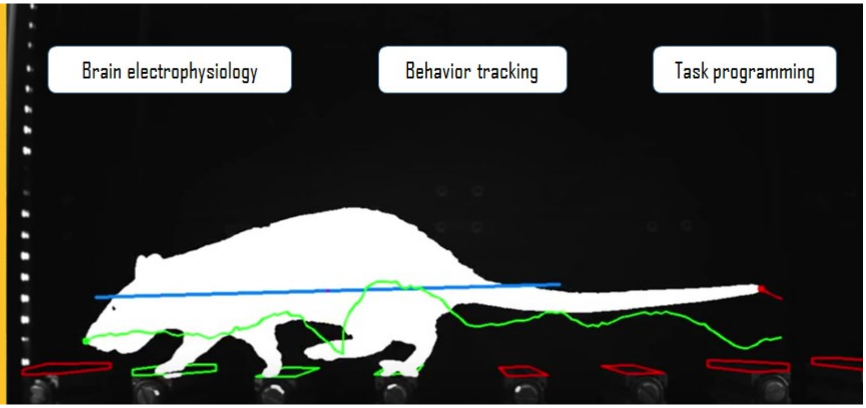
ADVANCED COURSE

Advanced Neurophysiology and Behavior



SUMMARY

Contemporary neuroscience relies on precise measurements of neural activity and behaviour obtained using sophisticated instruments controlled by computer programs. Commercial software packages are available for controlling behavioural and neural data acquisition but they are often **expensive, closed, inflexible** and specialised in a data modality, requiring researchers to constantly patch together diverse pieces of software. Moreover, the experimental approaches used to acquire data in the first place are **complex and interdisciplinary**, not to mention technically-challenging. Students and novel practitioners are therefore often overwhelmed, resorting to a **“black box”**, “need-to-know” strategy when learning these techniques and procedures.

Our ultimate goal with the course **"Advanced Neurophysiology and Behavior: Empowering and Open Source Experimental Neuroscience"** is to break down these barriers of understanding in two specific domains: the computerised **control of data acquisition and experimental protocols**, and the **theory and practise of neurophysiology**.

In one component of the course, we will provide training in basic concepts of the **Bonsai visual programming language**, which can be used to develop **software for recording, controlling, analysing, and manipulating video, as well as behavioural and neural activity data**. In the other, we will train students in the **theory and practise of neurophysiology**, with special emphasis on **patch-clamp**. Instead of equivalent circuit diagrams and other electronic engineering concepts, we will keep **real, biological neurons front and centre**, focusing on **how these concepts apply to understanding neuronal and brain function**.

This course concentrates top-level international expertise in a single hands-on program focused on applications to experimental systems neuroscience. The goal of the course is to empower students with the tools and skills to design and construct their own experimental instruments and setups, as well as to encourage a spirit of critical thinking, experimental boldness and theoretical de-mystification. This will enable participants to go back to their labs and immediately apply the acquired knowledge to design experiments that go beyond the available turn-key solutions.

PROGRAMME

Neurophysiology	**Behaviour**
Session 1 - Introduction to neurophysiology ● What is “special” about neurons and the nervous system? Evolutionary considerations on the function and modes of communication of the nervous system. ● What is neurophysiology and what tools do we use to study it? ● Why so many tools? Levels of analysis and scales in the nervous system. ● One neuron. Things they don’t tell you about spikes. ● Two neurons. Things they don’t tell you about synapses. ● Many neurons. Things they don’t tell you about extracellular recordings. ● Wrap-up: where we are in neuroscience, and why we’ll need micropipettes and electrodes for decades to come.	Session 1 - Introduction to data acquisition and behavioural control ● How to measure almost anything with a computer. From quantities to bytes. ● How to control almost anything with a computer. From bytes to effects. ● What is a programming language, and why should you care? Introduction to Bonsai. ● How to measure and control multiple things at the same time with one computer. ● The impact of measurement and control technologies in the study of behaviour: past, present, and future.
Session 2 - Neural electricity ● Membranes, why they matter, and what’s on them. ● Between -50 and -80 mV: where does the resting membrane potential come from? Equilibrium potentials, driving forces, Nernst and GHK equations. ● From -65 to +40 mV: ligand- and voltage-gated channels and the spike. ● From +40 to infinity: active and passive properties as functional-molecular fingerprints of neurons. ● Wrap-up: thinking of currents as if/while statements and simple lines of code.	Session 2 - Cameras, tracking and microcontrollers ● Measuring behavior using video. From photons to pixels. ● Recording real-time video from multiple cameras. ● Real-time tracking of colored objects, moving objects and contrasting objects: the basic toolkit. ● Measuring behavior using voltages and an Arduino. ● A primer on data synchronization: on what frame did the light turn on?
Session 3 - Recording from neurons with patch-clamp ● If you like it, then you should’ve put a seal on it: the art and science of patch-clamping. ● The whole-cell patch-clamp experiment: leaks, access resistance, capacitance. ● From whole-cell to cell-attached to extracellular - the same principles hold along a continuum of approaches. ● Current- and Voltage-clamp: when and why? ● Wrap-up: Limitations of patch-clamp: space-clamp and dendritic filtering.	Session 3 - Real-time closed-loop experimentation ● What can we learn from closed-loop experiments? ● Conditional effects. Triggering a stimulus based on video activity. ● Continuous feedback. Modulate stimulus intensity with speed or distance. ● Feedback stabilization. Record video centered around a moving object. ● Measuring closed-loop latency.
Session 4 - The Big Picture: what is the point of all this? Examples of practical applications. ● Exploiting equilibrium potentials: uncaging, intracellular solutions and distinguishing glutamate from GABA. ● Neurons do more than integrate and fire: burst and tonic firing modes in thalamic relay neurons. ● A safari of GABAergic interneurons: how active and passive properties relate to function in the nervous system.	Session 4 - Operant behavior tasks ● Modeling trial sequences: state machines and events. ● Driving state transitions with external inputs. ● Choice, timeouts and conditional logic: the basic building blocks of reaction time, Go/No-Go and 2AFC tasks. ● Combining real-time and non real-time logic for good measure. ● Student project brainstorming
Session 5 - Acute Slice Physiology practical demonstration and experiments ● How to prepare acute slices ● Whole-cell current clamp recordings ● Whole-cell voltage-clamp recordings ● Loose-seal recordings ● Extracellular recordings ● Optogenetic stimulation ● Basic analysis: event detection and feature extraction	Session 5 - Final projects ● Custom behavior tracking ● Interactive visual stimulation ● Audio acquisition and stimulation ● Student project preparation and presentation

ORGANIZATION AND TEACHING STAFF:

Andre Marques-Smith
Sainsbury Wellcome Centre, University College London, London, UK

Andre did an undergraduate degree in Psychology, at Universidade do Minho. He then moved to the University of Oxford, where he completed the Wellcome-Trust PhD programme in Neuroscience with Zoltan Molnar and Simon Butt, using slice electrophysiology, optogenetics and glutamate uncaging to map early circuits between excitatory and inhibitory neurons in the cortex. He followed up this research during a postdoc with Beatriz Rico at King's College London. He is currently a Sir Henry-Wellcome Postdoctoral Fellow at the Sainsbury-Wellcome Centre for Neural Circuits and Behaviour, where he collaborates with Sonja Hofer and Adam Kampff on investigating the anatomy, electrophysiology and in vivo role of inhibitory circuits in the thalamus.

Andre has extensive experience with patch-clamp electrophysiology in vitro and in vivo, as well as extracellular recordings in vivo with state-of-the-art Neuropixels probes.

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Gonçalo Lopes
NeuroGEARS Ltd
Sainsbury Wellcome Centre, University College London, London, UK

Gonçalo moved from software engineering to neuroscience to study the behaviour of intelligent systems. He joined the Champalimaud Foundation Neuroscience Programme and completed his PhD with Adam Kampff and Joe Paton, studying the role of motor cortex in the robust control of movement. Gonçalo developed the Bonsai visual programming language as a way to rapidly prototype real-time closed loop behavioral experiments and automating data acquisition protocols for neurophysiology. He followed up this research at the Sainsbury Wellcome Centre in London, before deciding to start a technology company, NeuroGEARS Ltd, with the goal of empowering scientists to build their own tools.

Gonçalo regularly teaches about technology and behavior in many hands-on experimental courses like TENSS or BNS, where he shares his experience developing interactive real-time systems.

Hugo Almeida
Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal
ICVS/3B's - PT Government Associate Laboratory, Braga/Guimarães, Portugal

Hugo Leite-Almeida is a researcher at the ICVS/3B's PT-Government Associate Laboratory and teaches in undergraduate (e.g. histology) as well as in multiple post graduation courses (e.g. Fundamentals in Neurosciences) at the School of Medicine, University of Minho. He holds a BSc degree in Biochemistry (University of Porto) and a PhD degree in Health Sciences (University of Minho). His main line of research deals with the causality relation between peripheral neuropathies and pain, mood and cognitive function. From a methodological point of view, his approaches have been diverse and include anatomical tracing, stereology, electrophysiology, immunohistochemistry, HPLC and rodent behavior. He and his colleagues have been developing diverse behavioral paradigms like the variable delay-to-signal (VDS) for impulsivity assessment in rodents.

He received the Early Career Research grant from the International Association for the Study of Pain (IASP)I in 2015.

Patrícia Monteiro
Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal
ICVS/3B's - PT Government Associate Laboratory, Braga/Guimarães, Portugal

Patricia Monteiro is a researcher at the Neuroscience Research Domain, ICVS/School of Medicine, University of Minho. She holds a BSc/MSc degree in Pharmaceutical Sciences (University of Coimbra) and a PhD degree in Neurosciences (international PhD program in Experimental Biology and Biomedicine, University of Coimbra). She did her Ph.D. training with Dr. Guoping Feng at the Massachusetts Institute of Technology (MIT, USA), where she focused on understanding brain circuitry mechanisms underlying repetitive behaviors present in obsessive-compulsive (OCD) and autism-spectrum disorders (ASD). During her postdoc, Patricia has been awarded an EMBO postdoctoral fellowship as well as a Branco Weiss fellowship, to study how stress impacts brain networks. Her research at ICVS now focuses on new approaches to tackle brain disorders.

Patricia has extensive experience with patch-clamp electrophysiology *in vitro* and *ex vivo*, as well as transgenic mice and molecular biochemistry.

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