Bright Brains
Newsletter

Issue No. 9
Summer 2018

Welcome to the summer edition of our 'Bright Brains' Newsletter! We are pleased to present you with an impressive variety of thought-provoking articles that have been composed and edited by BNA students, postdocs, and early-career researchers from a diverse array of neuroscientific disciplines throughout the UK.

Ever since computational neuroscience was introduced as a term by Eric Schwartz at a conference in California in 1985, it has developed into a major branch of study. In its pursuit of knowledge about how the brain works and the development of theories of brain function based on the information-processing attributes of the component structures of the nervous system, computational neuroscience connects psychology and neuroscience with disciplines such as computer science, electrical engineering and mathematics. The field is therefore characterised by multidisciplinary collaborations between computational neuroscientists and scientists and experimentalists from other disciplines.

Nonetheless, the way that neuroscience currently operates allows only for limited data sharing. The nervous system has many levels of organisation, spanning molecules, synapses, neurons, circuits, networks, layers, maps and systems. To connect our understanding across these different levels of brain organisation, close collaborations and extensive sharing of resources, tools and data among multidisciplinary teams are essential. Therefore, by embracing the modus operandi of big science, neuroscience could make good use of the variety of skills and talents of large teams as well as the technical tools and funds for multidisciplinary projects.

Only time will tell whether close multidisciplinary collaborations will enable computational neuroscience to produce a comprehensive theoretical account of how the brain works. This would necessarily involve the creation of a sequential and overlapping chain of explanations of what occurs from the lowest to the highest level of brain organisation. To enlighten you about projects that have emerged over the past few years that are steering neuroscience toward big science, 'Bright Brains' presents you with a list of large-scale brain-related initiatives.

This edition of 'Bright Brains' has many other exciting features in store for you. Our 'Nuntia' section provides you with excellent tips on how to become an open scientist, and presents an insightful student perspective on the Alzheimer's Research UK 2018 conference. Our 'Socialia' section tells you how to become a successful Brain Bee Ambassador, and introduces the unique collaborative platform for troubleshooting neuroscientific methods called NeuroMethods Slack group. The 'Varietas' section shows us how studying fruit flies could shed light on the mechanisms regulating sleep, and offers us the highlights of the Monitoring Molecules in Neurosciences conference. 'Numquid sciebat...?' provides a portrayal of a neurosurgeon who has been dubbed 'neurosurgeon of the millennium', while 'Quid novi?' directs our attention to the informative two-day Grid Cell Meeting in London. Last but not least, we are challenging you to a super-easy BNA crossword on cellular mechanisms and cognition!

Finally, we sincerely hope that you will have as much joy reading our ninth 'Bright Brains' newsletter as we had in producing it. On that note, we would like to encourage you to get involved in science communication by joining our newsletter team! Please direct enquiries to jayanthinykangatharan@gmail.com.

Jayanthiny Kangatharan, 'Bright Brains' newsletter coordinator

Large-scale initiatives aiming to generate a better understanding of the brain (with starting dates in brackets)	
China Brain Project (March, 2016)	Human Connectome Project (July, 2009)
Brain/MINDS (June, 2014)	BrainMaps (2005)
Human Brain Project (October, 2013)	Blue Brain Project (May, 2005)
BRAIN Initiative (April, 2013)	Allen Brain Atlases (September, 2003)

Stephen Eglen, PhD
Reader in Computational Neuroscience, University of Cambridge

Reproducible research and open science

At first glance, it might seem odd that you would need to prefix the term 'research' with the qualifier 'reproducible'. Surely, once you have a paper in your hands, you have all the details to reproduce someone else's work? That's certainly the theory when writing the paper, but often not the practice. Since 2004 we have set a problem for our master's students to reproduce key results from a paper within computational biology. However, students invariably find many missing details that preclude them from reproducing key figures or results. This failure to reproduce (1) is commonly termed the 'reproducibility crisis' (2). So, what might reproducible research entail? My interpretation is that when publishing results, labs should also provide all relevant datasets and methodology for transforming data into results. This means providing the spreadsheets or computational scripts to reproduce analyses.

This leads us naturally to the second term, open science. The competitive nature of science, such as limited funding, jobs and 'high-impact' publications, means that there is a natural tendency to withhold key datasets or analysis technologies. An alternative view gaining prominence in recent years is that sharing our resources allows others to build on our work and science as a whole should benefit. As an open scientist, you are increasing your chances of making your work reproducible.

Though being an open scientist may appear naive and altruistic, there are selfish reasons for sharing your research (3). Many funding agencies now require data management plans for sharing of data post-publication, and journals are increasingly asking for data and methods. My optimistic hope is that in 10 years we might be able to drop the qualifier 'open' and instead talk again simply about science.

TOP TIPS FOR BECOMING AN OPEN SCIENTIST:

1. Read the guidelines in Markowetz (3) and think if they would apply to you.

2. Read about personal experiences such as those of Erin McKiernan.

3. Do experiments? Try writing a registered report before doing the experiments to reduce publication bias. See www.nature.com/articles/s41562-016-0034

4. Talk to your local library to see what services they can offer to help archive and share your research. Find a local community of like-minded scientists!

5. Learn how to code, rather than using Excel, for your data analysis. See www.datacarpentry.org

Comments? Send them to me on twitter @StephenEglen

1. **Ioannidis JPA.** (2005) Why most published research findings are false. *PLoS Med* 2:e124.
2. **Baker M.** (2016) 1,500 scientists lift the lid on reproducibility. *Nature* 533:452–454.
3. **Markowetz F.** (2015) Five selfish reasons to work reproducibly. *Genome Biol* 16:274.

Anna Cranston
PhD student in Neuroscience, University of Aberdeen

Alzheimer's Research UK 2018 Conference

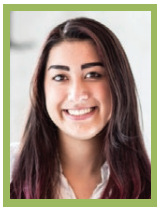
The annual Alzheimer's Research UK (ARUK) conference, the UK's largest gathering of dementia researchers, took place in London on 20–21 March, with over 500 scientists attending, 21 symposia, and 272 posters presented.

The mark of a good conference is one that inspires new ideas, collaborations, questions and, above all, an enthusiasm for science. The success of ARUK 2018 stems from all these aspects, promoting collaboration not only within the UK but among scientists worldwide. The conference also featured an 'Early Careers Day' event, in which PhD students had the opportunity to present their work as a symposium talk or during the poster session. The event concluded with a brilliant career Q&A panel, featuring academic and industry experts.

The main conference covered a wide range of scientific topics, including the potential role of astrocytes in synaptotoxicity in Alzheimer's disease, the contribution of cell and animal models in tauopathies, and the alterations in autophagy in frontotemporal dementia. The highlight of day one was, in my opinion, the lecture given by Jie Shen of Harvard University, on the genetic links between missense mutations in the presenilin gene and the amyloid precursor protein and familial Alzheimer's disease.

On day two, the main highlight came from John Skidmore's talk, in which he presented the latest research updates from the ARUK Cambridge Drug Discovery Institute, launched in 2015. The institute, which was established and funded by ARUK itself, is one of a network of institutes at UCL, Oxford and Cambridge, and aims to bridge the gap between academic research and drug discovery. As a PhD student working in the field of translational neuroscience, the recent development of such a platform is particularly exciting, and it is very encouraging to see a designated network of academic researchers and industry professionals working together towards a collective goal.

The success of ARUK largely comes from the large involvement of early-career researchers, including a busy poster session on both days at which many collaboration opportunities arise, the symposia chaired by early career post-docs, and the infamous networking banquet in the evening. Overall this year's event was a great success, and I look forward to attending again next year.



Ghalia Khan
Marketing Trustee, BrainBee

Becoming a Brain Bee Ambassador

Directed by founder Norbert Myslinski, the International Brain Bee is a worldwide competition that motivates students to learn about the brain, captures their imaginations, and inspires them to pursue neuroscience careers to help treat and find cures for neurological and psychological disorders.

Founded in 1999, more than 60 nations and 175 chapters are engaged in coordinating Brain Bee programmes around the world, and this number is rapidly increasing. About 50,000 students participate across six continents every year, and more than 600 neuroscientists have been involved with organising and judging the events. An Alumni Club has been established to sustain the global community of young scientists into their university and career tracks.

The Brain Bee competition platform is organised on three levels: local, national and international. Local scientific institutions are licensed by International Brain Bee to carry out city-wide or regional events, engaging students 14–19 years of age. The first-place prizewinners are granted the opportunity to compete at the national level. The national champions are, in turn, invited to represent their country at the annual International Brain Bee competition, which is hosted by different neuroscience organisations during an international conference.

Are you looking for a new challenge? Are you interested in neuroscience communication and engagement with schools? Would you like to contribute to and support the growing initiative that aims to promote neuroscience education and career in schools? Then join us as a Brain Bee Ambassador!

British Brain Bee is a non-profit organisation that runs outreach neuroscience initiatives in the UK. Our goal is to promote the advancement of neuroscience education at schools. We do this by running the British Brain Bee annual competition.

This year we are expanding massively and we have many ambitious plans. One of them is to visit schools to give talks to students about neuroscience research, careers and the Brain Bee competition. As a scientist would you like to become a Brain Bee Ambassador in your region? Your duties would be to:

- Promote the Brain Bee and neuroscience in schools of your region
- Organise a regional Brain Bee competition and select a regional winner
- Visit schools in your region
- Fundraise for the initiative
- Have fun…bzzz!

Inês Barreiros
PhD student in Neuroscience, University of Oxford

The NeuroMethods Slack Group

Have you tried setting up or optimising a new technique in the lab? Then you have likely run into endless, exasperating troubleshooting. With research articles' methods sections often missing critical details, fine-tuning or implementing a new technique can be challenging. But now you can find the help you need to make this endeavour more manageable at the NeuroMethods Slack group, a collaborative platform for troubleshooting methods in neuroscience.

Traditionally, researchers largely restrict themselves to advice from supervisors, labmates, or the local science communities, when trying to supplement the information gathered from papers on particular methods. This can be problematic if you belong to a small neuroscience community or the technique you are trying to implement is relatively new. While email technology has been around for a while and writing to distant authors asking for more details is also an option, something researchers are not famous for is swift email replies.

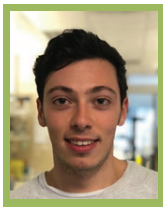
Instantaneous messaging and numerous social and teamwork media platforms have reinvented the way people communicate. Using these to promote open, collaborative research can revolutionise how we do troubleshooting in science. Thinking of this, Benjamin Saunders, group leader at the University of Minnesota, created NeuroMethods (neuromethods.slack.com), an open Slack (1) workspace that brings together researchers from 'different labs working on similar techniques that can share questions and insights'.

At NeuroMethods, researchers can quickly ask for advice and discuss practical details of research techniques with fellow neuroscientists from all over the world. Discussions are organised into specialised channels with topics ranging from experimental to theoretical, from molecular to systems neuroscience. Current channels include: mouse lines, *Drosophila* methods, immunohistochemistry, tracing, electrophysiology, *in vivo* imaging, statistical analysis and data visualisation. And you can easily set up a new channel if the method you are looking for hasn't been added yet.

So next time you try troubleshooting a new technique, keep calm and read the ongoing discussions or ask for more advice at its NeuroMethods channel. And, even if you are using methods fully established in your group, join the platform and share your expertise with the global neuroscience community.

Joining NeuroMethods: you can join by simply creating a Slack account, if your university email domain is listed at neuromethods.slack.com, or by invitation from any current member. If you would like an invitation, you can contact Benjamin Saunders via email (saunderslab.umn@gmail.com) or Twitter (@BenSaunders).

1. **Perkel JM .** (2017) How scientists use Slack. *Nature News* 541(7635):123.



Francesco Monaca
Undergraduate student in Biomedical Sciences, University of Southampton

Flies on a treadmill

Sleep is a scientific mystery. Now, fruit flies (*Drosophila melanogaster*) placed on a spherical treadmill are offering insights into the mechanisms regulating this marvellous yet poorly understood biological process.

In *Drosophila*, a population of dopaminergic neurons projecting to the 'dorsal fan-shaped body' (dFB) of the central complex (a region running across the midline of the insect brain) has been observed to induce sleep when stimulated. It is therefore plausible to believe that dFB neurons effectively act as a switch between quiescent and active states, with Dop1R2 receptors mediating the arousing effects of dopamine.

To test this idea and characterise the mechanisms underlying the dopamine-modulated switch, the behaviour of head-fixed experimental flies on treadmills was studied while wake-promoting signals resulting in dopamine release were delivered via optogenetics.

Interestingly, this research highlighted that optogenetic stimulation of dFB neurons resulted in their transient hyperpolarisation and concomitant awakening of flies. Both effects were mediated by dopamine interacting with Dop1R2 receptors.

Surprisingly, while single dopamine pulses silenced dFB neurons temporarily, prolonged dopamine supply switched these neurons to the OFF (inactive) state, in which they remained even in the absence of transmitter. The speed of transition between ON and OFF states suggested that the translocation of ion channels to the plasma membrane could effectively be the mechanism underlying this switch, accounting for the increased potassium conductances and subsequent hyperpolarisation of dFB neurons observed when flies wake up.

Two main types of channels are expressed in dFB neurons in their ON, electrically active state, namely Shaker and Shab. Currents associated with these two channels are downregulated when cells are switched to their OFF state by dopamine, whereas voltage-independent leak currents are upregulated through a channel termed Sandman.

Therefore, in response to dopamine, Sandman is internalised within the plasma membrane and its hyperpolarising current, along with the attenuation of Shaker and Shab, is responsible for the transition of dFB neurons into OFF state, triggering awakening of flies.

The next big step for sleep researchers would now be understanding the molecular players influencing this homeostatic switch.

This article together with references can be found at: **https://www.bna.org.uk/publications/bright-brains/bb-online/**.

Marios Panayi, PhD
Postdoctoral scientist in Neuroscience, University of Oxford

17th International Conference on Monitoring Molecules in Neuroscience

The University of Oxford hosted the 17th International Conference on Monitoring Molecules in Neuroscience (MMiN; www.2018.monitoringmolecules.org) on 25–28 March. This conference brought together scientists from around the world at the forefront of developing and using neurochemical tools to understand the brain and behaviour.

The meeting kicked off with a plenary symposium celebrating the inspirational life and work of Marianne Fillenz, who fled the Nazis as a child in Eastern Europe and eventually became a highly accomplished researcher and academic at Oxford. She was one of the first to develop and use voltammetry to measure dopamine release in the rat striatum, the focus of much of the research discussed at MMiN.

Dopamine was the neurotransmitter of interest in many of the posters and talks at this meeting. Dopamine release in the mesolimbic pathway (i.e. dopamine neurons projecting from the midbrain to the striatum) is commonly thought of as the pleasure molecule, and is associated with learning and rewards such as food, sex and drugs. However, the recurring theme at the meeting was that midbrain dopamine is not just involved in learning and pleasure, but also in surprise, novelty, pain and even punishment. For example, my lab (www.waltonlab.org) presented data showing dopamine release in the nucleus accumbens of mice in response to pairs of stimuli (e.g. neutral lights). Dopamine release showed stimulus-specific habituation: dopamine levels decreased if the same light was repeated twice, but remained high when both lights changed.

Following these interesting symposia were an impressive line-up of plenary speakers including **David Attwell** looking at the role of blood flow control in health and disease, **Andrew Ewing** measuring synaptic vesicle function at impressive scales, **Bita Moghaddam** discussing the multiple properties of prefrontal dopamine, and **Ann Graybiel** highlighting the importance of translational/cross-species approaches.

The conference also held a seminar to discuss the issues of attracting and retaining women and ethnic minorities in science. It was encouraging to see many senior and junior researchers at different stages attending and openly discussing this important issue.

The conference ended on a high with a picturesque reception and dinner at Somerville College, and many important conversations over drinks. The next MMiN conference will be held in Lyon (France) from 28 June to 1 July 2020, and is bound to be just as exciting.

VARIETAS NUMQUID SCIEBAS...?

Joshua Au-Yeung, MBBS
FY2 Doctor in Stroke Medicine,
NHS Northern Care Alliance

Neurosurgeon of the millennium

Robin Sengupta is a prominent neurosurgeon who has been dubbed 'neurosurgeon of the millennium' by the Indian Neurological Association. He was awarded an OBE and the Medal of Honour by the World Federation of Neurological Surgeons for his contributions.

Sengupta was born into poverty in Chittagong, India. His family could not afford to send him to school, so he would just read each and every book that he could get his hands on. Eventually he was able to pay for school by tutoring younger students. He soon defied all odds to gain a place in medical school in Kolkata, India. After graduating, he moved to study surgery in Newcastle-upon-Tyne, UK. He stayed in Newcastle for 51 years, working as a leading neurosurgeon, carrying out cutting-edge research and treating countless patients.

During his neurosurgical training, he became interested in cerebral aneurysm operations. An aneurysm is characterised by weakness in the walls of a vein or an artery. Aneurysms can be congenital or acquired through life and exacerbated by lifestyle factors such as diet, exercise, smoking and alcoholism. When the vascular wall components are weakened, the weak section can expand and 'balloon'. The danger is that a weakened aneurysm is prone to bursting or leaking. It goes without saying that the mortality and functional impact of a ruptured cerebral aneurysm can be very serious.

In a time where there was no protocol or consensus on how to manage intracranial aneurysmal haemorrhages, Sengupta strived to improve our knowledge and management of these patients.

He travelled across the world visiting different neurosurgeons to learn new skills and management styles. He identified risk factors and procedures that conferred good outcomes in aneurysm surgery and adapted them into his own practice. He then published a paper detailing 32 anterior communicating artery operations that he had carried out using what he had learnt; his ability to complete the operations with a mortality rate of zero was unheard of at the time. His pioneering technique and positive outcomes led to referrals from around the UK and internationally.

After dedicating much of his life to the NHS, Sengupta wanted to fulfil his own vision for delivering high-quality, affordable healthcare to people in India. He decided to return to Kolkata, where it all began, and established the Institute of Neuroscience, Kolkata (IN-K). Today, the IN-K is one of the best specialty hospitals in India for treatment, education and research in the field of neurology and neurosurgery.

This article in full together with references can be found at: **https://www.bna.org.uk/publications/bright-brains/bb-online/**.

VARIETAS QUID NOVI?

Inês Barreiros
PhD student in Neuroscience,
University of Oxford

Navigating cognitive map research

In 2014 the Nobel Prize in Physiology or Medicine was awarded to John O'Keefe and to Edvard and May-Britt Moser 'for their discoveries of cells that constitute a positioning system in the brain'. Four years later, neuroscientists from all around the world who do research on these cells gathered in London to discuss and put into perspective the advances in the field. The two-day Grid Cell Meeting was held at the Sainsbury Wellcome Centre for Neural Circuits and Behaviour on 21–22 May 2018.

Since the original work on place and grid cells that led to the Nobel Prize, research has revealed that these neurons are important for much more than the encoding of spatial location. Accordingly, talks were grouped into sessions that spanned navigation in physical space to the representation of abstract relational knowledge, and from experimental to theoretical research. At the end of the first day, a data blitz session covered some of the most recent research through a series of short five-minute talks. The poster session that followed was combined with a well-received barbecue.

The meeting closed with a panel discussion around what grid and place cells are and what they truly encode. It was noted that, due to the wide range of environmental features that can be represented by these cells, we may come to conclude that the hippocampus is a general-purpose information-mapping system. However, it was also pointed out that we still have a very poor understanding of how hippocampal cells encode fundamental features such as time. What is more, it was widely agreed that we must try to integrate cross-species experimental research with computational modelling.

The event was free to attend but oversubscribed, so not everyone interested managed to get a place. However, most talks were livestreamed. Being unable to secure a place myself, I 'attended' the conference from my sofa at home. Even though I missed the poster session and the opportunity to participate in the discussions, I could pause the talks and repeat some parts if I did not understand something well at first. Video recordings of the streamed talks will be made available on the meeting website. So, if you missed the event, you can still watch the talks at www.cognitive-map.com.

Panel discussion at the Grid Cell Meeting.

VARIETAS THE BNA CROSSWORD

How well do you know your brain?

Test your knowledge by completing this super-easy crossword on cellular mechanisms of the human nervous system. Answers will be revealed in the next edition, while answers to last edition's puzzle are provided at the bottom of the page.

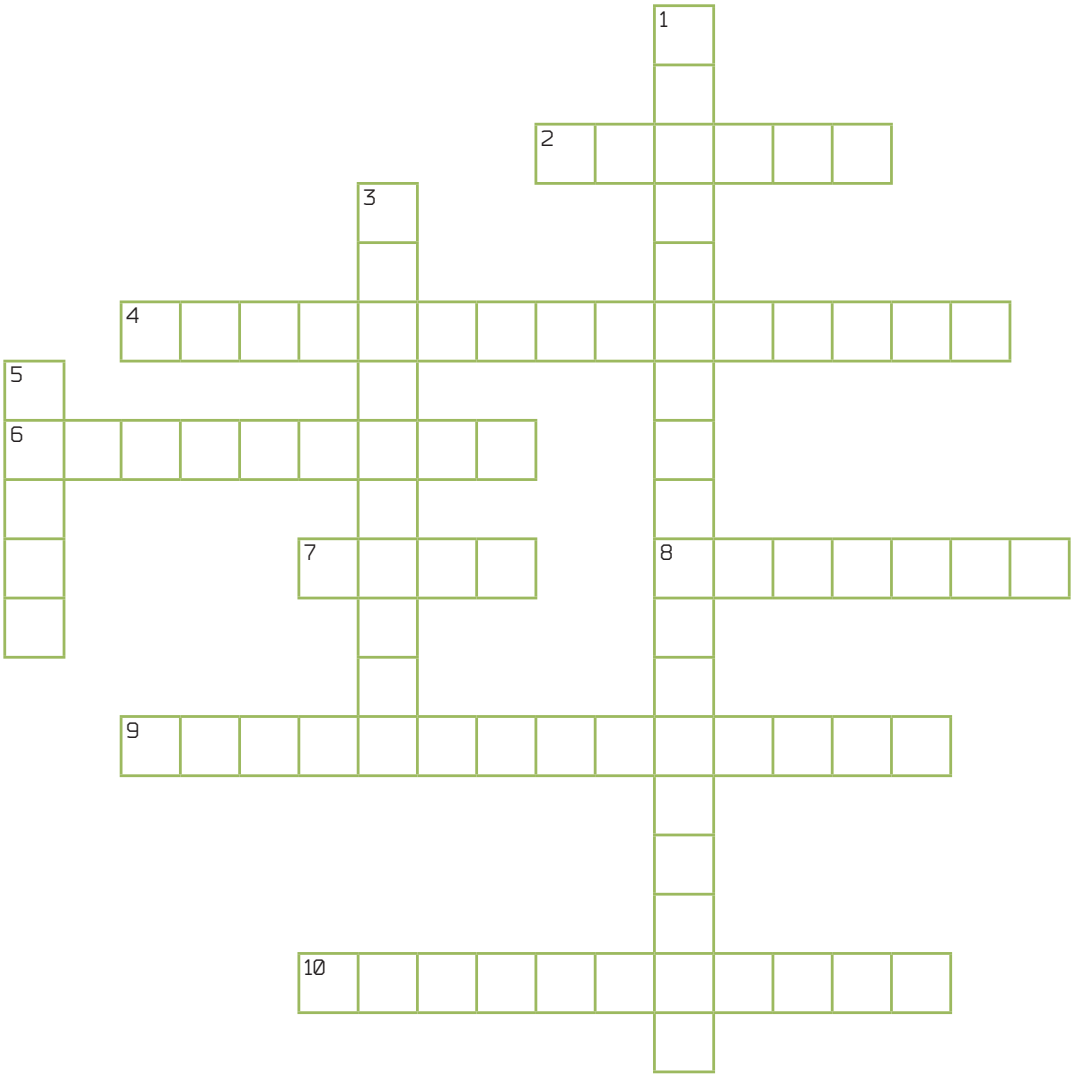
Enter this edition's competition by sending your answers to jayanthinykangatharan@gmail.com. Entries received before 1 September 2018 will be entered into a prize draw to win a unique contribution towards the 'Bright Brains' autumn edition!

ACROSS

2. What allows for the rapid transmission of an action potential down an axon via salutatory conduction?
4. What type of glial cell forms myelin in the central nervous system?
6. What type of glial cell forms the blood-brain barrier?
7. What is the body of a neuron called?
8. What are neurotransmitters also being referred to?
9. What equation is used to find the equilibrium potential for an ion?
10. What type of glial cell forms myelin in the peripheral nervous system?

DOWN

1. What does the asymmetrical distribution of ions across the membrane lead to?
3. By what process are neurotransmitters released in the synaptic terminal?
5. Ion channels can be either passive or...?



Answer to the puzzle from Issue 8 – Spring 2018

The answer to the first BNA Bright Brains puzzle is 'Keep expanding your consciousness.'