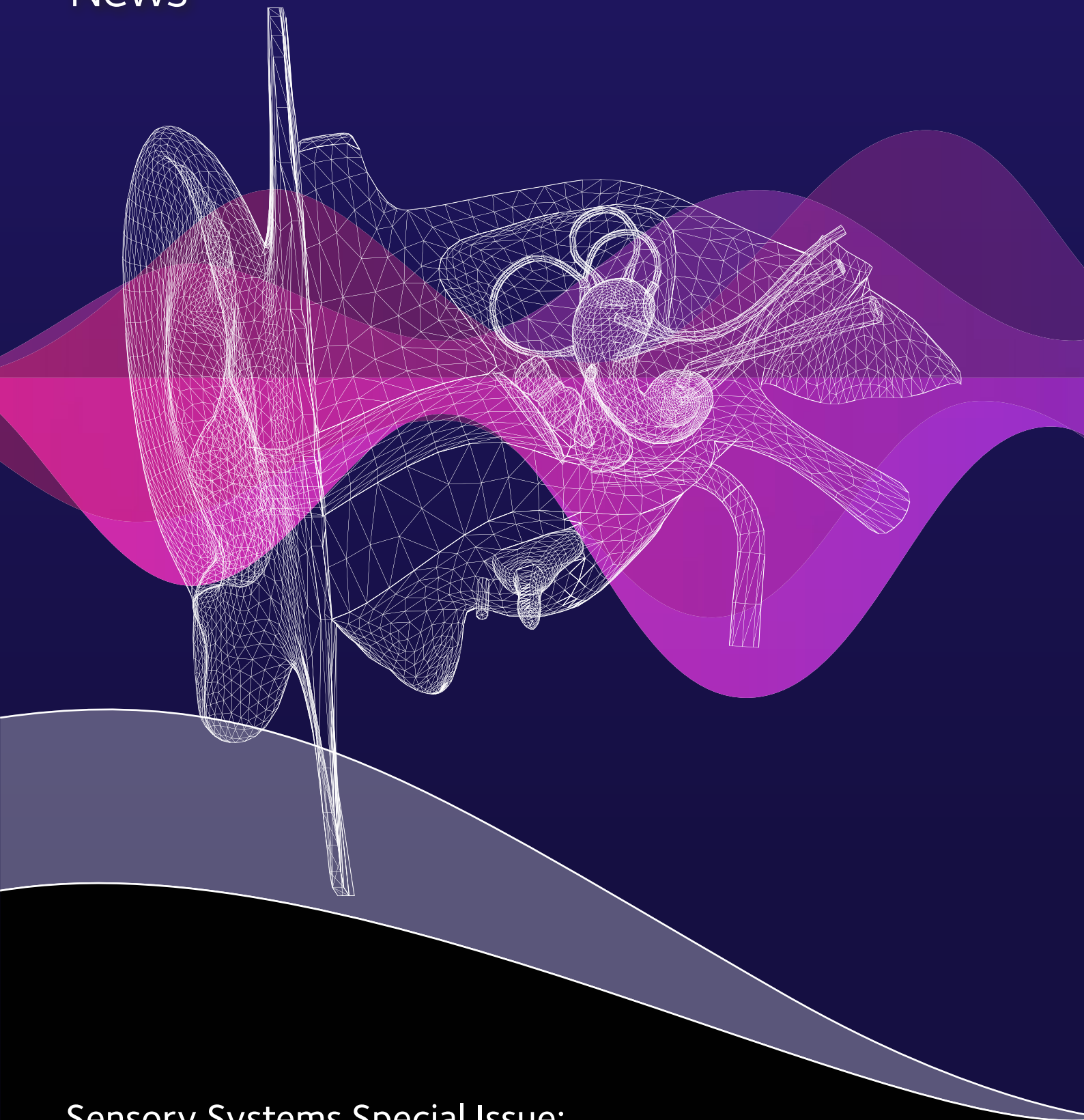


PN

Physiology
News

Issue 126/ Summer 2022



Sensory Systems Special Issue:
Delving into the physiology of sensation

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Processing and Modulation of Sensory Signals: From the Periphery to the Cortex

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20 – 21 June 2022

The Royal College of Physicians,
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Making sense of the world: Exploring the power of sensory systems

Dr Keith Siew

Scientific Editor,
Physiology News

When first teaching students about sensory physiology, one of my favourite tasks is to split the class into two teams and hand out a few markers. The rules are simple, each sense can only be written up on the board once, and like a relay race, when done you must nominate a new teammate to take your marker to write up the next one on the board. One point for the common name, two points if you can give scientific designation (or name the sensory organ system) too.

Predictably there is an initial scramble and the usual suspects: sight, hearing, smell, taste, and touch all appear within seconds, but things slow dramatically as visual, auditory, olfaction, gustation and somatosensation gradually fill the board. At this point there is usually a pause... and I'm greeted with a sea of perplexed looks as I break the silence and exclaim: "What are you waiting for? There are oh so many more still to go!"

It takes them a moment, but after some whispered mutters, eventually one brave soul thinks outside the box, will step forward and write something like... balance or pain on the board. A breakthrough! And with that spark the floodgates of ideas are once again open, eventually hunger, temperature, proprioception, baroreception, chemosensation, thirst, acceleration, etc... all populate the board. And for bonus points a few even manage to come up with a smattering of "non-human ones" (or so we generally tend to think of them for now at

least) like magnetoreception, electroreception, echolocation, infrared sensing, etc.

The exact number of senses is a matter of debate, but we as physiologists can at least agree that it's certainly not limited to five. And for our students, learning how real physical stimuli are transduced into neuronal signals that can be processed and responded to by our brains is perhaps one of the most fascinating areas of physiology they learn about.

It goes without saying that sensory physiology and its neuronal processing and modulation is a vast area of research, and in this special issue we've attempted to give you a broad flavour of some of the exciting work being carried out. From the evolution of our understanding of pain during development (a story beautifully told in five papers by our Honorary Fellow Member, Professor Maria Fitzgerald on p.42) to our recent recognition and redefinition of pain to include invertebrate species. Sensory research can have serious ethical, moral and legal implications for the ways our societies and scientific institutions will function going forward (see p.12 for the comparative physiology of nociception by Dr Lynne Sneddon).

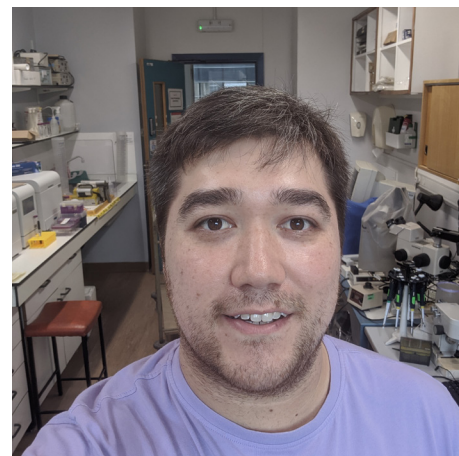
Not only that, but sensory physiology has the genuine power to radically improve lives (see p.10 for how organisations like Royal National Institute for Deaf People support translating research into treatments). I can think of no better example than the amazing work by Dr Lore Thaler and colleagues (see p.20), which shows that teaching our brains to process sensory signals in new ways can give us genuine superpowers! These amazing individuals with visual impairments can learn to navigate the world through echolocation (not unlike Marvel Comic

superhero Daredevil). Even our furrier friends have evolved incredible adaptations that resemble Daredevil's superpowers, with the blind desert golden mole being able to sense the seismic vibrations of wind passing through tufts of grass to navigate and search for food (see p.16 to learn more about Marvellous middle ears from Matthew Mason).

Even the study of perhaps less obvious sensory systems, like whiskers, can yield incredibly useful insights and drive technological innovation. With the aerodynamic shape of seal whiskers inspiring the latest generations of wind turbine blades or the utility of whisker-like probes for drone-like devices in sensitive areas like medical or archaeological environments being explored (see p.24 for Robyn Grant's article on whisker physiology).

Understanding how our brains process and respond to signals is itself an intriguing body of work, and the article by Kathleen Cullen (p.28) on the role of the vestibular system and the cerebellum's ability to generate models of our self-motion is an equally fascinating read. A computational marvel of our brains that's pretty important if you want to distinguish between a sudden slip on the ice or a graceful flying sit spin.

It becomes even more wondrous when the processing of these signals can become mixed up or disagree with one another, leading to strange phenomena like synaesthesia where people may hear a C# and see purple, or hear their boyfriend's name and taste bacon. There are even new senses being discovered like the gravitostat, whereby osteocytes in long bones can measure bodyweight and signal for its maintenance. There is a genuine plethora of material enough to fill a whole other issue! Who knows... maybe we will.



A hive of activity highlighting the value of physiology and creating new opportunities at The Society



Professor David Paterson

President,
The Physiological Society

In April we welcomed physiologists from across the world to our first in-person scientific conference since the start of COVID-19 pandemic. Biomedical Basis of the Elite Performance (BBEP) in Nottingham, UK was a vibrant display of the very best aspects of our conferences – discussing fantastic science while catching up with colleagues old and new (more on p.32).

Some key highlights from the meeting include:

- 179 attendees from 11 countries
- 20 invited speaker talks and lectures
- 6 oral communications
- 56 posters

Our online meetings have been really popular during the pandemic, and we intend to continue online events as part of our programme, but BBEP showed to me the real value in meeting together face to face. I'm looking forward to Sensory Signals in London, UK in June and Europhysiology in Copenhagen, Denmark in September.

Following a project last year focused on considering how the UK's research ecosystem should best recognise and foster interdisciplinary research, we have been working with Research England to feed into their plans for the 'next REF'. As many Society members will be aware, REF outcomes are used to inform the allocation of around £2 billion per year of public funding for universities' research. The 'Future Research Assessment Programme' (FRAP) was launched by the UK's higher education funding bodies in May 2021 and aims to explore possible approaches to the assessment of UK higher education research performance. A future exercise will continue to enable the funding bodies to allocate funding based on research quality and will continue to provide accountability for public investment in research.

The Society convened a high-level roundtable with Research England to discuss some of the key issues and concerns facing physiologists with the REF process. Topics covered included the cost/benefit of REF, the pros and cons of a metric-driven approach, and REF's sometimes negative impact on research culture. As physiologists, we were also particularly concerned that the current system often results in our discipline falling between the cracks, and therefore we discussed how the 'next REF' could better support disciplines like ours. Research England is currently considering responses to their consultation and will report back in the autumn.

The Society also recently held a workshop with the Biotechnology and Biological Sciences Research Council (BBSRC) to launch a report resulting from a project I chaired with BBSRC reviewing the opinions of researchers into the use of models in research. This is a complex area involving a range of experimental systems spanning the remit of *in vitro*, *in silico* and *in vivo* techniques to better understand biological processes.

As physiologists, we are engaged in many different areas of research into cell, tissue, organ, and system function (and malfunction), using various different experimental approaches. One key question for our study design must be "am I using the correct model for my research question?" With a plethora of animal models, *in vitro* experiments, and the growing use of *in silico* modelling, this choice is fundamental to ensure that the data produced are relevant (more on p.9).

The project aimed to understand the current use of experimental systems or models for human and animal research. It has also looked into how researchers perceive the future of animal models. The report is available on BBSRC's website.¹

In June I am looking forward to an event The Society is holding in Parliament to celebrate the role of physiology in teaching. The event will launch a new report from The Society and The Academy For Healthcare Science. This is based on an independent economic analysis by economists Emsi, which shows that the impact of graduates who studied courses with a core physiology component is over £22 billion a year to the UK economy. I'm looking forward to reading more in the report, which will be available on our website.

Finally, I am pleased to let you know that at our Board meeting in March we agreed to create a new role for a clinical Trustee. We saw during the COVID-19 pandemic the vital contribution of physiologists across academia and clinical settings working together, and The Society has well-established links with organisations such as the Intensive Care Society. We are now looking to go further by ensuring clinicians have a direct voice in The Society as a Trustee. This will build on work such as our "Questions from the Frontline" initiative and ensure The Society is representing the breadth and depth of the discipline.

This drive will be reinforced at our 2022 President's Lecture event in early December, where I am delighted to announce that the recipient of the 2022 President's Lecture Medal will be Sir Patrick Vallance. Sir Vallance spearheaded the UK's response to the pandemic and is an Honorary Fellow of The Society. More information about the event will be available soon.

From getting back to in-person conferences, engaging with BBSRC and Research England on the R&D landscape and our renewed focus on clinical physiology, this is a really exciting time for The Society. I look forward to seeing you soon at one of our events – keep an eye on our website for all the details.

References

- ¹ www.ukri.org/publications/bbsrc-survey-report-on-the-use-of-models-in-research

Setting new ambitions for The Society and strengthening our community

Daniel Burdass

Chief Executive,
The Physiological Society

One of my favourite parts of working for The Physiological Society is meeting our members who are actively engaged in a wide range of aspects of physiology, including discovery and translational physiology, clinical physiology, exercise physiology, nutritional physiology and comparative physiology. So I was particularly delighted to be able to attend our first in-person conference since the COVID-19 pandemic – The Biomedical Basis of Elite Performance at the University of Nottingham, UK, alongside our Member Roadshow, which celebrated physiology in Nottingham.

During the Member Roadshow we heard from Dr Angus Brown (University of Nottingham, UK) who gave a fascinating talk on *The Hodgkin and Huxley papers: still inspiring after all these years*. This was followed by three inspiring talks from early career researchers, Dr Matthew Brook, Esther Wainwright and Dr Jyoti Agrawal from the University of Nottingham, each elucidating thought-provoking questions from the audience. This was followed by a reception, which created a great networking opportunity – chances to catch up with old friends and make new ones too.

We recognise that a key element of science research is building collaborations. With physiology becoming less obvious as a distinct discipline within many institutions, alongside researchers who are physiologists not recognising themselves as such, we need to work to change this. We therefore recognise the importance of us getting back on the road to re-engage with our members in their institutions – to build our community through developing new connections and networking opportunities at a local level. There will be further Roadshow events that celebrate physiology during 2022 and 2023. I look forward to meeting many of our members and future members at these events.

As well as working more locally we also recognise the role that we play internationally and with travel restrictions lifting we were really pleased to be able to attend Experimental Biology 2022 held in Philadelphia, US. While at the event we had a busy few days, meeting with the senior leadership of the American Physiological Society (APS) to explore areas of synergy and potential collaborations as well as meeting physiologists on the stand and at their posters. Alongside this we also sponsored a symposium on *Causes and Consequences of Sympathoexcitation Across the*

Lifespan: Physiological or Pathological? and co-sponsored a symposium with the APS on *Physiological Consequences of Obesity During Pregnancy for Mother and Child*.

The highlight of the conference for me was being able to attend the Nobel Prize Award Lecture on *Grid Cells and Neural Coding of Space* given by Professor Edvard Moser from the Norwegian University of Science and Technology, Trondheim, Norway.

While at the event we asked the physiology community who came by our stand two questions:

What does physiology mean to you, in three words? The word cloud below is a visual representation of the frequently used words.

What is the most important scientific question that physiology can help answer and why?

At the end of the conference a competition winner was drawn and the winner was: Cole Jensen from the Mayo Clinic Cell and Regenerative Physiology Laboratory, Minnesota, US.

He wrote that the most important scientific question that physiology can help answer is “How do you treat heart failure with preserved ejection fraction (HFPEF), a common cause of hospitalisation and mortality?” He considers it is important because there are currently very few treatment options. We will be speaking to Cole Jensen about this further, which will be appearing on our blog in the near future.

During 2022, The Physiological Society will need to replace its existing strategy, which has served us well for the past five years but will soon expire.

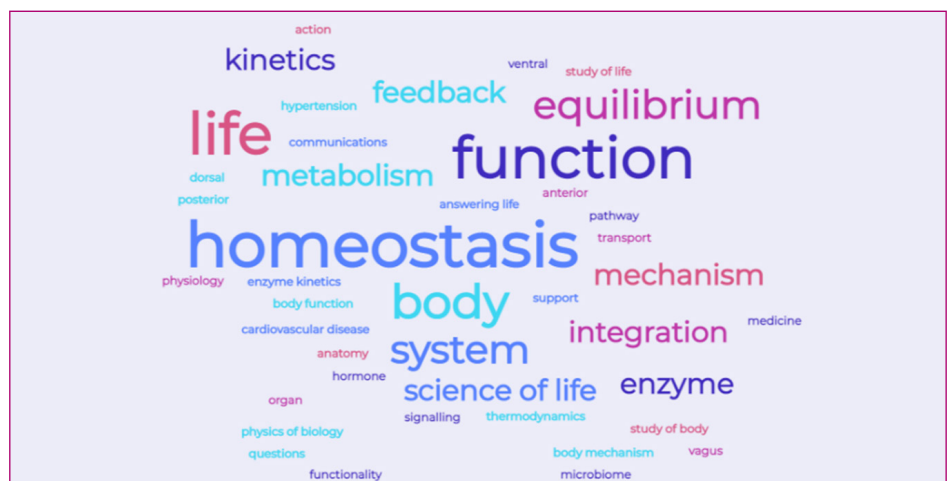
As we look to develop our next three-year strategy we are in a really strong place to build on these foundations and think ambitiously about where our Society goes next.

Our vision for The Society is to increase the visibility of physiology through an inclusive approach so that we are sustainable for the future. Over the coming months Trustees, with the Senior Management Team, will be spending time on developing The Society's new strategy, which will determine where and how we should focus our resources and what The Society's USP is. The plan will demonstrate how we will support physiology while providing that sense of community for members and a strong voice for our discipline through our publications, policy work, and conferences programme.

The Society's publishing plays a significant role in our mission through the dissemination of cutting-edge research. We want to keep the Society's journals at the forefront of scientific publishing, and we are therefore working with a consultancy firm who is conducting a strategic assessment of our journals programme. The aim of this assessment is to ensure that we have a publication strategy for today's market dynamics.

Our three journals lead the discipline, promoting best practice and pushing the boundaries of scientific endeavour and we would like to strongly encourage our members and the wider community to consider submitting their next article to one of our journals. We use the surplus from our international publishing operation to support our community of physiologists, advance physiology and increase the influence of The Society with the public, policymakers, and other stakeholders.

The Society is a membership organisation. As always, please call me, email me, invite me to come to your lab, and let me know what we do well, where we could do better, what we might stop doing and what we could do more of.



Word cloud shows the words most frequently used to describe physiology, with homeostasis being the most popular, at Experimental Biology 2022

We must talk!

Dr Peter Kohl

Editor-in-Chief, *The Journal of Physiology*

Physiology News (PN) welcomes the new Editor-in-Chief of *The Journal of Physiology*, Dr Peter Kohl, who started his tenure in April of this year. Peter studied Medicine and Biophysics in Moscow, did his PhD in Physiology at the Berlin Charité, spent 20 years researching cardiac mechano-electric feedback at Oxford, and another five years focused on heterocellular interactions at Imperial College London, before setting up the new Institute for Experimental Cardiovascular Medicine at Freiburg, Germany. He will have a regular column in *PN*, and hopes to engage our readership to join a discourse about physiology in general, and publishing physiology-based research in particular.

The phrase 'we must talk' triggers the startle reflex in me, running a quick mental check to probe potential recent transgressions. If that is the same for you – please excuse me: this is not what I intended.

But: I do think we need to talk.

If you read *PN*, most likely you will be a member of The Physiological Society. And – so at least I hope – you are an admirer of *The Journal of Physiology (JP)*. Of course, you should be, since you – as a member of The Society – 'own' *JP*.

Though – ownership obliges!

As a Society, we derive significant benefit from *JP*, in domains including science, reputation, and finance. Income from *JP* is crucial for enabling The Society's activities, upholding research and education in physiology for public benefit.

Like most journals, there will be increasing pressure on *JP* to consider switching to Open Access (OA). And while OA solves some problems (such as offering free access to papers for all) – it generates new ones (such as shifting costs to authors). One problem often overlooked is that Society-owned journals do not operate to generate profit, but resources for academic independence and self-organisation. If we wished to maintain the current levels of charitable income for The Society, yet switch to OA, *JP* would have to charge 'article processing fees' to authors that approximate those commanded by *Nature*.

Leaving aside the question of whether this would be desirable in general, or affordable in particular, it would not be viable. Few journals have the global impact of *Nature*, and the benefits of having a *JP* publication on an individual's CV – rightly or wrongly – will not match the prestige of a *Nature* paper. So when choosing where to submit what, the balance of journal-level metrics such as the impact factor (50 for *Nature*, 5 for *JP*) versus fees associated with publishing will affect author decisions.

Now, we all know that metrics can be surprisingly poor indicators of the actual standing of a journal in a field. And they are even less indicative of the quality of an individual paper.¹ In any case, metadata reflect at least some aspects of the *status quo*. One of these aspects is the fact that, in spite of tremendous efforts, *JP* has seen a continued reduction in the number of original papers submitted over the last few years. Also, just 16.5% of current Society members (postgraduate and above) have submitted original research to *JP* since the start of 2019.

This is equivalent to one paper submitted per member of The Society *every 20 years*...

So, this is what we need to talk about.

For *JP* to continue to flourish, and to be able to support the good work of The Society, we as members must take more conscious and more complete ownership of *JP*. First and foremost, this means that we submit our best work to *JP*.

If that may not be possible, then at least we should be aware of, acknowledge and share the amazing research published in *JP*.

Now we all know how difficult it is to deal with information overload: it is easy to miss relevant papers. *JP* therefore proposes to set up a "Readers Digest" service for members of The Society, which would inform you – just once every 12 months – of the most exciting *JP* papers in your area, published in the preceding calendar year. If this allowed members of The Society to discover just one additional recent *JP* paper relevant to their studies, and to consequently cite it, it would accelerate the transfer of knowledge in our field, improve journal visibility, and benefit the metrics that researchers evaluate when choosing where to publish.

I hope that this may be of interest to you. In any case – please let me know your thoughts and suggestions on where you see the future of *JP*, on how you would wish to exercise your ownership of the journal, or on any other aspect of the interrelations between The Society and *The Journal* – by writing to me via pkohl@physoc.org. I may not be able to respond to each message directly, but I would hope to sum up and address key points in future editions of this column here in *Physiology News*.

So let's talk.

References

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7974631/>.

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Building a better picture of the current use of experimental models for human and animal research

Tom Addison

Policy Manager, The Physiological Society

The *President's View* in the previous edition of *PN* was a timely reminder that ensuring a responsible and balanced *in vivo* landscape for our researchers is a critical part of The Society's mission.

As Professor Paterson noted in Issue 125, The Society was formed as "an association of physiologists for mutual benefit and protection", in part in response to Victorian anti-vivisection campaigns. While challenges undoubtedly remain in the *in vivo* regulatory environment, the UK Government's economic priorities following the UK withdrawal from the European Union and the role of science research and development (R&D) in the COVID-19 response have given The Society and its allies a number of opportunities to reinforce the value of *in vivo* skills. As such, The Society has been working on a number of projects in this area.

Since the last edition of *PN* was published, The Physiological Society has been working closely with the Biotechnology and Biological Sciences Research Council (BBSRC) to organise a webinar to launch their *Survey Report on the Use of Models in Research*. This report was developed in consultation with The Physiological Society and our President chaired the Expert Working Group that was responsible for discussing and ratifying the report's findings.

The report found that the most common reason for choice of a model was its physiological relevance (21%) and that 50% of respondents have been using their model for more than 10 years, with only 35% of respondents reporting changing from one model to another during their career. The most common model species was the fly (18%) followed by mouse and zebrafish (both 17%).

These findings give an interesting overview of the use of different models and species across those disciplines of most interest to BBSRC, and physiology will certainly have been represented within this survey. However, The Society is interested in building a better picture of the current use of experimental systems or models for human and animal research among

physiologists specifically. This will help inform the work of our Policy Committee and *In vivo* Taskforce, as well as engagement with other organisations interested in the role of *in vivo* work in the R&D landscape such as the Royal Society of Biology (RSB), Understanding Animal Research (UAR) and the Association of the British Pharmaceutical Industry (ABPI).

This work will be particularly important given the changes that are currently ongoing in the regulation and auditing of the UK *in vivo* landscape. The UK Government's Animals in Science Regulation Unit (ASRU) is currently in the process of being reorganised within the Home Office to focus exclusively on its role as a regulator. Its stakeholder engagement function is being taken over by a new cross-departmental policy unit, which will be responsible for coordinating animal welfare across all Government departments.

Ensuring that the challenges physiologists face in delivering high-quality research and teaching involving animals will be crucial as the UK Government looks to R&D as a key aspect of its strategy to build back better, both economically and through improvements in health outcomes, following the COVID-19 pandemic.

Reports of The Society's recent committee meetings

The purpose of this short update is to keep you informed about the work of our Communities Committee. Here is the summary detailing the spring meeting.

Communities Committee

April 2022

It was noted that this was the first meeting of the Communities Committee, which had been developed following the dissolution of the Education, Public Engagement and Policy (EPEP) Committee. Alongside the Communities Committee, a Policy Committee had also been established.

The Committee was provided with an update on engagement with the new grants programme, and associated support webinars, which was launched in 2021. The Committee also received an update on the outcomes of professional development sessions that had run in Q1 of 2022, including the successful workshop on securing promotion to professorship in teaching and learning. It

was agreed that the support for Techniques Workshops would be reviewed in 2023.

The Committee was updated with regard to plans for the implementation of an Early Career Funding Task and Finish Group, to determine how The Society could effectively and sustainably provide funding support for early career researchers not yet in a substantive post.

Recommendations from a Task and Finish Group reviewing the Education and Teaching Prize portfolio were presented; the Group provided ideas for changes to existing prizes and identified new areas for recognition. The Committee made further suggestions and the updated portfolio will be presented to the Prize Nominations Committee for consideration.

As Scientific Editor of The Society's magazine, *Physiology News*, Dr Keith Siew invited the Committee to suggest ideas for the upcoming climate change issue and general theme ideas for the 2023 calendar year. Since this was the first meeting of the newly termed Communities Committee, members were asked to consider the remit of the group and its focus moving forwards. The ideas will be gathered over the coming months and fleshed out ready for the next meeting.

The Committee Chair announced that Chrissy Stokes will be leaving The Society. She was thanked sincerely for all of her hard work and her career move to The Royal Society was celebrated.



RNID: Making life inclusive for deaf people and those with hearing loss

Our research priorities and themes

Dr Tracey Pollard

Research Programme Lead, Royal National Institute for Deaf People (RNID)

Hearing loss affects 1 in 5 adults in the UK. It's an invisible condition that can have a devastating effect on relationships, education and job prospects. It's also a growing problem in an ageing population – we estimate that 15.6 million people in the UK will have hearing loss by 2035. Tinnitus, noise in the ears or head that doesn't have an external source, affects around 7.1 million people in the UK. It can have a serious impact on people's quality of life, causing problems with sleep and concentration, as well as stress and anxiety.

There's a frustrating lack of patience, empathy and understanding for people who are deaf or have hearing loss. Barriers to work, travel and communication take a toll on mental wellbeing and cause social isolation.

RNID have been helping people with hearing loss for more than 100 years, and we've already changed the lives of millions. We want to make life fully inclusive for deaf people and those with hearing loss or tinnitus. We campaign for an inclusive society, connect people to practical advice and fund research to support the development of new treatments for hearing loss and tinnitus.

We've been funding research into treatments since 1999. Back then, most applications were for research into medical devices – hearing aids and cochlear implants. There were fewer applications from researchers working on hair cell regeneration, tinnitus, ototoxicity (caused by medications that damage cells in the inner ear as a side effect,

leading to hearing loss) or protection of the auditory system from noise damage.

Over time, that has shifted – in particular, we now see more applications focused on developing specific treatments for hearing loss or tinnitus. In response to this shift in the field's priorities, we set up a new programme to fund translational research in 2011, providing a dedicated source of funding to move potential therapies along the research pipeline. More recently, we set up our Hearing Therapeutics Initiative, through which we offer a broad range of support to innovators within academia and biotech or pharmaceutical companies.

We currently focus on three main areas of research:

Preventing hearing loss

We fund research to better understand the cellular and molecular mechanisms that underlie hearing difficulties and advance the development and testing of treatments to prevent any type of hearing disorder.

Restoring hearing

We fund research that will lead to transformative improvements to the quality of hearing gained from medical devices. We also fund research to advance the development and testing of drug, gene or cell-based therapies to repair damage to any part of the auditory system to improve hearing.

Silencing tinnitus

We fund research to improve our understanding of the biological mechanisms involved in tinnitus and to develop and test new approaches to reduce the perception of tinnitus.

Through our funding schemes, we aim to accelerate the discovery and development of new treatments. We're also working to ensure

that we include the needs of people with hearing loss or tinnitus when setting priorities for our research funding, to ensure that the work we fund will bring them the benefit that they want.

We fund project grants (at both the discovery and translational research stages), fellowships and PhD studentships. We also have a pump-priming pilot grant scheme to kickstart new lines of research. Applications to our schemes go through a rigorous peer-review process so that we can be sure we're funding the best research.

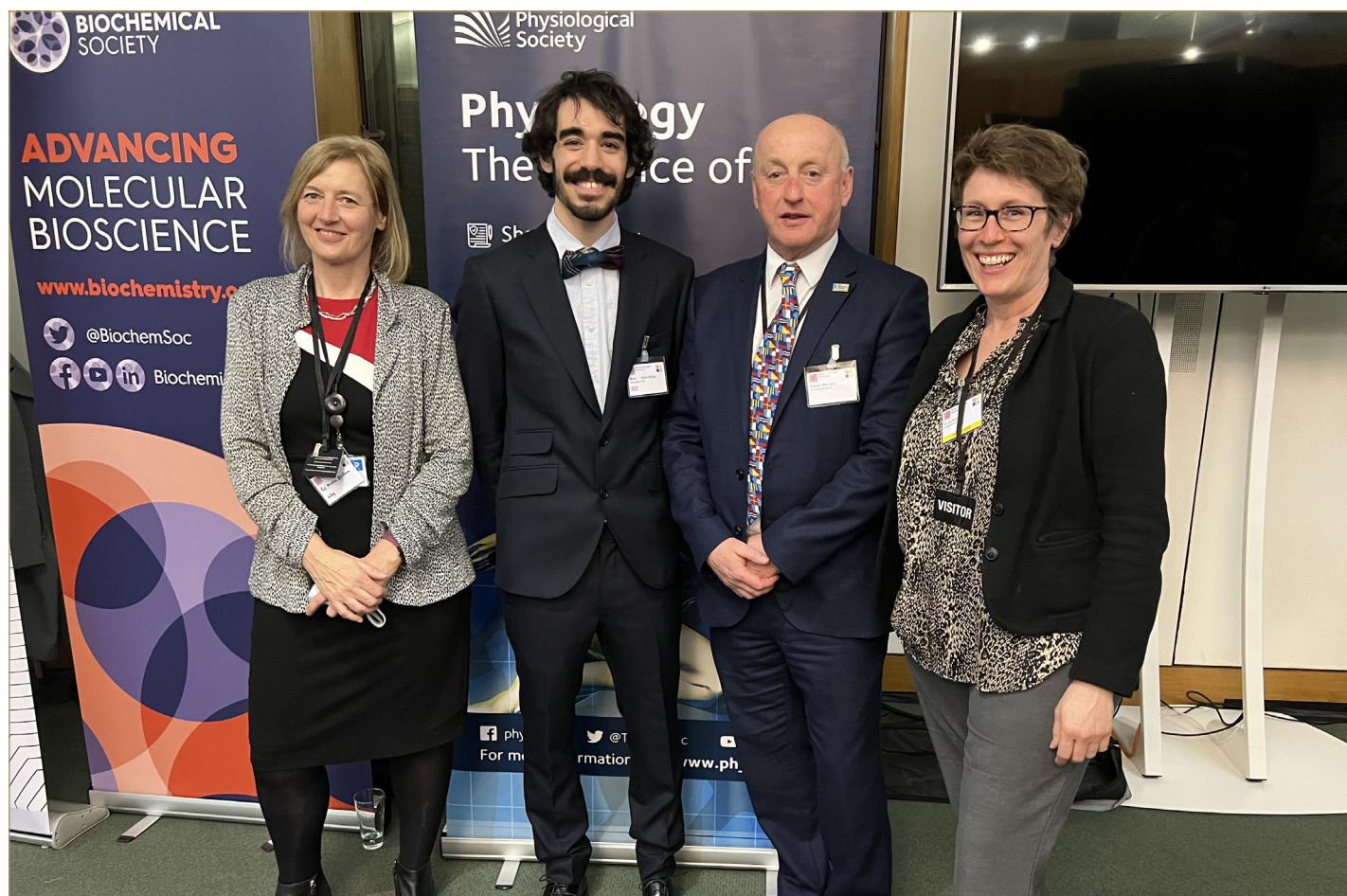
Our grant schemes have deadlines throughout the year. We want to see applications from researchers we've not had contact with before, so if your research fits our remit, please consider applying to us – there's more information on our website: <https://rnid.org.uk/researchfunding>.

Recently, our funding helped researchers at King's College London to identify 44 new genes linked to age-related hearing loss¹. The researchers used data from the UK Biobank (which tracks different health characteristics in 500,000 people aged between 40 and 69 over time) to find these new genes. Before this, only a handful of genes had been linked to the condition. The discovery of these genes will improve our understanding of the mechanisms involved in age-related hearing loss, allowing the development of more targeted treatments to slow the onset of, or treat, hearing loss.

References

- 1 Wells HRR *et al.* (2019). GWAS identifies 44 independent associated genomic loci for self-reported adult hearing difficulty in UK biobank. *The American Journal of Human Genetics* **105**, 788–802 <https://doi.org/10.1016/j.ajhg.2019.09.008>.

The Physiological Society Prize winner announced at STEM for BRITAIN



Daniel Burdass (CEO at The Society), Miquel Serna Pascual (King's College London, UK), Professor Mike Tipton (Chair of The Society's Policy Committee Chair) and Dr Lucy R Green (Chair of Communities Committee).

The Physiological Society Prize was awarded to Miquel Serna Pascual from King's College London, UK at STEM for BRITAIN. Miquel also won the Gold Bioscience Prize.

On 7 March 2022, early career research scientists, politicians and a panel of expert judges attended Parliament for STEM for BRITAIN, a major scientific poster competition and exhibition. The event is organised by the Parliamentary & Scientific Committee to give members of both Houses of Parliament an insight into the outstanding research being carried out at UK universities by early career researchers.

The Physiological Society Prize was judged by a panel of physiologists, including Chair of The Society's Policy Committee Chair, Professor Mike Tipton, and Chair of Communities Committee, Dr Lucy R Green.

Speaking after presenting the award to Miquel, Professor Tipton said:

"The Physiological Society is proud to support STEM for BRITAIN, which gives the opportunity for early career physiologists to talk directly to politicians about their research."

"Every year we award The Physiological Society Prize to an early career researcher in physiology whose research stands out for being novel, robust and important. This year was no different. I was really impressed by the first-class science on display. It was also fantastic to see Miquel win the overall competition prize; this is a testament to Miquel's excellent research and also shows how critical physiology is for understanding disease processes."

Miquel's poster on research about "Hidden disease signs in the pattern of breathing" discussing how to improve diagnostics for respiratory diseases was judged against dozens of other scientists' research in the only national competition of its kind.

Miquel was shortlisted from hundreds of applicants to appear in Parliament and is studying a PhD in Bioinformatics. He is applying a novel mathematical method, termed Symmetric Projection Attractor Reconstruction, to analyse large amounts of biomedical waveform data. From this data, Miquel can search for patterns to help inform clinicians about early changes in the human body in response to treatment or disease.

On winning The Physiological Society Prize, Miquel said:

"It was a great experience to present my research in Parliament and to get feedback and questions from both academics and policymakers. I thank The Physiological Society for my award and The Parliamentary and Scientific Committee for awarding me the Biological and Biomedical Sciences Award. I would also like to take this opportunity to thank my research team and my supervisor Dr Manasi Nandi, King's College London, UK, for making this project possible."

The impact of nociception and pain: Implications for animal welfare legislation



Dr Lynne U Sneddon

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Nociception (from the Latin *nocēre* “to harm”) is the simple detection of noxious, potentially damaging stimuli and is usually accompanied by a reflex withdrawal response away from the danger. Receptors for nociception, termed nociceptors, are the subject of intense study, from their anatomy and molecular biology through to their electrophysiological properties (Sneddon, 2018). These neurons convey information about tissue-damaging stimuli to the central nervous system and alert the animal to the risk of injury. In effect, they act as an alarm system and elicit the adaptive response of retreating from the offending stimulus. Nociceptors also underlie the sensation and affective dimension of pain where tissue damage leads to feelings of discomfort and suffering.

The International Association of the Study of Pain (IASP), a clinical society, recently changed their definition of pain from “An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (Merskey, 1979) to “An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage” (Raja *et al.*, 2020). This may appear as a slight change to the terminology, but it is an incredibly important one as it recognises that pain may occur in other animals and not just humans. Previously, criticisms of the original definition included the concept that pain could only be felt by humans who could self-report their pain and thus excluded infants, adult humans with medical conditions that make communication difficult or impossible, and of course animals who we do not share common language with. This is a dramatic

shift in the dogma surrounding pain and this definition accepts that pain is not just a human experience. Of course, animal models of nociception and pain, which have yielded so many important insights into our fundamental knowledge of human pain, must experience some form of pain to be relevant otherwise why study them? In humans, self-reporting of the pain experience is the gold standard; however, with humans and animals that cannot communicate using spoken language, how do we tell if they are in pain? The primary way in which pain is assessed is in behavioural responses and so under the new IASP definition if an individual is displaying behavioural and physiological changes that resemble pain then it should be accepted that pain is occurring. So, it is the insertion of this word “resembling” that creates a paradigm shift in the doctrine surrounding pain and acknowledgement of its existence in other animals.

Why study pain in animals?

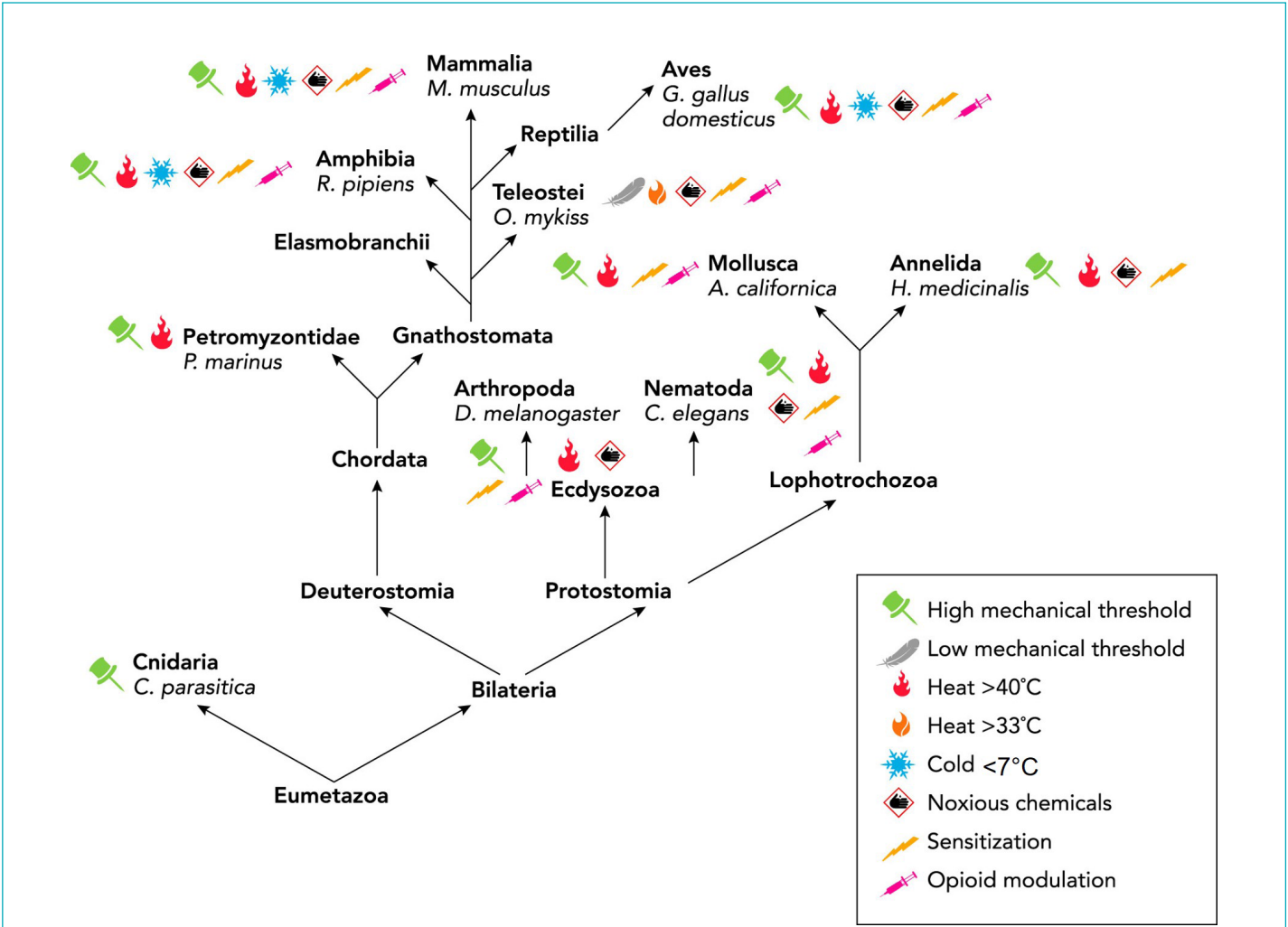
The use of animals in nociception and pain studies has led to dramatic discoveries and has really fuelled our understanding of the basic biology of this important sensory system. Pain can be debilitating and reduce the quality of human life and this also poses challenges for the welfare of animals.

We must ask ourselves, why have animals become such important experimental models for the study of clinical pain? Using animal models with perhaps a less complex nervous system (e.g. invertebrates) may not be immediately intuitive, but their study can yield insights into the mechanisms of nociception and pain that lead to the discovery of new therapeutics. Their less complex structure can allow much more detailed analysis of how the nervous system works using genetic, physiological and molecular tools and, further, they are considered as Replacement under the 3Rs umbrella and are believed to be a more ethical choice to replace vertebrates without the requirement for acquiring experimental licensing or governmental permits. Studying animals

can also help us understand the comparative aspects as well as the evolutionary conservation of nociception and pain. Finally, many laws and guidelines demand we keep animals in a pain-free state. So by studying the occurrence of pain from nociceptors through to whole-animal responses we can inform pain management and seek to avoid, minimise, or alleviate pain in captive contexts such as the laboratory or in farming.

Invertebrate models of nociception, where neuronal activity can easily be linked to behaviour, include the sea slug (*Aplysia californica*), roundworm (*Caenorhabditis elegans*), fruit fly (*Drosophila melanogaster*) and the leech (*Hirudo medicinalis*) and so on. These have advantages over rodent models due to the lack of need for ethical permission and due to easier monitoring of their nervous system. Much of the underlying molecular biology and physiology of nociceptors is strikingly similar to that of mammals, including opioid modulation (Fig.1; Sneddon, 2018; 2019), and this has led to the identification of new targets for the alleviation of pain (e.g. analgesics). For example, a chronic pain model

in *Drosophila* has demonstrated that the Bone Morphogenetic Protein (BMP) pathway downstream of the hedgehog (Hh) signalling pathway, known to be involved in nociceptive sensitisation in response to injury, has been thoroughly dissected and yielded new insights into the mechanism of chronic pain. In a recent study, the proteins Brinker (Brk), and Schnurri (Shn) were suppressed in nociceptors using an RNA-interference (RNAi) knockdown approach in *Drosophila*. Knockdown of Brk resulted in hypersensitivity in the absence of injury, suggesting a role in suppressing nociceptive sensitivity. Whereas when Shn was knocked down in the *Drosophila* nociceptors, allodynia (pain response to a stimulus that does not normally provoke pain) was not seen after injury, showing that this transcriptional activator is involved in promoting hypersensitivity after injury (McParland *et al.*, 2021). Both Brk and Shn can now be considered as novel targets in chronic pain treatment in humans and other animals. So, do fruit flies experience chronic pain given these results? If so, should we safeguard their welfare? This is certainly becoming a growing concern amongst scientists and the public (Delvendahl *et al.*, 2022).



Why is pain so important in animal welfare legislation?

When deciding which animals to protect under legislation and guidelines, pain is the key factor. Indeed even in 1789, the philosopher Jeremy Bentham provided a famous quote: "the question is not, Can they reason? nor, Can they talk? but, Can they suffer?" Providing sound scientific evidence that an animal is capable of experiencing pain and the associated suffering and discomfort makes a compelling case for their protection. The scientific legislation concerning the use of adult vertebrate animals and cephalopods in the EU and the UK states that pain should be avoided or minimised to reduce suffering in laboratory animals. However, this is often not applied equally to different species. For example, pain relief protocols are routinely used and the assessment of pain is well developed in rodents (see Fig.2 for rat grimace scale, Sotocina *et al.*, 2011; mouse and rabbit grimace scales can be found on the NC3Rs UK website). This is not the case for fish models where the assessment of pain is less well studied and analgesic drugs are rarely used or reported. In some regions there are no welfare laws pertaining to fish and only local ethical review occurs in experimentation. With the first publication of nociceptors in fish 20 years ago (Fig.3; Sneddon, 2002), the situation has been transformed and the treatment of fish has been enhanced through a better understanding of the biology of pain in these animals (Sneddon, 2019). Thus far we know fish nociceptors are comparable with mammals because the underlying molecular biology is similar and behavioural and physiological responses to painful treatment are prevented by analgesic drugs. By studying neuroanatomy, electrophysiology, stress physiology and behavioural responses to pain, it is now largely accepted that fish experience pain. This research has informed changes in attitudes not only in science but in other fields. In aquaculture, a recent report adopted by the European Union states "There is growing evidence that fish, like other vertebrate animals, are sentient beings, and that they can experience pain and distress" (SCAR, 2018).

Pain in cephalopods and decapod crustaceans

Headlines from many media outlets were emblazoned with the outcome of a UK government-funded report on the existence of pain in cephalopods and decapod crustaceans. Currently adult cephalopods such as octopus, squid, cuttlefish and *Nautilus* are included in the EU and UK science legislation (e.g. laboratory animals) but not in the UK Animal Welfare Act, which pertains to animals held in captivity (e.g. companion and production animals) but not to wild animals. Decapods such as crab, lobsters, prawns and shrimps were not included in the European science legislation in 2010 as there was not enough evidence for pain in these animals at that time. This new report on these decapods and cephalopods reviews the scientific evidence for nociception and pain in these animal groups and comes to the conclusion that they should be afforded protection under UK law.

In decapods, there is behavioural evidence that resembles pain (review in Elwood, 2019). Application of noxious chemicals to antennae in prawns results in rubbing and this is reduced by morphine (an opioid receptor agonist). Shore crabs avoid shelter when they receive an electric shock and hermit crabs, which are soft-bodied and live in mollusc shells, will abandon a high-quality shell after a shock only to remain in a "safer" yet poorer-quality shell afterwards. Studies have also demonstrated a physiological stress response after potentially painful treatment in crabs. Few studies have performed a classic electrophysiological characterisation of nociceptors in crabs and we know relatively little about central nervous system responses. Therefore, it is imperative that we fill this knowledge gap.

In contrast, nociceptors have been identified and recordings have been taken that demonstrate the evolutionary conservation of

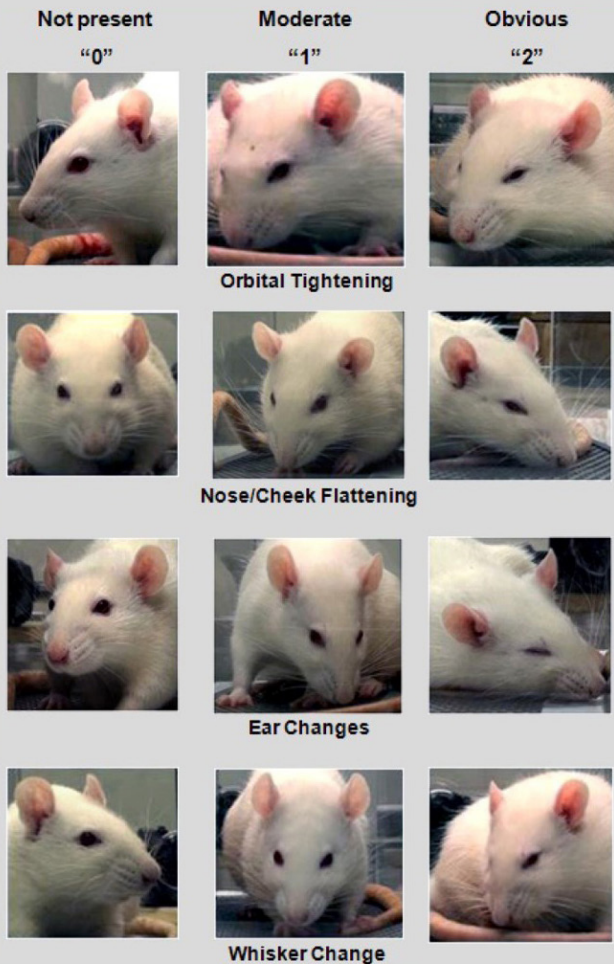


Figure 2. The four action units of the Rat Grimace Scale (RGS).

1. Orbital Tightening: Rats in pain display a narrowing of the orbital area, manifesting either as (partial or complete) eye closure or eye "squeezing." 2. Nose/Cheek Flattening: Rats in pain display successively less bulging of the nose and cheek (see above), with eventual absence of the crease between the cheek and whisker pads. 3. Ear Changes: The ears of rats in pain tend to fold, curl and angle forwards or outwards, resulting in a pointed shape. The space between the ears may appear wider. 4. Whisker Change: The whiskers of rats in pain move forward (away from the face) from the baseline position, and tend to bunch, giving the appearance of whiskers standing on end (Reproduced from Sotocina *et al.*, 2011 under the terms of the CC BY 3.0).

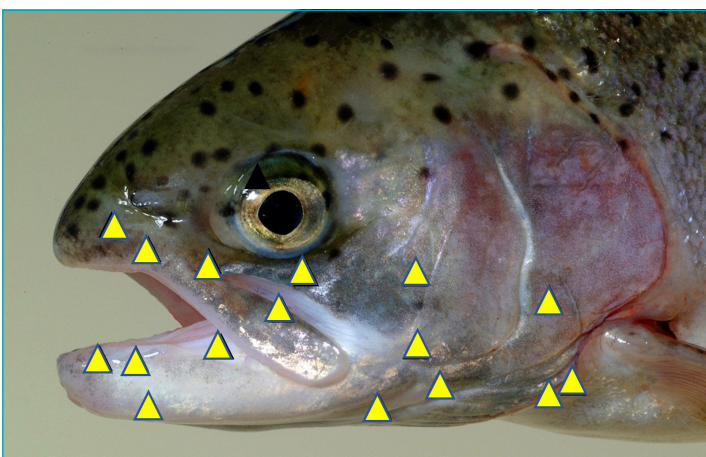


Figure 3. Polymodal nociceptors on the head of the rainbow trout. The position of polymodal nociceptors (triangles) characterised by electrophysiology that responded to mechanical, thermal (heat) and noxious chemical (acetic acid) stimuli (created by LU Sneddon from data obtained in Sneddon, 2002).

nociceptor properties in cephalopods. A very elegant study performed by Robyn Crook measures both behaviour changes and nociceptor activity in the octopus (Fig.4; Crook, 2021). Octopuses avoided areas where pain was experienced, demonstrating that pain is aversive, whereas they exhibited a preference for an area where they experienced pain relief. These animals also groomed the acetic acid injection site but this was prevented by the use of a pain-relieving drug, the local anaesthetic lidocaine. Electrophysiological recordings demonstrated the presence of nociceptor activity when a pain stimulus was given and its absence after pain-relief administration. What this study tells us is that octopuses are motivated by pain and will avoid an area associated with it, so it must be a detrimental experience. Conversely, providing pain relief resulted in the octopus showing a clear preference for the area where pain was reduced by lidocaine administration, demonstrating that the relief of a negative internal affective state, pain, alters the animal's preferences. Animals with no pain showed no preference for either area, demonstrating that pain was the motivational stimulus behind the animals' behavioural decision-making (Fig.4).

Should we protect animals where there is evidence for pain?

Given the heightened awareness of animal welfare issues by the general public and the growing calls for inclusion of decapods and cephalopods into existing animal welfare legislation, decisions regarding other animal groups may rise to prominence. Governments and regulatory bodies will need scientific evidence to base their decisions on. This is a unique opportunity for physiologists to ensure their science makes a wider impact. There are many different opinions on whether non-human animals can experience pain. Irrespective of one's own opinion, there are many advantages to ensuring good animal welfare for human benefit. In the context of experimental research, pain may present a confounding factor and so minimising pain after an invasive procedure ensures you are measuring the response to your experimental treatment rather than pain symptoms. Keeping animals in good welfare may lead to reduced individual variation, lower sample sizes and better reproducibility. When studying pain itself, animal models with more accessible nervous systems, which

allow easier monitoring, can help us find novel ways of improving human pain treatment. Further, the work can provide new insights into the comparative biology and evolution of nociception and pain, not only adding to our understanding but informing decisions regarding the welfare of all animals.

References

Birch J et al. (2021). Review of the evidence of sentience in cephalopod molluscs and decapod crustaceans. <https://www.lse.ac.uk/business/consulting/assets/documents/Sentience-in-Cephalopod-Molluscs-and-Decapod-Crustaceans-Final-Report-November-2021.pdf>.

Crook RJ. (2021). Behavioral and neurophysiological evidence suggests affective pain experience in octopus. *iScience* **24**(3), 102229. <https://doi.org/10.1016/j.isci.2021.102229>.

Delvendahl N et al. (2022). Edible insects as food–insect welfare and ethical aspects from a consumer perspective. *Insects* **13**(2), 121. <https://doi.org/10.3390/insects1302012>.

Elwood RW. (2019). Discrimination between nociceptive reflexes and more complex responses consistent with pain in crustaceans. *Philosophical Transactions of the Royal Society B* **374**(1785), 20190368. <https://doi.org/10.1098/rstb.2019.0368>.

Merskey H. (1979). Pain terms: a list with definitions and notes on usage. Recommended by the IASP Subcommittee on Taxonomy. *Pain* **6**, 249–252.

McParland A et al. (2021). The brinker repressor system regulates injury-induced nociceptive sensitization in *Drosophila melanogaster*. *Molecular Pain* **17**, 17448069211037401. <https://doi.org/10.1177/17448069211037401>.

Raja SN et al. (2020). The revised International Association for the Study of Pain definition of pain: Concepts, challenges, and compromises. *Pain* **161**(9), 1976–1982. <https://doi.org/10.1097/j.pain.0000000000001939>.

Standing Committee on Agricultural Research. (2018). Strengthening fish welfare research through a gap analysis study. https://scar-europe.org/images/FISH/Documents/Report_CWG-AHW_CASA_FISH-welfare.pdf.

Sneddon LU. (2002). Anatomical and electrophysiological analysis of the trigeminal nerve in a teleost fish, *Oncorhynchus mykiss*. *Neuroscience Letters* **319**(3), 167–171. [https://doi.org/10.1016/S0304-3940\(01\)02584-8](https://doi.org/10.1016/S0304-3940(01)02584-8).

Sneddon LU. (2018). Comparative physiology of nociception and pain. *Physiology* **33**, 63–73. <https://doi.org/10.1152/physiol.00022.2017>.

Sneddon LU. (2019). Evolution of nociception and pain: Evidence from fish models. *Philosophical Transactions of the Royal Society B* **374**, 20190290. <https://doi.org/10.1098/rstb.2019.0290>.

Sotocina SG et al. (2011). The Rat Grimace Scale: A partially automated method for quantifying pain in the laboratory rat via facial expressions. *Molecular Pain* **7**(55), 1744–8069. <https://doi.org/10.1186/1744-8069-7-55>.

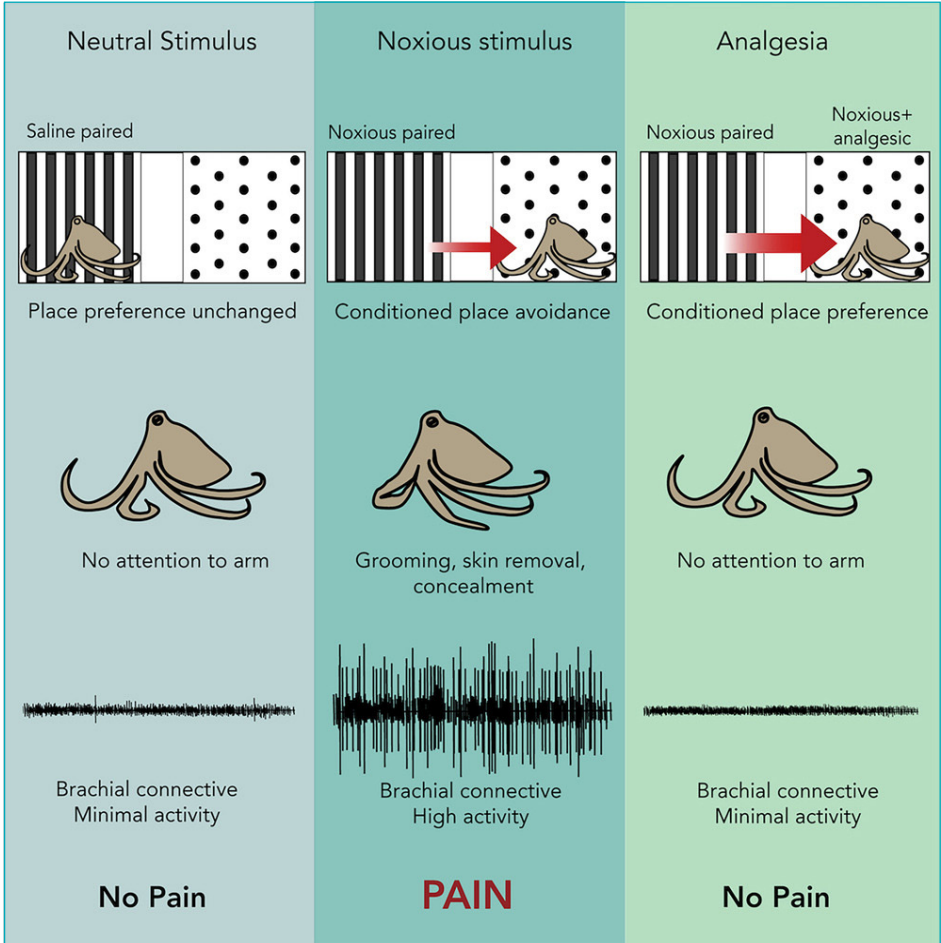


Figure 4. Investigation of pain in the octopus. In conditioned place preference assays, octopi avoided contexts in which pain was experienced (middle panel), preferred a location in which they experienced relief from pain (right panel), and showed no conditioned preference in the absence of pain (left panel). Injection site grooming occurred in all animals receiving acetic acid injections, but this was abolished by local anaesthesia. (reproduced under the Creative Commons CC-BY-NC-ND license from Crook, 2021).

Marvellous middle ears:

Structure and function in some unusual mammals



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Mason*

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Bridging the gap between the external ear canal and the cochlea, the middle ear apparatus has long attracted a level of interest from biological scientists disproportionate to its small size. Its development requires all three germ layers, and involves the neural crest. The possession of three middle ear ossicles – malleus, incus, and stapes – is a defining characteristic of mammals, and the discovery that the malleus and incus evolved from the jaw bones of ancestral vertebrates is regarded as a triumph of comparative anatomy. Exactly how the middle ear is constructed can also help us to determine what an animal can hear. This link between structure and function forms the basis of my research.

Beyond drawing pins and wheelbarrows: How the middle ear really works

Vertebrate inner ears are filled with fluid, which creates a problem for the detection of sound travelling in air. Impedance (strictly, specific acoustic impedance) is the ratio of pressure to velocity: a high impedance means that you need to apply a high pressure to a structure in order to move it. Because air has a lower impedance than the much denser cochlear fluids, most of the energy in sound would reflect back from the air–liquid interface if the sound were to impinge upon those fluids directly. A similar impedance mismatch means that it is difficult to hear someone talking if your head is underwater.

The middle ear is used as a way of reducing the impedance mismatch so as to improve sound energy transmission. The impedance of the thin, flexible tympanic membrane is close to that of air; thus, more of the sound energy is absorbed and less reflected than if the

sound reached the cochlea directly. Vibrations of the eardrum in turn vibrate the ear ossicles, which are suspended within the air-filled middle ear cavity. The stapes footplate moves like a piston within the oval window, the entrance to the inner ear, conveying the sound vibrations through to the cochlea.

Textbooks highlight two features of the middle ear that help with impedance-matching (Fig.1). One is the area ratio: the tympanic membrane is larger in area than the stapes footplate. This increases pressure at the footplate, like a drawing pin increases pressure at the sharp end. The other is the lever ratio: the processes of the malleus and incus are unequal in length. This increases the force (but decreases the velocity) at the stapes, just as it is easier to lift a load in a wheelbarrow when the load is closer to the wheel than the handles are. For many years, zoologists have measured the area and lever ratios of mammals, including fossil species, and have used them to calculate the efficiency of impedance matching by the middle ear as an index of auditory acuity.

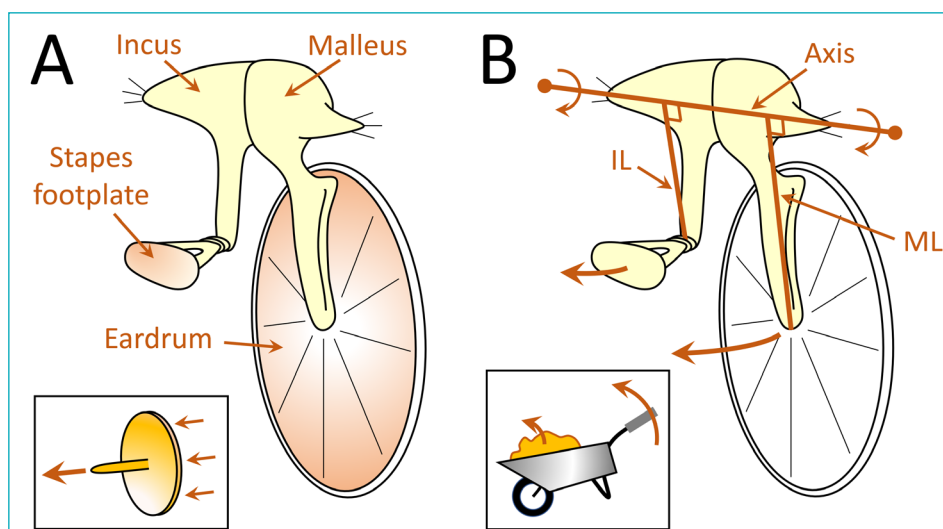


Figure 1. Diagrammatic illustrations of the textbook concept of middle ear function. Panel A illustrates the area ratio. The area of the eardrum exceeds that of the stapes footplate, increasing pressure at the stapes. This is analogous to the function of a drawing pin (inset). Panel B illustrates the lever ratio. The ossicles vibrate about a rotatory axis. The length of the malleus lever arm (ML) exceeds that of the incus lever arm (IL). This increases force but decreases velocity at the stapes, forming a class II lever. This is analogous to the function of a wheelbarrow (inset).

One striking pattern, first noted in the 19th century, is that small desert mammals such as gerbils and kangaroo rats tend to have very large middle ear cavities relative to the sizes of their skulls.

Unfortunately, there are problems with this concept of how the middle ear works. One is that the response of the tympanic membrane and ossicles is highly frequency-dependent, as we know from laser interferometric experiments. Moving a step beyond the textbooks, the simplest models which take frequency into account suggest that, as for other vibrating systems, compliance should be the dominant factor affecting the low-frequency response of the middle ear, while mass should be dominant at high frequencies (Mason, 2016a).

Compliance is the reciprocal of stiffness. It can be increased by increasing the volume of the middle ear cavity or by loosening the tympanic membrane and ligaments of the ossicular chain. Increasing compliance would be expected to improve low-frequency sound transmission. The mass of the middle ear relates to the size of the middle ear ossicles: the smaller the ossicles, the better we might expect sound transmission to be at high frequencies. However, the pattern of vibrations gets much more complicated at high frequencies, and it is not clear from experimental studies that high-frequency sound transmission is actually affected by ossicular mass. The limits to high-frequency hearing in mammals remain unclear, and very likely involve parts of the auditory system other than the middle ear.

Air heads

As a comparative physiologist, I look for similarities in how the middle ear has evolved in different groups of animals, and how they might suggest common evolutionary selective pressures. One striking pattern, first

noted in the 19th century, is that small desert mammals such as gerbils and kangaroo rats tend to have very large middle ear cavities relative to the sizes of their skulls. This is taken to an extreme in the elephant shrew (*Macroscelides flavicaudatus*), in which the volume of the two air-filled cavities added together exceeds the volume of the brain (Mason, 2016a). The middle ear cavity in most mammals (humans are an exception) is contained within a bony swelling on the basicranium known as the auditory bulla. In *Macroscelides*, each bulla wraps all around the posterior skull to reach even the dorsal aspect (Fig.2).

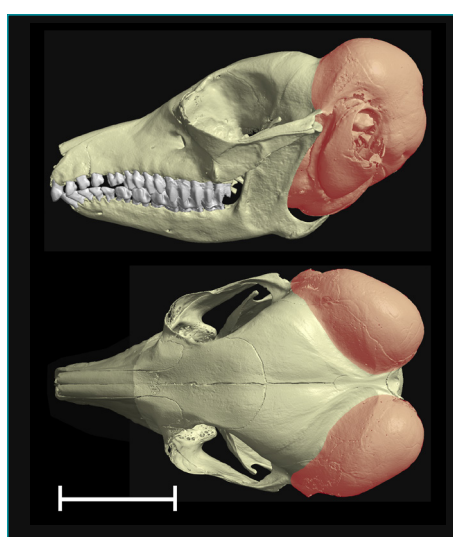


Figure 2. CT reconstructions of the skull of the elephant shrew *Macroscelides flavicaudatus*. Above: lateral view. Below: dorsal view, the snout added on from a different scan. The extent of the relatively enormous middle ear cavities is indicated with red shading. Scale bar 10 mm.

Michael Ravicz and John Rosowski (1997) have shown that having a large middle ear cavity volume increases acoustic compliance and improves low-frequency sound transmission (<3 kHz) in gerbils, which are known from behavioural studies to have excellent low-frequency hearing for their size. Elephant shrews have not yet been tested, but we would certainly expect that they would also be able to hear well at low frequencies. This ability may be especially important in desert environments, because lower-frequency sound travels further in dry air (Huang *et al.*, 2002). Having good low-frequency hearing could help animals in dispersed populations communicate with each other, or detect predators from further away. Large animals have no trouble hearing low frequencies because of their large middle ears, but because acoustics depends on absolute dimensions, small mammals need to fit relatively enormous middle ears into their small skulls in order to achieve the same feat.

Going underground

Caliban's plea to his companions, "Pray you, tread softly, that the blind mole may not hear a foot fall", drew on a longstanding belief that moles must hear very well to make up for their poor vision. In fact, European moles have eyes hidden in their fur and are not blind (Fig.3). As for their hearing, studies of subterranean mammals (mostly mole-rats, to be fair to Shakespeare) have shown them to have unusually *poor* auditory acuity when tested under experimental conditions, even at the low frequencies of a few hundred Hertz, which propagate best in underground tunnels. Unlike gerbils and elephant shrews, subterranean mammals such as the naked mole-rat (*Heterocephalus glaber*, Fig.4) do not have grossly enlarged middle ear volumes. *Heterocephalus* has no pinna, a very narrow ear canal, flimsily constructed ossicles and no stapedius muscle. Turning to the inner ear, it has recently been shown that this species has abnormal outer hair cells and no cochlear amplifier (Pyott *et al.*, 2020).



Figure 3 European mole (*Talpa europaea*), with hair parted to show the eye and the entrance to the external auditory meatus. This species has no pinna (Mason, 1999).

Nearly half a century after *The Tempest* was written, Edward Topsell commented that moles "dig about their lodging long passages, which bringeth noises and voices to them, being spoken never so low and softly, like as the voice of a man carryed in a trunk, reed or hollow thing". This has become known in the much more recent literature as the "stethoscope effect". It has been suggested that the stethoscope effect might compensate for the poor hearing of subterranean mammals; i.e. these animals would not need acute audition if sound is amplified within the burrows that they

normally inhabit (Lange *et al.*, 2007). I remain to be convinced by this hypothesis, but it is an intriguing idea.

Good vibrations

So, if moles are indeed very sensitive to foot-falls, must that be because of a stethoscope effect of their burrow systems? Not necessarily. Foot-falls result in vibrations propagating in air, which is what we would normally call "sound", but they also cause seismic vibrations to propagate in the soil. Ground vibrations might in principle be picked up by the somatosensory system. Talpid moles have specialised somatosensory structures called Eimer's organs on their noses, and disproportionately large representations of both noses and forefeet in the somatosensory cortex (Catania, 2000).

The somatosensory system is not the only means of detecting seismic vibrations. Vibrations applied directly to the skull can be conveyed to the cochlea through a number of possible routes collectively known as "bone conduction". In human medicine, bone conduction is used as a diagnostic test for conductive hearing loss. A vibrating tuning fork is applied to the skull of a person who appears to be deaf: if the person can hear it, the cochlea and neural pathways must be intact, suggesting that it may be the middle ear that is damaged.

Although it remains unclear whether talpid moles and mole-rats detect ground vibrations primarily through their somatosensory or auditory systems, one group of subterranean mammals has very striking adaptations of the middle ear that strongly suggest that they use a form of bone-conducted hearing. These are the golden moles of southern Africa (Chrysochloridae), some of which have relatively enormous mallei. The malleus of the mouse-sized desert golden mole *Eremitalpa granti*, for example, is twice the mass of its human equivalent (Mason *et al.*, 2006) (Figure. 5) In normal hearing, airborne sound sets the ossicles vibrating, leading to relative movement between stapes and inner ear. This vibrates the cochlear fluids, which activates the hair cells. The mallei of golden moles are so large and dense, and their eardrums so small, that airborne sound would not be expected to result in much ossicular movement. However, if the head is in firm contact with the ground, the skull will be set into motion by low-frequency seismic vibrations. The inertia of the huge ear ossicles will tend to result in them staying in one place, with the head vibrating around them, leading to the relative movement between stapes and inner ear that is required for hearing (Mason, 2003). Field studies in Namibia have shown that desert golden moles – which really are blind – are able to navigate from one grassy clump to the

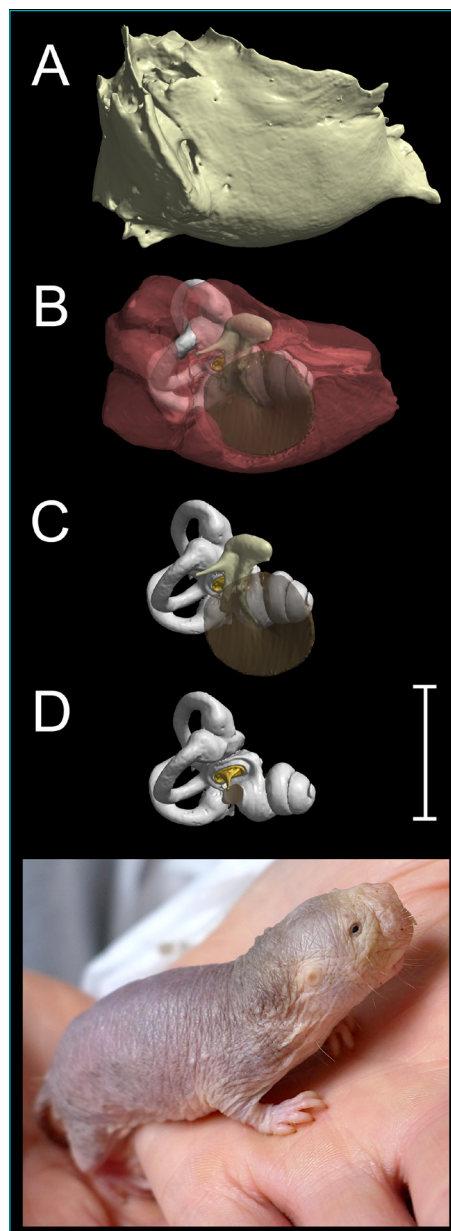


Figure 4. CT reconstructions of the right ear region of the naked mole-rat, *Heterocephalus glaber* (inset). A: Auditory bulla, lateral view; the entrance to the bony external auditory meatus is top left. B: Bullar walls removed to reveal the extent of the middle ear cavity (red) and the tympanic membrane (brown). C: Tympanic membrane, synostosed malleus and incus (cream) and bony labyrinth (white). D: Bony labyrinth, round window (brown) and stapes (yellow). Scale bar for reconstructions 3 mm.

next in their search for food. It has been proposed that ground vibrations produced as wind passes through the grass, measured at around 30 dB above background noise at 300 Hz, allow the clumps to act as “seismic beacons”, which the moles can detect and orient towards, using their massive mallei (Narins *et al.*, 1997).

Middle ear frontiers

Although we are learning more all the time about hearing, studies tend to focus on certain model species. These include arid-

region rodents such as gerbils and chinchillas, since their capacious middle ears offer easy surgical access. How the middle ear works in other species often remains to be tested experimentally, especially when it comes to subterranean mammals. Surprisingly, big questions remain about human middle ears too. For example, what is the function of the tensor tympani muscle? It is not required to tense the tympanic membrane, as its name suggests, since several mammals lack this muscle and still have perfectly tense eardrums. By taking a comparative perspective, we can see what is necessary and sufficient for hearing, better appreciate

the similarities and differences between human ears and those of model species, and develop a deeper understanding of how structure links to function.

Acknowledgements

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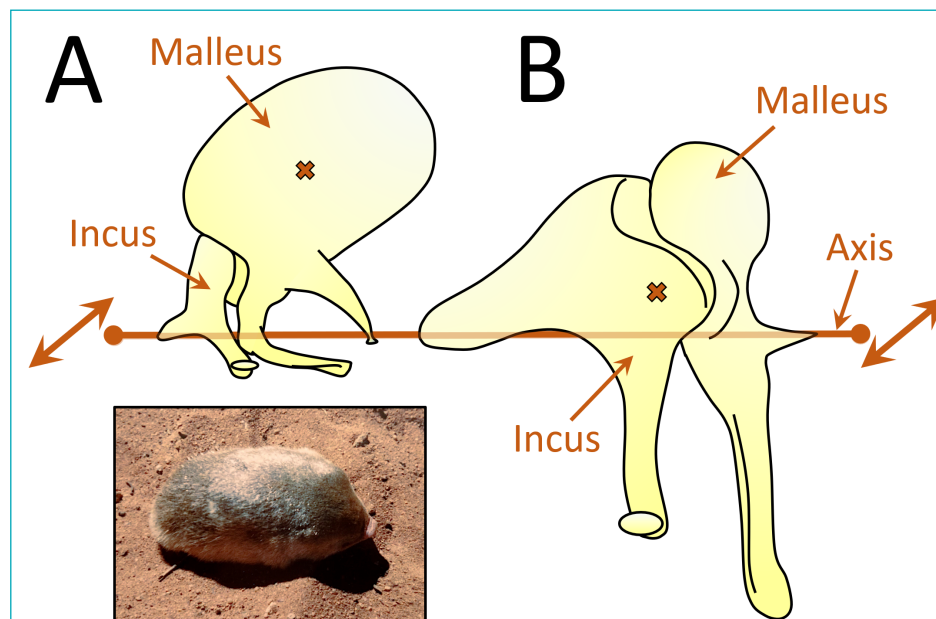


Figure 5. Diagrammatic illustrations of the left malleus and incus of (A) a golden mole *Eremitalpa granti* and (B) a human, drawn to scale. An axis is drawn through the main ligamentous tether-points. Although the golden mole (inset) is only the size of a mouse, its malleus is twice as heavy as the human malleus. The displacement of the centre of mass of the mole's ossicles (cross) away from the axis makes the ossicles “unstable”, predisposing them to the detection of bone-conducted vibrations when the head is shaken (arrows).

Large animals have no trouble hearing low frequencies because of their large middle ears, but because acoustics depends on absolute dimensions, small mammals need to fit relatively enormous middle ears into their small skulls in order to achieve the same feat.

References

- Catania KC (2000). Cortical organisation in Insectivora: The parallel evolution of the sensory periphery and the brain. *Brain, Behavior and Evolution* **55**(6), 311–321. <https://doi.org/10.1159/000006666>.
- Huang GT *et al.* (2002). Mammalian ear specializations in arid habitats: Structural and functional evidence from sand cat (*Felis margarita*). *Journal of Comparative Physiology A* **188**(9), 663–681. <https://doi.org/10.1007/s00359-002-0332-8>.
- Lange S *et al.* (2007). Living in a “stethoscope”: burrow acoustics promote auditory specializations in subterranean rodents. *Naturwissenschaften* **94**(2), 134–138. <https://doi.org/10.1007/s00114-006-0168-0>.
- Mason MJ (1999). The Functional Anatomy of the Middle Ear of Mammals, with an Emphasis on Fossorial Forms. PhD Thesis, University of Cambridge, UK.
- Mason MJ (2003). Bone conduction and seismic sensitivity in golden moles (Chrysochloridae). *Journal of Zoology* **260**(4), 405–413. <https://doi.org/10.1017/S0952836903003868>.
- Mason MJ (2016a) Structure and function of the mammalian middle ear. I: Large middle ears in small desert mammals. *Journal of Anatomy* **228**(2), 284–299. <https://doi.org/10.1111/joa.12313>.
- Mason MJ (2016b) Structure and function of the mammalian middle ear. II: Inferring function from structure. *Journal of Anatomy* **228**(2), 300–312. <https://doi.org/10.1111/joa.12316>.
- Mason MJ *et al.* (2006). Ossicular density in golden moles (Chrysochloridae). *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology* **192**(12), 1349–1357. <https://doi.org/10.1007/s00359-006-0163-0>.
- Narins PM *et al.* (1997). The use of seismic signals by fossorial southern African mammals: A neuroethological gold mine. *Brain Research Bulletin* **44**(5), 641–646. [https://doi.org/10.1016/s0361-9230\(97\)00286-4](https://doi.org/10.1016/s0361-9230(97)00286-4).
- Pyott SJ *et al.* (2020). Functional, morphological, and evolutionary characterization of hearing in subterranean, eusocial African mole-rats. *Current Biology* **30**(22), 4329–4341. <https://doi.org/10.1016/j.cub.2020.08.035>.
- Ravicz ME, Rosowski JJ (1997). Sound-power collection by the auditory periphery of the Mongolian gerbil *Meriones unguiculatus*: III. Effect of variations in middle-ear volume. *Journal of the Acoustical Society of America* **101**(4), 2135–2147. <https://doi.org/10.1121/1.418275>.

Echolocation in people

Humans can learn how to use echolocation, aiding the mobility, independence and wellbeing for people who are partially sighted or blind

One day in 2009 (when I was a postdoc at Western University in Canada), I came across reports of people who were totally blind and could do things such as riding their bike, playing basketball and hiking using echolocation. Together with my postdoc advisor Mel Goodale I watched video clips about remarkable people like Daniel Kish and Juan Ruiz, nicknamed *Human Bats*. Juan Ruiz and Daniel Kish are blind and exceptionally skilled at echolocation to the degree that they go mountain biking or can tell what objects are without touching them. They also teach others (Fig.1). This was when I started working on human echolocation. Today in my lab we investigate human echolocation as a topic in its own right, and use it to understand how the human brain adapts to learning new skills.



Dr Lore Thaler

Associate Professor, Department of Psychology, Durham University, UK



Figure 1. Photograph of Daniel Kish teaching echolocation to a child who is blind. Echolocation works well together with other mobility methods, for example the long cane. Credit: World Access for the Blind.



Figure 2. Photograph of the setup used to make recordings of echolocation mouth clicks. Recordings are made in rooms that are insulated against outside noise, and the walls, ceilings and floors of which are covered in special foam. Thin metal poles covered with cotton wool are used to hold microphones, and another metal pole is provided for positional guidance for the person making mouth clicks. During recordings only the person making clicks is inside the room. The experimenter controls the equipment from outside the room. Credit: Lore Thaler

How do humans use echolocation and how does this differ from other animals?

Bats and dolphins are well known for their ability to use echolocation. They emit bursts of sounds and listen to the echoes that bounce back to perceive their environment. Human echolocation uses the same technique. It relies on an initial audible emission, and

subsequent reflection of sound from the environment. When people echolocate, they make audible emissions like mouth clicks, finger snaps, whistling, cane taps, or footsteps. These are all in the audible spectrum, as opposed to the ultrasound emissions that bats or dolphins use. Even though every person, blind or sighted, can learn how to echolocate, to date the most skilled human echolocators are blind (Kolarik *et al.*, 2014; 2021).

The emissions that proficient echolocators prefer to use are mouth clicks. In our work we have measured thousands of these clicks (see Fig.2), and have found that they are very brief (~5 ms), and that the beam of sound spreads out in a way that I like to refer to as a “beam of an acoustic flashlight” (Thaler *et al.*, 2017) (see Fig.3). We have also found that people adjust clicks dynamically. For example, people will make more clicks or louder clicks when the echo is comparably weaker (Thaler *et al.*, 2018) or to compensate for interfering noises (Castillo-Serrano *et al.*, 2020). This dynamic nature is likely to be important when using echolocation out and about.

We also use motion capture to investigate how echolocation is related to body movement, for example during walking. The motion capture technology we use is the same used to create CGI movies such as Avatar or The Polar Express. Reflective markers are placed on a person's body, and movements of these markers are captured with special cameras (see Fig.4). Using this technology, we found that echolocation can support walking in a similar way to vision (Thaler *et al.*, 2020). We found that people who are blind and who have experience using echolocation walk just as fast as people using vision. They also have walking paths that are very similar to sighted people using vision, for example when navigating around obstacles.

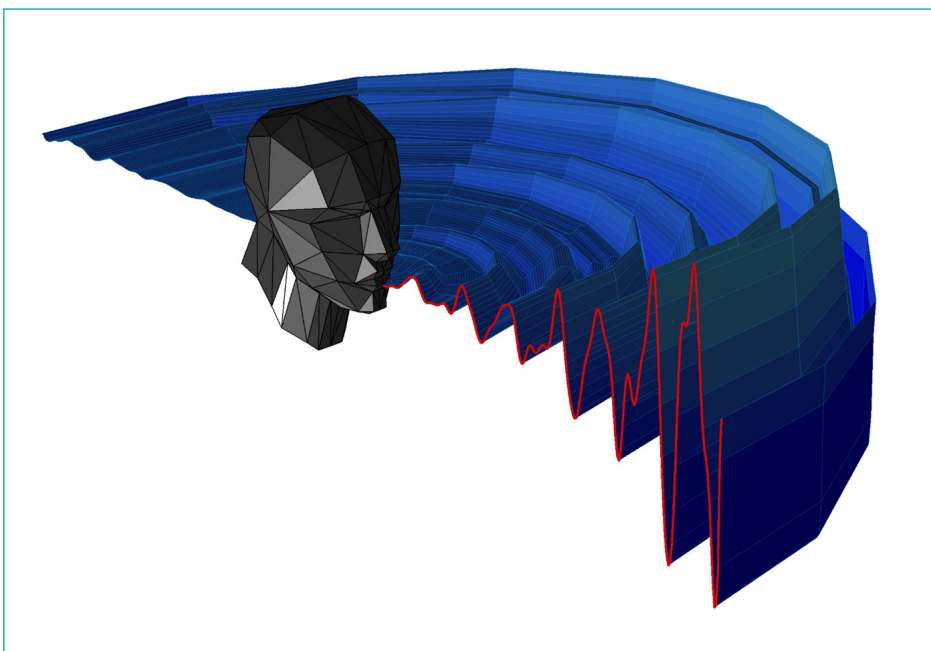


Figure 3. Illustration of the waveform of echolocation mouth clicks. The red line illustrates the waveform of a mouth-click (i.e. change in air pressure over time) measured right in front of the echolocator. Larger waves indicate more intense sound. The blue curve illustrates how the sound is less intense as it is measured at the side or the back of the echolocator, somewhat similar to the way the beam of a flashlight distributes, which is why I like to refer to this as an ‘acoustic flashlight’. Credit: Galen Reich

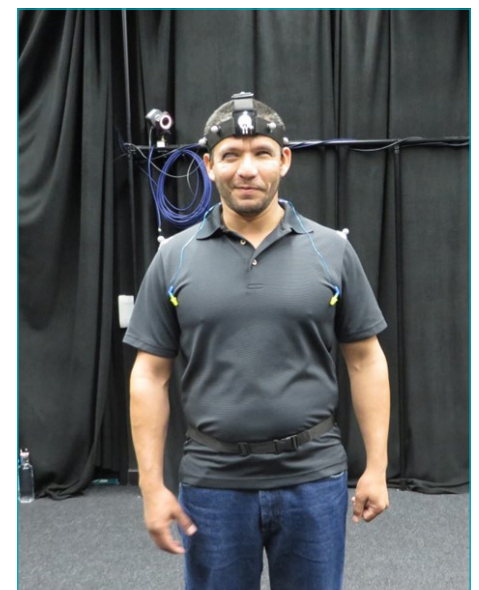


Figure 4. Photograph of the experimental set up used to record head movements that echolocators make during echolocation. Juan Ruiz is wearing reflective markers on his head. Special cameras track these markers, and we can use these data to reconstruct the movements of the head. Credit: Nina Ruiz

Brain Activity related to Echoes

Echolocation Expert

Control Participant

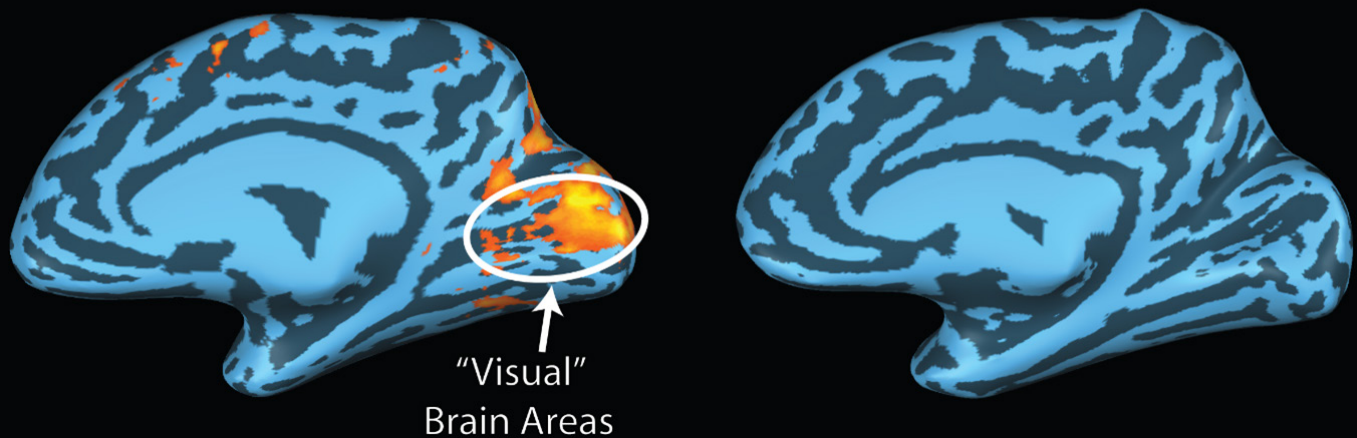


Figure 5. Illustration of MRI results for echolocation. Areas highlighted in warm colours show an increase in brain activity when the participant listened to echolocation sounds, compared with control sounds. The echolocation expert showed a relative increase in the primary “visual” cortex. For the age- and gender-matched sighted control participant, no relative increase was observed. Credit: Lore Thaler

Understanding brain activity related to echoes

We are also interested in the brain basis for echolocation in people. Neuroimaging methods such as functional magnetic resonance imaging (fMRI) are suitable for investigating this. One of the problems we face when using fMRI to investigate echolocation is the scanner is a very confined space, with not enough room to actually echolocate. In fact, during scanning, the participant lies inside a narrow tube that is only 60 cm in diameter, and the inside of that tube is about 10 cm from your eyes or mouth, so really very close. This can be overcome by using “virtual” echo acoustic spaces.

In my lab we make use of passive listening scenarios. To do this, we first make recordings inside the ears of a participant whilst they are echolocating scenarios outside of the scanner. Subsequently, inside the scanner, these scenarios are recreated by playing the recordings back using special in-ear headphones. Other labs have overcome this issue by recording the clicks that people make inside the scanner, and then processing them to create a virtual scene, which is played back to the participant via headphones. The advantage of this technique is that the participant can make their own emissions

during scanning. Further to this, we also use special scanning sequences, so that the MRI scanner is silent whilst the participant is listening to the echolocation sounds. If we used regular scanning sequences, it would be too noisy for the participant to hear anything.

Which parts of the brain are activated?

Studies using these techniques have shown that people who are blind and skilled in echolocation use not only the hearing part of their brain to process echoes, but that they also use those parts of the brain that process vision in sighted people (Thaler *et al.*, 2011; Wallmeier *et al.*, 2015). In people who are normally sighted, early visual cortical areas, such as primary visual cortex, are activated by visual stimulation in a specific pattern that is referred to as retinotopy. We have found that in blind echolocators, the primary visual cortex is activated by acoustic stimulation in a specific pattern that resembles retinotopy (Norman and Thaler, 2019) (See Fig.5). Our results suggest that “retinotopic” activity can also be driven by sound, and that this is facilitated by experience with echolocation. This result challenges our classical understanding of the organisation of brain function by sensory modality and opens other ways of understanding the human senses.

Understanding the brain’s ability to adapt and learn new skills

Current research in my lab is investigating how these changes arise in the human brain. The findings will be useful for learning about the inherent ability (or limitations) of the human brain to adapt to learning new skills. Echolocation is a perfect paradigm for measuring these changes because people start from scratch (unless they already have experience in echolocation), so that there is a good baseline from which change can be measured. It also provides large scope for improvement. This will also be useful for determining rehabilitative effects of training for people who are blind. Specifically, we can track change over time and compare effects before and after training, both on the behavioural and the brain level.

The benefits of click-based echolocation for people who are visually impaired or blind

Echolocation is a learnable skill that can be acquired by people who are blind as well as by people who are sighted. In a recent study we investigated if training in click-based echolocation leads to meaningful benefits for people who are blind (Norman *et al.*, 2021).

In our study we trained people who were sighted, and people who were blind (aged 21–79 years) over the course of 10 weeks. People were trained to use their own mouth clicks to determine the size, location and orientation of objects placed in front of them at various distances. They were also trained in a computer-based echolocation task, where they used buttons on a computer keyboard to navigate their way around a set of corridors using echolocation sounds that they heard over headphones. Everyone improved their echolocation skills, i.e. accuracy or speed of responses in these various tasks got better. Importantly, neither age nor blindness was a limiting factor in participants' rate of learning (i.e. their change in performance from the first to the final session) or in their ability to apply their echolocation skills to new, untrained tasks.

Three months after training was completed, we found that all blind participants reported improved mobility, and 83% of blind participants also reported improved wellbeing and independence in their daily lives. All blind participants in this study were independent travellers, and had mobility skills (See Fig.6) before taking part in the study (e.g. long cane or guide-dog users). Thus, any benefits of click-based echolocation we observed were in addition to those pre-existing skills. The results from this work suggest that echolocation might be a useful skill for people who are blind, and that even 10 weeks training can lead to measurable benefits in terms of mobility, independence and wellbeing. The fact that the ability to learn click-based echolocation was not strongly limited by age or level of vision has

positive implications for the rehabilitation of people with vision loss or in the early stages of progressive vision loss.

Ongoing and future work in my lab will continue investigating issues relating to human echolocation and using echolocation as a paradigm to better understand the human brain and cognition. For example, we would like to use echolocation to learn more about the brain's ability to adapt to change as a function of age. For example, how do children acquire echolocation skills, and how does this compare to adults and how is this related to sensory loss? Better understanding of such issues might also have potential applications for timing of rehabilitative interventions for children and young people.

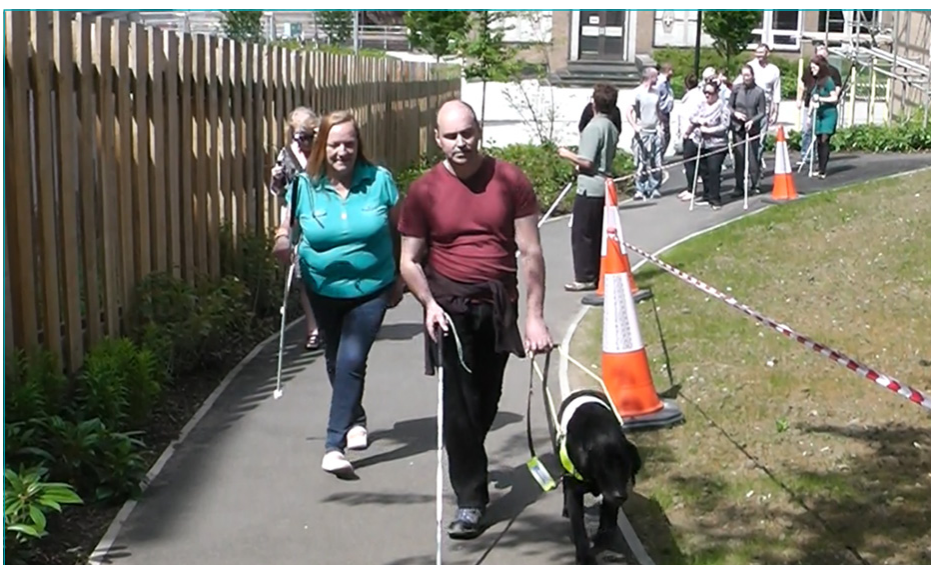


Figure 6. Echolocation users at Durham University. Echolocation works well together with other mobility methods such as guide dogs or the long cane. Credit: Lore Thaler

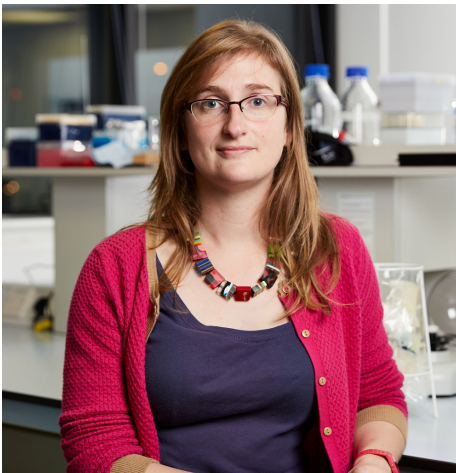
People who are blind and skilled in echolocation use not only the hearing part of their brain to process echoes, but that they also use those parts of the brain that process vision in sighted people

References

- Castillo-Serrano JG *et al.* (2021). Increased emission intensity can compensate for the presence of noise in human click-based echolocation. *Scientific Reports* **11**(1), 1–11. <http://doi.org/10.1038/s41598-021-81220-9>.
- Kolarik AJ *et al.* (2014). A summary of research investigating echolocation abilities of blind and sighted humans. *Hearing Research* **310**, 60–68. <https://doi.org/10.1016/j.heares.2014.01.010>.
- Kolarik AJ *et al.* (2021). A framework to account for the effects of visual loss on human auditory abilities. *Psychological Review*, **128**(5), 913. <https://doi.org/10.1037/rev0000279>.
- Norman L, Thaler L (2019). Retinotopic-like maps of spatial sound in primary 'visual' cortex of blind human echolocators. *Proceedings of the Royal Society: Series B Biological Sciences* **286**(1912), 20191910. <https://doi.org/10.1098/rspb.2019.1910>.
- Norman L *et al.* (2021). Human click-based echolocation: Effects of blindness and age, and real-life implications in a 10-week training program. *PLoS ONE* **16**(6), e0252330. <https://doi.org/10.1371/journal.pone.0252330>.
- Thaler L *et al.* (2011). Neural correlates of natural human echolocation in early and late blind echolocation experts. *PLoS ONE* **6**(5): e20162. <https://doi.org/10.1371/journal.pone.0020162>.
- Thaler L *et al.* (2017). Mouth-clicks used by blind human echolocators – Signal description and model based signal synthesis. *PLoS Computational Biology* **13**(8): e1005670. <https://doi.org/10.1371/journal.pcbi.1005670>.
- Thaler L *et al.* (2018). Human echolocators adjust loudness and number of clicks for detection of reflectors at various azimuth angles. *Proceedings of the Royal Society: Series B Biological Sciences*. **285**(1873), 20172735. <https://doi.org/10.1098/rspb.2017.2735>.
- Thaler L *et al.* (2020). The flexible Action System: Click-based echolocation may replace certain visual Functionality for adaptive Walking. *Journal of Experimental Psychology: Human Perception and Performance* **46**(1), 21–35. <https://doi.org/10.1037/xhp0000697>.
- Wallmeier L *et al.* (2015). Aural localization of silent objects by active human biosonar: Neural representations of virtual echo-acoustic space. *European Journal of Neuroscience*, **41**(5), 533–545. <https://doi.org/10.1111/ejn.12843>.

Why don't we have whiskers?

What we can learn from mammalian whisker touch sensing



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I am a sensory biologist, specialising in whisker touch sensing. My job is to try to understand what animals perceive from their whisker sensations. It is a challenging job, made even harder by not being able to draw parallels from my own experiences – while most mammals have whiskers, humans, along with rhinos and some species of apes and cetaceans, do not. Most whisker research has focused on laboratory animals, such as rats and mice, and some species of zoo animals, such as seals. It is only now that we are beginning to study whiskers comparatively (Grant and Goss, 2022). By looking at lots of mammalian species, we are starting to truly understand which species have whiskers and why. Therefore, we can start to answer the questions *why don't we have whiskers?* And *why should we care about them?*

What are whiskers?

The whiskers I will focus on in this article are mystacial whiskers – the whiskers on the moustache area of mammals. There are lots of different types of whiskers, including around the jaw, chin, eyes and feet, but

mystacial whiskers have garnered the most attention from researchers because they are the longest and can also be moved. However, we are only starting to understand what the mystacial whiskers can do and the function of the other types of whiskers are still poorly understood (Fig.1, Table 1).

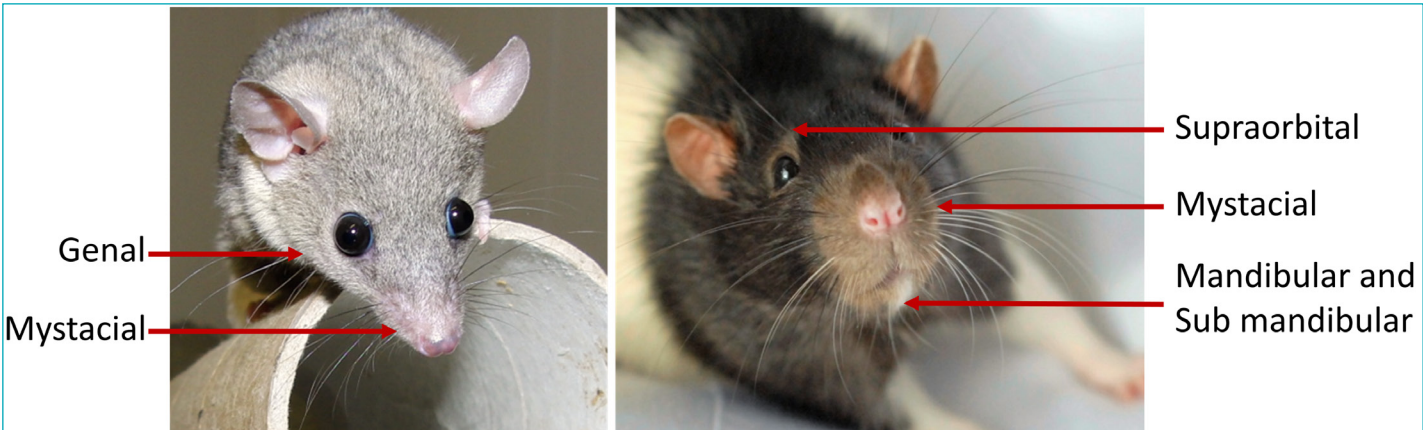
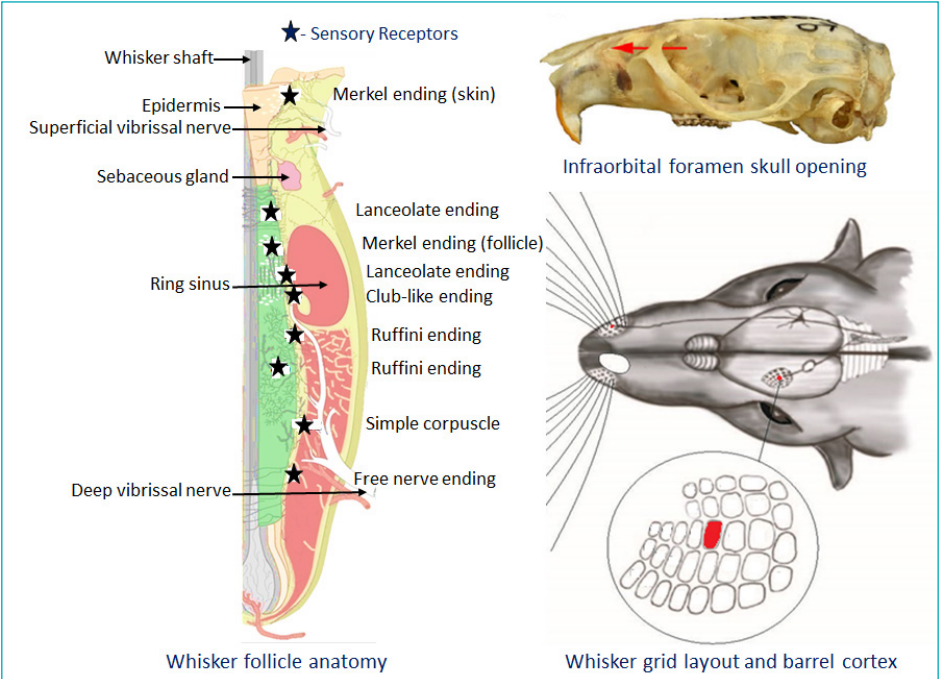
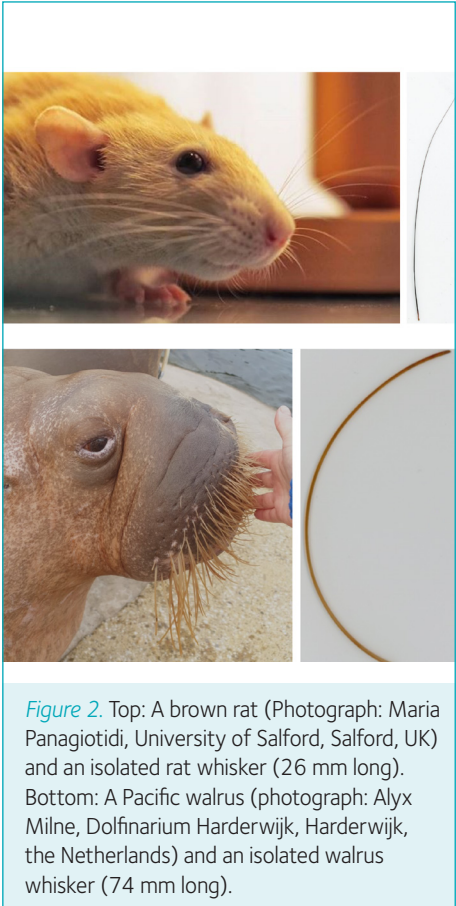


Figure 1. Different types of whiskers of grey short-tailed opossum (left) and brown rat (right) (photographs: Active touch sensing lab, University of Sheffield, Sheffield, UK)

Whisker	Location	Possible function
Genal	Cheek	Unknown
Mystacial	Moustache area	Guiding locomotion, foot placements, foraging, exploration
Supraorbital	Above eyes	Unknown – possibly eye protection
Mandibular/submandibular	Jaw and under chin	Detection of self-motion i.e. speed
Leg/Foot	Leg/Foot	Guiding foot placements

Table 1. Different types of whiskers and their suggested functions.



Whiskers are similar in structure to hair and fur, although they are typically a little thicker and longer than other hair. Whiskers are made of keratin, and are flexible, tapered and curved (Fig.2) (Dougill *et al.*, 2020). These properties are likely to help them to deform and vibrate against different surfaces, which is better for sensing. Mammals that live in aquatic environments have thicker and stiffer whiskers than terrestrial mammals (Fig.2), probably to make sure they can be accurately positioned in high-drag aquatic environments (Dougill *et al.*, 2020).

How do whiskers work?

What really sets whiskers apart from other hair, such as fur, are their specialised follicles. Much like our hair, the whisker itself cannot “feel”. Rather, the hair sits within a complex and sensitive follicle, called the follicle sinus complex (Ebara *et al.*, 2017). Each follicle

is surrounded by large blood sinuses, which is why mystacial whiskers are sometimes called sinus hairs (Fig.3). The follicle is densely innervated by a variety of different nerve fibres (Fig.3) that can translate whisker vibrations into neural information. As the whiskers are deformed, such as by contact or water movement, these deformations are detected by the different nerve endings in the follicle and are conveyed as spike impulses to the brainstem (trigeminal nuclei). Properties of whisker deformation, such as which whisker was deformed, and the force, duration and direction of deformation are all useful properties that are detected and encoded by these nerves.

This information from the whisker follicle travels via the deep vibrissal nerve to the infraorbital nerve – a division of the trigeminal nerve. The infraorbital nerve passes through a small skull opening – called the infraorbital foramen – and into the brain

Whiskers can be moved in quite complex patterns too, including changing their spread, speed and position. It is thought that, much like our fingertips, whiskers are an active touch sensing system.

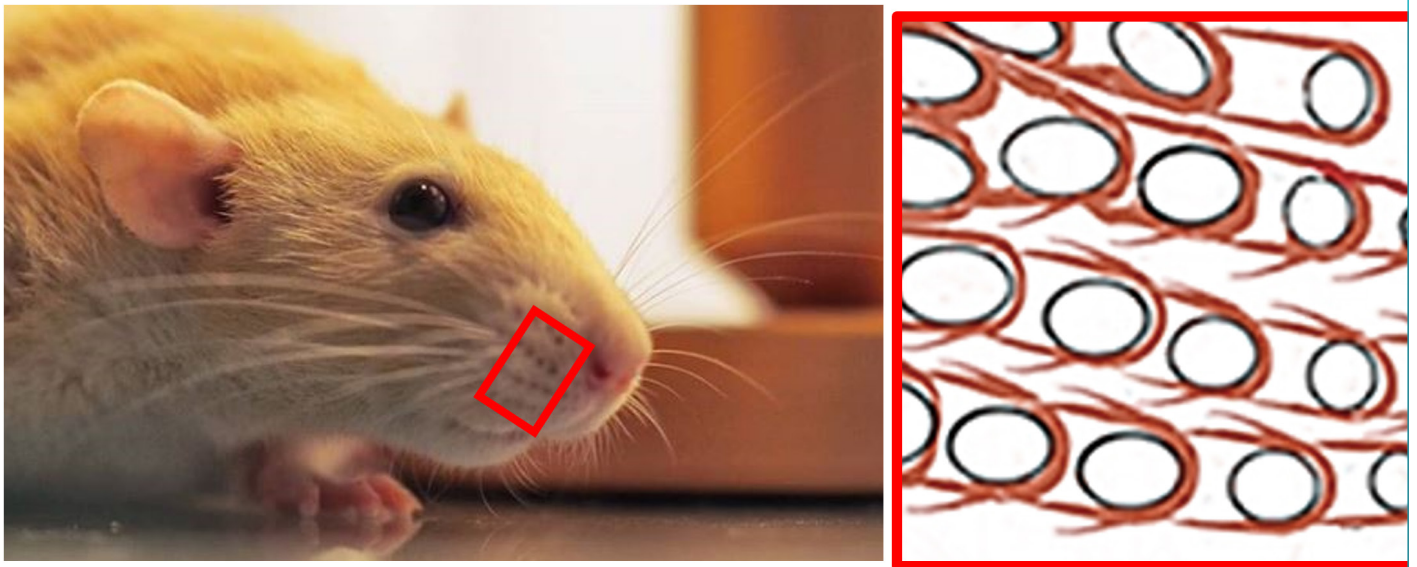


Figure 4. Whiskers and whisker intrinsic muscles. Left: Photograph of a brown rat (Photograph: Maria Panagiotidi, University of Salford, Salford, UK); Right: Magnified illustration of the whisker muscles within the red box from the photograph. Black circles correspond to individual whisker follicles. The brown sling muscles around every follicle are the intrinsic muscles. Follicles within the same row are coupled together via their intrinsic muscles.

Whiskers can vary in numbers from 4 in porpoises, to around 300 in walruses and several thousand in manatees.

(Fig.3). Whiskers can vary in numbers from 4 in porpoises, to around 300 in walruses and several thousand in manatees. Animals with more whiskers have a larger infraorbital nerve and foramen, since more whiskers tend to carry more sensory information. Therefore, the size of this skull opening is a good proxy of how sensitive an animal's whiskers are (Muchlinski *et al.*, 2020).

Whiskers are arranged in a grid-like pattern on an animal's face, in rows and columns (Fig.3). In some species, this same pattern can be seen throughout the brain in physical structures called barrelettes in brainstem, barreloids in thalamus and barrels in cortex (Fig.3). This one-to-one mapping of whiskers to topographic structures in the brain has fascinated neuroscientists for decades as they are able to trace a sensory signal from an individual whisker follicle, all the way from the trigeminal complex through the brain to the cortex (Fig.3). This has established whisker touch sensing as a useful model for understanding sensory processing in the brain (Grant and Goss, 2022).

Whiskers do not just sense, they can also move. In most species, each whisker has its own individual intrinsic muscle (Fig.4), which contracts to move the whiskers forward. Some animals, such as rats and mice, move their whiskers forward and backward, almost constantly, in a process called *whisking*. This occurs at around 8 times per second in rats, and 25 times per second in mice, which are amongst the fastest movements that mammals can make! This muscle architecture is present across mammals, from marsupials to primates, but is absent in some species, including deer, horses, diurnal primates, apes and humans (Muchlinski *et al.*, 2013). Humans even have some vestigial

muscle remnants just above our lips, in the moustache area, although they are probably not functional.

As well as simple scanning motions, whiskers can be moved in quite complex patterns too, including changing their spread, speed and position. It is thought that, much like our fingertips, whiskers are an active touch sensing system. They are moved across objects to focus on important (salient) features to identify and distinguish between objects. For instance, by feeling around the edges of things that are differently sized and stroking across the surfaces of different textures (Milne *et al.*, 2021), in much the same way that we would do with our fingertips.

Why don't humans have whiskers?

Perhaps the high sensitivity and mobility of our own fingertips means that they play a similar role to whiskers and is one of the reasons why humans don't need whiskers. Certainly, it is challenging to answer the question *why don't humans have whiskers?*

One way to approach the question is to look at the animals that have great whiskers – those with long, numerous whiskers, with large infraorbital foramen and lots of intrinsic muscles. These species tend to forage in dark, complex habitats, such as underwater (e.g. seals and sea lions) or be nocturnal, climbing specialists (e.g. mice and shrews) (Muchlinski *et al.*, 2020). Indeed, many small, quadrupedal mammals use their whiskers during walking and climbing to guide safe foot placements in the dark (Grant *et al.*, 2018). Therefore, perhaps being upright makes whiskers useless for us, as they cannot be positioned ahead

of our movements to guide locomotion and foraging.

In addition, we notice that more diurnal or visual mammals have fewer whiskers, which are also less organised with fewer whisker muscles (Grant and Goss, 2022). Therefore, perhaps our reliance on other senses, such as vision, also make whiskers less useful for us. Odontocete cetaceans (such as dolphins) have very few, or no whiskers, with no intrinsic whisker muscles, as echolocation is instead an important sense for them. We also see that while nocturnal primates have whiskers and intrinsic muscles, diurnal primates have fewer whiskers with no muscles, and whiskers are entirely absent in some apes and humans (Muchlinski *et al.*, 2013). Being upright, relying on vision, and having sensitive and moveable hands and fingers, probably makes whiskers a less important sense for humans.

What can we learn from studying whiskers?

Neuroscientists use whiskers as a model to address fundamental questions around sensory processing in the brain. Most drugs and treatments are developed in laboratory rats and mice before human trials. We have found that measuring whisker positions and movements in these animals reveals impacts from disorders such as Motor Neuron Disease, Huntington's disease, Parkinson's disease, Alzheimer's disease, Cerebellar Ataxia, Somatosensory Cortex Development Disorders and Ischaemic stroke (Simanaviciute *et al.*, 2020). We notice that whisker movements can be impacted earlier than any other behavioural measure (including balance beam tests, swim tests and gait analysis). By looking at whisker movements in these animals, we may be able to detect diseases and treatment effects earlier.

As well as applications for human neuroscience and disease, whisker research is also driving technological innovation too. The aerodynamic shape of seal whiskers has been used to inspire wind turbine blades (Ahlman *et al.*, 2020). There are also many tactile whiskered sensors and robots being developed for a wide range of medical, industrial and environmental applications, such as underwater exploration of archaeological sites, autonomous inspection of off-shore wind and wave generators and environmental monitoring of ocean currents.

Why should we care about whiskers?

Whiskers can also give important insights in animal biology and evolution. Comparative studies looking at the infraorbital foramen of extant and extinct mammals suggest that the first mammals are likely to have had

functional whiskers and even the ancestors of mammals, the therapsids, may also have had whiskers (Muchlinski *et al.*, 2020; Grant and Goss, 2022). In addition, the importance of whiskers to nocturnal and aquatic mammals in guiding their feeding and locomotion behaviours has huge implications for captive mammals. Sometimes whiskers can be lost, for example, rats and mice can engage in barbering, where a dominant animal removes the whiskers of their subordinate cage mates. I have seen this especially in some strains of female mice. Whisker removal reduces the social and locomotor functioning of an animal. It is extremely stressful and negatively affects brain development. Rats and mice without whiskers walk with a shrunken posture, struggle to balance and swim and do not engage in fighting; therefore, whisker barbering probably establishes a dominance hierarchy (Grant and Goss, 2022). Mother cats sometimes trim their offspring's whiskers, perhaps to establish a dominance hierarchy or to keep the kitten close to the nest. We need to make sure that whiskers are stimulated in captive animals that rely on their whiskers, perhaps by increasing tactile stimuli around their enclosures and designing feeding

enrichment to encourage natural whisker movements (Grant and Goss, 2022). This might be something for all of us to try with our pets at home, especially if you have cats, rabbits, guinea pigs or hamsters – as these all have quite prominent whiskers.

As well as the direct applications of my whisker research, studying whiskers has also given me lots of surprises too. Did you know that in Guiana and bottlenose dolphins, their whiskers fall out and the remaining follicles then become electrosensors (Hüttner *et al.*, 2021)? And that the whiskers of all species that we have tested so far fit to the shape of an Euler spiral (Dougill *et al.*, 2020)? This is a shape whose curvature changes linearly with its length and was first described by Leonhard Euler in 1744.

I truly think that whisker science has the power to inspire us all by demonstrating the complex and ingenious innovations of the natural world. While it is still a challenge for us to picture how a rat whisker “feels” or how a dolphin electrosenses, we can wiggle our fingers around, think very hard, and try our best to understand it all.

References

- Ahlman R *et al.* (2020). Wake flow structure of a seal-whisker-inspired power turbine blade. In *AIAA Scitech 2020 Forum*. <https://doi.org/10.2514/6.2020-2020>.
- Dougill G *et al.* (2020). Ecomorphology reveals Euler spiral of mammalian whiskers. *Journal of Morphology* **281**(10), 1271–1279. <https://doi.org/10.1002/jmor.21246>.
- Ebara S *et al.* (2017) Vibrissal mechanoreceptors. *Scholarpedia* **12**(3), 32372. <https://doi:10.4249/scholarpedia.32372>.
- Grant RA *et al.* (2018). Whisker touch sensing guides locomotion in small, quadrupedal mammals. *Proceedings of the Royal Society B* **285**(1880), 20180592. <https://doi.org/10.1098/rspb.2018.0592>.
- Grant RA, Goss VG (2022). What can whiskers tell us about mammalian evolution, behaviour, and ecology? *Mammal Review* **52**(1), 148–163. <https://doi.org/10.1111/mam.12253>.
- Hüttner T *et al.* (2021). Behavioral and anatomical evidence for electroreception in the bottlenose dolphin (*Tursiops truncatus*). *The Anatomical Record*. <https://doi.org/10.1002/ar.24773>.
- Milne AO *et al.* (2021). California sea lions employ task-specific strategies for active touch sensing. *Journal of Experimental Biology* **224**(21), jeb243085. <https://doi.org/10.1242/jeb.243085>.
- Muchlinski MN *et al.* (2013). Comparative histomorphology of intrinsic vibrissa musculature among primates: Implications for the evolution of sensory ecology and “face touch”. *American Journal of Physical Anthropology* **150**(2), 301–312. <https://doi.org/10.1002/ajpa.22206>.
- Muchlinski MN *et al.* (2020). Good vibrations: the evolution of whisking in small mammals. *The Anatomical Record* **303**(1), 89–99. <https://doi.org/10.1002/ar.23989>.
- Simanaviciute U *et al.* (2020). Recommendations for measuring whisker movements and locomotion in mice with sensory, motor and cognitive deficits. *Journal of Neuroscience Methods* **331**, 108532. <https://doi.org/10.1016/j.jneumeth.2019.108532>.

The neuroscience of balance

From athletes to the elderly



Dr Kathleen E Cullen

Johns Hopkins University, US

Aristotle described five senses, namely sound, sight, touch, smell, and taste, that provide us with a conscious awareness of the world around us. But he missed one of our most important senses: the vestibular (inner ear) system, which makes critical contributions to our sense of balance. In this article, I will focus on how single neurons, organised into dedicated circuits, support our ability to stay on our feet.

The vestibular system – a 6th sense

The vestibular system detects head motion to generate essential reflexes required for stable gaze and balance, and to provide us with our sense of motion relative to our world (self-motion) and spatial orientation. This essential sensory system is located in the inner ear just next to the cochlea, within the petrous part of the temporal bone (Fig.1).

In mammals, the vestibular system comprises five sensory organs on each side of the head, namely (i) the three fluid-filled semicircular

canals, which sense rotational head acceleration in three axes and (ii) the two otolith organs (the saccule and utricle), which sense linear head acceleration (i.e. gravity and translational movements).

Accordingly, the vestibular system detects and encodes the angular and linear components of motion separately, with the semicircular canals and otoliths functioning as miniature gyroscopes and linear accelerometers that provide online feedback about our current head motion during our daily activities.

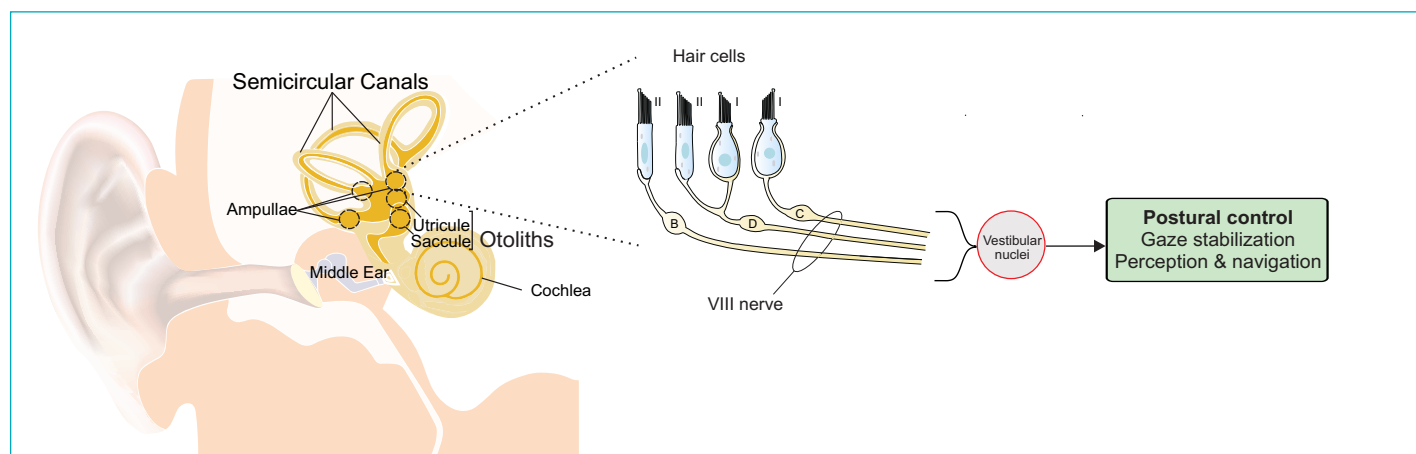


Figure 1. Vestibular sensors are located in the inner ear. Three semicircular canals (horizontal, anterior and posterior) detect head rotations in three dimensions. The two otoliths (saccule and utricle) detect linear head movements in three dimensions. Signals detected by specialised hair cells are carried by vestibular nerve fibres to the vestibular nuclei and result in generation of reflexes required for postural and perceptual stability.

Rapid multimodal integration ensures stable gaze and posture

As we explore our environment, the brain takes advantage of information from multiple sensory systems – vestibular, proprioceptive, and visual – to keep track of our movement and spatial orientation. In turn, the integration of this multimodal information underlies our ability to rapidly generate robust behaviours to remain stable and upright.

In this context, the vestibular system is incredibly fast. This is because the vestibular system is unique among sensory systems in that the same neurons that receive peripheral afferent nerve input, also send direct projections to motoneurons and motor centres. Likewise, the proprioceptive system, which senses the relative position of arms, legs, etc. in relation to each other, is also remarkably fast. Indeed, when we experience unexpected self-motion, the vestibular and proprioceptive systems work together to generate compensatory postural responses within ~10 ms (reviewed in Cullen, 2019).

By comparison, the visual system's contribution to behaviour is an order of magnitude slower (~100 ms) due to the inherent delays of the pathways that transform visual information into movement. Because patients with complete vestibular loss must rely more strongly on vision during everyday activities such as walking, they demonstrate impaired gaze and postural stability.

Accordingly, during everyday life, the vestibular and proprioceptive systems effectively work together to provide us with our essential "6th sense". Indeed, when the vestibular system is functioning normally, we are unaware of a distinct sensation because vestibular information is integrated with proprioceptive and other sensory inputs to encode sense of motion.

Did I really want to do that?

The brain combines vestibular and proprioceptive information to maintain balance. But the brain also needs to constantly keep track of the vital question: Did I really want to do that?

Consider the fact that both unexpected motion and intended motion relative to the world will result in activation of the vestibular system (Fig.2). If the goal is to maintain posture, then the brain will use this sensory information to generate the postural adjustments required to stabilise ourselves relative to our environment via vestibulo-spinal pathways. For instance, the unexpected motion experienced when slipping on ice will activate the vestibulo-spinal pathways to generate rapid compensatory postural responses. Alternatively, the requirements are different when we voluntarily move through the world. While we will also experience vestibular sensory input, the resulting activation of the vestibular system is a consequence of our own behaviour and thus represents motion that was intended. Thus, in this case, it would actually be counterproductive for the brain to generate postural stabilising responses, since our goal is to move through rather than stabilise ourselves relative to the world. Accordingly, the efficacy of vestibulo-spinal pathways is modulated in a manner that depends on whether the experienced self-motion is the result of unintended or intended behaviour.

Indeed, we now know that during intended behaviours the brain computes an "internal model" (Fig.3) of the expected sensory consequences of our self-motion (Brooks *et al.*, 2015). The computation is performed in the cerebellum, an area deep in the brain that plays an important role in the coordination of movement and balance. During our everyday activities, the cerebellum plays an essential role in the real-time regulation of movement required for coordinated behaviour and maintenance of posture. For instance, the act of suddenly slipping on ice would effectively produce a mismatch between the brain's

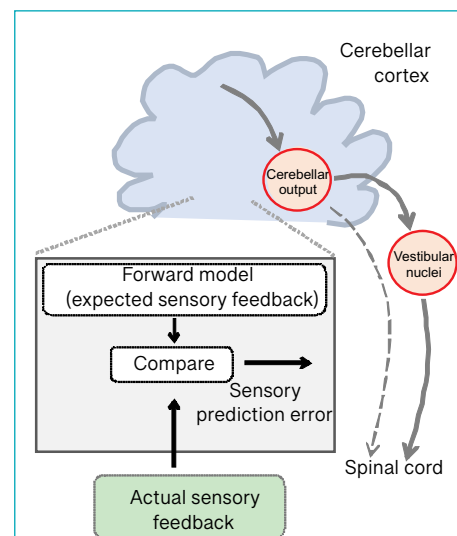


Figure 3. The vestibular cerebellum computes an "internal model" of the expected sensory consequences of our intended self-motion. In turn, this estimate is compared to the actual sensory inflow to determine whether there is a mismatch.

expectation of sensory input and the actual sensory input that is experienced. In response to such a mismatch, vestibulo-spinal pathways quickly send a robust signal to the spinal cord to maintain balance, which (hopefully) allows us to stay on our feet (Brooks and Cullen, 2013).

Accordingly, the cerebellum's internal model allows us to effectively distinguish sensory input caused by our own actions versus unexpected self-motion. Athletes can compute this mismatch for very complex motions – consider a gymnast doing a back flip on a balance beam. In contrast, patients with severely impaired cerebellar function – due to either hereditary or acquired conditions – cannot do this, even for a simple movement like placing a foot on a step.

In addition to being important for postural control, the ability to distinguish between self-generated and externally applied stimuli is also vital to ensure perceptual stability. Notably, in 1867, Helmholtz made the salient observation that tapping on the canthus of the eye results in an illusory shift of the visual world. However, we never see the world "shift" when we make rapid active eye movements (i.e. saccades) to look from one side of the room to the other. Indeed, the visual world remains stable because the brain can predict and suppress the visual stimulation produced by these active eye movements. Similarly, self-generated tactile stimulation in human subjects does not result in the same tickling sensation that arises when stimulation is externally produced (Witney *et al.*, 1999). In the context of balance, single-unit recordings from the thalamocortical vestibular pathway have further shown that neurons selectively encode unexpected motion, thereby providing

Unexpected self-motion



Intended self-motion



Figure 2. Both unexpected self-motion and intended self-motion relative to the world result in activation of the vestibular system. (Photograph by Vesperholly, CC BY-SA 2.5, via Wikimedia Commons)

During our everyday activities, the cerebellum plays an essential role in the real time regulation of movement required for coordinated behaviour and maintenance of posture.



BP/Barcroft Media

Loss of hair cells with age

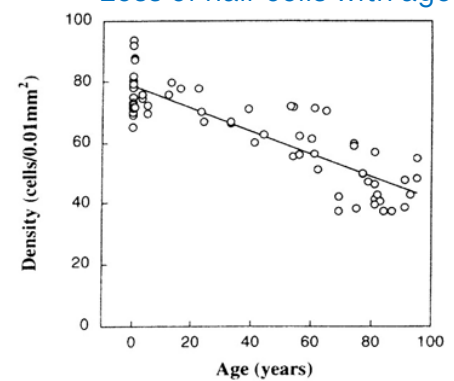


Figure 4. We lose receptor cells in the vestibular sensory organs as we age (plot from Rauch et al., 2001). Exercises such as Tai chi and Pilates are thought to help improve balance by upweighting the brain's reliance on self-motion information from the faster vestibular and proprioceptive systems versus the slower visual system.

a neural correlate for ensuring perceptual stability during active versus externally generated motion (Dale and Cullen, 2017).

Thus, overall, the computation of a mismatch between expected and actual vestibular input is necessary for robust postural control and our subjective awareness of self-motion as we explore the world. Elite athletes demonstrate superior performance in their abilities to anticipate the sensory consequences of motor commands when learning new complex actions (reviewed in Yarrow *et al.*, 2009). In contrast, as discussed below this ability declines as we age.

The role of motor signals in sensory processing

Recent experiments have provided circuit-level insight into the question of where and how the brain compares expected and actual sensory feedback. As we move through our world, cerebellar output neurons dynamically track the difference between the predicted versus actual sensory inflow that is experienced (Fig.3). As a result, these neurons effectively compute a representation of the unexpected motion that is experienced, which in turn is then used within milliseconds to adjust our balance. This signal is then relayed to vestibulo-spinal neurons that connect the cerebellum to the spinal cord to drive rapid compensatory postural responses to “unexpected” motion (Cullen, 2019). By repeatedly practising a complex action the brain can build sophisticated internal models of the expected feedback—as demanded by sports such as gymnastics and artistic pursuits such as dance.

Additionally, the brain learns to update its cerebellar internal model of what to expect, as our muscles and bodies change. Recordings from single cerebellar output neurons have demonstrated this updating in real time. Such updating achieves the flexibility required to continuously calibrate relationships between

motor signals and the resultant sensory feedback across our life span.

Ageing and balance

Over our life span, we lose an increasing percentage of the vestibular receptor cells that we had when we were younger (Fig.4). Thus, much like how we lose hearing with age, we also lose our vestibular sense. As a result, we have less reliable vestibular sensory information to estimate how we are moving relative to world to maintain balance. Further, as we age, we typically become more sedentary, and as we move less our brains often learn to rely more on vision. However, this is not ideal since, as noted above, vision is a very slow sensory input compared to vestibular and proprioceptive systems. In patients with vestibular loss, rehabilitation programmes focus on retraining the brain's strategy for integrating sensory information so that it learns to again use faster sensory inputs such as the vestibular system and proprioception to better maintain balance. Similar training as well as exercises such as Tai chi and Pilates have also proven to be beneficial for improving balance in the elderly and are thought to upweight the brain's reliance on self-motion information from the vestibular and proprioceptive systems (Sun *et al.*, 2021).

Cognitive aspects of vestibular disorders

The ability to form a picture of where we are heading relative to where we currently are requires knowledge of our current location and the direction of our self-motion. There is evidence to show that the hippocampus plays a vital role in such spatial navigation, and that the vestibular system provides a key input (Brandt *et al.*, 1994). Interestingly, there is also increasing evidence that cognitive decline in patients with Alzheimer's disease is linked to peripheral vestibular loss observed during

ageing. For example, patients with cognitive impairment have poorer vestibular function (most notably, impaired otolith responses) relative to age-matched controls (Harun *et al.*, 2016). Understanding the links between peripheral vestibular loss and cognitive impairment in disease, as well as in normal ageing will be an essential direction for basic and clinical future research.

Conclusion

The brain's ability to distinguish externally applied from self-generated sensory inputs underlies our ability to achieve both perceptual stability and accurate motor control during everyday activities. Recent studies have provided circuit-level insight into the neural computations performed in vestibular pathways to ensure these vital functions. Nevertheless, several open questions remain regarding the computations that the brain performs on vestibular information to ensure stable perception and accurate motor control. For example, further studies are needed to establish exactly how the cerebellum builds a neural representation of the expected sensory consequences of our voluntary self-motion. Additionally, further research is required to elucidate how functional changes in cerebellar versus higher-level cortical processing contribute our ability to maintain balance across our life span.

Ultimately, an improved understanding of these vestibular neural mechanisms can be leveraged to advance the development of more targeted training and rehabilitation strategies to counter deficits due to neurological disorders and/or ageing. Moreover, such fundamental knowledge can be leveraged to determine the extent to which the performance of complex movements can be optimised through extensive practice versus to what extent innate inter-individual differences simply make elite athletes different from the rest of us.

References

- Brandt T *et al.* (1994). Vestibular cortex lesions affect the perception of verticality. *Annals of Neurology* **35**, 403–12. <https://doi.org/10.1002/ana.410350406>.
- Brooks JX, Cullen KE (2013). The primate cerebellum selectively encodes unexpected self-motion. *Current Biology* **11**, 947–55. <https://doi.org/10.1016/j.cub.2013.04.029>.
- Brooks JX *et al.* (2015). Learning to expect the unexpected: Rapid updating in primate cerebellum during voluntary self-motion. *Nature Neuroscience* **18**, 1310–7. <https://doi.org/10.1038/nn.4077>.
- Cullen KE (2019). Vestibular processing during natural self-motion: Implications for perception and action. *Nature Reviews Neuroscience* **20**, 346–363. <https://doi.org/10.1038/s41583-019-0153-1>.
- Dale A, Cullen KE (2017). The ventral posterior lateral thalamus preferentially encodes externally applied versus active movement: Implications for self-motion perception. *Cerebral Cortex* **29**, 1–14. <https://doi.org/10.1093/cercor/bhx325>.
- Harun A *et al.* (2016). Vestibular impairment in dementia. *Otology & Neurotology* **37**, 1137–42. <http://dx.doi.org/10.1097/MAO.0000000000001157>.
- Rauch SD *et al.* (2001). Decreasing hair cell counts in aging humans. *Annals of the New York Academy of Sciences* **942**, 220–7. <https://doi.org/10.1111/j.1749-6632.2001.tb03748.x>.
- Sun M *et al.* (2021). The effect of exercise intervention on reducing the fall risk in older adults: A meta-analysis of randomized controlled trials. *International Journal of Environmental Research and Public Health* **18**(23), 12562 <https://doi.org/10.3390/ijerph182312562>.
- Witney AG *et al.* (1999). Predictive motor learning of temporal delays. *Journal of Neurophysiology* **82**(5):2039–48. <https://doi.org/10.1152/jn.1999.82.5.2039>.
- Yarrow K *et al.* (2009). Inside the brain of an elite athlete: The neural processes that support high achievement in sports. *Nature Reviews Neuroscience* **10**, 585–596. <https://doi.org/10.1038/nrn2672>.

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Meeting report

The Biomedical Basis of Elite Performance 2022

12 – 13 April 2022

University of Nottingham, UK

After not being able to meet face to face at a Society conference since December 2019, we were delighted to be at the University of Nottingham on 12 – 13 April for The Biomedical Basis of Elite Performance 2022.

This conference, in its third addition, once again provided an overview of the physiological responses to exercise, in the context of human adaptation and performance, and the central role that biomedical science is playing in directing understanding in this area. The programme covered cardiovascular, neuronal, and neuromuscular physiology, along with molecular and cellular metabolism, and the application of transformative methods in human physiology.

179 people from 11 countries shared their science at 20 invited talks, 6 oral communications and one poster session of 56 posters.

We are grateful to Professor Paul Greenhaff (University of Nottingham, UK) and his co-organisers for putting together such a vibrant and inspiring meeting.

Two of the prize winners and a first-time attendee share their thoughts on the conference.



Oral Communications: Isabel Ely, University of Nottingham, UK presenting her research on knee extensor force accuracy

Thomas Inns
University of Nottingham, UK



Winner, Michael J Rennie Oral Communication Prize

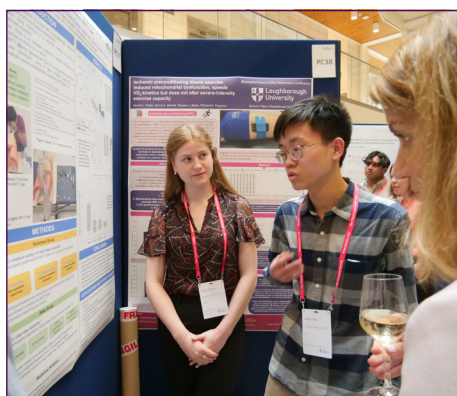
The Biomedical Basis of Elite Performance 2022 was a wonderfully organised in-person conference, the first of which I and many others had attended since before the COVID-19 pandemic. The atmosphere was fantastic, drawing researchers from across the globe, and the quality of work presented and displayed was excellent.

One of the things that impressed me the most was how well each of the presenters delivered a wide range of topics throughout various areas of performance and health science. Presentation topics ranged from the tissue level to studies containing elite athletes, epigenetics to exercise training and

fatigue, and were communicated at levels understandable to both scientists and clinical researchers with varied understanding of the topic at hand.

It was also a pleasure to interact with other researchers from undergraduate and early-stage postgraduate through to those who had devoted many years to their work. We were honoured to hear an extremely insightful keynote talk from Professor Claude Bouchard, focusing on his various careers and interests over his long and impactful time pushing the boundaries of human physiology and performance work. The absolute silence in the room during this talk was telling of the utmost respect he had gained. It was encouraging to hear him discuss both successes and failures of his and his colleagues' hypotheses during his work, highlighting an important personal lesson as an early career researcher to understand that it's okay if you don't find what you expected!

I was honoured to receive the Michael J Rennie prize for best oral communication following the presentation of findings from my primary PhD study investigating neuromuscular adaptation to immobilisation in humans. This was especially humbling given the quality of presentations, and I am grateful to both The Physiological Society for the opportunity to present and to my supervisors Professor Beth Phillips and Dr Mathew Piasecki for their constant support.



Poster session

Joseph Bass
University of Nottingham, UK



Winner, The Physiological Society Early Career Poster Competition

I have been a member of The Physiological Society for several years and have been fortunate enough to participate in many of their Annual Conferences and events, with this year's Biomedical Basis of Elite Performance being my first in-person attendance since the COVID-19 pandemic.

The atmosphere and character of the event was fantastic, and it was great to be able to see the enthusiasm of new and old colleagues, with the research they were presenting and the discussions that sprang from these. This was especially evident in other early career researchers, who may have been presenting in-person for the first time and embraced the experience.

It was nice to have a varied and balanced range of sessions within the area of elite performance, with a great mix of invited speakers, who were able to place into context many years of research. Similarly, the engagement and questions from the audience throughout the conference were excellent and allowed open and honest discussions to be had. These sessions allowed a greater appreciation and understanding of physiology not typically within my area. Seeing how physiological research has been shaped and

changed over time was inspiring to see, and I am intrigued to see where it continues.

Overall, the whole event was thoroughly enjoyable and refreshing to attend. I look forward to attending the next Biomedical Basis of Elite Performance conference and thank The Physiological Society for supporting the event.

Robyn Aitkenhead
Edinburgh Napier University, UK



The Biomedical Basis of Elite Performance 2022 was my first in-person conference. This was a fantastic opportunity and it felt great to network and speak to others in person rather than online. I felt very privileged to present my Master's research at the poster session. This was also a great opportunity to speak to other researchers and learn about the other incredible research going on. In addition, having the posters up before and after the sessions allowed for greater insight into the posters I didn't get to view during the dedicated poster session. It was great to have some very interesting conversations about my research during the poster session and it has definitely sparked some ideas for future work.

The conference was very well organised by The Physiological Society and the line-up of

oral talks was of a very high quality. There was a focus on early career researchers, which was great to see. The oral talks allowed me to learn about other areas of research completely new to me, specifically neuromuscular research. It was an amazing opportunity to hear an online presentation from Professor Louise Burke on her research and I thoroughly enjoyed the many presentations focusing on sex differences and female athletes. Furthermore, it was very inspiring to hear from the keynote speaker Professor Claude Bouchard.

Attending my first conference solo was particularly nerve-wracking but everyone I spoke to was very welcoming and kind. Overall, I thoroughly enjoyed my two days at the conference and I hope that this will be one of many Society conferences I attend in the future!

Organising Committee

Professor Paul Greenhaff
University of Nottingham, UK

Dr Matthew Brook
University of Nottingham, UK

Dr Carrie Ferguson
Lundquist Institute, California, US

Professor Ylva Hellsten
University of Copenhagen, Denmark

Dr Mathew Piasecki
University of Nottingham, UK

Professor Claire Stewart
Liverpool John Moores University, UK

Dr Gareth Wallis
University of Birmingham, UK

Dr Daniel Wilkinson
University of Nottingham, UK



Conference attendees



Dr Emma Hart, University of Bristol, UK

EUROPHYSIOLOGY 2022

COPENHAGEN, 16-18 SEPTEMBER 2022



europhysiology2022.org



Europhysiology 2022 pre-conference symposia

15 September 2022
Europhysiology in Copenhagen, Denmark

Our Annual Conference in 2022 will be taking place as part of Europhysiology in Copenhagen, Denmark from 16 – 18 September 2022. The main conference is preceded on Thursday 15 September by a day of eight symposia, bringing together communities for focused scientific discussions and networking followed by a canal tour in the evening. Pre-conference symposia are free to attend but you must be registered for Europhysiology 2022. The most up-to-date programmes can be found at: <https://europhysiology2022.org/presymposia-on-15-september-2022/>.

A snapshot of the pre-conference symposia

Young Physiologists Symposium

The Young Physiologists Symposium is organised by Early Career Researchers and will run from 08:00 to 11:30 CEST. We want to support the early career journey with an event where you can learn about opportunities to further your academic or non-academic careers. The event starts with talks on ways to increase your academic impact and expertise. These will be given by a successful Editorial Board Fellowship candidate and a Programme Officer for a Research Foundation, both of whom will share skills and paths to widen your academic opportunities. After a networking break, you will hear about innovative new projects and programmes beyond academia, including the experience of people working in the pharmaceutical industry or those translating their research into start-ups. Following this morning symposium, you'll have your pick of afternoon symposia, where you can interact with speakers and attendees in your research field and beyond!

The organising committee:

- Dr Felix Beinlich, University of Copenhagen, Denmark

- Dr Gustavo Chaves, Klinikum Nürnberg Medical School, Germany
- Dr Ana Cruz, University of Exeter, UK
- Dr Rehan Junejo, Manchester Metropolitan University, UK
- Dr Dominik Lenz, Philipps University of Marburg, Germany
- Dr Andreas Ritzau-Jost, University of Leipzig, Germany

Special Interest Group meetings run from 12:00–17:00 CEST

Vascular Physiology

Our central aim is to showcase the work of early career researchers selected from a range of prominent groups across Europe. The focus will be on topical areas of vascular physiology, including: research on transcriptional control in vascular cells, hormonal regulation of vascular tone, *in vivo* imaging and global health problems. By interspersing presentations by early career and senior physiologists we have created an exciting and interactive programme that will stimulate discussion. The Vascular Physiology symposium has been jointly organised by the special interest groups of The Physiological

Society, the Scandinavian Physiological Society and the German Physiological Society.

The organising committee:

- Professor Christopher Garland, University of Oxford, UK
- Professor Thomas Korff, University of Heidelberg, Germany
- Professor Michaela Kuhn, University of Würzburg, Germany
- Dr Vladimir Matchkov, Aarhus University, Denmark

Comparative Physiology

This will be the inaugural symposium for the newly formed Special Interest Group for Comparative Physiology from the Scandinavian Physiological Society. We have assembled interesting speakers on a variety of timely topics in comparative physiology, from mechanisms of stress tolerance in tardigrades, to Arctic chronobiology and anoxia-tolerant fish. We will also use this opportunity to host a discussion on future activities in our group. Comparative physiology offers unique insight to an intelligent choice of animal models for biomedical research, but also has a fundamental value in its own right. We hope this symposium will highlight the many wonderful and exquisite adaptations to various environments and provide both academic insight and a firm understanding of animal physiology to show how and why the current destruction of natural environments will lead to extinction of species worldwide.

The organising committee:

- Dr Sjannie Lefevre, University of Oslo, Norway
- Professor Tobias Wang, Aarhus University, Denmark

Cardiac Physiology

Building on the success of the pre-conference symposium at Europhysiology 2018 we have arranged this symposium on cardiac physiology. The scientific programme for this pre-meeting includes four exciting sessions on human, human-induced pluripotent stem cell-derived cardiomyocytes, the microtubule network in health and disease, protein turnover and quality control and novel potential therapies for heart disease – meet the industry. We have organised an international programme that includes speakers from Scandinavia, Germany, UK and US and invited both established researchers and early career scientists for exciting scientific talks and networking. In London, more than 100 physiologists met at the Cardiac Physiology

pre-conference symposium. We are sure to surpass this number in Copenhagen!

The organising committee:

- Dr Andrew James, University of Bristol, UK
- Professor William E Louch, University of Oslo, Norway
- Professor Wolfgang A Linke, University of Muenster, Germany
- Dr Morten B Thomsen, University of Copenhagen, Denmark

Renal Physiology

The Renal Physiology pre-conference symposium is broadly focusing on key topics in renal transport physiology and mechanisms underlying renal disease. We have secured many notable speakers who will deliver specific insight into new methodologies and novel physiological findings in their respective areas. The focus will be on three main topics: a session on claudins and paracellular transport in kidney, a session on renal ion transport proteins involved in transcellular transport and finally a session on the molecular mechanisms underlying renal disease. There will be ample room for scientific discussion, and we welcome all interested at any career level to participate.

The organising committee:

- Dr Henrik Dimke, University of Southern Denmark, Denmark
- Professor Markus Bleich, Christian-Albrecht University-Kiel, Germany

Skeletal Muscle

The Scandinavian Physiological Society's Special Interest Group in Skeletal Muscle is looking forward to hosting a pre-conference symposium entitled Novel Approaches and Insights on Skeletal Muscle Structure and Function in Health And Disease. The symposium comprises six invited talks covering exciting skeletal muscle subjects such as stem cells to performance, analyses of cellular responses to exercise using single-cell sequencing, studies of the role of circulating factors in exercise-induced tissue remodelling, as well as mitochondrial function and dysfunction. Also, four short talks will be chosen from abstracts – so we encourage students, postdocs, and colleagues to submit your work for presentation. In addition to sharing and discussing our most recent understanding of skeletal muscle function and adaptation in health and disease, we aim to boost scientific interactions between researchers in the skeletal muscle community in Scandinavia and Europe.

The organising committee:

- Professor Theresia Kraft, Hannover Medical School, Germany
- Dr Johanna Lanner, Karolinska Institutet, Sweden
- Dr Julien Ochala, University of Copenhagen, Denmark
- Dr Kristian Vissing, Aarhus University, Denmark

Human, Exercise and Environmental Physiology

This Human, Exercise and Environmental Physiology pre-conference symposium is organised by the The Physiological Society's Theme Leads for Human, Exercise and Environmental Physiology and is entitled Is There a Norm in Human Physiology? Biological Influences in Health and Disease. Speakers from all career stages will talk about their research into different aspects of physiological diversity. We will hear about how sex and hormones affect responses to exercise, how age impacts key aspects of human movement, as well as how race and skin pigmentation influence physiological function. We will also discuss the need to widen the demographic in physiological research, and why this is important to study the human body comprehensively to optimise outcomes for all humans.

The organising committee:

- Dr Paul Ansdell, Northumbria University, UK
- Dr Irene Di Giulio, King's College London, UK

Neuroscience

The Neuroscience pre-conference symposium will bring together world leaders in the study of histamine and the nervous system, and the wider community for face-to-face networking to create international connections. This symposium aims to showcase the latest research, methodologies, and developments in the field. The topics will range from studies in the healthy nervous system at the level of synapses, neuronal circuits to whole animals. We will also outline the latest technological developments and methodologies to accurately measure histamine in the nervous system and recent studies of histamine dysregulation in disorders of both central nervous as well as the peripheral nervous system disorders.

The organising committee:

- Dr Tommas Ellender, University of Oxford, UK

Paton Prize Fund: The value of historical research

Dr David Miller

University of Glasgow, UK

Dr David Miller, a recipient of the Prize, will be delivering the Paton Prize Lecture at Sydney Ringer and physiological discovery in its historical context symposium taking place at Trinity College Dublin, Ireland on 1 September 2022. He shares the importance of digging into the life and research of physiologists.

Understanding how and why any given research was done is a core skill in science. The "Introduction" sections of papers (and theses) often provide context by outlining what had led to the latest study. Beyond that, the broader sweep of research, scholarship and teaching demands insight into key techniques and personalities that are only identified with significant advances.

In 1990, Sir William Paton FRS (1917–93) donated £5000 to The Society, a sum which The Society matched, to sponsor the eponymous Fund. Through the fund, Sir Paton sought to encourage and recognise those key aspects of research. The Paton Historical Studies Fund (The Society, 1990). offers grants of up to £1000 or more to support work explicitly aimed at improving our knowledge of the broadly "historical" aspects of physiology. Paton was particularly keen to encourage better understanding of methodological developments as well as of the researchers themselves.

The scientific and clinical eminence of Professor Sydney Ringer

Fifteen years ago, I was fortunate to be awarded funding from the Paton Historical Studies Fund for my own early studies of Professor Sydney Ringer (1835–1910). As well as being an eminent physician, appointed Professor of Clinical Medicine at University College Hospital (UCL), UK, it was through his physiological and pharmacological research that he became the father of "physiological saline". Most notably, Ringer was the first to recognise the crucial importance of extracellular calcium for cardiac contraction (and, as it has turned out, for very much more in cellular physiology!).

I spoke about Ringer at the recent unveiling of a blue plaque to commemorate him at UCL (The Society, 2022), where he had spent



Sydney Ringer (centre – pale suit) at his home in Lasingham with friends and family c.1885 (original courtesy of the late Mrs Marjorie Paris. Photo DJM.)

his entire career. I have now been given the honour of delivering the Paton Prize Lecture this year at Trinity College Dublin, Ireland in September. This is part of Trinity's "100 Years of Physiology" celebration..

In tune with Paton's idea, I have sought to reveal how Ringer could focus his research on the key physiological ions, such as calcium, sodium, potassium, etc. and their nearest chemical relatives, such as strontium and rubidium, at a time in the early 1880s when current understanding of the relevant chemical solution of ionic dissociation had yet to emerge. A booklet summary of my work, largely written for a lay audience, was published by The Society (Miller, 2007).

Wonders found from unravelling the past

Understanding the context in which important discoveries were made is valuable as well as potentially deeply fascinating. And the same is true of digging into the "life and times" of those who did the work. As a result of pursuing my interest, I often found myself in the lovely Dales village of Lasingham, North Yorkshire, UK where Ringer and his family spent holidays and to which he retired.

In 2005, the "Dead Ringer Society's" *ad hoc* meeting saw a group of my cardiac muscle friends assemble there to help clean up the

churchyard and Ringer's grave (Dead Ringer Society, 2005). On an early visit there, I first saw previously unknown photos of "my hero" in the very house he had owned. I can fairly claim to have discovered both the presence of imposing Florentine-stained glass, nearly unique to Britain, that he endowed at Lasingham's ancient church, St Mary's, as well as the reason for it being there. I've been delighted to meet two of his great-great granddaughters and a man who, in 1920, was baptised by Ringer's brother-in-law.

In Norwich, UK, where Ringer was raised, I held a monaural wooden stethoscope that Ringer himself had used. These represent aspects of the "sociology of science" that I never anticipated I would unravel. But the experience has helped form a more rounded view of someone who was previously little more to me and many others than "Ringer (1883) ...". (In my case, those are the very first words in my own PhD thesis of 1973.)

Paton Prize Fund highlights

I would like to showcase a few other recipients of the Paton Prize Fund. The first is Dr Martha Tissot van Patot, University of Oxford, UK, who researched Mabel Purefoy FitzGerald (1872–1973) (Van Patot, 2015). FitzGerald became a member of The Society at the great age of 100! She had worked with eminent colleagues such as William Osler, John Scott Haldane, Claude Gordon Douglas and Charles



Wooden stethoscope used by Sydney Ringer, given to his senior assistant, Dr Harold Batty Shaw MD, of UCH. (Courtesy of the late Dr Anthony Batty Shaw. Photo DJM).

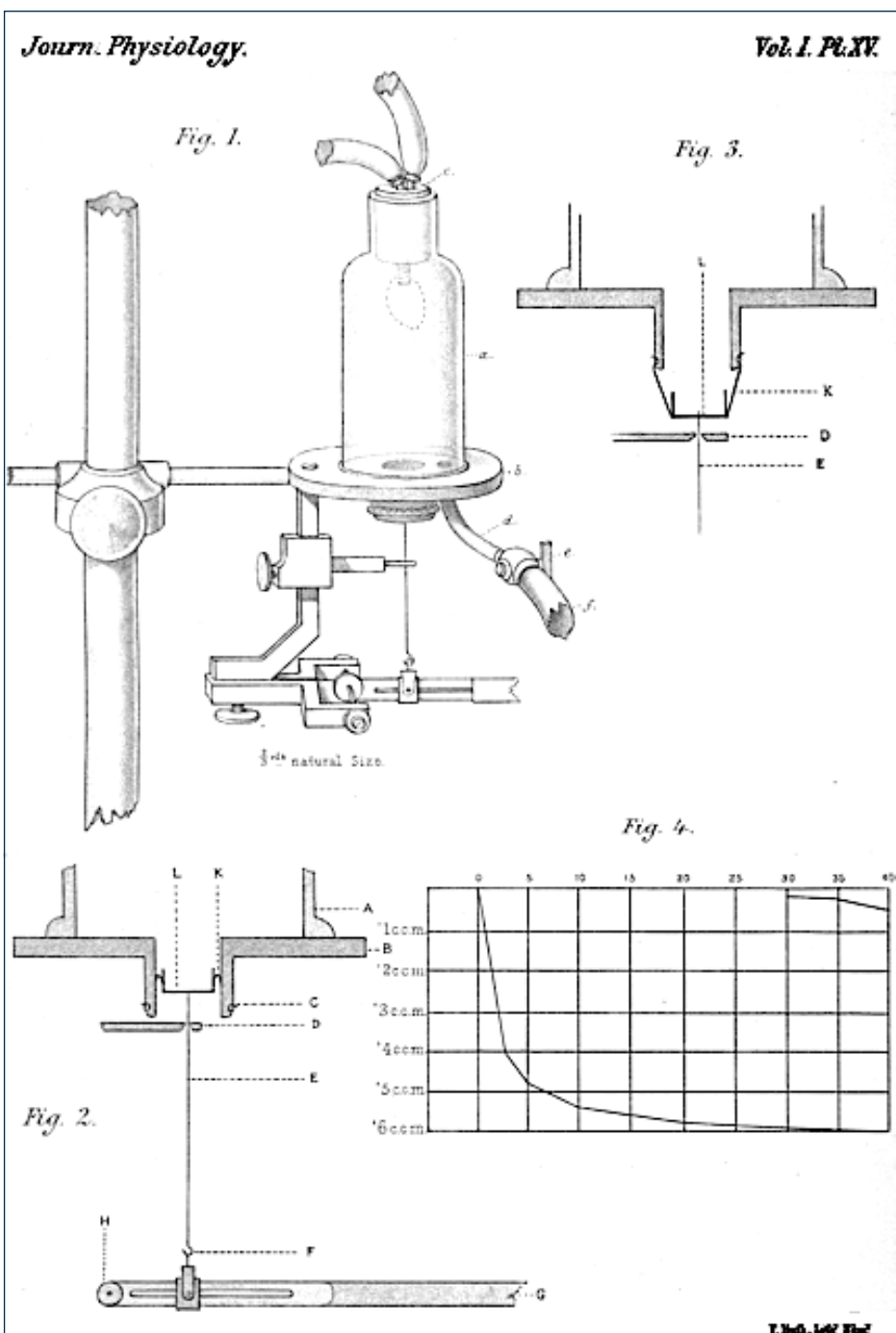
Scott Sherrington. FitzGerald carried out pioneering work on the control of breathing and the effects of altitude.

The second is Professor Oksana Zayachkivska, Danylo Halytsky Lviv National Medical University, Ukraine, very much in our thoughts just now. Oksana researched the life and work of Adolf Beck (1863–1942), an early, eminent cortical and spinal cord neurophysiologist and founder of the Physiology department at the Medical University of Lviv in the 1920s (Zayachkivska, 2014).

I encourage anyone with an interest in researching the historical context of their own heroes or important techniques to consider applying for the Paton Historical Studies Fund. You might even find an unexpectedly well-cited article or two can emerge to burnish and broaden your CV! (e.g. Miller, 2004 – has been cited over 100 times).

References

- Dead Ringer Society (2005). The Dead Ringer Team clean up at Lasteringham. *Physiology News* **58**, 44. <https://bit.ly/3sWsRK1>
- Martha Tissot van Patot (2015). The science and sagacity of Mabel Purefoy FitzGerald. *Physiology News*, **100**, 26 – 31. <https://doi.org/10.36866/pn.100.26>
- Miller DJ (2004). Sydney Ringer; physiological saline, calcium and the contraction of the heart *Journal of Physiology* **555**, 585–587. <https://doi.org/10.1113/jphysiol.2004.060731>
- Miller DJ (2007). *A Solution for the Heart: A brief biography of Sydney Ringer (1835–1910)* –revised 2014, 2020. The Society. <https://bit.ly/38lm1B0>
- Oksana Zayachkivska (2014). Remembering the 150th anniversary of the birth of Adolf Beck (1863–1942) *Physiology News* **94**, 12–13. <https://doi.org/10.36866/pn.94.12>
- Ringer S (1883). A further contribution regarding the influence of the different constituents of the blood on the contraction of the heart. *Journal of Physiology* **4**, 29–42. <https://doi.org/10.1113/jphysiol.1883.sp000120>
- The Society (1990). *The Paton Historical Studies Fund*. The Society. <https://bit.ly/3sWQ7Ym>
- The Society (2022). *Plaque unveiled in London to celebrate Professor Sydney Ringer*. Society News <https://bit.ly/3wDW5iV>



Roy's tonometer- the device used by Ringer to monitor cardiac contraction. (Fig.1 from Charles S Roy, 1879. On the influences which modify the work of the heart *Journal of Physiology* **1**, 452–496)

What is it like to lose one's sense of taste and smell?



Noemi Vadaszy, PhD Student

University of Leicester, UK

Member, Noemi Vadaszy, University of Leicester, UK describes the sensory impact of COVID-19, sharing the onset and sensation of losing her sense of taste and smell when infected with the virus.

.....

Before getting COVID-19, I thought this symptom was the same as when you have a cold, and flavours of foods are altered or decreased. However, it was not like that at all.

.....

A sudden loss of taste

I lost my sense of taste on the third day of my illness. While brushing my teeth, I noticed that my toothpaste tasted very different. Thinking back, it tasted like a weird medicine that you resist as a child. At the time I was quite ill and did not give too much attention to it; I noted the difference in my head and went to bed.

The next morning my coffee tasted like warm water. It was then that I realised that I had lost or partially lost my taste. At the time I was not too worried because I assumed it would come back, despite having heard it could take people months to regain their taste.

Ongoing symptoms

I lost my sense of taste and smell for a month. For about 2-3 weeks, I couldn't taste anything apart from salt. Then, I gradually regained my sense of taste. I remember my first "symptom-free" day was three weeks after I got my positive test. My friend and I ordered a meal to celebrate our recovery. At that point, I was craving a big burger but with the first bite, I realised something was still off. I could not taste the meat in the burger at all. Instead, I could feel a strange blood-like taste in my mouth with cheese (apologies if this is too grotesque).

There were some funny situations too though. I made a spaghetti bolognese about a week later and as you do, I added some garlic. When I asked my friend whether I put enough garlic in or not; with tears in her eyes, she replied: "Yes, you definitely did!" Even then I couldn't taste the flavours of foods, only detecting the basic taste range.

The psychological impact

Before getting COVID-19, I thought this symptom was the same as when you have a cold, and flavours of foods are altered or decreased. However, it was not like that at all. It is a partial or complete loss of taste. Psychologically this was the hardest symptom of my illness. When sick, all you want is a nice cup of tea or a meal that is easy to consume. However, when you have no taste or smell and are too ill to do anything else, you are just waiting for the illness to go. Because of having very little taste, I could only eat Pho soup as it was hot and salty, and I felt it helped me relax. I lost 4 kilograms during my illness simply because I did not want to eat. I felt like I was poisoned; my tongue felt odd too, which made it difficult to eat.

Lack of interest in food

It certainly changed my interest in food. When I tried to eat some brownies during the height of my illness, it left me with some strange memories. The brownie felt like moulded mud in my mouth (again apologies for being too grotesque). I could not look at brownies for a while after that. It is odd how it only influenced my interest in food though. I kept drinking coffee and tea even though I could not taste them. This may be because of how weird my tongue was feeling physically; when you drink your tongue is less involved. Or it could be related to how losing my sense of taste affected my psychological wellbeing and I wanted these drinks because they usually help me relax.

A newfound like

Luckily, there were no real lasting effects. It took me a while to start eating properly again and every time I ate something I was cautious because I wasn't sure if I would be able to taste it. The only major lasting effect is that I really like Pho soup now.

A “tasty” cough: My unusual sensory symptom of COVID-19 infection



Dr Katherine Rogers

Queen’s University Belfast, UK

Dr Katherine Rogers, Queen’s University Belfast, UK shares the sensory changes she experienced during two bouts of infection with COVID-19.

It is very difficult to describe the sensory change, as it is nothing that I have ever experienced before with a cough. The ‘cough taste’ was the first noticeable symptom that rang alarm bells for me.

I caught COVID-19 twice, with the second infection happening exactly two months after the first. During my first infection, I never had any of the three official symptoms at that time, except for slight nasal congestion and a runny nose for a couple of days. My constant refrain during that time was that “I’ve experienced worse colds”. Had it not been for the positive PCR test, I wouldn’t have known I had COVID-19 because I never tested positive by lateral flow test (LFT) during the first infection – was this because my symptoms were extremely mild?

Four weeks after the first infection I developed a nasty cough that was deep and irritating but non-productive. I had no other COVID-19 symptoms but the cough was so bad that I took a PCR test just for reassurance; it was negative. This is significant because it suggests that the positive test I got later by LFT at the end of February was probably not due to a lingering infection from my positive PCR result in December.

A month after the cough started, I tested positive for COVID-19 by LFT; the onset of symptoms happened quite quickly. Over the course of an hour or so, I could feel a change develop in myself. My cough that had been going on for over a month by then quickly worsened. It got more frequent and I felt like I could actually “taste” the cough. It is very difficult to describe the sensory change, as it is nothing that I have ever experienced before with a cough. The “cough taste” was the first noticeable symptom that rang alarm bells for me.

Throughout that night I had a combination of all the symptoms including chills, fever, hot and cold sweats, and a sustained restlessness that disturbed my sleep. The following morning, I was exhausted and by then, I had no appetite whatsoever.

I also noticed that my sense of taste and smell had changed. I didn’t lose either sense but certain types of tastes changed for me. At one point, water had a metallic taste but thankfully that only lasted a couple of days at the height of the infection. By the time I

was testing negative, water tasted fine again. Since I had no appetite, all I consumed for four days was Lemsip drinks (an over-the-counter lemon-flavoured hot drink containing paracetamol and phenylephrine hydrochloride [a decongestant]) with a spoon of honey. At times, I thought that the sour lemon taste was different.

After four days my appetite began to return but I still found that sour and spicy tastes were less “strong”. Sweet tastes seemed to remain the same throughout; the honey tasted fine and never changed. Within a few days of my appetite returning my sense of taste also returned to normal. The whole experience lasted just over a week.

The tiredness thankfully only lasted for the early days of the infection and I tested negative by LFT on day 5 and 6. Was that because this was a second infection? Interestingly, the cough lingered on. For a couple of weeks after the infection it was still quite debilitating and I required a prescribed salbutamol inhaler (for the first time ever) – just to get relief from the constant harsh cough. Five weeks post infection I still had a slight cough, which has been my only remaining symptom.

I have had two different COVID-19 infection experiences in a relatively short space of time, which is possibly due to the variants I had, but I also wonder about the severity of the symptoms in relation to perhaps waning immunity post-vaccination? Furthermore, was my relatively quick and full recovery from sensory symptoms due to immunisation from vaccination and/or the previous infection?

I have had no antigen tests, nor were my variants confirmed, so a lot of my thinking is circumspect but the sensory changes I experienced during the second infection were unusual and markedly different from anything I have ever noticed with previous colds. Over time, with more research, we will build a clearer picture of the immediate and possibly chronic sensory symptoms associated with infection by SARS-CoV-2 and the COVID-19 illness it causes.

Lab spotlights

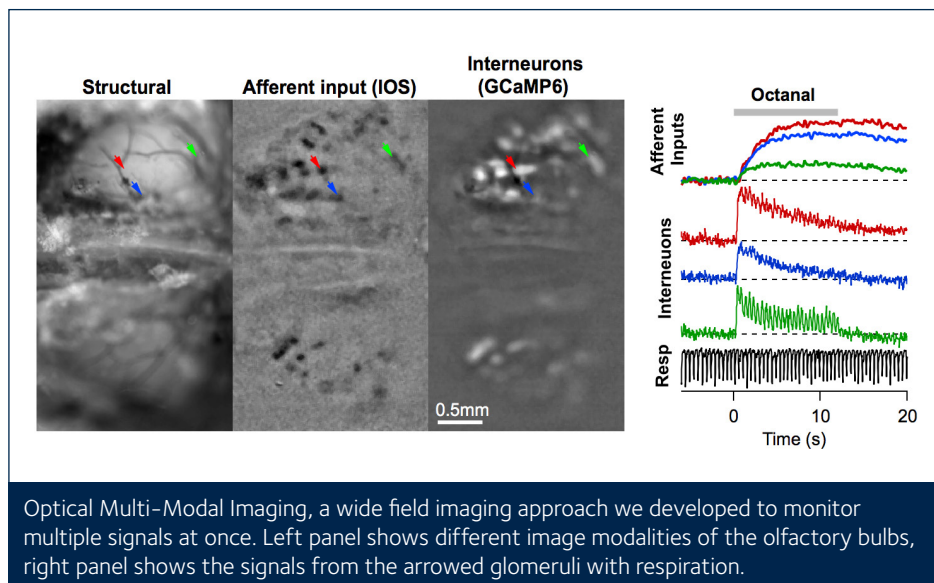
Two speakers presenting at the *Processing and Modulation of Sensory Signals: From the Periphery to the Cortex* conference on 20 – 21 June discuss their lab's sensory physiology research.

Exploring neural circuits

Dr Jamie Johnston
University of Leeds, UK

Having been enamoured with potassium channels during my undergraduate studies, I began my research career by poking neurons to see how these ion channels enabled neurones in the auditory system to match their excitability to their function. I then broadened a growing interest in sensory physiology by moving to work in the olfactory and then visual systems. During these transitions my interests expanded from how an individual neuron functions to include how networks of neurons work together in circuits to encode sensory stimuli.

In 2016, I moved to the School of Biomedical Sciences at the University of Leeds, UK and started my own lab to continue exploring neural circuits. We are now a multinational lab with members from Belgium, Romania, UK, Turkey, China and even as far away as Newcastle. Most of the



lab is working on the olfactory bulb with projects ongoing on the role of interneurons, regulation by metabolic state, learning, and through collaboration, we have also been investigating sensory neurons within the spinal cord.

We like to see what the brain is up to when we stimulate it. So, many of our experiments involve imaging neural activity with multi-photon microscopy while we deliver odours, but we also employ electrophysiology, behaviour, and computational modelling when necessary. We are also a maker lab and proponents of open-source and community-developed tools. Most of

our equipment is custom built to suit the experiments we want to do. This includes imaging rigs, behaviour enclosures and microcontrollers to measure physiological signals and synchronise recording of multiple parameters across an experiment. We have hosted engineering students for projects focused on tool development.

Our lab sits within a broad neuroscience community at Leeds that is both supportive and collaborative. The campus sits on the edge of Leeds city centre and with the fantastic Yorkshire Dales National Park on our doorstep it provides an excellent place to live and work.



Lab outing to the Yorkshire Dales, left to right: Niannian Wang, Emma Smith, Jamie Johnston, Andreea Pantiru, Merve Oncul, Mark Conway.

Studying pain perception

Professor Nikita Gamper
University of Leeds, UK



Nikita Gamper in his lab

I am a neuroscientist and biophysicist with interests in neuronal communication, intracellular signalling and mechanisms of pain transmission. I graduated in Biology/Biochemistry from the St Petersburg State University, Russia in 1995. In 1999 I obtained a PhD in Physiology from the Sechenov Institute of Evolutionary Physiology and Biochemistry (Russian Academy of Science) St Petersburg, Russia.

After six years of postdoctoral study at Tubingen University, Germany and at the University of Texas Health Science Center at San Antonio, US, I joined the Faculty of Biological Sciences at the University of Leeds in 2006, where I am currently appointed as a Professor of Neuroscience. Since 2011, I have carried out research at the Department of Pharmacology at Hebei Medical University in Shijiazhuang, China as an adjunct professor of pharmacology.

Our research, both in Leeds and in Shijiazhuang, is focused on cellular, molecular and biophysical principles of neuronal communication, especially in relation to somatosensory physiology and pain processing. One of our main focuses is on our recent discovery of GABAergic modulation of throughput spike conduction in the spinal somatosensory ganglia. These findings are highly discussed in the field and could amount to a novel principle of somatosensory processing in mammals.

We also have a long track record in studying ionic mechanisms of nociception and pain. Our group have contributed to elucidation of the role and modulation of TMEM16A (ANO1), M-type K^+ channels and T-type Ca^{2+}



The Neuroscience Research Group

channels in the peripheral pain pathways. Several current projects are focused on the modulation of these channels in sensory neurons by G protein-coupled receptors (GPCRs). Specifically, we are looking at the molecular organisation of localised GPCR signalling in sensory neurons in relation to inflammatory pain.

We also reported on transcriptional and epigenetic regulation of sensory neuronal gene expression associated with chronic pain. One specific focus of this line of enquiry is on transcriptional repressor REST (neuron-restrictive silencer factor (NRSF)) and its role in neuropathic remodelling of peripheral nerves in chronic pain states.

Our group is keen on the development of new methods and approaches for molecular neuroscience research. We recently developed, and modified for use with sensory neurons, single-molecule localisation methods (STORM, DNA-PAINT, proximity ligation), an all-optical method for simultaneous measurement of intracellular Ca^{2+} dynamics and chloride channel activity.

We are also developing neurophysiological approaches for simultaneous *in vivo* recordings from multiple sites along the somatosensory circuits. Lately, we adopted tissue clearing and light sheet imaging of whole spinal somatosensory ganglia for accurate morphometry, as well as developing multiple computational approaches to evaluate neuronal activity.



The Neuroscience Research Group

My top five papers



Professor Maria Fitzgerald

Professor of Developmental Neurobiology at University College London (UCL), UK

Maria Fitzgerald is an Honorary Member of The Society and a world leader on the neurobiological processes involved in the development of pain pathways. Maria reflects on the papers that have most influenced her career.

I am a Professor of Developmental Neurobiology at University College London (UCL), UK. My research has focused upon the development of touch and pain pathways in the peripheral and central nervous system, from late fetal life to adolescence. I was drawn to Physiological Sciences as my first degree because I knew that I wanted to study biological processes in living animals but also knew that I did not want to be a doctor.

After a very enjoyable PhD in the Physiology department at UCL (with Bruce Lynn) recording from individual nociceptors, I accepted a postdoc position with Patrick Wall, the father of pain physiology. He was an amazing mentor and an inspirational scientist; through him I developed a passion for understanding pain in infants and children that remains today.

Wall PD (1960). Cord cells responding to touch, damage, and temperature of skin. *Journal of Neurophysiology* 23, 197-210. doi: 10.1152/jn.1960.23.2.197.

This classic paper had a great influence on my (and others') understanding of sensory processing in the spinal cord. The senses of touch and pain were classically described in terms of simple lines of information from the skin (via primary afferents) up to the spinal cord dorsal horn and subsequently on up to the brain, with specific "lines" for each modality. Wall showed in this paper that although spinal cord neurons detect the characteristics of sensations, the circuitry in which they operate is not fixed and can be "gated" by controlling peripheral sensory nerve inputs. It formed the basis of his famous "gate theory of pain" and taught me a very important lesson – be prepared to think beyond the accepted scientific dogma.

Woolf CJ (1983). Evidence for a central component of post-injury pain hypersensitivity. *Nature* 306(5944), 686-688. doi: 10.1038/306686a0.

This deceptively simple paper provided the first clear evidence that spinal cord circuits actively enhance and spread pain beyond a site of injury. It demonstrated that nociceptive signals from an injury site generate "central sensitisation" within dorsal horn circuitry, leading to the enhanced and widespread pain. Central sensitisation meant that pain could be maintained even when the original nociceptive input was silenced with local anaesthetics. This elegant study led me to understand the importance of the central nervous system in generating pain, independent of an injury.

Owens ME, Todt EH (1984). Pain in infancy: Neonatal reaction to a heel lance. *Pain* 20(1), 77-86. doi: 10.1016/0304-3959(84)90813-3.

I had always been interested in developmental physiology and had begun to ask questions about how nociceptors and spinal cord circuits ever developed to process pain in the first place. Reading this paper made me realise how important this question was in humans – in other words, that this scientific question had real-life impact. The paper shows significant increases in heart rate and crying follow a tissue-damaging stimulus in human infants and suggests that, contrary to received wisdom at the time, infants experience pain and that pain in infants can be reliably measured in clinical settings. This pioneering paper stimulated me to begin research on human infant pain in collaboration with colleagues at University College London Hospital, alongside my ongoing lab experiments.

Johansen JP, Fields HL (2004). Glutamatergic activation of anterior cingulate cortex produces an aversive teaching signal. *Nature Neuroscience* 7(4), 398-403. doi:10.1038/nn1207.

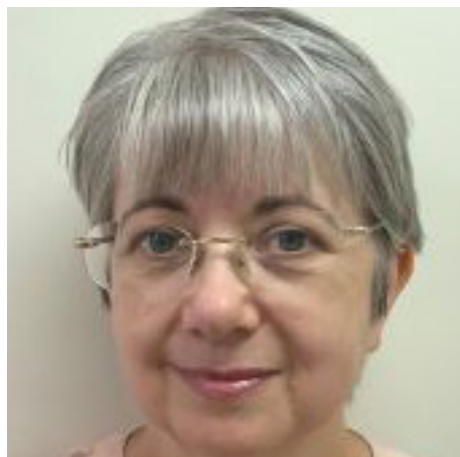
This paper introduced to me to the concept that noxious stimuli do not simply cause pain, but also have motivational power and can support associative learning. The study shows the role of neural circuitry in the anterior cingulate cortex (ACC) in the affective response to noxious stimuli and the motivational properties of conditioned stimuli that predict noxious stimulation. Using conditioned place aversion in rats, the authors showed that ACC neuronal activity is necessary and sufficient for noxious stimuli to produce an aversive teaching signal. This exciting paper made me realise that, despite my love of spinal cord pain circuits, it was time to move into the brain to really understand pain experience.

Duerden EG, Grunau RE, Guo T et al. (2018). Early procedural pain is associated with regionally-specific alterations in thalamic development in preterm infants. *Journal of Neuroscience* 38(4), 878-886. doi: 10.1523/JNEUROSCI.0867-17.2017.

My lab was building evidence that early life pain does not only cause suffering but, at critical stages of development, may cause longer-term changes in connections within the developing spinal cord and brain. This paper provided convincing evidence of this in humans. It shows that early exposure to repetitive procedural pain in very preterm neonates disrupts the development of regions involved in somatosensory processing, leading to poor functional outcomes. Specifically, early pain is associated with thalamic volume loss in the territory of the somatosensory thalamus and is accompanied by disruptions in thalamic metabolic growth and thalamocortical pathway maturation, associated with cognitive and motor outcome at 3 years corrected age. The data convinced me that it was indeed important to understand the underlying physiology of this vulnerability to early pain.

These five papers summarise my overall research philosophy. Be brave – science moves on, so open your mind to new ideas and evidence and be prepared to change the focus or direction of your research. And make sure that your laboratory work has relevance to the human condition.

Promotion to professor in teaching and scholarship: My top tips



Professor Louise Robson

School of Biosciences, University of Sheffield, UK

Louise Robson has over 25 years teaching experience. Winner of the Otto Hutter Prize (2017) and a National Teaching Fellowship (2021), she champions the use of digital technologies in teaching, providing an inclusive learning environment. In 2021 she was promoted to Professor of Digital Innovation in Learning and Teaching.

When I got my first academic position, back in 1996, teaching-only roles were rare, and were typically used to free up research time for other staff. Over the years, universities have started to realise the value of having teaching specialists – individuals that not only teach but also participate in scholarship, leadership and wider engagement activities. As a consequence, teaching roles have gone from being a stop-gap job, to having specific and dedicated career pathways that take an individual from junior lecturer level all the way through to professor. However, successful promotion in teaching and scholarship requires a different approach to the research-orientated pathways. In this article I would like to share my experience of promotion to professor in learning and teaching.

The first thing to do is **read the promotion documentation as soon as you can**. Make a plan (short, medium and long term). Identify what criteria you already meet, and how you will evidence this. Make sure you build your evidence portfolio as you go (it's not easy to go back to collect evidence). Seek more evidence if you need to. For those areas that you still need to meet, plan

how you can achieve them. Talk to your line manager and ask for support to help you achieve what is needed. Make it known you are open to positions that will help you with, e.g. leadership and wider impact – you will need to have held leadership positions, and demonstrate you have impact and influence across your institution, and often the wider HE sector. Talk to people who have already been promoted, and ask them their top tips. Ask them to look at your application, and take their feedback on board. If at first you don't succeed, reflect, plan and try again. It took me 3 attempts to get promoted.

Next, **identify something you will specialise in**. In my case this was digital technologies and their role in enhancing student learning and support. Pick something that you are passionate about, that has the potential to influence the institution and HE sector. Having something you specialise in means you are more likely to be recognised as an expert in that area, and it allows you to build a portfolio of activities that evidence your work. I started by using lecture capture in my modules, and evaluating the impact. I took my scholarship work to internal and external conferences, and this led to my institution asking me to lead on the implementation of lecture capture across the institution, helping me demonstrate leadership and impact in my promotion application. I was able to provide a joined-up narrative in my application that showed I was working at professorial level in this area.

Networking and collaboration are a great way of enabling a wider impact of your work. My championing of lecture capture meant a Sheffield colleague linked me on Twitter with someone who subsequently invited me to collaborate in a cross-institution, multi-discipline paper on lecture capture (Nordman *et al.*, 2020a,b). That paper had a huge impact across the sector, and it was used by other institutions to support staff and students. As part of my promotion application I contacted those institutions and asked for a statement, and several were very happy to provide this, evidencing my impact across the wider HE sector. This collaboration led to another paper in April 2020 around tips for a temporary online pivot (Nordmann *et al.*, 2020c). It helped institutions plan for the 2020/21 academic year, and I could evidence this from e-mails and comments on social media about the paper.

The next key point is to **share your scholarship work**. You can speak at

conferences, but should also consider publishing work in blogs and online magazine articles. Why not consider sharing via the National Teaching Repository. Plus make sure you publicise your talk and work on social media, linking to your organisation and relevant groups. Participate in HE social media activities, e.g. the LTHE Twitter chat each week can be a great source of ideas and an excellent way to start networking and collaborating. Twitter posts about my work provided some great evidence I could use in my application.

Don't say yes to all the impact and scholarship opportunities that are presented to you. Make sure that you evaluate what each opportunity is going to do for you. This sounds quite callous (we all want to help others out), but for me I was asked to do so many things I realised that I needed to prioritise what I was doing, to ensure I got the most out of what I did to allow me to evidence my standing in the field. One thing I did do was engage with opportunities at The Physiological Society, sitting on committees and eventually chairing the Education and Outreach Committee. This allowed me to work outside of my institution, and become known across the wider physiology community.

For me, these are the top tips I wish I had known at the start of my journey to becoming a professor, because they would have helped me massively. They are also, of course, tips that apply to anyone considering promotion in learning and teaching.

References

- Nordmann E, Kuepper-Tetzl CE, Robson L, Phillipson S, Lipan GI, and McGeorge P (2020a). Lecture capture: Practical recommendations for students and instructors. *Scholarship of Teaching and Learning in Psychology*. Online. <https://doi.org/10.1037/stl0000190>.
- Nordmann E, Kuepper-Tetzl CE, Robson L, Phillipson S, Lipan GI, and McGeorge P (2020b). Lecture capture: Practical recommendations for students and instructors (pre-publication). Student guide. <https://psyarxiv.com/sd7u4/>.
- Nordmann E, Horlin C, Hutchison J, Murray JA, Robson L, Seery MK *et al.* (2020c) Ten simple rules for supporting a temporary online pivot in higher education. *PLoS Computational Biology* **16**(10): e1008242. <https://doi.org/10.1371/journal.pcbi.1008242>.

National Teaching Repository: https://figshare.edgehill.ac.uk/The_National_Teaching_Repository.

LTHE Twitter chat: <https://ltthechat.com/>.

Career spotlight with Rob Clarke Award winner



Dr Laura Riggall

University College London, UK

*Rob Clarke Award winner, Dr Laura Riggall
shares her career journey*



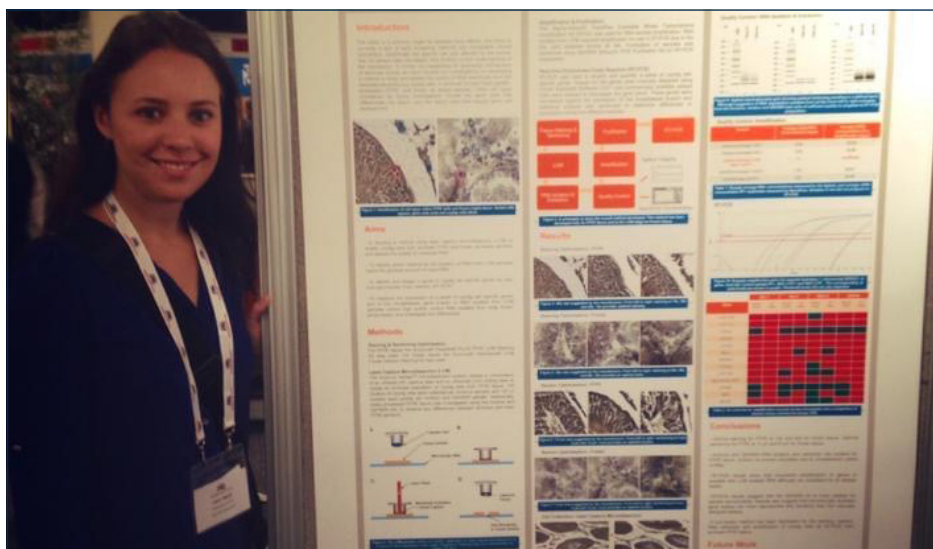
Group photo: Laura with Dr Jim Morrison and her peers at the University of Glasgow, having been awarded the Short Courses in Integrative Pharmacology & Physiology scholarship by The Physiological Society in 2014.

I completed my BSc Medical Sciences (Industrial) degree at the University of Leeds, UK, where I was presented with the Rob Clarke Award for my final-year dissertation project. Undertaking this degree provided me with the relevant technical knowledge and skillset to enable me to pursue my postgraduate studies at both Imperial College London, UK (MRes) and University College London, UK (PhD).

Furthermore, my dissertation project allowed me to realise my passion for neuroscience, which I subsequently specialised in during my masters and doctoral degrees. When I was given the Award, I was both surprised

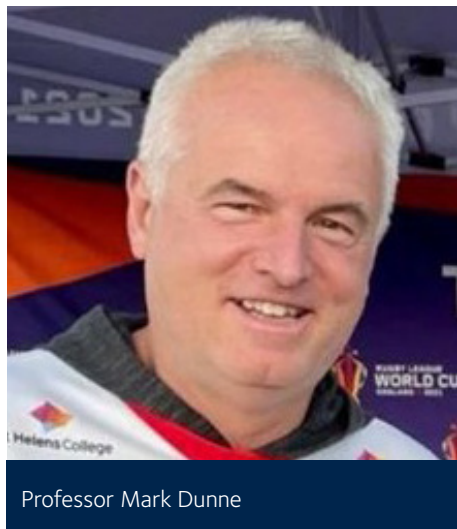
and delighted that my research had been recognised by such an esteemed society and was incredibly excited to have the opportunity to present my findings at The Society's renowned annual conference.

The Award greatly influenced my career path; having the chance to attend Physiology 2015 enabled me to discuss my research goals and ambitions at length with experts in the field, arming me with the confidence and enthusiasm to pursue a lifelong scientific career. In addition, the Award reinforced my passion for scientific writing, and I now regularly contribute to several scientific organisations as both a writer and editor.



Laura attending the 50th Congress of the European Societies of Toxicology during her industrial placement year at GlaxoSmithKline in 2014

Obituary: Professor Mark Dunne (1961–2021)



Professor Mark Dunne

Mark Dunne, who died unexpectedly from a heart attack in his sleep on 18 December 2021, was born in St Helens, one of three children of Eddie, a professional driver, and Pat, who worked at a school for children with special educational needs. Mark's friends from his teenage years remember him as a leader in mischief and in obscure "alternative" music appreciation – both familiar to Mark's later colleagues. He was also a keen schoolboy rugby and football player. Mark retained his St Helens ("it's not Scouse!") accent, and a devotion to St Helens Rugby (League) Football Club, all his life, passing on his enthusiasm for sport, and his allegiance to "The Saints", to his daughters Maija, Anya and Orla-Mae.

After a Biochemistry BSc at Warwick (1983) Mark got a job as a Research Assistant in Ole Petersen's famous electrophysiology group in Liverpool, where he was ultimately to spend 7 years as a PhD student and latterly postdoc. After some initial work on Ca^{2+} -activated K^{+} channels he switched to the then recently discovered ATP-sensitive potassium channel. Using the insulinoma cell line RINm5F, Mark helped to map out the sensitivity of KATP to different nucleotides in a series of papers. This formative period set him on his scientific path for the rest of his career.

By the start of the 90s, Mark was ready to start his own lab, and moved in 1990 to a Lecturer post in Sheffield. Here he rapidly established a young and lively research group. Of his early "alumni", two, Jonathan Jaggar and Paul Squires, have become Professors, at the University of Tennessee Memphis, US and the University of Lincoln, US, respectively. Other key figures in the Dunne lab in the

Sheffield years were Mark's long-time lab manager Ruth Shepherd, and his later life partner and long-time collaborator Karen Cosgrove. Ruth and Karen both moved with Mark to Manchester in early 2003.

Early in the Sheffield years, Mark took the key decision to focus the lab on working with human beta-cells, rather than with rat or mouse cells, or with the cell lines he and others had earlier used to study KATP channels. Human islets were available from islet transplant programmes, though accessing them required establishing a lot of collaborations with clinicians around the UK, which Mark did with his usual energy and people skills. Over the next couple of years, Mark and his lab worked out the details of how to isolate and patch-clamp human beta-cells.

In the mid 90s, the human beta-cell work led to what was to become Mark's primary research interest for the rest of his career, the rare but serious disease of congenital hyperinsulinism. Mark had forged a link with clinicians at Great Ormond Street treating children with severe forms of the disease. These children often required pancreatectomy to stop uncontrolled insulin secretion and severe hypoglycaemia, and Mark was able to obtain cells from the tissue to test. The striking result was that KATP channels, so prominent in normal beta-cells, could not be detected, leaving cells permanently depolarised. Mark's lab collaborated with Lydia and Joe Aguilar-Bryan, who had earlier established the molecular identity of the KATP channel. A landmark case report in the *New England Journal of Medicine*, and other publications, showed that mutations in the sulphonylurea receptor led to non-functional KATP channels, and that this was the cause of at least some of the most severe cases of congenital hyperinsulinism. This work put Mark's Sheffield group firmly on the map, and in 1998, at only 37, he became the University's then-youngest full Professor.

In 1999 Mark took on the job of Society Meetings Secretary for 3 years, which made him a familiar figure to UK physiologists. Running six meetings a year gave Mark's personal, diplomatic and organising skills a workout, and the late 90s saw the start of a continuing trend to joint meetings with sister societies in Europe and elsewhere. Mark was always in his element at scientific meetings, though he did not enjoy the time-honoured Phys Society custom of the Meetings

Secretary having to compose light-hearted "minutes of the previous meeting" and read them aloud after the meeting dinner. The practice was finally dropped just after the end of his tenure.

In the late 90s and into the 2000s, Mark's interest in diabetes and hypoglycaemia led him, like many others in the beta-cell field, to get interested in the idea of "replacing" beta-cells, particularly with cells derived from stem cells. On moving to Manchester in 2003, Mark was one of the prime movers in setting up a facility for stem cell biology. In Manchester he and Karen started a series of collaborations with local clinicians and endocrinologists, on subjects as diverse as fish-oils and extracellular matrix influences on beta-cell development. The core of the lab's work remained hyperinsulinism, and a number of the region's junior clinician scientists passed through the lab. Mark's enthusiasm for new scientific ventures never flagged, as his 120+ career publications testify.

The 2003 move to Manchester shifted Mark into a senior organisational and leadership role, and during his first Manchester decade he served as Head of Physiology & Pharmacology and Chair of the Biomedicine Teaching and Exam Boards. He steered the phys/pharm grouping through two building moves whilst shouldering his full share of admin, teaching and examining duties. He also took on jobs outside the University, including for hyperinsulinism charities, and was rarely without an undergraduate External Examinership on the go. As one contributor to his memorial page noted "it would be hard to imagine a more balanced and collegial colleague". The page, set up to honour Mark, has 100+ appreciations, including from undergraduate students past and present, as well as from friends and colleagues.

Mark and Karen's Manchester family home in Marple, on the edge of the Peak District, reflected their joint love of the outdoors. Mark was a keen cyclist, often cycling the dozen or so miles into the University – though in latter years he switched to an electric bike to help with the hills on the way back. Mark was above all a proud and devoted father. His social media feeds were full of their three girls' academic and sporting achievements, or family pictures at Saints' games, most recently their 2021 Grand Final victory.

Written by Dr Austin Elliott, University of Manchester, UK

Obituary: David Charles Ogden (1948–2021)



David Charles Ogden

I could scarcely believe it when I heard of David Ogden's sudden death at the age of only 73.

David was born in London, the first child of Charles Joseph and Doris Edith Ogden.

David Ogden joined UCL in the 1960s. For a while he was a technician in my lab. I recall that he had Higher National Diplomas (at the time that was a technical qualification). I have always liked late developers (being one myself) and I encouraged him to go further. He became a Member of the Institute of Biology (MIBiol), which was deemed to be a degree-equivalent qualification. That was enough to qualify him to start as a research assistant in Bernard Katz's famous Biophysics Department in 1972.

He worked there with Rolf Niedergerke and Sally Page who, after a tussle with the University of London dinosaurs about whether his MIBiol was a sufficient qualification, got him enrolled for a part-time PhD. For his first three years in Biophysics he overlapped with another research assistant, David Gadsby, with whom he collaborated on aspects of the sodium pump in skeletal muscle. (Gadsby, Niedergerke and Ogden, 1977). His PhD thesis was "Analysis of the hyperpolarisation associated with active exchange of sodium for potassium in skeletal muscle" (1981). Sally Page pointed out that some of his characteristics reminded her of Rolf Niedergerke: "the hands-on skill with equipment, the collecting of possible spare parts, the scrupulous analytical approach and concern for sources of error, the lack of self-promotion". His modesty was legendary. That hasn't helped with writing this obituary, but it was an appealing characteristic in a time when self-promotion became increasingly part of the job of academics.

In 1970 I had left for the US and didn't get back to UCL until 1979. I was delighted to be reunited with David. He stayed in our C-floor lab until 1986. They were heady times, the early days of single ion channel recording. I had met Bert Sakmann in 1977, the year after his first publication on single ion channels (Neher and Sakmann, 1976), and he and I had agreed to test some predictions made by Colquhoun and Hawkes (1977). Subsequent visits to Göttingen gave us early access to the methods published by Hamill *et al.* (1981). We got a circuit for a patch clamp via Erwin Neher, and I recall clearly David and I in the lab soldering together our first patch clamp in 1979 or 1980. It involved a search through catalogues for the least noisy 50 GW resistors. David's knowledge of electronics and his talent for building of apparatus proved invaluable and that led to the first publication of single ion channels from UCL using the gigohm seal method (Ogden, Siegelbaum and Colquhoun, 1981). During the 1980s, David proved himself to be a superb experimenter and he published several highly original studies on single ion channels.

In 1984, while continuing his research, David took on the huge task of organising the course on Microelectrode Techniques for Cell Physiology. Professor Anne Warner had proposed a course to teach methods, but from the start David did the work and kept it going over the next 37 years. It was a huge amount of work because the course was intensively practical. It involved the organisation and erection of six, and later ten, electrophysiological rigs from scratch at the Marine Biology lab in Plymouth. Over 600 students from around the world have now had the chance to do experiments with

their own hands with the help of experienced scientists at each setup. The experiments were accompanied by lectures that explained the necessary theory. David asked me to talk about the practice and theory of single channel measurements and I loved the annual trip to Plymouth every year but one from 1984 to 2017. At the first meeting the speakers included Bernard Katz and Richard Keynes.

In 2021, the course had to be virtual because of COVID-19 and the lectures were recorded. Of course, they are a poor substitute for the real course because the main virtue of the course was that students were able to do experiments with their own hands.

At least we can be grateful that if it were not for COVID, the lectures might never have been recorded. They will form part of his memorial.

After David left UCL he had a 3-year stint as a lecturer in Pharmacology at King's College London, but soon moved on to spend 16 years as a Senior Scientist at the MRC National Institute for Medical Research, London (later the Crick Institute). There he worked with David Trentham, John Corrie and George Papagiorgiou, developing photo-cleavable caged compounds, in particular caged neurotransmitters, to study synaptic receptor activation and properties *in situ*. From then on, David concentrated on optical methods. His deep knowledge of optics and electronics, and his legendary ability to make equipment, made a brilliant career.

In 2004, together with Céline Auger, he moved to Université Paris Descartes where



David Ogden and David Colquhoun with students at the Plymouth Cell Physiology Workshop in 2016



David Ogden teaching at Plymouth Cell Physiology Workshop in 2017

he stayed until his untimely death. He worked on further development of caged compounds and optical approaches to localise photolysis to a single synapse. David was never far from synapse biophysics. His last paper was published in 2018 (Palma-Cerda, Papageorgiou, Barbour, Auger and Ogden, 2018).

I can't put it better than Stephen Brickley: "Like many people who will contribute to this document, Dave gave me his time and

knowledge selflessly, teaching me about amplifiers, optics, scientific integrity, and the dying art of humility".

David is survived by his wife, Céline Auger, their two children, Eleanor and Félix, by his first wife, Judith and their two children, Vanessa and Clara, and by his brother, Paul, and sister, Marian.

Written by Professor David Colquhoun, University College London, UK

Footnotes

There are more pictures and reminiscences on my blog: <http://www.dcsience.net/in-memorial/the-diary-june-2013-may-2014/#070913>.

His publications can be found at <https://www.researchgate.net/profile/David-Ogden-4/research>.

To learn more about how much David Ogden was loved by his friends, there are tributes from many of them at <https://docs.google.com/document/d/1CiG4s5BPTRE3KioPOD8QZGB6fs81dof0D-XlnuVbmvm/edit>.

David had a lifelong passion for football. You can read about it here: <https://www.hamhigh.co.uk/news/obituaries/david-ogden-has-died-aged-73-8561236>.

I owe thanks to many people who've helped with this tribute, especially Dr Céline Auger, Dr Sally Page and Dr Loise Morgan, and his younger brother, Paul Ogden.

References

Colquhoun D, Hawkes AG (1977). Relaxation and fluctuations of membrane currents that flow through drug-operated channels. *Proceedings of the Royal Society of London. Series B, Biological Sciences* **199**, 231–262.

Gadsby DC, Niedergerke R, Ogden DC (1977). The dual nature of the membrane potential increase associated with the activity of the sodium/potassium exchange pump in skeletal muscle fibres. *Proceedings of the Royal Society of London. Series B, Biological Sciences* **198**(1133), 463–472. doi:10.1098/rspb.1977.0110.

Hamill OP, Marty A, Neher E, Sakmann B, Sigworth FJ (1981). Improved patch clamp techniques for high resolution current recording from cells and cell-free membrane patches. *Pflügers Archive – European Journal of Physiology*, **391**, 85–100.

Neher E, Sakmann B (1976). Single channel currents recorded from membrane of denervated frog muscle fibres. *Nature* **260**, 799–802.

Ogden DC, Siegelbaum SA, Colquhoun D (1981). Block of acetylcholine-activated ion channels by an uncharged local anaesthetic. *Nature* **289**, 596–598.

Palma-Cerda F, Papageorgiou G, Barbour B, Auger C & Ogden D (2018). Photolysis of a caged, fast-equilibrating glutamate receptor antagonist, mni-caged gamma-d-glutamyl-glycine, to investigate transmitter dynamics and receptor properties at glutamatergic synapses. *Frontiers in Cellular Neuroscience* **12**, 465. doi:10.3389/fncel.2018.00465.

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