari and Javdan, 2016; Rae and O'Malley, 2017), but never in our large-cohort, introductory physiology course.

I tend to be sceptical about new educational practices, but Mazur was a lecturer whose cohort of students was very similar to my own. Might an approach which works in Cambridge, Massachusetts also improve teaching in Cambridge, England? An opportunity to put this to the test presented itself when I was asked to give three lectures about nutrient acquisition to 187 first-year biology undergraduates, as a sabbatical replacement.

Implementation

I uploaded the material from last year's lecture course, only slightly altered, onto the students' virtual learning environment, and asked them to read it in advance of the three presentations. In the presentations themselves, students were asked to form groups of 4 – 6, each of which was given a Turning Technologies ResponseCard RF "clicker".

"There was a buzz in the lecture theatre which one does not get in a traditional session, with periodic cheering as groups got answers right"

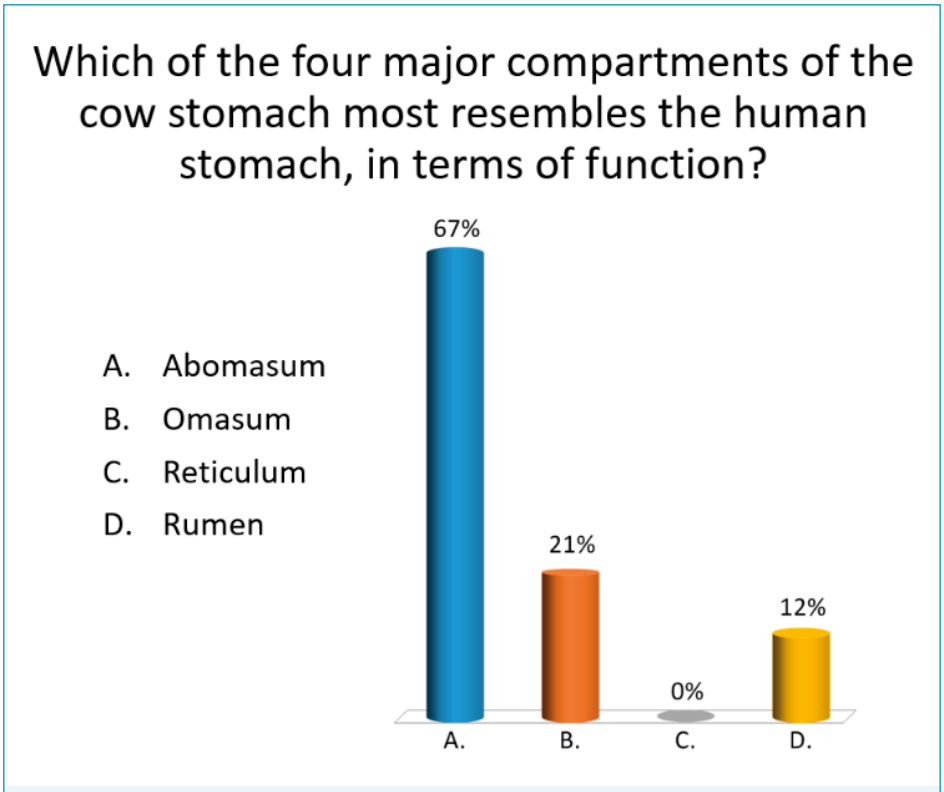

Figure 1. "Clicker" responses to one of the multiple choice questions (MCQs) asked in the flipped-classroom presentations.

The format I followed was to ask a question which the students would work in groups to solve, and then I would go through the answer. Questions took four general forms:

1. **Multiple choice**. The groups were given a few minutes to select an answer using their clickers. The range of answers was presented on-screen immediately afterwards as a bar-chart, in which the performance of individual groups remained hidden (Fig. 1). As well as helping the students to see where their understanding might be deficient, the ability to get real-time feedback from the class as a whole allowed me to move on quickly when the class was comfortable with a particular topic, or spend more time explaining when there was some uncertainty.

2. **Calculation questions**. The groups were asked to perform calculations, for example "What rise in [K^+] would be expected if all the potassium in five bananas were dumped into the extracellular fluid?". This particular question led to a follow-up calculation about the expected effects of this on resting membrane potentials, which in turn led to a discussion of what the body would have to do to render banana consumption safer.

3. **Diagram completion**. Groups were asked to sketch out a cell diagram, showing the transporters responsible for sodium chloride secretion by a salivary acinar cell. After their first attempt, I showed them how they might work this out logically, and later in the presentation I asked them to perform a similar exercise on a different cell type, to see if they had mastered the concepts.

4. **Open-ended discussion**. Groups were invited to consider how they might structure different parts of an essay comparing human and ruminant physiology. For example, how do we get away from the limp, default introductory sentence of "In this essay I shall [*insert essay title here*]"? What does the reader really need to know? I suggested ideas afterwards, while making it clear that there is no single correct answer to such questions.

Student Feedback

Would Cambridge undergraduates, used to a traditional lecture format, accept the flipped-classroom approach? Numerical results from the questionnaire at the end showed that they collectively felt that they had learned more than they would have from a traditional lecture course (mean score 3.55, where 1 indicated "much less", 3 "about the same" and 5 "much more"; $n = 121$ students), and had a deeper understanding of the material (mean score 3.50; $n = 123$). Our students also felt that this flipped-classroom course, with its emphasis on getting them to answer questions for themselves and think more about essay structure, helped them to prepare better for exams (mean score 3.63; $n = 120$).

A remote "clicker" allowing students to answer MCQs posed in the lectures. Other brands are available!

Interestingly, our students did not seem to regard flipped-classroom teaching as superfluous despite having weekly "supervisions", in which lecture topics and associated problems are discussed in small groups led by academics.

Some representative student comments about the benefits of the flipped classroom approach:

"I feel more confident with this series and have a clearer understanding, rather than just remembering the process"

"The interactive nature of the lectures helped me to think through and understand the material used in the lectures better"

"It's a different flavour from what we get usually; it's definitely more exciting".

Before plunging into flipped-classroom teaching it is important to consider some cautionary points, however, including the following:

- While most students said that they were able to prepare for these sessions adequately, one possible consequence of delivering a higher proportion of lectures in this format is that students might find it more difficult to allocate the necessary preparation time.
- This form of teaching might not suit conceptually difficult topics such as neuroscience, which would be harder for students to assimilate on their own. What came out strongly from the follow-up interviews was that students saw this approach as a useful complement to the traditional format, rather than a replacement.
- Our traditional lecture theatre, with tiered seating, was not conducive to group discussions among students.

Going forward

Although a little nervous in advance about what reactions I would get from students and colleagues, I genuinely enjoyed giving these flipped-classroom presentations. There was a buzz in the lecture theatre which one does not get in a traditional session, with periodic cheering as groups got answers right. Concerns about whether students would prepare sufficiently in advance, and whether interactive teaching in supervisions renders flipped classrooms redundant, proved not to be justified: the student response was more positive and far less polarised than I had anticipated. Whether this approach translates into improved exam performance requires careful analysis, but even if not, the enhanced levels of energy and interest among the students made the exercise more than worthwhile.

Restructuring existing lectures is a lot of work but there is much to be said for flipped-classroom teaching, perhaps especially in end-of-course recaps when students are flagging. This is certainly something that I will be doing again – and I will work on converting the other sceptics out there!

Acknowledgements

We thank Andrew Murray for letting us use his lecture material, Matthew Moss and Turning Technologies for granting us a temporary license to use their software, and Darerca Owen and the Department of Biochemistry for the loan of the clickers. Many thanks also to the students for taking the time to provide such extensive and constructive feedback!

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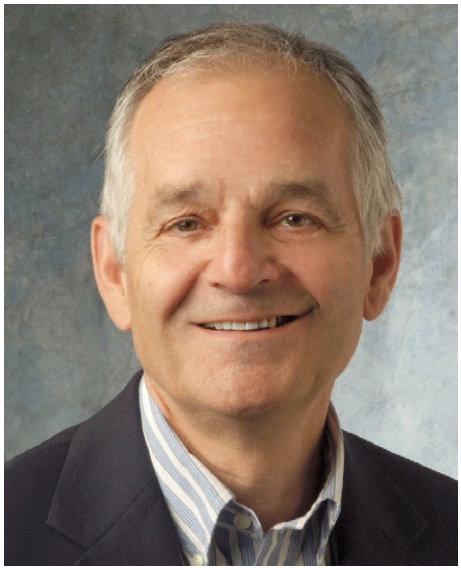
Neural WiFi

A new form of communication in the brain by electric fields



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The current thinking about spontaneous brain rhythms is that they result from the interaction between the intrinsic properties of individual neurons and their extrinsic interactions via classical chemical or electrical synaptic transmission. Therefore, extracellular electric fields and voltages recorded in neural tissue are thought to be only a reflection of the underlying neural activity. While non-synaptic effects by electric fields (i.e. ephaptic mechanisms) have been suggested to play a role in modulating ongoing activity, these effects are thought to be reasonably limited, at least during physiologically relevant activity (Anastassiou *et al.*, 2011), but this may not be so.

Neural communication without synapses

While carrying out experiments to study the role of synaptic transmission in the propagation of signals in the brain, we noticed something odd and unexpected. After blocking synaptic transmission by removing extracellular calcium from the environment of the cells, we observed that spontaneous neural events were still propagating. The speed of this propagation was quite fast, around 0.1 m/s. This speed was too fast for diffusion of neurotransmitters and/or ions. Another possible mechanism was the presence of electric synapses (also known as gap junctions), whereby neighbouring cells' cytoplasms are electrically conductively linked through connexins to form intercellular short circuits that achieve signalling more rapid than that of chemical synapses. However, additional experiments blocking these synapses revealed that those same spontaneous neural events still propagated throughout the tissue (see Fig. 1A) (Chiang *et al.*, 2019; Qiu *et al.*, 2015; Shivacharan *et al.*, 2019; Zhang *et al.*, 2014).

At that point in our research we were left wondering how these events could propagate. After eliminating the usual suspects, we had no choice but to entertain the only remaining viable possibility: electric fields generated during cell activation could recruit neighbouring neurons. This idea was highly controversial since the latest experiments indicated that electric fields could modulate neural activity but were too small to excite neurons by themselves. To convince ourselves that electric field coupling could actually explain our experimental results, we conducted several computer simulations with electric field as the only means of communication between neurons. Computer models did indeed show that electric fields can be sufficient to mediate propagation within the neuronal tissue. However, simulations only show what is theoretically possible and experiments must be designed to directly test the mechanism. We therefore adapted an old method known as voltage clamp to this problem by creating an electrical field clamp system, whereby measurements from detectors sensing the electric field within the tissue were used to generate its

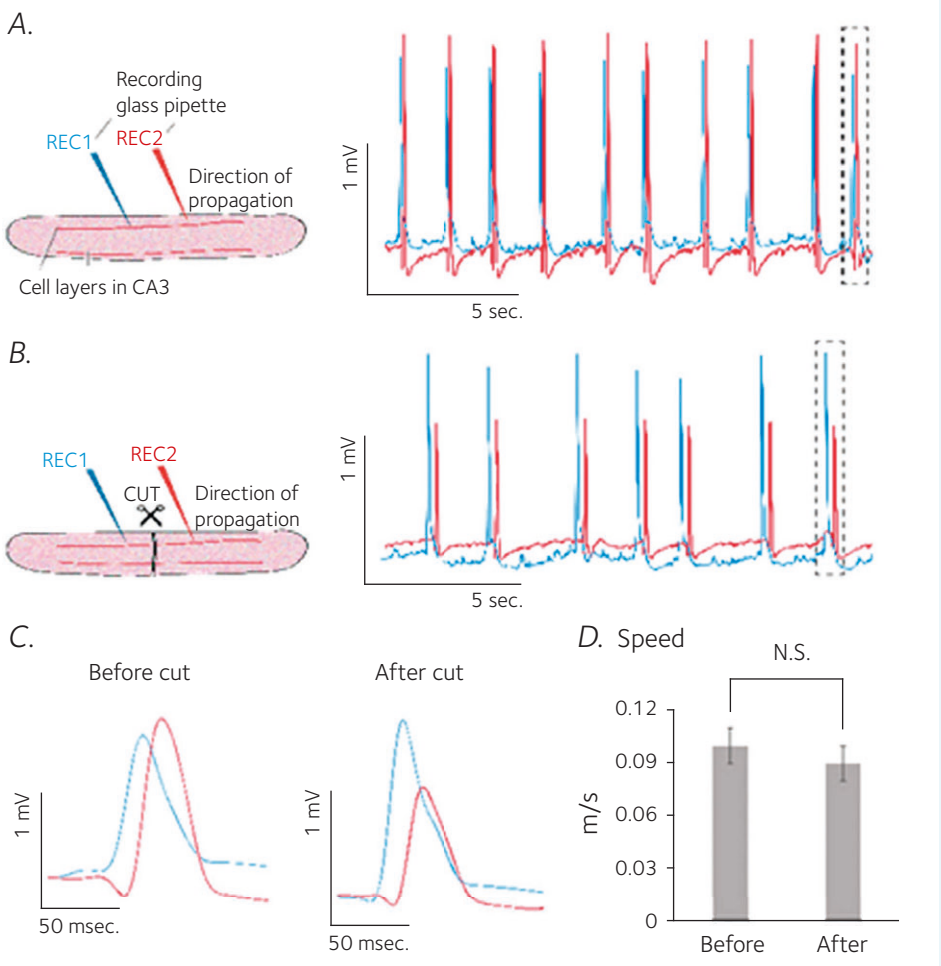

Figure 1. Slow hippocampal oscillation propagation along the tissue with a complete cut in an *ex vivo* mouse hippocampal slice preparation.

A. Slow hippocampal oscillations propagate from recording electrode 1 (REC1) to recording electrode 2 (REC2) at a speed of 0.10 ± 0.01 m/sec before the cut.

B. Propagation through a complete cut in the hippocampal slice. Slow hippocampal oscillations were observed to be propagating along the slice with a cut from REC1 to REC2 with speed similar to that recorded in an intact slice by activation of the neurons of the other side of the cut.

C. Expanded windows of the single event of the slow hippocampal oscillations before and after the cut revealing similar delays between two recording electrodes.

D. Speeds of slow hippocampal oscillations before and after the cut. There is no significant (N.S.) difference between the two speeds.

corresponding cancelling anti-field that can set and hold (i.e. clamp) the electrical field to zero. This clamp, applied locally was able to block the propagation of the events exactly at that site. Notably, this neural activity was not only eliminated, but could also be modulated or even regenerated by imposed electrical fields. In particular, the application of electric fields with amplitudes in the observed range of the endogenous fields (1 to 5 mV/mm) to the tissue could control the speed of the propagation (Chiang *et al.*, 2019). Therefore both the experiments and simulations confirm that electric field coupling between neurons plays a crucial role in mediating non-synaptic signal propagation.

Self-propagating waves

It is well known that action potentials self propagate along axons at speeds determined by the diameter of those axons. However, brain waves recorded during neural activity are not thought to be self-propagating and rather viewed as simply reflections of the underlying neural activity generated by neuronal firing and synaptic transmission. However, our experiments reveal the presence of neural waves that are indeed self-propagating. They maintain their amplitude within the tissue in the absence of synaptic transmission or gap junctions. The speed is also constant at about 0.1 m/s. These data therefore suggest that endogenous electrical fields generated by neural firing in a group of neurons are sufficient to excite their neighbors and generate a wave of activity (see Fig. 2). This hypothesis also implies that endogenous electrical fields can excite other neurons. Stimulation experiments with electrodes placed to generate electrical fields similar to those observed experimentally were indeed observed to induce a propagating wave at the same characteristic speed (Chiang *et al.*, 2019).

Ephaptic effect in sleep waves

This newly found form of communication was discovered while studying the propagation mechanism of brain waves similar to those generated during sleep (Sanchez-Vives and McCormick, 2000). These waves are observed during slow wave sleep and they can be generated in an *ex vivo* preparation of mouse hippocampal slices, where the waves propagate at the same speed reported above (0.1 m/s). These waves are associated with the regulation of synapses that have been potententiated during wakefulness. In particular these waves are thought to be involved in downregulating synapses that have a low synaptic weight and consolidating the synapses with high weight (i.e. the strength or amplitude of a connection between two neurons). These "sleep" waves were shown to propagate non-synaptically and were not blocked by either presynaptic junction blockers or gap junction blockers (Chiang *et al.*, 2019). Therefore, our results suggest that neural activity during slow wave sleep may regulate synaptic weight by a process involving electric field coupling, a non-synaptic process that would not require presynaptic input into the synapse thereby avoiding generating new potentiation of existing weights.

Propagation through a complete cut of the tissue

All along we have been trying to design new experiments to disprove this hypothesis of electric field coupling, without success. Indeed, the idea that electric field coupling, or ephaptic coupling, could allow communication between neurons was met with some resistance and incredulity on the part of other scientists and reviewers. *That's not possible! Did you try this or that experiment?* Finally, we predicted that if our hypothesis is correct, then propagation should go through a complete cut of the tissue since coupling by electric fields is carried without any delay through volume conductors. This experiment would cut axons and eliminate gap junctions and synaptic transmission simultaneously.

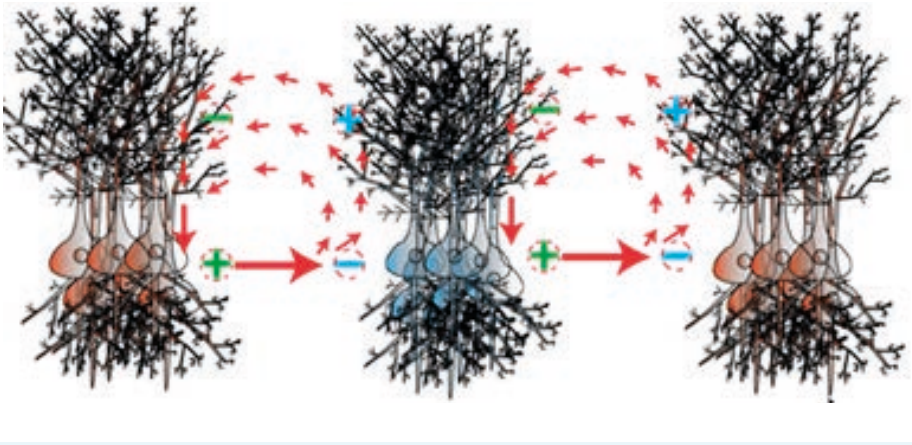

Figure 2. Electric coupling mechanism. A group of pyramidal cells (1st group of cells in brown) become excitable and depolarize in the dendritic tree (NMDA dependent), creating a current sink in the dendrites. An electric field is generated between the soma and dendrites in the extracellular space (green dipole). This electric field passively depolarizes the neighbouring neurons (cells in blue) as indicated by the blue dipole, and the cycle repeats.

"The function and role of this self-propagation in physiological and pathophysiological neural activity is still a mystery"

Ex vivo experiments carried out in hippocampus slices confirmed that indeed waves can travel across a physical void in the neural tissue as long as the gap is not greater than 400 µm, at which point the field strength would be too weak due to the inverse-square law (Chiang *et al.*, 2019; Shivacharan *et al.*, 2019) (see Fig. 1 B-D). Similar preliminary results were obtained in mice *in vivo* and neural activity was observed to cross through a complete transverse cut of the hippocampus. These results indicate that endogenous fields thought to be too small can indeed be large enough to excite other neurons located close by. In addition, the results indicate that the endogenous electric fields can no longer be considered simply as a passive reflection of the underlying neural activity and should instead be thought of as active players in and contributors to neural function.

Endogenous fields can recruit and synchronize neurons in epilepsy

Epilepsy is characterized by increased neuronal firing and hypersynchrony of neural activity. Our recent experiments have implicated these endogenous electrical fields in recruiting neurons during seizures without any involvement of synaptic transmission (Chiang *et al.*, 2018; Chiang *et al.*, 2019). Seizure-like activity was observed to propagate through a cut of the tissue and the propagation could be blocked by cancelling the tissue electric field locally using the newly developed extracellular field clamping circuit. Therefore, our results indicate that this new form of communication plays a significant role in how seizures recruit neurons and could lead to new treatment modalities for seizure control. In particular these results could explain failures of surgical transections of the brain in some patients with epilepsy.

Why is this important?

Until now there were four known ways that neurons could "talk" to each other in the brain: via synaptic transmission, diffusion, axonal transmission and what are known as "gap junctions" between the neurons. Yet when many neurons fire together they generate weak electric fields that can be recorded with the electroencephalogram (EEG) or within neural tissue such as field potentials. These fields were thought to be too small to contribute to neural activity. However, our recent experiments have shown that these electric fields can excite cells which in turn produce electric fields of their own thereby generating a self-propagating wave of activity. Although waves have been observed before, these experiments are showing that these waves can be self-sustained and propagate on their own without synaptic transmission. The function and role of this self-propagation in physiological and pathophysiological neural activity is still a mystery. However, brain waves such as theta waves or sharp-wave ripples are thought to be involved in memory encoding and consolidation. Information is encoded into a neural circuit by a phenomenon called long-term potentiation, which involves simultaneous firing of both pre- and post-synaptic elements. To trim synaptic weights without encoding new information, a mechanism that does not potentiate synapses is required. Waves propagating by ephaptic coupling could regulate synaptic weight during sleep without the need for presynaptic stimulation, since it would not interfere with the synaptic weights already set in the neuronal dendrites.

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Microcirculation, metabolic syndrome and exercise

Does exercise dose matter?

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The microcirculation is a branching network of vessels less than 150 µm, only visible through a microscope (Fig.1). This network, composed of arterioles, capillaries, and venules, is primarily responsible for perfusing organs and tissues with blood. Some functions, such as the delivery of oxygen and nutrients and removal of waste products from the tissue, occur almost exclusively in the microcirculation. Because of that, an adequate perfusion via the microcirculatory network is essential for the integrity of tissues and organs. Notwithstanding, abnormalities in microvascular structure and/or function, might contribute to several diseases like myocardial ischemia and stroke.

In recent years, our research group has been dedicated to evaluating the mechanisms and consequences of diseases like hypertension and metabolic syndrome (MS) on the microcirculatory function. MS is the term used to characterise all the risk factors for cardiovascular disease (CVD) that arise from the association of obesity, diabetes mellitus, increased levels of lipids and elevated blood pressure in humans. The association of two or more of these factors significantly increases the likelihood of having damage in organs like the brain, the heart, and the kidneys and consequently increases mortality rates. Here we will provide a brief overview of our data about the dose and benefits of exercise training in the treatment of MS.

How MS impairs microvascular perfusion?

Microvascular rarefaction is broadly defined as a reduction in the number of perfused capillaries in an area of tissue. The rarefaction can be structural, characterised by the absence of capillaries, or functional, in which capillaries are present but they are not perfused. There are currently several pieces of evidence that MS is directly involved with both structural and functional capillary rarefaction in the skeletal muscle, heart and brain (Nascimento *et al.*, 2013; Estato *et al.*, 2017; Machado *et al.*, 2014; Machado *et al.*, 2016).

Although the pathophysiological mechanism involved in microvascular dysfunction during MS is multifactorial and complex, it is widely recognised that the interaction between hyperactivity of the sympathetic nervous system and dysregulation on the release of hormones and pro-inflammatory cytokines is the likely link between the metabolic dysfunctions and microvascular abnormalities (Levy *et al.*, 2008).

The sympathetic nervous system plays a main role in several cardiovascular functions. However, the sympathetic hyperactivity observed both in hypertension and in MS, seems to be an important factor for the microvascular dysfunction and the incidence of CVD. Arterioles are richly innervated by the sympathetic adrenergic

"Exercise is one of the most powerful lifestyle interventions to repair the damage caused in the microcirculation by metabolic syndrome"

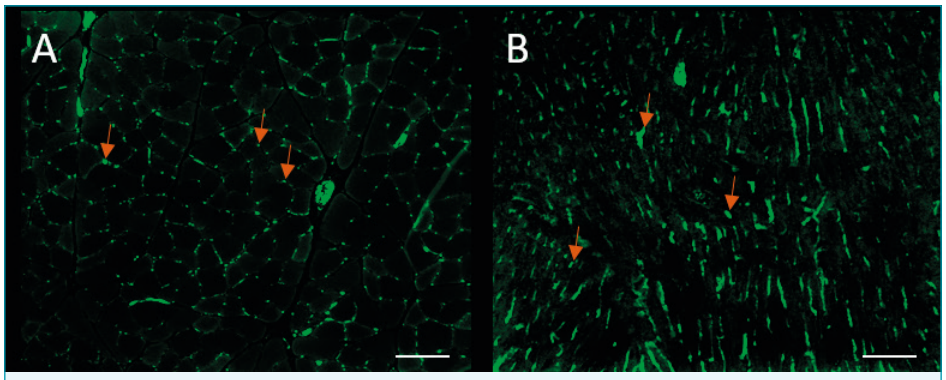

Figure 1. Example of the microcirculation in the skeletal muscle (A) and heart (B) obtained via intravital fluorescence video microscopy. Endothelial cells (shown in green, and examples indicated with red arrows) were labelled with fluorescein isothiocyanate (FITC)-conjugated lectin *Griffonia simplicifolia*. Scale bar is 100 µm.

Groups	Aerobic Capacity	Body Weight	Body Fat	Adipocyte Diameter	Liver Fat	Systolic Blood Pressure	Lipid Profile	Glucose Metabolism	Muscle Capillary Density	Heart Capillary Density
Lean	↓	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Obese	↓↓	↑↑↑↑	↑↑↑↑	↑↑↑↑	↑↑↑↑	↑↑↑↑	↑↑↑↑	↑↑↑↑	↓↓↓↓	↓↓↓↓
Obese + 30 min/ 3 times week/ moderate intensity	↑	↑↑↑	↑↑↑	↑↑↑	↑↑↑	↓↓↓	↑↑↑	↑↑↑	↓↓	↓
Obese + 30 min/ 3 times week/ high intensity	↑↑	↑↑	↑↑	↑↑↑	↑↑	↓↓↓	↑↑	↑↑↑	↓	↑
Obese + 60 min/ 3 times week/ moderate intensity	↑↑	↓↓	↑↑	↑	↑	↓↓↓	↑↑	↑↑↑	↑	↑
Obese + 60 min/ 3 times week/ high intensity	↑↑	↓↓	↑↑	↑	↑	↓↓↓	↑	↑↑↑	↑↑	↑↑↑
Obese + 30 min/ 5 times week/ moderate intensity	↑↑	↓↓	↑↑	↑↑	↑↑	↓↓↓	↑	↑↑	↑↑	↑↑
Obese + 30 min/ 5 times week/ high intensity	↑↑↑	↓↓	↑↑	↑↑	↑↑	↓↓↓	↑↑	↑↑	↑↑	↑↑↑
Obese + 60 min/ 5 times week/ moderate intensity	↑↑↑↑	↓↓↓↓	↑	↑	↓	↓↓↓↓	↓↓↓↓	↑	↑↑↑↑	↑↑↑↑
Obese + 60 min/ 5 times week/high intensity	↑↑↑↑	↓↓↓↓	↑	↑	↑	↓↓↓↓	↓↓↓	↑	↑↑↑↑	↑↑↑↑

Table 1. Effect of different dose of exercise on aerobic capacity, anthropometric and metabolic parameters as well as muscle and heart capillary density in rats with metabolic syndrome (Machado *et al.*, 2017). (↑) represents the degree of increase of the assessed variable compared to lean rats; (↓) represents the degree of decrease of the assessed variable compared to lean rats; (N/A) non applicable.

fibres and highly responsive to sympathetic vasoconstriction via α_1 and α_2 adrenergic receptors. Sympathetic system-induced vasoconstriction directly contributes to the functional and structural rarefaction of capillaries, as well as to high blood pressure (Nascimento *et al.*, 2013).

We also investigated some molecular pathways related to the deleterious effects of MS and recently reported increased protein expression of angiotensin-converting enzyme (ACE) and angiotensin II type 1 receptor (AT1R) in an MS model induced by a high-fat diet (Frantz *et al.*, 2017). It is well established that ACE and AT1R can exert deleterious effects on skeletal muscle, such as activation of inflammatory pathways, reactive oxygen species production, and impairment of insulin signalling (Zhou *et al.*, 2015). In addition, ACE activity drives the formation of angiotensin II (ANG II), which stimulates the production of adhesion molecule-1 and macrophage colony in the endothelial wall, increasing vasoconstrictor action and plays a strong atherogenic role (Lyon *et al.*, 2003).

The activation of the inflammatory response through increased expression of proteins involved in the acute-phase reaction and systemic inflammation, such as tumour necrosis factor-alpha (TNF-α) and interleukin 6 (IL-6), increases the expression of adhesion molecules by the vascular endothelial cells and makes their surface adhesive to leukocytes. In the post-capillary venules, increased recruitment of leukocytes may result in capillary obstruction and decreased capillary perfusion. Furthermore, these cytokines stimulate the synthesis of acute-phase proteins by liver hepatocytes (e.g. C-reactive protein [CRP] and fibrinogen), increasing systemic inflammation, platelet aggregation, and plasma viscosity, increasing risk of developing CVD and stroke (Gray and Kim, 2011; Frantz *et al.*, 2017).

Which dose of exercise is beneficial in MS?

Exercise is one of the most powerful lifestyle interventions to repair the damage caused in the microcirculation by MS. Although there is consensus on the relationship between physical activity and health, the amount of exercise needed to improve several metabolic dysfunctions and reduce the risk of CVD is not clear. In a recently published article "Exercise training dose differentially alters muscle and heart capillary density and metabolic functions in obese rats with metabolic syndrome" (Machado *et al.*, 2017), we provided novel evidence on the adaptive response induced by different combinations of weekly frequency, duration of the session and intensity of exercise effort on metabolic parameters and structural capillary density in rats with MS. A summary of the data on the effects of different combinations of exercise frequency, duration, and intensity on MS parameters and microcirculation is shown in Table 1.

In our study, the animals were fed with a high-fat diet (HFD), and the sedentary group developed obesity, hypertension, diabetes and hepatic steatosis. They also reduced capillary density in the skeletal muscle and heart. On the other hand, even the lowest exercise training dose (30 min/3 times week/moderate intensity) used in this study was able to reduce adipocyte size and the fatty liver (nonalcoholic fatty liver disease – NAFLD).

Interestingly, our results showed that haemodynamic variables (blood pressure and heart rate) were reduced in all animals subjected to exercise regardless of dose. In other words, an increase in frequency, duration or intensity did not provide additional reductions in arterial blood pressure and heart rate in our obese rats.

Regarding glucose metabolism, any exercise dose was able to reduce fasting blood glucose levels, but the glucose intolerance determined by intraperitoneal glucose tolerance test (IGTT) was completely reversed only in the animals who trained five times per week. Therefore, our data showed that an increase in exercise frequency seems to be more advantageous than duration or intensity in reversing insulin resistance (a pre-diabetic state) induced by metabolic syndrome.

Complementarily, we found that exercise frequency (3 or 5 times/week) and duration (30 or 60 minutes) were the main factors improving anthropometric (body weight and body fat) indications, and glucose metabolism (insulin sensitivity and lipid profile) as well as microvascular density in skeletal muscle. The intensity of exercise (high intensity groups) was not the main contributing factor to increased capillary density in skeletal muscle but was nonetheless beneficial to microvascular density in the heart.

In summary, our results demonstrated that exercise frequency and duration are the main factors that improve MS parameters and capillary density in skeletal muscle. The increased intensity was the major factor in reversing microvascular rarefaction in the heart alone. It was noteworthy that while a low dose of the exercise (30 min/3 times week/moderate intensity) was not able to completely reverse the MS dysfunctions, we did observe that this dose was sufficient to normalize blood pressure and attenuate metabolic dysfunctions.

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Metabolic physiology in flux

A Theme Lead report

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We are a few months into our roles as co-Leads of one of the Society's newest themes, and though the decision to separate Metabolism from Endocrinology was not our own we both welcome this development. The opportunity to fly the flag for Metabolic Physiology comes at an exciting time, with technical advances in metabolic research arriving in the nick of time as we tackle problems that include some of the gravest health issues facing society.

For ordinary people living in the developed world it has, it seems, never been easier nor cheaper to acquire food packed with calories yet containing little else of nutritional value. Equally, it has become easier to avoid using those calories by adopting increasingly sedentary lifestyles and spending our days staring at screens in our homes and offices. The consequences of this behavioural shift have arrived in various forms – obesity, diabetes, cardiovascular disease, fatty liver disease – all well documented to be on the rise but still incompletely understood, and with life spans increasing, each a significant and growing burden for our society and health services.

The scope of metabolic physiology reaches beyond the realm of metabolic diseases, however, arguably touching upon all other areas of physiology. As such, this is a diverse and dynamic area of physiology, combining fundamental research with a broad range of applications to health and disease. A taste of this came recently when, in one of our first tasks as Theme Leads, we found ourselves reviewing abstracts for Physiology 2019. Of the 408 abstracts submitted, 94 were submitted under the Metabolism & Endocrinology theme. This was the most for any theme, and perhaps explains the rationale for separating the two areas in future. Alongside research investigating the consequences of malnutrition in various forms and the aetiology of diabetes and fatty liver disease, were abstracts submitted for symposia on the circadian regulation of metabolism, the roles of free radicals in skeletal muscle function, and the physiology of brown adipose tissue (BAT). We also came across studies investigating metabolic regulation in contexts as diverse as excitation-contraction coupling in muscle, cell-cell tethering in renal tubule epithelia, and placental function in hypoxia. In the latter case, this reflects one of two trends in metabolic research that bookend the life-course. On one hand, there is growing interest in the metabolic aspects of fetal development and in how the intrauterine environment shapes metabolic function in the offspring with consequences for lifelong health. At the other end of the lifespan we find great interest in the role of mitochondrial function in the ageing process, and in the lifestyle factors that might permit or prevent a healthy ageing phenotype.

Metabolic physiology is therefore naturally interdisciplinary, and the links with endocrinology are particularly profound. Despite the separation of these two themes,

we will continue to work closely with the endocrinology Theme Leads particularly at a time when the boundaries between the two areas are becoming a little more blurred. The hormonal control of tissue metabolism and appetite regulation, for example, are well established and understanding these mechanisms has been essential to our comprehension of how metabolic function is integrated at a whole-body level and what happens when it goes wrong. Of more recent interest, however, are the signalling roles now known to be played by many small molecule metabolites. There are, for instance, a number of G-protein coupled receptors known to be activated by metabolites including various fatty acids, lactate and ketones, which in turn, regulate aspects of metabolic function, e.g. by potentiating insulin secretion at pancreatic β cells or suppressing lipolysis in adipocytes. Similarly, a number of nuclear hormone receptors are also activated by metabolic ligands. Perhaps the best known example being the PPAR family of transcription factors which are expressed in a tissue-specific manner, and which alter the expression of genes involved in fat metabolism to match tissue metabolism to substrate supply when activated by fatty acids or their derivatives.

There is therefore a growing recognition that many metabolites, previously considered mere substrates in pathways or building blocks for various macromolecules, are themselves cellular mediators of metabolic function and/or distinct plasma-borne signatures of physiological and pathophysiological states. The term oncometabolite was initially coined in reference to R-2-hydroxyglutarate (Ward *et al.,* 2010), and later extended to encompass succinate, fumarate, lactate and S-2-hydroxyglutarate. These intermediates accumulate in cancer cells downstream of mutations to genes encoding metabolic enzymes, and have been shown to aid tumorigenesis through various oncogenic signalling cascades that result in immunosuppression and epigenetic remodelling. More recently, oncometabolites have been found to accumulate in non-cancerous tissues under pathological conditions, influencing cardiac metabolism and contractile function (Karlstaedt *et al.,* 2016), and with succinate in particular proposed to play a role in ischaemia/reperfusion injury by mediating mitochondrial reactive oxygen species (ROS) generation (Chouchani *et al.,* 2014). Meanwhile, the term immunometabolite has been proposed for small molecules which act as signatures of immune cell activation including succinate, itaconate, serine and S-2-hydroxyglutarate (de Goede *et al.,* 2019), the latter of which alters DNA methylation to play a role in T-cell differentiation and proliferation (Tyrakis *et al.,* 2016).

The discovery of active BAT deposits in adult humans, reported in several articles published in 2009, catalysed a wave of studies that aimed to understand its functional significance, particularly regarding body weight regulation (Betz *et al.,* 2015). As a fat-burning form of adipose tissue, BAT naturally represents an attractive target for the treatment of obesity and its comorbidities, and a great deal of research has since sought to understand the mechanisms regulating BAT thermogenesis and uncover any factors that promote the expansion of BAT deposits. A number of peptide mediators of BAT development and function have been uncovered, including for example the hormone irisin. Notably, a handful of small molecule mediators of the browning process have been described, including inorganic nitrate and β-aminoisobutyric acid (BAIBA), which is secreted by myocytes and rises in human plasma in response to exercise training. BAIBA was shown to increase the expression of BAT-specific genes in the white adipose tissue of mice, enhancing metabolic rate and improving whole-body insulin sensitivity (Roberts *et al.,* 2014).

The discovery of novel metabolic mediators of physiological function has been aided by the development of high-throughput technologies, initially developed as tools for analytical chemistry and subsequently applied to the metabolic profiling of tissues and biofluids (Griffin *et al.,* 2011). Alongside the development of data analysis software, and aided by data sharing platforms, techniques such as NMR spectroscopy and mass spectrometry have greatly expanded our capacity to comprehend global metabolic disturbances. Collectively termed metabolomics, these techniques can be applied in a targeted manner to fully profile adjustments to intermediates across a metabolic pathway or a collection of related pathways, or in an unbiased manner to aid biomarker discovery and provide fodder for hypothesis generation. Advances in lipid-profiling are revealing distinct patterns of change across the many classes and species of lipid, and shedding new light on the possible functional properties of a hitherto overlooked class of metabolites, whilst the novel application of mass spectrometry imaging is highlighting the importance of their distribution across tissues (Hall *et al.,* 2017).

This quantum leap in our capacity to understand the full metabolic state-of-play in our model systems is perhaps the metabolic equivalent of the Human Genome Project. The challenge for metabolic researchers contemplating such a rich resource of data will be to extract the signal from the noise and to determine the physiological significance of these findings. Metabolic physiology is in flux; there are challenges ahead but it is an exciting time to come along for the ride.

"The scope of metabolic physiology reaches beyond the realm of metabolic diseases, arguably touching upon all other areas of physiology"

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My experience as a PhD student adapting to a new country and culture

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"Social integration is one of the most important factors in any international student's life and adjusting to accents has been one important step in getting used to life in Ireland."

Adapting to the new position

A PhD is about more than learning how to do the best science; it's about developing as an individual and learning from international colleagues. Going abroad for a PhD is a big decision but I felt it would be worth the journey, so I moved from Jordan to Ireland to take up a PhD at University College Cork (UCC) in 2017. Since then, I have grown as a scientist, not just in terms of the knowledge and skills I have gained, but getting to know others in my community.

Back in 2013, I earned a BSc in pharmacy from the University of Jordan followed by an MSc degree in pharmaceutical sciences. Changing discipline was a worry, and moving from pharmacy to physiology was challenging, especially in a team of students that are all physiologists. Currently, I am a third year PhD student in the Department of Physiology at UCC.

My interests are in autonomic reflexes (afferent sensory and efferent nerves) that regulate renal and cardiorespiratory function in hypoxia. At the start, my PhD project choice was between a project utilising molecular biology and biochemistry approaches, *ex vivo* experiments and biomolecular analysis of muscle, and an *in vivo* project that required surgical training and some molecular biology approaches. I chose the third project because I was keen to learn the techniques involved, although some advised me against transitioning from pharmacy to a project that is broad and involves integration of many physiological systems (cardiovascular, renal, respiratory and carotid sensory bodies).

In contrast, all of my technical training and experience during my masters was focused on transdermal drug delivery systems, HPLC, infrared spectroscopy and gas chromatography in addition to organic chemistry and synthesis reactions. Therefore, the first years of my PhD in physiology were a steep learning curve going from the very routine techniques such as ELISA or immunofluorescence, which were not especially difficult to do with a background and experience in pharmaceutical chemical reactions and analysis, to the more involved protocols like hypoxia induction or surgical procedures. Acquiring those surgical skills and generating results within a short period of time proved particularly challenging and training was divided into cardiovascular surgical techniques (arterial and venous cannulation), renal surgical procedure (intra-renal administration of drugs) and renal nerve recordings, which required the most time given the difficulty and relative rarity of the technique. I have received substantial support and direction to gain these techniques from a supervisory team in the department. Now that I am comfortable and competent in the surgical techniques, they have become my favourite part of my PhD work and I am thankful that I had the opportunity to choose between various projects offering different skill sets at the beginning of my studies.

Adapting to the new country

In Jordan, we start learning English at six years of age. All of my studies at the University of Jordan were in English. Despite this, I wasn't prepared for the sheer speed at which many Irish people speak nor the overwhelming variety of accents that co-exist on the small green island. Fortunately, I did not experience any major language barriers in terms of research and scientific discussions with my supervisors. Due to the many accents and, at least what seems to me, a very fast way speaking, the rapid bombardment of information given in short presentations by Irish researchers was not without its struggles. However, with time, my ear is gradually adjusting and dealing with the many accents is starting to become easier. Social integration is one of the most important factors in any international student's life and adjusting to accents has been one important step in getting used to life in Ireland.

Like any students coming from a foreign land, there is also the inevitable culture shock. Not only for the student but sometimes for the locals too. This can lead to well intentioned, although cringeworthy questions born out of curiosity that may not always come across the way they were intended. For instance, many have asked questions related to the conservative culture present in many Arabic countries such as "are women allowed to drive in Jordan?" However, Jordan is one of the most liberal countries in the region. While the formulation of the question can be a shock to me, it is great that people ask about how Jordan may be different to surrounding countries. Another major aspect that I found difficult was the initial exposure to the drinking culture that is prevalent in many Western societies and was noticeable at many of the social events I wanted to attend.

Jack Leacy, Maria Casacão, Sara AlMarabeh, Karen O'Connor, Eric Lucking and Michael Vaughan at the Western Gateway Building, University College Cork.

This can be difficult for students, especially those from areas where this is not what they are used to (Clarke *et al.*, 2018). However, I've grown more comfortable and enjoy having a laugh and socialising with colleagues at these events with my coffee in hand.

A country adapting to the needs of others

For 30 days every year during Ramadan, Muslims don't eat or drink between sunrise and sunset. There are approximately 1.8 billion people fasting every year (a quarter of the world's population). Ramadan has a special and warm atmosphere between family and friends and is one of the most important months. It can be more challenging for an international Muslim student in a non-Muslim country. Due to very long fasting hours in Europe, I usually reduce my practical work in that month and focus on the theoretical work.

Regarding Ramadan this year, I had a lot of practical and theoretical work to do. Due to the flexible nature of the project, work during Ramadan was limited to the theoretical parts and allowed the possibility of doing it in Jordan. Also, colleagues are usually very caring and considerate around Ramadan. Many of them try to hide their meals. This consideration is appreciated but I always urge colleagues not to worry about eating or drinking in front of me during Ramadan because part of the fast is the discipline of our abstinence. During this time when I might feel tired or cranky from lack of food and water, other students are always understanding and try to support me by having light-hearted conversations with me.

In addition to being accommodating during Ramadan, UCC takes my religion into consideration in other ways. When I needed sterile clothing to perform surgical work, they provided me some in a style that would be appropriate for me as a Muslim female. There is also a prayer room for Muslims in the Brookfield Health Science building as well as a canteen that offers halal food every Friday.

The adventure of conducting my research training in Ireland included many other challenges such as being apart from family and friends. I also have to go each year with many documents to renew my visa, which is quite exhausting. To participate in a conference, internationals need to apply for a visa for each country in Europe, and this can be a long process. Finally, the colder weather in Ireland really takes time to get comfortable with (and I'm not sure I ever fully will!).

Studying abroad has many advantages such as being in a different academic system, a different research team, learning new skills, attending different conferences and meeting different researchers. The adventure of being different in a country and a university helped me recognise my strengths and weaknesses and grow as a student and person as a whole. Recently, I have even had my first physiology review article published (AlMarabeh *et al.*, 2019) which is my first paper in the field of physiology.

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Art and science together can change the world: Seven Thousand Feet and The Fascinating Family

Christine Wilcox-Baker

Lead artist and organiser,
Seven Thousand Feet exhibition

Project website

sites.google.com/view/seven-thousandfeet/home

Project collaborator websites

mmu.ac.uk/mssm/news-and-events/

diabetes.org.uk/

researchforthefuture.org

ncl.ac.uk/magres/research/diabetes/reversal/#publicinformation

research.manchester.ac.uk/portal/martin.rutter.html

research.manchester.ac.uk/portal/karen.e.cosgrove.html

research.cmft.nhs.uk/our-team/mr-naseer-ahmad

mmu.ac.uk/mssm/our-expertise/meet-the-director/

mmu.ac.uk/cheshire/our-staff/department-of-exercise-and-sport-science/profile/index.php?id=1589

art.mmu.ac.uk/profile/emulhearn

My maternal grandmother had type 2 diabetes; I didn't know much about this disease and wanted to find out more. Will my mother develop it? Will I? I've been a visual artist for many years, and completed a Masters in Art as Environment in 2008 at Manchester Metropolitan University (MMU). A few years ago, I felt a new urge to do something "useful" with my artwork. I met Martin Rutter, Professor of Cardiometabolic Medicine at the University of Manchester and Honorary Consultant Physician at Manchester Diabetes Centre, who became my mentor.

We had an initial discussion about the potential merits of trying to use visual art to portray messages, about diabetes, to the general public in ways different from the usual health education routes. Martin and I then had a number of meetings and discussed aspects of the condition. We identified a need to try new ways of bringing this information to the general public and encourage them to take this condition seriously.

As he put it, "It has to be worth a try... more people are developing the condition and current health information routes are not working well enough." The project takes its title, *Seven Thousand Feet*, from the approximate number of diabetes-related lower limb amputations performed in the UK each year at that time. The scale of the problem was made clear by the fact that by the time of the exhibition the figure had risen to 8,793 amputations per year. I had been very shocked by this statistic and it kept coming back to me, hence choosing it as the title.

Martin then introduced me to a number of other health practitioners who also thought this was a good idea to pursue. These expert practitioners, who also supported the project, agreed that traditional health education has a role but it is not reaching everyone. Using creative interventions is a new way to engage on the topic of diabetes. It adds a different dimension to information already out there.

From a little idea the project started to grow. I met diabetes dietitians, nurses, researchers, medics and an impact and engagement manager (Edwin Colyer), from both the University of Manchester and MMU, along with Newcastle University. Everyone I met immediately "got on board" and I have had a huge amount of support from these people for which I am immensely grateful.

I subsequently developed a portfolio of proposed artworks and interactive events, informed by and in collaboration with them. Some ideas involved animation and illustration and I wanted to involve other artists and students in order to add to the variety

Visitors to the Manchester Science Festival immersed in the *Seven thousand feet* installation.

of visuals and have different age groups' interpretations. With this plan in mind I contacted MMU's *Illustration with animation* course leaders. They too welcomed the project and put it out to their students as a "live" project. Four BA students, three BA graduates and two MA graduates took up the challenge and tutor Eleanor Mulhearn took the lead.

Working with Katherine Grady, Programme Development Manager at Research for the Future, the Salford-based organisation who supply participants to numerous diabetes research projects, I wanted to create a visual "family" as tools for their public engagement events. Also working closely with Neil Reeves and Gladys Pearson, from MMU, I successfully applied for a grant from The Physiological Society.

I thought that the figures should be contemporary-styled 21st century images but, for me, they were also inspired by the 18th century anatomical wax figures I have extensively researched at the Josephinum in Vienna and the Museo Delle Cere Anatomiche in Bologna. I also had the privilege to spend a day in an operating theatre at Manchester Royal Infirmary where I observed operations to remove calcium deposits from main arteries. These procedures, aimed at reducing the risk of amputation, were carried out by Naseer Ahmad, Consultant Vascular surgeon, and his team. This experience helped me with the concept and in particular for one of the figures – "Jack" who has had one leg amputated and has blocked veins and ulcers on his other leg.

I pulled everything together and the concept for *The Fascinating Family* was born. The plan was to have a "family" of three free-standing cut-out figures who could show us some of the symptoms and outcomes of diabetes. We wanted the figures to be interactive, so we installed motion sensors that would start playing the voice recordings. Each figure tells a story of their experiences of diabetes and also has a series of "blue dots" which represent symptoms and outcomes. One blue dot on each figure acts as a door knob and reveals further potential outcomes. I commissioned MMU student Fabia Fowler to do the illustrations in her fabulously engaging style.

Seven Thousand Feet is a collection of visual art informed by diabetes. The central installation for the exhibition comprised 7,000 individual socks, representing the aforementioned UK annual diabetes-related amputation statistic. The individual socks were stitched onto mesh panels by an army of volunteers. The panels were then fixed to a scaffolding frame. Other exhibits included illustrations, animations, a card game, silk scarf, artist book, sculptures and interactive pieces. Many were created by MMU students and graduates and images of all pieces can be found on the project website. Clothes in bespoke fabrics adorned mannequins and portrayed patterns with "traffic light" backgrounds showing illustrations of healthy (green), not so healthy (amber) and very unhealthy (red) diets.

The Fascinating Family. Visual engagement tools for Research for the Future, an NHS-supported campaign which encourages people to get more involved with health research in their local area.

The exhibition gained a large amount of coverage in the press, on social media, websites and on TV. We had been working with Diabetes UK during the planning and research and they were immensely helpful and supportive. Following the success of the Manchester exhibition, Diabetes UK asked if we could bring the exhibition to their Professional Conference in March 2019. This took place at the Liverpool Arena and Conference Centre and attracted over 3,000 delegates. This was an opportunity that was too good to miss and, despite having no funding left, we decided we had to be there. We received amazing responses from delegates; as one of them put it "you're all over social media."

We'd thought along the way that *The Fascinating Family* could perhaps be a prototype for other "families" who could illustrate other health conditions and would be delighted to talk to anyone who may be interested. Also many of our artworks are available to those involved with diabetes and we have produced a website to show the work (**google.com/view/seven-thousand-feet/home**). Images can be used in presentations and publications too – please don't hesitate to get in touch via the project website or my website **axisweb.org/p/christinewilcoxbaker** or via the websites listed.

Responses from our various events tell us that many visitors, including some already diagnosed with diabetes, learned a lot from our endeavours, found the use of visual art powerful and want to make some lifestyle changes. Some of the comments included: "it made me decide to eat healthier as I have a family history of diabetes and I am borderline"; "I definitely need to reduce my sugar intake as I eat a lot and did not realise the impact diabetes could have"; "your info has been a reawakening of my need to be aware"; "7,000 socks – what a brilliant concept to get a very important message across."

I've learnt a lot too, including ways to minimise my own risk of diabetes by watching my diet and keeping active and that it isn't a given that you'll develop it because it is in your family. Looking ahead to the future, I'm very interested in working on other health-related projects though I might perhaps let others share the lead in future! The whole project has been a fantastic (if exhausting) experience and I have met many amazing people along the way. I am extremely grateful to all those who participated; attended the exhibition, conference and events; the crowdfunders, volunteers and supporters; and particularly to The Physiological Society for being midwife to *The Fascinating Family*.

STEM for Britain 2019: Preventing type 2 diabetes using wrinkled peas

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Exploring ways to present important and novel scientific results and methods to lay audiences is a key part of a scientist's job. My participation in the STEM for Britain 2019 competition allowed me to appreciate the importance of communicating and popularising science. As a PhD candidate, I had the opportunity to present my work entitled "Unique food structures and their effects on glucose homeostasis" and I was honoured to receive the Inaugural Physiological Society Prize.

In 2017, there were over 3.7 million people in the UK diagnosed with type 2 diabetes (T2D) and rates are expected to rise to 5 million by 2025. The risk of T2D is thought to increase with age because of poor control of blood glucose levels. This in turn is due to a progressive decline in the capacity of cells in the pancreas (beta-cells) to secrete insulin, the hormone that controls glucose levels. The decline in beta-cell function can be accelerated by poor diet and lifestyle, thus increasing the risk of developing T2D. Epidemiological and clinical evidence suggests that changes in the diet and lifestyle can prevent or delay the development of T2D.

"In 2017, there were over 3.7 million people in the UK diagnosed with type 2 diabetes (T2D) and rates are expected to rise to 5 million by 2025"

Nevertheless, despite national campaigns to promote healthy eating, T2D diagnosis rates continue to rise. An alternative dietary strategy to maintain normal blood glucose rates at the population level is to improve the composition of commonly consumed foods. There is much evidence that diets rich in a type of carbohydrate called resistant starch have a positive impact on controlling blood glucose levels, and hence reduce susceptibility to T2D. Resistant starches, as the name suggests, are not completely digested in the upper parts of the digestive tract and are available for fermentation by bacteria in the colon. The products of fermentation, known as short-chain fatty acids (SCFA), are thought to improve beta-cell function and thus insulin secretion. There are a variety of fruits and vegetables that contain various amounts of resistant starch, but UK diets are generally low in resistant starch. Thus, there is great potential to reduce the incidence of T2D in the long term by promoting the widespread consumption of resistant starch.

My research focuses on wrinkled peas, a range of naturally occurring variants of peas known to contain different types of resistant starch and less available carbohydrate content. In a series of state-of-the-art experiments, I recruited healthy volunteers, gave them a meal including wrinkled peas (rr peas), and in a series of control experiments smooth peas (RR peas), and I examined: (i) how resistant starch affects the rate at which ingested food moves through the stomach and gastrointestinal tract; (ii) how resistant starches influence the digestion of food in the stomach and gastrointestinal tract; (iii) how resistant starch fermentation in the colon affects metabolism and glucose levels; and (iv) if resistant starch from peas improves beta-cell function. To study the acute effect of food processing and associated health outcomes, we repeated the experiments using pea flour. To further investigate the impact of long-term consumption of resistant starches on glucose responses, I recruited a group of volunteers and asked them to consume pea hummus (rr and RR type) and mushy peas (rr and RR type) for a period of 4 weeks.

As a scientist in the field of human nutrition I was grateful to win this prize and for the new exciting opportunities that have been offered to me. Apart from The Physiological Society prize I have also received an Affiliate membership with The Society and have been invited to join The Physiological Society's Membership Review Task and Finish Group. Also, as a winner of The Physiological Society prize, I was invited to Parliamentary Links Day, one of the largest science events of the annual Parliamentary events. My participation in the STEM for Britain competition was one of the highlights of my doctoral studies, and I would strongly encourage early career researchers and PhD candidates to participate and present their work.

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