Imperial College Centre for Neurotechnology

ANNUAL REPORT | 2015

Centre for NEUROTECHNOLOGY

Director's foreword

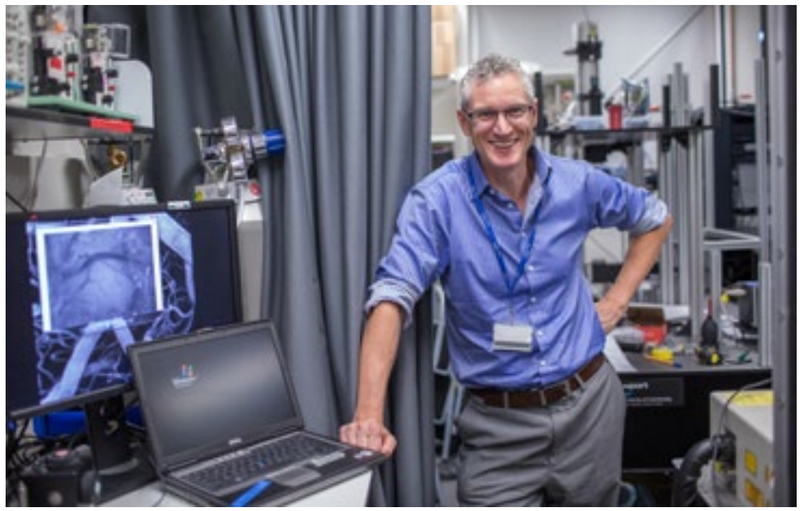
I am delighted to introduce the first Annual Report of the Centre for Neurotechnology.

The Centre brings together interdisciplinary teams working at the interface between Neuroscience and Engineering, and spans three Faculties at Imperial College (Engineering, Medicine and Natural Sciences) and numerous academic departments. Brain-related illnesses affect over two billion people worldwide, and are having an increasing impact on healthcare resources. By harnessing novel technological approaches, we hope to not only improve our understanding of how the brain works, but also to develop new therapeutic strategies to treat its disorders.

The Centre was initiated with the launch of the EPSRC Centre for Doctoral Training in Neurotechnology for Life and Health (the CDT), which brings together government, industry and charity funding to train a new generation of multidisciplinary researchers working to develop and harness new technologies for understanding and treating brain disorders. You will read more about the CDT – and the remarkable students who have made up its first intake – in the pages of this Annual Report.

However, the Centre clearly is becoming a catalyst for a larger focus on research in this area having already attracted substantial additional funding, including over £500,000 of funding from the EPSRC and from industry collaborators to establish equipment and collaborative research facilities for the Centre, and a £500,000 philanthropic donation for research applying a biomedical engineering approach to Alzheimer's Disease. I hope that it will continue to provide the critical mass necessary to attract new investment into this area. Above all, the Centre creates a thriving environment for bringing different disciplines and perspectives together to solve difficult problems in neuroscience - a "hothouse" of inter-disciplinary activity that we hope will result in new ways of thinking, new approaches to studying brain function, and new tools for treating brain disorders.

On behalf of Imperial College, I would like to thank all those who have provided the support that has allowed us to get the Centre off the ground. I hope that in reading this report, you will see not only quite how substantial the activity that you have helped to create is already, but also how the Centre will "change the landscape" of UK brain research, bringing new ways of looking at problems of great importance to our society.



Dr Simon Schultz
BSc BE ME(Res) DPhil FIET

ABOUT US

Established in 2014, the Centre for Neurotechnology is one of the research centres of Imperial College's Institute of Biomedical Engineering (IBME). The centre spans the Faculties of Engineering, Medicine and Natural Sciences at Imperial College and has satellites at Oxford, UCL and the Francis Crick Institute.

The Centre hosts the EPSRC Centre for Doctoral Training in Neurotechnology for Life and Health (the CDT), which offers a unique training programme, created by Imperial College in collaboration with 20 partners in industry and the charity sector. Working in cross-disciplinary teams, CDT students will undertake 4 years of training which will allow them to develop and harness new technologies for understanding and treating brain disorders

People

Centre Management

Simon Schultz
Director

Reader in Neurotechnology
Royal Society Industry Fellow
Department of Bioengineering

Paul Matthews
Co-Director

Edmond and Lily Safra Chair of Translational Neuroscience and Therapeutics
Head, Division of Brain Sciences
Department of Medicine

Bill Wisden
Co-Director

Chair of Molecular Neuroscience
Department of Life Sciences

ADMINISTRATIVE STAFF

Kate Hobson	Centre Administrator
Harry Lamble	Research Development Director (Institute of Biomedical Engineering)

OPERATIONS BOARD

Simon Schultz	Director
Kate Hobson	Centre Administrator
Paul Chadderton	Academic member (Bioengineering)
Adam Hampshire	Academic member (Brain Sciences)
Claudia Clopath	Academic member (Bioengineering), CDT mentor, cohort 1
Dan Goodman	Academic member (Electrical & Electronic Engineering), CDT mentor, cohort 2

RESEARCH BOARD

Mauricio Barahona	Mathematics
Martyn Boutelle	Bioengineering
Stephen Brickley	Life Sciences
Denis Burdakov	Crick Institute
Paul Chadderton	Bioengineering
Claudia Clopath	Bioengineering
Tim Constandinou	Electrical & Electronic Engineering
Aldo Faisal	Bioengineering/Computing
Dan Goodman	Electrical and Electronic Engineering
Adam Hampshire	Brain Sciences
Paul Matthews	Brain Sciences
Mark Neil	Physics
Richard Reynolds	Brain Sciences
Simon Schultz	Bioengineering
David Sharp	Brain Sciences
Richard Syms	Electrical & Electronic Engineering
Ravi Vaidyanathan	Mechanical Engineering
Bill Wisden	Life Sciences

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John Daniel	Vice President, Research & Development, Stryker Neurovascular
Caroline Hargrove	Technical Director, McLaren Applied Technologies
Stéphanie Lacour	Chair in Neuroprosthetic Technology, EPFL
Keith Mathieson (chair)	Director of Institute of Photonics, University of Strathclyde
John O'Keefe	Professor of Cognitive Neuroscience, University College London
Thomas Stieglitz	Head of Biomedical Microtechnology Laboratory, Bernstein Centre
Keith Wafford	Principal Research Scientist, Eli Lilly Research Laboratories UK
John White	Professor of Biomedical Engineering University of Boston

Centre Members

IMPERIAL COLLEGE ACADEMIC STAFF

Mauricio Barahona	Mathematics
Anil Bharath	Bioengineering
Martyn Boutelle	Bioengineering
Stephen Brickley	Life Sciences
Denis Burdakov	Crick Institute
Etienne Burdet	Bioengineering
Paul Chadderton	Bioengineering
James Choi	Bioengineering
Claudia Clopath	Bioengineering
Tim Constandinou	Electrical & Electronic Engineering
Vincenzo De Paola	Institute of Clinical Science
Simone di Giovanni	Brain Sciences
Manos Drakakis	Bioengineering
Aldo Faisal	Bioengineering/Computing
Giorgio Gilestro	Life Sciences
Dan Goodman	Electrical & Electronic Engineering
Adam Hampshire	Brain Sciences
Thomas Knöpfel	Brain Sciences
Mirko Kovac	Aeronautics
Andrei Kozlov	Bioengineering
Holger Krapp	Bioengineering
Rob Leech	Brain Sciences
Nick Long	Chemistry
Danilo Mandic	Electrical & Electronic Engineering
Paul Matthews	Brain Sciences
Dipankar Nandi	Brain Sciences
Mark Neil	Physics
Kenji Okuse	Brain Sciences
Tobias Reichenbach	Bioengineering
Richard Reynolds	Brain Sciences
Esther Rodriguez-Villegas	Electrical & Electronic Engineering
Simon Schultz	Bioengineering
Barry Seemungal	Brain Sciences
David Sharp	Brain Sciences
Molly Stevens	Materials/Bioengineering
Richard Syms	Electrical & Electronic Engineering
Mengxing Tang	Bioengineering
Ravi Vaidyanathan	Mechanical Engineering
Ramon Vilar	Chemistry
Bill Wisden	Life Sciences

SATELLITE MEMBERS

MRC Brain Network Dynamics Unit, University of Oxford
Director – Peter Brown
Deputy Director – Peter Magill

Francis Crick Institute
Denis Burdakov
Ede Rancz
Andreas Schaefer

Sainsbury Wellcome Centre, UCL
Troy Margrie

RESEARCH FELLOWS

Amir Eftekhar	Electrical & Electronic Engineering
Amanda Foust	Bioengineering
Peter Hellyer	Bioengineering

RESEARCH STUDENTS

Cher Bachar
Tamara Boltersdorf
Tiffany Chan
James Clarke
Darije Custovic
Sofia Dall'Orso
Catriona Egan
Andrea Fiorentino
Lewis Formstone
Patricia Gallego
Katie King
Tim Kirby
Rajinder Lotay
Carl Lubba
Diana Lucaci
Gerald Moore
Konstantinos Petkos
Peter Quicke
Tom Robins
Benedikt Schoenhense
Hugo Weissbart
Aidan Wickham
Georgios Zafeiropoulos

SPONSORS AND PARTNERS

The Centre and CDT are grateful for the support of the following partner organisations:

EPSRC
Engineering and Physical Sciences Research Council

NIHR Imperial BRC
Translating research into patient benefits

gsk GlaxoSmithKline

McLaren APPLIED TECHNOLOGIES

Medtronic

Scientifica
Experts in Electrophysiology

In addition the Centre has developed significant relationships with the affiliates listed below and is working to form links with new companies.

Biorobots LLC

ELEKTA

JAMES DYSON FOUNDATION

GREAT LAKES NEUROTECHNOLOGIES

NEURAL SIGNALS

Johnson & Johnson

Office of Naval Research ONR Science & Technology

ÖSSUR

stryker

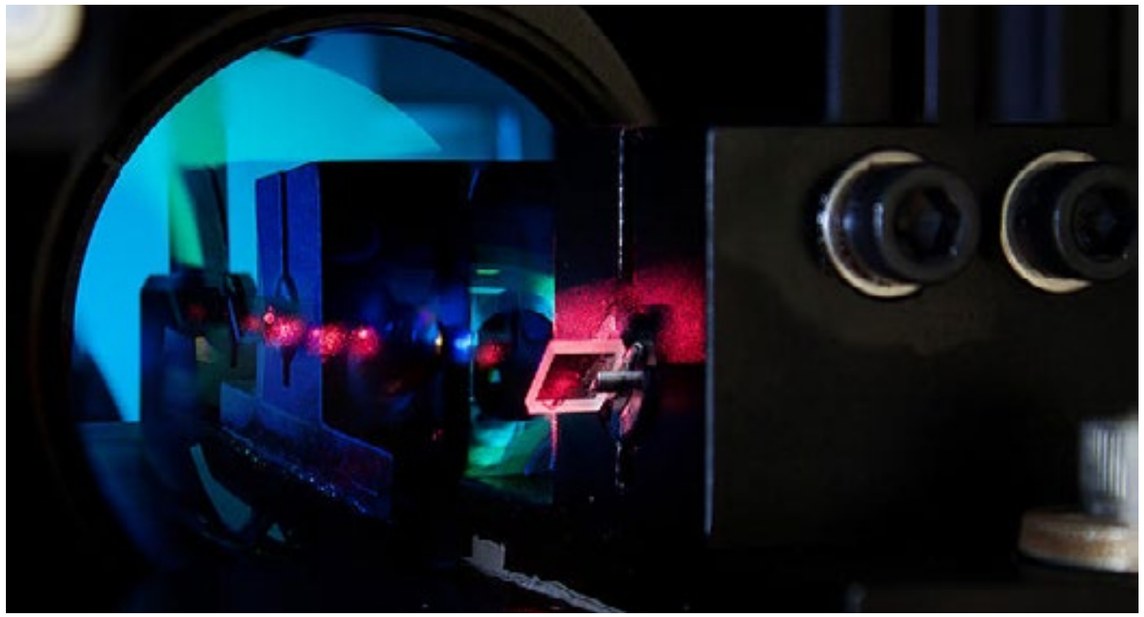
Medfield DIAGNOSTICS

Sapiens Steering Brain Stimulation

PARKINSON'S UK
CHANGE ATTITUDES. FIND A CURE. JOIN US.

VERTEX
THE SCIENCE of POSSIBILITY

We would like to thank our current partners and affiliates who, along with our academic partners (satellite members), have provided valued input and support to the Centre and CDT, from helping to shape the thematic structure of the Centre and prepare the initial proposal for the CDT itself, through offering expertise, equipment and supervision to our members and students, to providing internships for our CDT students and funding for studentships.



Research facilities

Recent funding from the EPSRC has enabled the Centre to establish state-of-the-art research facilities which build on existing resources available at the College for neurotechnology research.

CONNECTOMICS FACILITY

Connectomics is the production and study of comprehensive maps of an organism's nervous system. It uses high-throughput imaging and histological procedures to map neural connections – the underlying premise being that, to understand (and repair) a circuit, it is necessary to obtain its "wiring diagram". Connectomic studies of cortical tissue show substantial promise to make advances in understanding brain disorders such as dementia, a major translational focus of the CDT in Neurotechnology for Life and Health. The Centre for Neurotechnology has, thanks to equipment funds from the EPSRC, together with contributions from a number of research laboratories at Imperial, recently been able to establish a cellular resolution Connectomics Facility based on a TissueVision TissueCyte1000 serial two photon tomography platform. This platform allows axon tracing to be performed, with single cell resolution, in whole mouse brains, or large sections of a human brain. While the microscopy hardware is now in place, and working, substantial research still needs to be carried out on the informatics tools required to analyse these very large datasets. The development of this technology will be a key activity within the Centre.

NON-INVASIVE HUMAN BRAIN SIGNAL RECORDING AND STIMULATION FACILITY

Noninvasive technologies for assessing cognitive processes, diagnosing brain impairments and brain-machine interfacing are a key component of neurotechnology. The development of novel noninvasive biomarkers is a key diagnosis technology for dementia and other brain disorders; similarly, noninvasive techniques for brain stimulation using transcranial electrical stimulation (TES) offer the possibility of advances in treatment for brain disorders, but needs substantial research in order to understand the neurobiological basis of their effects.

This facility comprises a number of noninvasive recording (EEG, EMG, fNIRS) and stimulation (TES) technologies, which complement existing resources at Imperial College (fMRI, DTI, TMS). The Facility is distributed between South Kensington and Hammersmith campuses, with support and training capacity shared across user groups.

Wireless EMG system

The Delsys Trigno system from AD Instruments provides wireless recordings of muscle activity using surface electromyography (SEMG) electrodes. A diseased neurone will struggle to hold its membrane potential and so will spontaneously discharge, known as a fasciculati on potential. These fasciculation potentials result in muscle twitches that can be visible in motor units close to the skin surface. The wireless EMG system allows these fasciculations to be recorded and is completely non-penetrative; traditionally these potentials are recorded using needle EMG which can be very uncomfortable for the patient and is an unpleasant experience. The added wireless feature allows the patient to feel even more comfortable and relaxed. The Delsys Trigno system can communicate over 16 channels at a time; the current setup uses just 8 channels. Data recorded by the EMG system is then fed into an 8 channel PowerLab for signal analysis. The LabChart software is a powerful tool that can perform many different signal analyses to the incoming signal in real time.

High density, high temporal resolution EEG and EMG

This is a high-density EEG system from BrainProducts with 64 active electrodes that can sample electrical brain signals at rates of up to 100 kHz. The associated amplifier actiCHamp also allows connection of EMG sensors.

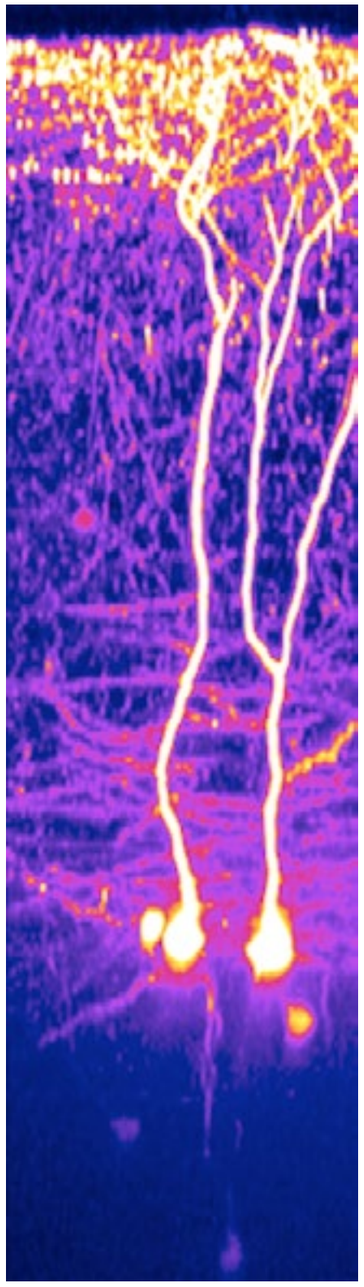
EEG compatible MRI system

This system is designed to do simultaneous EEG/fMRI experiments and can also be used to perform simultaneous EEG and brain stimulation experiments. The system is composed of a 32-channel amplifier with an additional 8 channel bipolar amplifier extension, which can be used to record electrooculogram or motor evoked potentials. It is equipped with a SyncBox to synchronize the EEG and MRI scanner clocks and a trigger cable to send TTL triggers to the EEG system from a computer running a behavioural task. The system has a USB 2 adapter (BUA) that allows the recording of up to 128 channels. The equipment includes two 32-channel MR compatible caps to fit different head sizes.

Multi-channel functional near-IR spectroscopy

Functional Near-Infrared Spectroscopy (fNIRS) is the use of non-invasive near-infrared spectroscopy for the purpose of functional neuroimaging without the need for an MRI scanner. Using fNIRS, brain activity is measured through hemodynamic responses associated with neural activity. fNIRS is a non-invasive imaging method involving the quantification of chromophore concentration resolved from the measurement of near infrared (NIR) light attenuation, temporal or phasic changes. This is achieved through a cap studded with IR LEDs and IR photosensors, and can be worn in virtually all situations in which EEG data can also be collected, providing great flexibility in terms of use scenarios and the ability to combine with other sensor modalities, such as integration with EEG and in experimental settings and applications were conventional scanner-based neuroimaging may not be suitable, such as brain -machine interfaces, wheelchairs, or moving subjects. fNIRS is a recently developed Neurotechnology that has great potential in terms of applications, and proved early successes in Brain -Machine -Interfaces, neonatal neuroimaging and combination with EEG in many situations (e.g. motor control etc.) were neuroimaging is not suitable or not effective. The hemodynamic response characteristics of the fNIRS signal and much of its analysis techniques are matching those encountered in fMRI data.

The Centre's research facilities are available for use by CDT students, members of the Centre and the wider academic community at Imperial College.



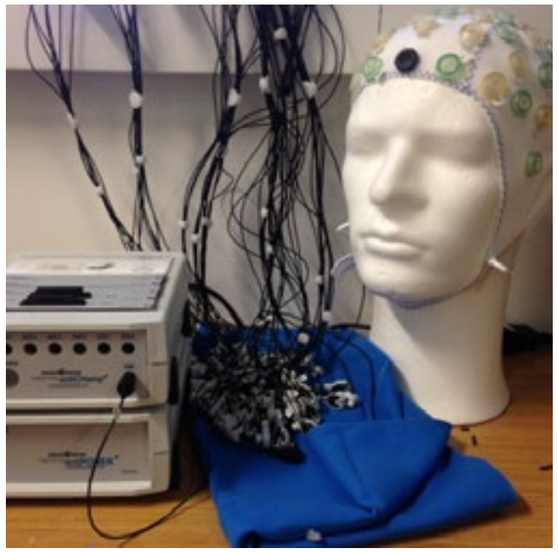
ORCA-FLASH SCMOS CAMERA

The Hammamatsu ORCA-flash sCMOS camera is a state-of-the-art digital camera for attachment to a microscope for imaging brain activity in animal models. The camera will allow novel widefield imaging applications of genetically encoded voltage sensors

to be pursued, maintaining Imperial at the forefront of this technology.

HIGH-PERFORMANCE COMPUTER SERVERS

Three new servers provide data storage as well as high-performance computing capability for the Centre research facilities. In addition to providing just over 32TB of RAID L5 storage, each machine also has a 8-core CPU, 64GB of RAM and 4 NVIDIA GPUs which are well-suited to analyzing large spatial datasets from imaging studies. With such hardware we can make use of both parallelisation and virtualisation, the former enabling the training of large



machine learning models and the latter allowing multiple application environments on the same physical machine. In addition to data storage, the servers have also been used to provide free training courses on high-performance GPU computing to industrial collaborators and researchers working on computationally demanding problems.

MULTIPHOTON IMAGING LAB

The Centre has use of a Two Photon Laser Scanning Microscopy Facility, established as a result of collaboration between Scientifica Ltd and the Schultz Laboratory. The facility comprises three Scientifica Multiphoton laser scanning microscopes: two galvanometric microscopes and one resonant scanning microscope. These microscopes allow fluorescence signals related to neural signalling to be imaged in live brain tissue

FLIM MODULE FOR TWO PHOTON MICROSCOPE

Attaching a Fluorescence Lifetime Imaging (FLIM) module to a two-photon microscope enables us to perform two-photon FRET-FLIM to monitor the activation of key signalling molecules such as cAMP, metabolic molecules such as glucose, ATP and calcium activated proteases such as calpains in light scattering tissue, i.e. in the cell natural environment. Centre equipment funds allowed a FLIM module to be installed on a two photon microscope located at Imperial College's MRC Clinical Sciences Centre, for the use of Centre members.

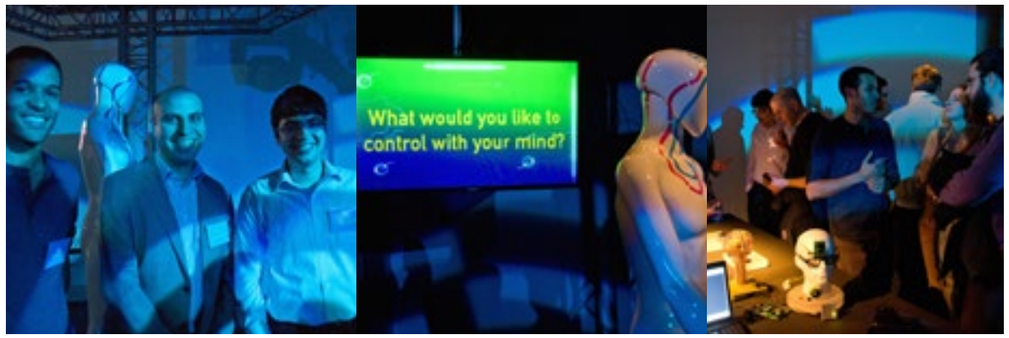
News | events

Some recent and upcoming activities and events involving Centre members are described below.

Neurotechnology Colloquium Series

Established in autumn 2014, the Centre for Neurotechnology colloquium series comprises monthly seminars on a variety of neurotechnology topics, presented by external speakers from the UK and overseas. The colloquia are open to Centre members and the wider academic community at Imperial College. A list of titles from the 2014-15 colloquium series is below:

- **Antoine Adamantidis, University of Bern**: *Optogenetic dissection of sleep-wake circuits in the brain* (Nov 2015)
- **Etienne Koechlin, INSERM, ENS, Paris**: *A computational approach to prefrontal executive function and human adaptive behavior* (Oct 2015)
- **John Duncan, University of Cambridge**: *Frontoparietal control systems in the assembly of cognitive episodes* (Sept 2015)
- **Peter Brown, University of Oxford**: *Novel temporally-patterned electrical stimulation techniques to treat Parkinson's disease and Tremor* (Jul 2015)
- **Richard Wade-Martins, University of Oxford**: *Translating Parkinson's: Modelling disease in human iPS cell and transgenic rodents for target discovery* (Jun 2015)
- **Dario Farina, Georg-August-University**: *Bionic Reconstruction of Upper Limb Function* (May 2015)
- **Tobias Moser, University of Göttingen**: *Optogenetic stimulation of the auditory pathway for research and future prosthetics* (Apr 2015)
- **Silvestro Micera: EPFL**: *Closing the loop in neuroprosthetics* (Mar 2015)
- **Andrew Jackson, Newcastle University**: *Applications of low-frequency local field potentials for Brain-Machine Interfaces* (Feb 2015)
- **Rodolphe Sepulchre, Cambridge University**: *Sensitivity analysis of neuronal behaviours* (Jan 2015)
- **Ted Milner, McGill University**: *Robot-assisted rehabilitation of hand function following stroke* (Nov 2014)



Neurotechnology Grand Challenges Event

A "Neurotechnology Grand Challenges" event was held in July 2014, bringing together engineers, scientist and clinicians to brainstorm projects for the CDT in Neurotechnology for Life and Health for October 2015. The day was a mix of facilitated discussion and short talks to set the scene, with perspectives on future prospects for neurotechnology. The event was well-attended with participants from the three academic faculties at Imperial College, plus representatives from the UK Dementia Platform and the Centre's industry partners including GlaxoSmithKline, Stryker Neurovascular and Scientifica. The Centre aims to run the event biennially with the next Grand Challenge provisionally scheduled for 2016.

Science Museum Lates

Centre member Tim Constandinou participated in the Science Museum Festival "You have been upgraded" on the topic of human enhancement in March 2015. Along with researchers from the Next Generation Neural Interfaces Lab/Centre for Bio-Inspired Technology, Dr Constandinou hosted the section on "implantable devices".

CDT Festival of Science and Engineering

Students from the CDT Neurotechnology participated in the fourth CDT Festival of Science at Imperial College, on 23rd April 2015. This annual event is a great opportunity for the 12 Imperial College CDTs to collaborate and gain a more detailed understanding of the work that is carried out in each field in order to present a showcase of current research and scientific issues to the research community of Imperial College London. This year's festival focussed on the theme of "Criticism & Science" and featured speakers from a number of disciplines and positions from both within and outside of academia.

Imperial Festival

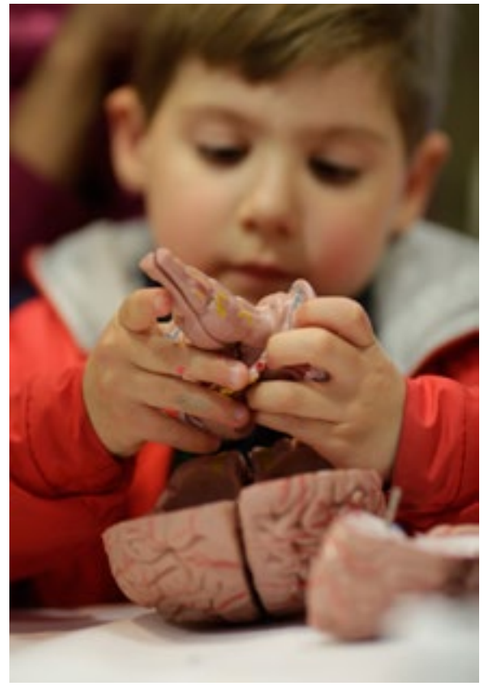
The annual Imperial Festival is dedicated to sharing the best science and arts on offer from Imperial College. This year more than 15,000 public and alumni visitors attended the festival to enjoy the stands, workshops, tours, talks and performances on offer. Members of the Centre were involved in a number of the activities taking place at the Festival and students from the Centre for Doctoral Training hosted two interactive stands in the Brain Zone: the "Brain Chain" stand demonstrated, via a hands-on exhibit, the path of electrical signals in the nervous system and how they are affected by disease, whilst the "Mind Control" stand invited volunteers to control a drone quadricopter using an EEG headset.

More than 15,000 visitors attended the Imperial Festival in 2015

Additional activities at the stands included the "Brain Anatomy Challenge", which invited visitors to assemble a model brain in the shortest time possible, and the "Design a Mind-Machine" table, where visitors were encouraged to draw or model their own brain-controlled machine. Both stands proved extremely popular, receiving an estimated 600 visitors over the two days. The festival provided a fantastic opportunity for the CDT students to work together to produce stimulating exhibits showcasing neurotechnology research, as well providing them with valuable experience of engaging with a wide audience to discuss their own research and the wider themes of the CDT and Centre.

Centre for Neurotechnology Research Symposium

The Centre's first research symposium was held on 9th September. The event brought together researchers from Imperial College and beyond for an afternoon of presentations and discussions on the subject of neurotechnology, with poster presentations from first CDT cohort. The symposium is the first of what will become an annual event. Future symposia will involve input from industry partners and will be organised by the CDT student cohorts.



Cybathlon 2016

The Cybathlon, dubbed the "bionic Olympics", is an inclusive event that will enable people living with disabilities to compete in a range of challenges, with the aid of restorative neurotechnology. The ultimate aim is to use the championships as a platform to further develop assistive technologies that are useful in daily life for people living with physical disabilities. A group from Imperial College London, led by Centre member Aldo Faisal and including Centre member Etienne Burdet, is teaming up with severely paralysed athletes including quadriplegics and high-level amputees to enter into the Cybathlon, which will take place in October 2016. The team propose to enter into four of the race categories; the arm prosthesis race, the BCI race, the powered exoskeleton race and the powered wheelchair race.

RESEARCH

Research strategy

Research in the Centre spans, in broad terms, multi-disciplinary research at the interface of engineering and neuroscience.

Within this, we have focused more heavily on certain topics, based on existing strengths, enabled development opportunities, and importance to society. Applications of novel technology to both clinical research, and underpinning basic neurobiology, are both considered to be vitally important. While our research has applications to a wider range of neurological conditions, dementia is a particularly strong focus of the Centre. The Centre's research is broadly structured along the technology and health themes described below.

TECHNOLOGY THEMES

- Microelectronics, devices & biosensors
- Optical & genetic neurotechnology
- Computational modelling and data analysis tools
- Neuroprosthetics & neural interface technology
- Robotics & human-machine interaction
- Imaging

Microelectronics, devices & biosensors.

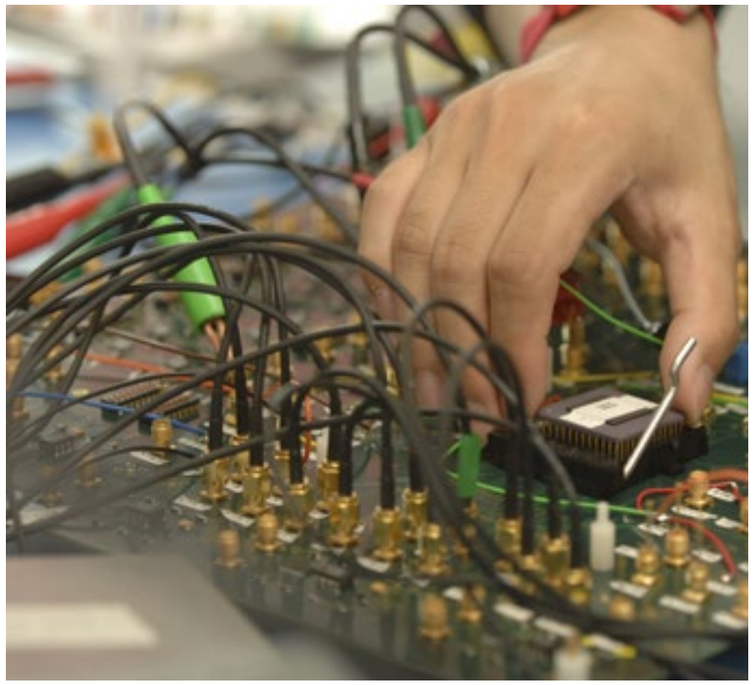
Real-time measurement of the brain, nervous system and the tissue under neuronal control is at the heart of Neurotechnology. To achieve transformational improvements in diagnosis, health and well-being requires measurement and control of physiological signalling mechanisms timescales of milliseconds to days. We have world-leading expertise in the engineering of complex 3D structures for tissue penetration and biosensing. Some of these in vivo sensing devices are currently being used "in the clinic" in neurointensive care units. This expertise is complemented by strength in the development of innovative nanotechnology based biomaterials that can control the implant-tissue interface. Key cross-College expertise in low-power innovative electronics and bionics, in "fabrication of Micro-Opto-ElectroMechanical Systems (MOEMS) and real world" signal processing and conditioning, makes Imperial a "one-stop shop" for device technology.

Optical & Genetic Neurotechnology.

The development and application of novel optogenetic technology for interrogating cortical circuits is a core theme. A cross-College team funded by a Wellcome Trust Networks of Excellence award is developing novel multiphoton optical imaging and opto-electrophysiological tools for reverse-engineering cortical circuit functional properties.

> Dementia is a particularly strong focus of the Centre

This strength is enhanced by the world-leading Photonics Research Group in Physics who will contribute expertise on novel microscope development and micro-endoscopy.



The Division of Brain Sciences has also recently hired Prof Thomas Knöpfel, a world-leading optogeneticist and developer of the genetically encodable voltage sensitive protein (VSFP), from RIKEN, Japan, to provide critical mass for this area. Troy Margie and colleagues at the Crick Institute and Sainsbury-Wellcome Centre will enhance this area further e.g. by providing training in *in vivo* circuit tracing technology.

Computational modelling and data analysis tools.

Researchers associated with the Centre have key expertise in Computational Neuroscience, from stochastic simulation of millions of interacting molecules in neurons, to high-performance very-large-scale simulations of cortical dynamics. Multi-scale simulation is a particular strength; another is the development of novel algorithms for analyzing large-scale neural recordings, particularly based on information theory, sparse sampling, graph theory and nonlinear dynamical systems. As improvements in Neurotechnology often result in new data analysis requirements, training related to this theme will be involved in many projects.

Neuroprosthetics.

Interfaces between neural tissue, computational software, and cybernetic hardware have become vital tools for the study of mechanisms of neural function and dysfunction, as well as for the development of new therapeutic strategies for assisting patients. Imperial College has a substantial track record in this area, with the development of the world's first totally implantable cochlear prosthesis, pioneering new approaches for spike-sorting for prosthetic control, the development of vestibular prosthesis for balance rehabilitation and proprioceptive feedback for upper-limb prostheses. The Imperial College Neuromodulation Group, who specialize in surgical implantation of Deep Brain Stimulation devices in patients, together with specialists in our satellite affiliate in Oxford, will be an important resource for this theme.

Robotics & human-machine interfaces.

Robotics provides critical tools to improve neurosurgery, to interact with human motion and investigate the sensorimotor function, and to model the motor control at system level. All these aspects are well represented in the research carried out at Imperial, with particular achievements including spinning off the robotic surgery company 'Acrobot', development of MRI-compatible robotic interfaces, the development of a robotic electrophysiological workstation, and the use of robotic technologies to investigate human sensorimotor control.

Imaging.

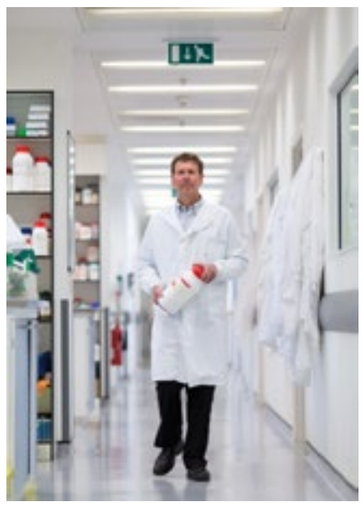
A new technology theme – imaging – has been added recently to reflect the fact that a considerable amount of the research being carried out in the Centre and CDT involves the use of various imaging techniques.

HEALTH THEMES

- Diagnostics & clinical monitoring
- Modulation of peripheral disease-controlling neural circuits
- Brain repair & neuroregeneration
- Brain circuits in health & disease
- Rehabilitation & augmentation
- Lifelong health & well-being

Diagnostics & clinical monitoring.

Monitoring and diagnosing brain disease and injury is challenging due to the problem of penetrating the skull. This is particularly true in a clinical setting. The CDT projects will collectively provide important tools to stimulate, sense and model the brain. This will allow us to fully characterize the dynamic responses of neuronal systems to stimuli, disease and injury



by using a range of measurement modalities. This information will facilitate creation of better disease models, and knowledge of optimised stimuli and responses will allow us to translate the technologies into a clinical setting.

Modulation of peripheral disease-controlling neural circuits.

Neurotechnology targets not only the central nervous system, but also the peripheral nervous system – virtually all organ functions are influenced by neural circuits. Control of peripheral nervous patterns of activity will allow therapeutic intervention in a wide variety of disease states, from chronic neuropathic pain to diabetes, effectively replacing pharmacological with more precise and targeted electrophysiological modulation – "electroceuticals". GSK Division of Bioelectronics have partnered with us to develop this technology theme, to which they will contribute studentships.

Brain repair & regeneration.

One of the most exciting opportunities for Neurotechnology is to repair the brain – after damage caused for example by trauma or stroke, or even by neurodegenerative disorders. We will bring a range of platform technologies to bear upon this problem, including stem cell therapy, nano-engineered 3D-scaffolding biomaterials for axonal growth guidance, and optogenetic patterned stimulation to induce and direct rewiring. The initial target will be brain repair following traumatic brain injury (TBI), in which Imperial has a concerted research effort, but wider applications include spinal cord repair, stroke, and repair of neurodegenerative effects in Parkinson's and Alzheimer's disorders.

Brain circuits in health & disease.

Fundamental to all of these advances in clinical translation is the transformative progress in our basic understanding of brain function. Most of the neurological disorders are disorders of neural circuits, with their symptoms ultimately caused by loss of network information processing functionality. We will apply optical and electrophysiological technologies for large-scale monitoring and perturbation of neural circuits, developed in the technology themes, to understanding the operating principles of cortical circuits and how they are affected in brain disorders.

Rehabilitation & augmentation.

Human augmentation and rehabilitation stand at the confluence of all thematic areas in the Neurotechnology CDT. Projects in these areas will cross all disciplines in focused applications such as: fully cybernetic limbs combining in vivo micro sensors, prosthetic interfaces, computational modelling/learning, and robotics or neural rehabilitation/therapy devices leveraging brain recording/stimulus, adaptive cognitive feedback, and recursive machine learning mapping neural plasticity. Research will combine key elements from each theme with direct focus on clinical application.

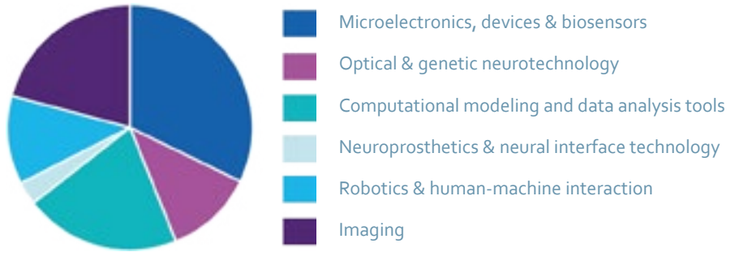
Lifelong health & well-being.

Life-long health & well-being is the core challenge to our ageing society, with the largest impact in healthcare and societal cost. As dementia, neurological and motor disorders are directly linked to age, our themes from Diagnostics to Repair will deliver novel solutions to maintain life-long health, while our understanding of large scale brain circuits and augmentation will deliver technological solutions to maintain mental wellbeing and activity. Key challenges will be the development of physiologically principled biomarkers of ageing, early diagnostics for dementia, the prevention of falls in the elderly, coordinated treatment of multiple co-incidental disorders, and the use of invasive and non-invasive devices to support or replace brain functions, providing a basis for preventative rehabilitation.

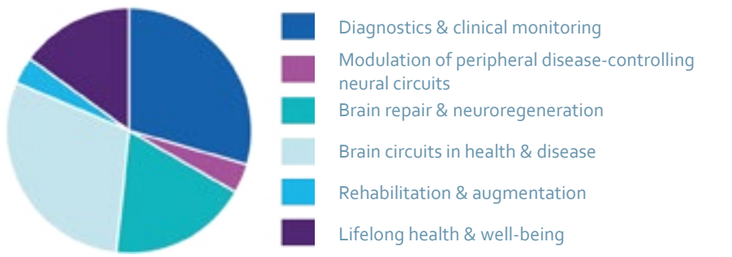
Centre for Doctoral Training projects commonly span multiple themes.

Centre for Doctoral Training projects commonly span multiple themes. The distribution of projects according to themes, for cohorts 1 and 2, is shown below.

TECHNOLOGY THEME



HEALTH THEME

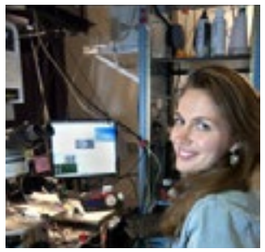


Research funding

Recent grants/funding awarded to Centre members include:

- 2015-20|Fellowship – ENGINI: Empowering Next Generation Implantable Neural Interfaces – project to create truly wireless, autonomous chip-scale implants for distributed sensing|£1M|EPSRC – Tim Constandinou
- 2015-20|Senior Investigator award|£450,000 (£375,000 to ICH Trust) |NIHR – Paul Matthews
- 2015-19|COGIMON: COGnitive Interaction in MotiON|€831,813|EU-H2020 – Etienne Burdet (total award: €5,688,126)
- 2015-19|Information transmission through cross-frequency coupling: revealing the frequency structure of information exchange in the brain|£80K|Wellcome Trust/NIH award – CD Martin, B Averbeck & SR Schultz
- 2015-18|Three dimensional holography for parallel multi-target optogenetic circuit manipulation|US$ 1.25M|NIH 1U01NS090501-01 – S Picaud et al. [IC, Simon Schultz £217,918]
- 2015-18| Grant EP/M012425/1 "Lab-on-an-Organ: A sensor"|£678,310|EPSRC – Xize Niu (PI - Southampton) Prof MG Boutelle (Co-I)
- 2015-18|"SenseBack" IDEAS Factory project to develop enabling technologies to restore sensory feedback in assistive devices, such as prosthetic hands|£1.44M|EPSRC – led by Newcastle University and involving the universities of Leeds, Essex, Keele, Southampton and Imperial College. The team at Imperial (led by Tim Constandinou) will develop the electronic neural interface that will directly communicate with the nervous system.
- 2015-17|Mechanical Muscle Activity with Real-time Kinematics (M-MARK): A novel combination and application of existing technology designed to improve arm recovery following stroke|£1.07M|NIHR – Ravi Vaidyanathan
- 2015-16|Seed Award|£100K|Wellcome Trust – Andrei Kozlov
- 2015-16| ITMAT Call for Experimental Medicine Proposals, Predicting response to disease modifying treatments for multiple sclerosis using a dynamic multimodal "omics" approach|£81,545|NIHR Imperial Biomedical Research Centre (BRC) – Paul Matthews
- 2015| Award to support clinical fellow to work with EPSRC CDT student Aidan Wickham on ALS project |£75K| MNDA (Motor Neuron Disease Association) – Shaw (KCL), Boutelle, Drakakis, Mills (Oxford)
- 2015|First Grant scheme "brain-inspired non-stationary learning"|£125K|EPSRC – Claudia Clopath
- 2015|Google Faculty Research Award (Computational neuroscience)|£50K – Claudia Clopath
- 2015|ENHANCE grant for multi-modal interfaces and orthotic robotic control to restore movement function to Spinal Cord Injury and Muscular dystrophy|€1.2M – Aldo Faisal (total award: €4M)
- 2015|Deep Phenotyping in Neurodegenerative diseases using wearable technology and diagnostic algorithms (joint with UCL) |NIHR – Aldo Faisal
- 2015|Equipment grant|£15K|The Royal Society – Andrei Kozlov
- 2015|Network of Excellence Award|£100K|ISSF – Andrei Kozlov
- 2014-|Neurotechnology for memory enhancement: cortical circuits and Alzheimer's Disease|£500K| Philanthropic donation – Simon Schultz
- 2014-22|Capital Equipment for Training in Next Generation Neurotechnologies|£451K|EPSRC – Simon Schultz
- 2014-22|Centre for Doctoral Training in Neurotechnology for Life and Health|£10,281,291| EPSRC – Simon Schultz
- 2014-17|Biogen IDEC, The OPTIMISE Portal: a flexible, eTRIKS-based platform for MS data capture and sharing|€725K – Paul Matthews
- 2014-17|A Tele-Operative Sensory Motor Control Interface|$375K|US Office of Naval Research – Ravi Vaidyanathan
- 2014-16|Structured healthcare data mining for neuroscience patient stratification and new therapeutic target discovery|£37,466|EPSRC Institutional Sponsorship Award – Paul Matthews
- 2014-16|UK Dementias Platform Capital Research Infrastructure Bid: Integrated DEmentiA research environment (IDEA)|(co-PI for £20M multi-institution imaging component [£5.6M to Imperial College] with UKDP Lead as PI)|MRC Capital Award – Paul Matthews
- 2014-16|Towards rapid, expression-based pharmacodynamic medicines stratification|£200K| Imperial College Healthcare Trust NIHR Biomedical Research Centre – Paul Matthews
- 2014-15|Innovation Grant: Assessing myelostructure as an index of grey matter disease progression in multiple sclerosis using high-resolution, 1 dimensional MRI|£40K|MS Society of Great Britain and Northern Ireland – Paul Matthews
- 2014-15|International Progressive MS Alliance Pilot Grant: Novel enabling infrastructure for outcomes monitoring: dynamic remote performance capture to assess disability in progressive multiple sclerosis| €74,995 – Paul Matthews
- 2014-15|Multiscale computational tools for optogenetics|£185K|BBSRC BB/L018268/1 – K Nikolic, SR Schultz
- 2014-15|Optical sensing of peripheral nerve action potentials using genetically encoded voltage indicators|£331K| GSK|SR Schultz, T Knöpfel
- 2013-16|Physiology of perivascular drainage of the brain and how it is affected by advancing age BB/K015540/1 |£765K total award, [IC £274,576]|BBSRC – R Carare, SR Schultz (co-PI)
- 2013-16|A platform for high throughput two-photon targeted in vivo cellular physiology BB/K001817/1|£565K (+ £55K industry contribution)|BBSRC Industry Partnership Award|SR Schultz (PI), P Chadderton, W Wisden
- 2012-16|Neural Engineering Transformative Technologies|€5.3M, co-PI. Imperial College (led by S Schultz) has largest component, with 4 fellow positions, €1.1M. [IC £900K]| EU Marie-Curie Initial Training Network (EU FP7 289146)|A Torcini, B Kappen, W Erlhagen, J Minguez, J Garcia-Ojalvo, S Schultz and S Coombes

Highlighted research



Computer-Generated Holography for Neural Circuit Reverse Engineering

Amanda Foust
Research Fellow,
Department of Bioengineering

A new project at the Centre for Neurotechnology is taking shape to capitalize on the "optogenetic revolution," innovation of technology to electrically activate neurons and to detect their activity with light. Following Gabor's legacy, they are engineering a holography-based microscope to pattern light onto neural circuits in genetically modified mice. Their goal is to manipulate the flow of electrical information between many neuron simultaneously in patterns mimicking the spatial and temporal complexity of naturally occurring activity. Holography provides two keys advantages over previous methods for stimulating light-sensitive neurons: (1), micrometer precision with, (2), the ability to distribute light simultaneously over multiple targets. Importantly, holography enables the experimenter to "paint" light onto desired targets within a microcircuit and to modify this pattern on a rapid (10 ms) time scale.

Spearheading the system design and construction is research fellow Amanda Foust who comes to Imperial after postdoctoral training in Professor. Valentina Emiliani's Neurophotonics lab at Paris Descartes University. There, Amanda studied the theory and implementation of computer-generated holography, along with the latest advances pioneered by the Wavefront Engineering Group. Synthesizing this experience with a previous training in neurophysiology, electrical and optical engineering, Amanda endeavours to translate recent advances in holographic technology into instruments and interfaces that will enable neuroscientists to test, for the first time, theoretical predictions about how neurons wire and process information.

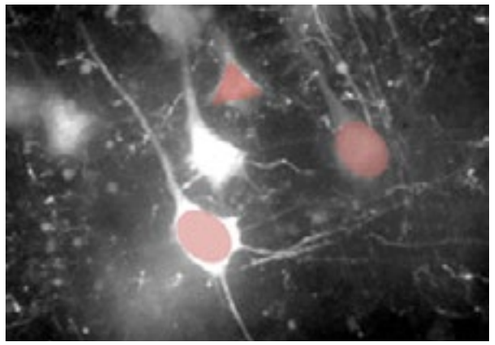
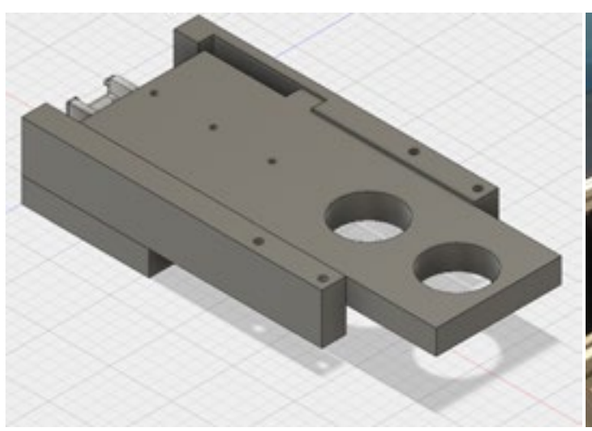
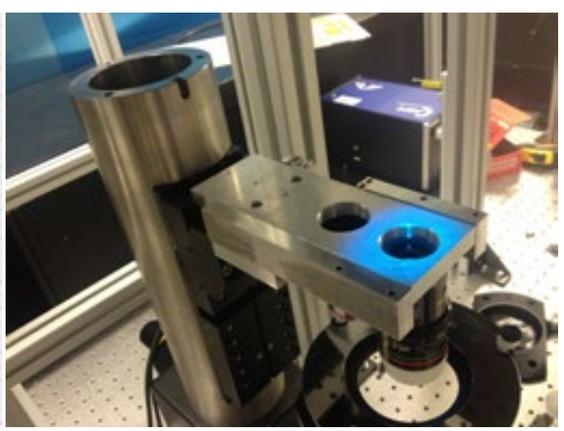


Image of cortical pyramidal neurons from mice expressing enhanced green fluorescent protein. Red shape masks drawn over three cells in the field illustrate how holography could target selected cells with micron precision

Together with Prof Emiliani and Dr Schultz, Amanda co-wrote a successful USA NIH BRAIN Initiative Grant, establishing a consortium to iteratively optimize and adapt holographic light sculpting for neuroscience applications. Amanda is currently developing a new prototype in collaboration with Prof. Emiliani's team and Dr Schultz's Neural Coding Group, as well as experts in laser physics, optogenetics, neurophysiology, mechanical and electrical engineering throughout Imperial College. Together they are adapting the optical design and its implementation for investigation of cortical circuit coding.





The holographic microscope prototype integrates several custom opto-mechanical components (e.g. the objective switcher, below), designed in house to achieve micron-scale repeatability, low-friction motion, and "quiet" docking required during neural recording

Tapping into the "Wandering" Nerve

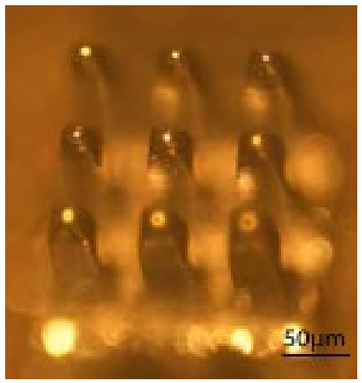
Amir Eftekhar
Research Fellow in Medical Devices,
Department of Electrical and Electronic Engineering

The peripheral nervous system, an extensive network of nerves, over 45 miles long, is the vital communication network between the brain, and spinal cord, to our limbs and organs. First documented in Roman Times (Galen, 130-210AD), our nerves control both conscious movements, to subconscious control of heart rate and even appetite. The nerve Galen identified, later illustrated by Leonardo da Vinci (1452-1519), was the Vagus nerve, from the Latin "wanderer". Extending from our brain stem the Vagus nerve communicates with all our vital organs: heart, lungs, stomach, liver etc.

Centuries later, there is still little known about many of its functions. It was until the late 19th and early 20th Century that the electrical signalling of nerves was recorded (Edgar Adrian, Herbert Gasser and Joseph Erlanger). It was Adrian's student Alan Hodgkin, with a colleague Andrew Huxley that described the chemical ionic behaviour that regulates nerve activity. This spawned nearly a century of work in deciphering the function of this extensive network. The Vagus nerve included, which has links to therapy across a diverse range of healthcare problems including obesity, epilepsy and several inflammatory disorders. Its role has even been linked to stress and anxiety, with its activity indirectly measured via heart rate and respiratory information (vagal tone).

It is then of no surprise that now, as technology has advanced in microelectronics and fabrication, to high-resolution imaging, interest in the Vagus nerve has grown and is now being investigated to identify its role in many diseases, and has become a target for therapeutic strategies.

Enter technology, directed at peripheral nerves and fuelled by the need for complementary and alternative solutions for some of the most devastating healthcare epidemics, including obesity[1], diabetes, and chronic pain. Obesity, for example, is an epidemic affecting almost one third of the world's population with accumulated costs of $2trillion and no effective non-surgical therapy.



Microelectrode spike array used to record intraneural electro-chemical profiles of subdiaphragmatic vagal activity. Device is 3x3mm, with spike heights of 300µm

This technological drive aims to capture or modulate nerve behaviour to identify, assess and regulate bodily functions. This has supported by a selection of Vagus Nerve Stimulation (VNS) devices that invasively and non-invasively stimulated, electrically, the Vagus nerve and have shown effectiveness in several conditions that include depression, epilepsy and arthritis, and currently being trialled for several more. Most recently, the work of Kevin Tracey's lab has shown how VNS lowers key inflammatory markers (serum TNF-α)[2].

The next generation of technology and research is now a multi-disciplinary approach using combing surgical techniques with micrometre scale nerve electrodes and microelectronics. Coupled with the knowledge of nearly a century we are closer to deciphering nerves, specifically the Vagus.

That has been the goal of my lab, the Centre for Bio-Inspired Electronics, over the last few years. Utilising the low-power, low-noise electronics and microfabrication at the Centre, Prof Christofer Toumazou, its director, has teamed up with world obesity expert, Prof Sir Steve Bloom. Together, combining physiological knowledge with state of the art technology we are tapping into the Vagus nerve's role in appetite, which is funded by a €7million European Research Council Synergy grant.

We have developed a lab that combines microscale electrodes to monitor electrical and chemical activity (Figure 1) inside the nerve, and low-power low-noise microelectronics. Combined with traditional cuff electrodes, we are, for the first time, able to capture real-time electro-chemical activity associated with gut/stomach activity. Closing the loop, we are creating a device that will decipher the Vagus nerve's appetite signalling and stimulate enhance satiety. By intelligently tapping into the "wandering" nerve, we can provide a novel solution to obesity and state of the art technology for a wealth of applications.

1 H-R Berthoud, "The Vagus Nerve, Food Intake and Obesity", Regulatory Peptides, 149:15-25, 2008.

2 Olofsson, et al "Single-pulse and unidirectional electrical activation of the cervical vagus nerve reduces tumor necrosis factor in endotoxemia", Bioelectronic Medicine, 2:37-42, 2015.

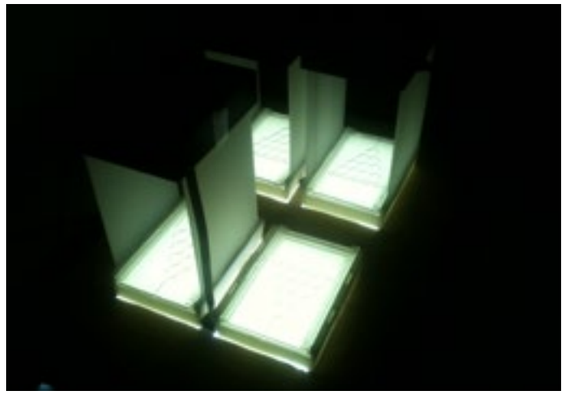
Of Sleep and Fruitflies – On the path to understanding the functions of sleep

Giorgio Gilestro
Lecturer in Systems Neurobiology,
Department of Life Sciences

Drosophila melanogaster is the most successful model organism in genetics. In the past 100 years, fruitflies have helped researchers uncover some of the most puzzling and fundamental principles of biology. Among these: genetic inheritance, chromosomal structure, impact of genes on development and behaviour. Flies were the first complex organism to have their genome fully sequenced, in 2000, and they still are the organism of choice for high-throughput genetic screens.

Beside this unbeaten role in genetics, Drosophila has encountered in the past 15 years a neurobiological renaissance. From the neurobiological point of view, flies do offer a perfect blend of resources: the availability of high throughput genomic manipulation, the possibility of studying complex behaviours, a brain composed of only 100 thousands cells and a very thorough functional & anatomical map of brain circuits – on top of this: virtually every neuron in the fly brain is genetically targettable and modifiable so that even the smallest neuronal activity in a given circuit can be altered ad libitum using light and temperature.

Taking a lead into this new neurobiological renaissance, our laboratory is using Drosophila to tackle one of the most puzzling problem of neuroscience: why do we sleep? Sleep is an extremely conserved yet mysterious behaviour: all animals, from invertebrates to mammals, encounter sleep with inexorable daily frequency, dangerously shutting down their conscious state for a good part of the day. Why do we do so? Why do we sleep and why does lack of sleep carry such a heavy burden?



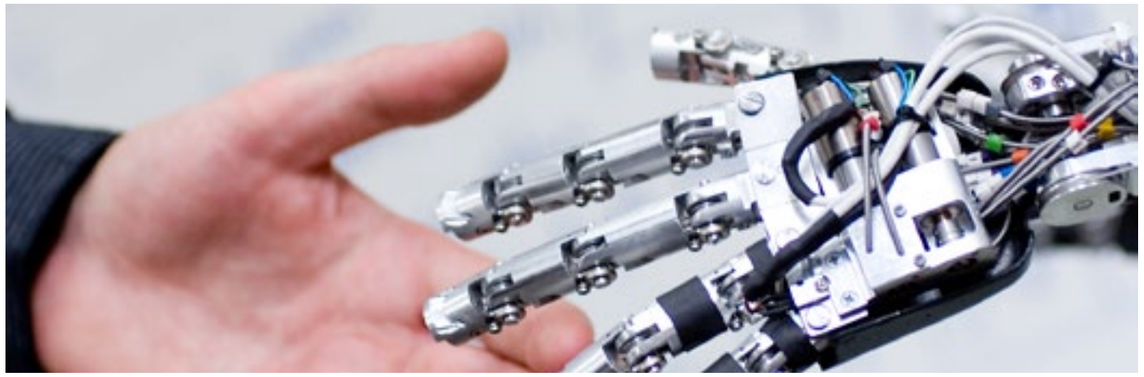
A photo of ethoscopes analysing how sleep deprivation affects decision making in fruitflies.

Drosophila sleep is a pioneering field, therefore a good proportion of our efforts has gone into building the neurotechnological tools that are needed to address this question on the first place. In particular, in the past few years, we constructed new hardware and software that allow for extremely precise detection of sleep in a multitude of conditions - from the lab to the wild. We use them to study not just how genes regulate sleep, but also how sleep affects learning, memory, decision making and social interactions. Using a powerful combination of consumer grade, raspberry-PI computers and 3D printing we constructed machines that use real time video tracking and machine learning to monitor, analyse and interfere with behaviours of Drosophila. We call these machines "ethoscopes". We use ethoscopes to study how flies sleep, interact, make decisions, learn – and how genes modulate all this. The real time analysis in ethoscopes allows for immediate feedback on animals' behaviour: we can, for instance, use small robotic to poke and wake up sleeping flies or use LEDs to shine particular wavelengths and activate optogenetically specific circuit in the brain.

Beside the PI, the laboratory is currently composed of a computer scientist, a bioinformatician, a geneticist, two behavioural scientists. Our work is funded by BBSRC, EMBO and the Edmond J. Safra Foundation.

Drosophila melanogaster is a new main player in neurotechnology of behaviour.

Recent publications/ patents



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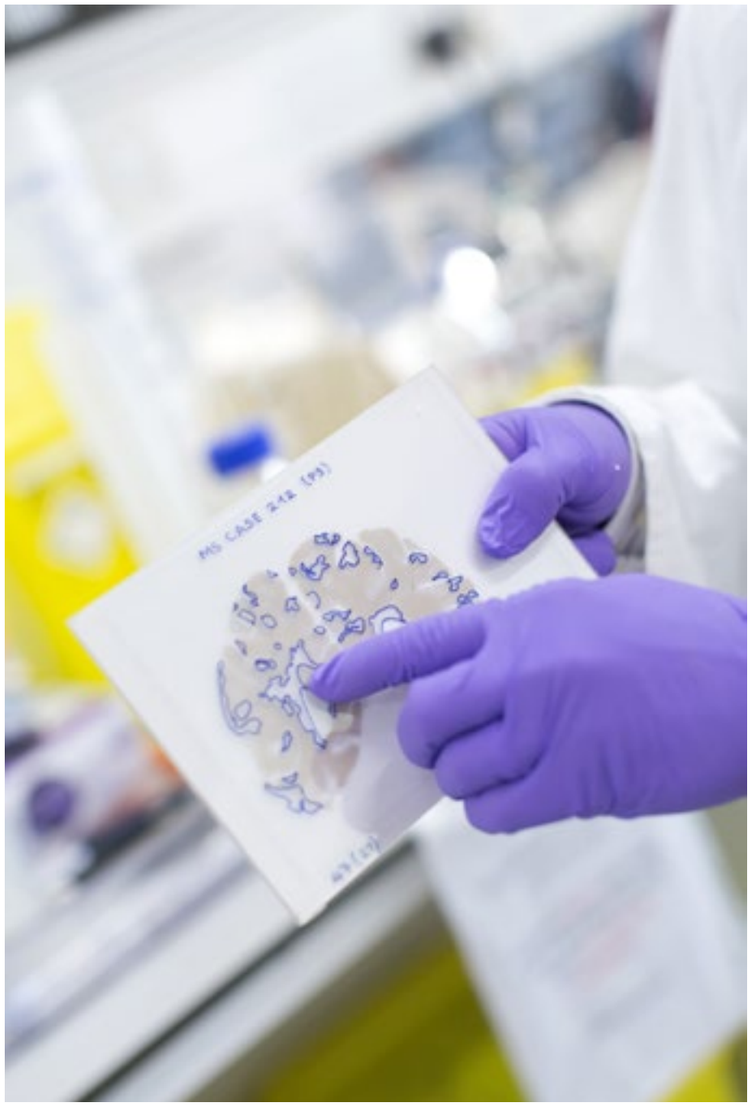


Research profiles

IMPERIAL COLLEGE ACADEMIC STAFF

Mauricio Barahona
Department of Mathematics

I am broadly interested in applied mathematics in biological, physical and engineering systems.

- Dynamics of networks of interconnected nonlinear systems: graph theory and dynamics, theory of synchronization
- Algorithms for nonlinear signal analysis
- Dimensionality reduction and graph clustering for data science: community detection
- Mathematical and computational biology: metabolic and genetic networks (deterministic and stochastic); structural analysis of proteins through graphs

Martyn Boutelle
Department of Bioengineering

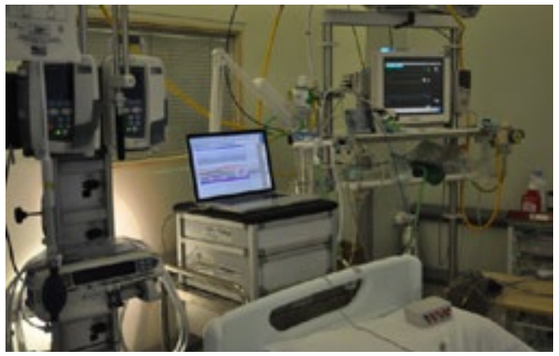
The biomedical monitoring research group is multidisciplinary, embracing both the development of fundamental physical/ analytical science methods and the use of these new techniques in a programme of neuroscience and clinical science research. Our approach is to combine real-time measurement of neurochemical, electrical and physical measurements such as blood flow and local brain pressure to give a clear picture of the dynamics of tissue response to stimulation or trauma. The same measurement techniques are used in patients and in experimental models allowing genuine translational research. Areas of interest include both acute monitoring of traumatic brain injury and degenerative conditions such as Amyotrophic lateral sclerosis.

Measurement methodologies

- Use of microdialysis to sample neuronal tissue in real-time
- Digital microfludicis - microfabricated flow-segmentation devices for microdialysis
- Development of biosensor systems for key neurochemicals and energy metabolites
- Design of smart wireless instrumentation
- Development of signal processing algorithms to fuse data from different real-time measurement techniques and identify complex events.
- Measurement of local blood flow using laser speckle and near-infrared methods
- Measurement of brain electrical activity – electrocorticography and EEG.

Clinical neuroscience research

- Clinical detection and characterisation of spontaneous electrical depolarisation waves in traumatic brain injury patients.
- Clinical monitoring of neurochemistry in brain injury
- Translational study of transient neurochemical mechanisms underlying brain injury
- Monitoring of progression of Amyotrophic lateral sclerosis



Real-time monitoring of the injured brain in the intensive care unit

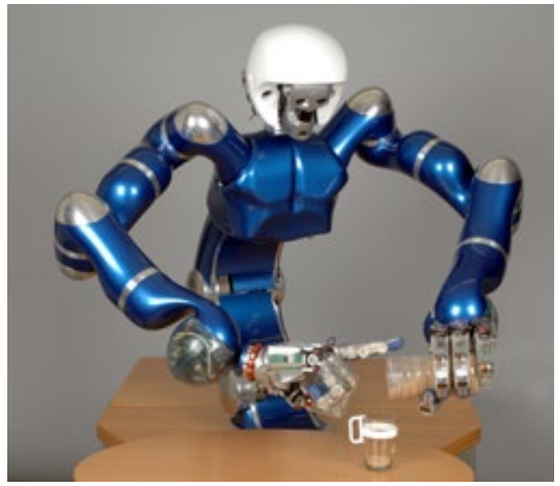
Stephen Brickley
Department of Life Sciences

My laboratory studies the control of neuronal excitability and combines biophysical and imaging approaches with computational models to help advance current theories of brain function with a particular emphasis on the control of sleep/wake states. My work has helped demonstrate the remarkable adaptive plasticity of the mature brain and helped identify key molecular targets for both neuroactive steroids and sedative drugs. My close collaboration with Professor William Wisden has enabled the development of tools for the study of defined neuronal populations using cutting edge molecular biology techniques. I am currently examining age-related changes in synaptic transmission within defined circuits of the prefrontal cortex in collaboration with Dr Paul Chadderton in the Department of Bioengineering.

Etienne Burdet
Department of Bioengineering

The Human Robotics Group at Imperial (HRG) headed by Prof Etienne Burdet uses an integrative approach of neuroscience and robotics to i) investigate human sensorimotor control, and ii) design efficient systems for training and rehabilitation which are tested in clinical trials. This approach has generated significant achievements including:

- The first clear evidence and computational model of how humans use learn appropriate force and impedance to control movements in unstable situations (Nature 414: 446-9, J Neuroscience 28(44): 11165-73, see figure).
- This translated to the first nonlinear adaptive robot controller able to deal with unstable situations typical of tool use, by learning appropriate force and mechanical impedance (Best Paper Award, IEEE Transactions on Robotics 27(5): 918-30).
- The first fMRI-compatible haptic interfaces, which are used in five labs in Japan and Europe in order to investigate the neural mechanisms of human motor control and rehabilitation.
- Robotic devices for decentralized rehabilitation of hand function in home and rehabilitation centres (best paper award at IROS06, the dominant conference for robotics applications).
- Some of these devices have been spun off to rehabilitation technology companies.
- A low-cost robotic wheelchair system based on path guidance assistance, which was shown to significantly reduce the effort necessary to control the wheelchair, and was tested by cerebral palsy and traumatic brain injury individuals.
- The first brain controlled wheelchair able to manoeuvre in a building environment.

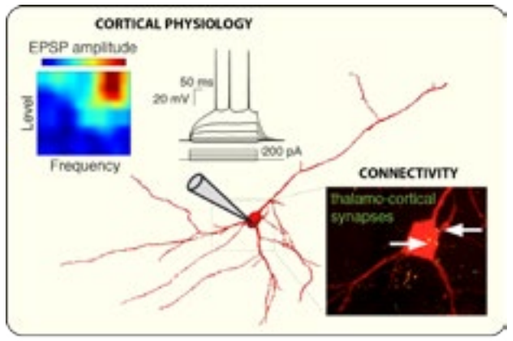


Burdet lab robotic devices

Paul Chadderton
Department of Bioengineering

Information received by the brain is transformed by individual neurons and distributed via synaptic connections. Great effort has been invested to extract an accurate and detailed circuit diagram of information flow in the mammalian cortex, based on anatomical connections. However, effective functional connectivity of cortical circuits is highly dynamic, and can vary on a moment-by-moment basis depending on the behavioural needs of the situation. My laboratory performs electrophysiological recordings using multi-site silicon microelectrodes and

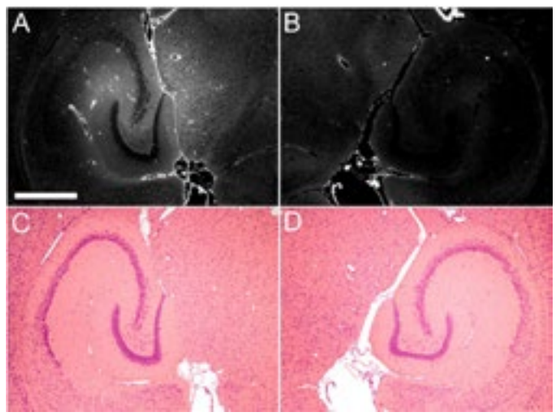
whole cell patch clamp in anaesthetized and awake mice, combined with targeted optogenetic perturbations to dissect the functional organization of cortical circuits. We are exploring cortical sensory representations in both single neurons and populations, allowing us to sample and manipulate circuit activity on multiple levels.



Relating neural physiology and connectivity to understand sensory processing

James Choi
Department of Bioengineering

Dr. Choi is a Lecturer in Bioengineering at Imperial College London and principal investigator of the Noninvasive Surgery & Biopsy laboratory. His laboratory studies how noninvasive energy (e.g. ultrasound), can be used to manipulate biological microenvironments deep in our body. His current focus is on the use of ultrasound with and without acoustically-responsive particles to generate different mechanical forces: pushing, expansion, and contraction. Three neurotechnology themes of work include: (Theme 1) the expansion and contraction of microbubbles within capillaries to safely open the blood-brain barrier for enhanced drug delivery; (Theme 2) the pushing – or palpation – of tissue to evaluate changes in stiffness related to brain diseases (e.g., Dementia); (Theme 3) the pushing of interstitial fluid to enhance the distribution of drugs in the brain (e.g. improved distribution of chemotherapeutics to glioblastoma); and (Theme 4) the development of devices and methods for localizing ultrasound through the human and murine skulls.



Safe and effective drug delivery across cerebral capillaries. The (A, C) left hippocampus was treated with ultrasound and microbubbles while the (B, D) right was the control. (A, B) A labelled model drug was delivered to the treated region (diffuse white area in A) (C, D) without damage as assessed histologically. The white bar in depicts 1 mm.

Theme 1 is our most advanced project and we are working on using this blood-brain barrier opening technology to treat glioblastomas and Alzheimer's disease.

Claudia Clopath
Department of Bioengineering

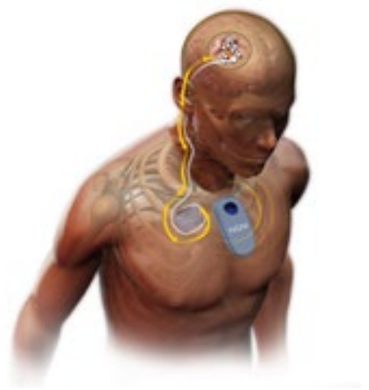
The lab is broadly interested in the field of neuroscience, especially insofar as it addresses the questions of learning and memory. Learning is thought to change the connections between the neurons in the brain, a process called synaptic plasticity. Using mathematical and computational tools, we model synaptic plasticity across different time scales that reproduces experimental findings. We then study the role of synaptic plasticity, by constructing networks of artificial neurons with plastic synapses. We are working to tight collaboration with experimental laboratories, which measure connectivity changes and behavioural learning.

Tim Constandinou
Department of Electrical & Electronic Engineering

The Next Generation Neural Interfaces Lab (www.imperial.ac.uk/neural-interfaces) utilises integrated circuit and microsystem technologies to create advanced neural interfaces enabling new scientific and prosthetic applications. The ultimate goal is to develop devices that interface with neural pathways for restoring lost function in sensory, cognitive and motor impaired patients. Previously we have worked on sensory prostheses (retinal, cochlear and vestibular) and brain machine interfaces.

Current research is focused on creating platform technologies for improved spatial selectivity, temporal resolution and energy efficiency. Ongoing projects include:

- ENGINI – creating chip-scale distributed neural implants
- iPROBE – investigating highly scalable (1k+) channel neural recording
- CANDO – developing a closed-loop optoelectronic pacemaker for epilepsy
- AnaeWARE – monitoring awareness during anaesthesia using a multi-modal approach
- SenseBack – developing PNS interfaces for sensory feedback in assistive devices.



Wireless, multi-channel neural recording interface with on-node spike sorting for real-time motor prosthetic contro

Other research is exploring entirely new modalities for neuromodulation and recording of neural activity.

Examples include:

- Functional neuroimaging using ultra-wideband impulse radar
- Large scale direct optical neural recording (without external markers)
- Thermal microstimulation for the modulation of neural activity

Vincenzo De Paola's Neuroplasticity and Disease

Vincenzo De Paola
Institute of Clinical Science

laboratory studies the mechanisms of synapse formation, elimination and regeneration, i.e. the synaptic life cycle, at the molecular, cellular and circuit level.

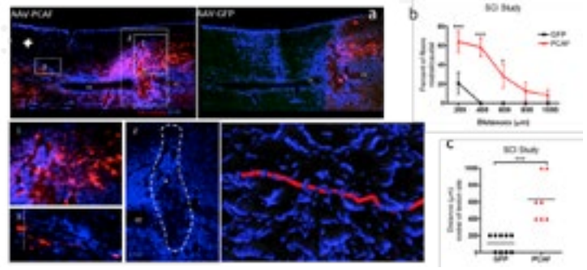
The team combines molecular genetics with high resolution multiphoton imaging, opto/pharmacogenetics and computational methods to quantitatively define the dynamics of axonal and synaptic plasticity directly in the living brain.

The aim is to shed light on the regulation of synaptic connectivity and repair in the adult brain, as such knowledge will inform potential therapeutic strategies for a vast array of neurocognitive disorders.

Simone di Giovanni
Division of Brain Sciences

My lab is interested in the characterization and discovery of the signalling, transcriptional and epigenetic mechanisms that are at the basis for regenerative failure. The final goal is to modulate these mechanisms to enhance nerve regeneration and recovery in several neurodegenerative conditions, including spinal cord injury and stroke. In fact, acute axonal damage in the brain and spinal cord, such as after trauma or stroke, leads to a more or less severe impairment of neurological function causing long term disability.
This is largely due to the incapacity of injured neurons to regrow their axons and re-establish functional connections, which is the primary cause of the lack of functional recovery in several neurological disorders, including Stroke, traumatic brain (TBI), spinal cord injury (SCI). Lack of effective disease-modifying treatments is largely due to a lack of understanding of the basic molecular mechanisms that govern gene expression and the intrinsic capacity of injured axons to re-growth following injury.

In vivo mouse animal models in my laboratory that are necessary to address these research questions include peripheral nerve lesions, spinal cord and optic nerve injury. In these models, we employ RNA-seq, proteomics, gene therapy, mouse genetics combined with anatomical and behavioural assessment of functional regeneration and recovery.



a, MicroRuby tracing of the dorsal columns shows regenerating fibers invading into and past the lesion site after AAV-PCAF overexpression (upper right) versus a control AAV-GFP virus (upper left). Insets show higher magnification of regenerating axons. D-R-C-V: anatomical coordinates, dorsal-rostral-caudal-ventral. cc: central canal. Scale bar, 250µm. b, Quantification of regenerating axons, N = 9 (AAV-GFP), N = 7 (AAV-PCAF), c, Quantification of longest regenerating axon per animal.

(PCAF-dependent epigenetic pathways promote axonal regeneration. Puttagunta et al., Nature comm, 2014).

Manos Drakakis
Department of Bioengineering

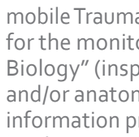
Dr Drakakis' group's research activities revolve around two axes: a) "Circuits for Biology" (inspiration drawn by the need for innovative instrumentation as dictated by a specific biological or medical need e.g. a new instrument for

mobile Traumatic Brain Injury patients or a new instrument for the monitoring of cell cultures), and b) "Circuits from Biology" (inspiration drawn by operational, architectural and/or anatomical characteristics encountered in natural information processing systems, e.g biomimetic cochlear implant processors or vision chips).

The Group has strong expertise in the design and fabrication of ultra low power high-performance application-specific integrated circuits (ASICs) and PCB-level instruments (miniaturised or not).

Research & expertise highlights: new instrumentation for the neuro/electrochemical monitoring of Traumatic Brain Injury (TBI) patients currently used in the ICU, world's first instrument (up to 128 channels) for the physical and chemical monitoring of stem cell cultures, world's lowest power (6μW per channel) and highest performance (80-120 dBs) cochlear implant processor filterbanks, world's lowest power pulse-oximetry front-end (sub-mW), world's first micropower chip (1.26μW) which computes in real time nonlinear cellular/molecular dynamics (e.g. intracellular calcium oscillations, mammalian cell cycle dynamics etc.), optoelectronic/optobionic arrays needed for the photostimulation of photosensitised retinal ganglion cells. The Group's research has been funded by a variety of research and translational sources including the Royal Society, EPSRC and BBSRC, Wellcome Trust-Dept of Health, the Human Frontier Science Program, FSRF, Imperial Innovations and the Bagrit Trust, ERC and the UK/US industry.

Dr Drakakis has received 6 personal academic/research awards, has served as Associate Editor in 6 journals and his Group have won 3 distinctions/prizes at international conferences.



Aldo Faisal

Department of Bioengineering/
Department of Computing

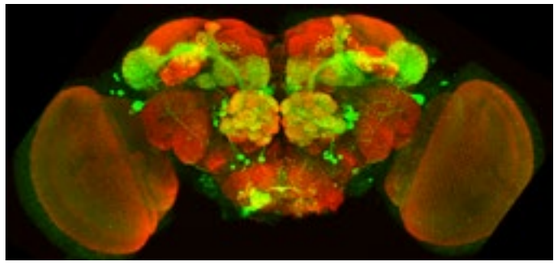
Our research fuses neuroscience with technology contributing to the emerging discipline of neurotechnology. We combine methods from computing, physics and engineering with experimental human studies to understand how the brain works: We pursue both basic science and translational work by a) reverse engineering from first principles the algorithms that drive brains and behaviour and b) translating this understanding into technology that helps patients and people in general. Experimental methods involve non-invasive experiments on sensorimotor control with human healthy and motor disabled volunteers in daily life environments as well controlled augmented reality settings. Physiological techniques established in the lab include EEG, EMG, MMG, fNIRS paired with theory driven experiments to uncover the algorithmic basis of human motor control with an aim to improve Brain-Robot-Interfaces and Neuroprosthetics.

Current funded restorative engineering developments include restorative Neurotechnology in form of Brain-Robot-Interfaces and Neuroprosthetics for a) amputees and b) muscular dystrophy and c) spinal cord injured (through the ENHANCE grant, PI Faisal). These technologies are deployed in the upcoming bionic Olympics, the Cybathlon, of which Dr Faisal is the Captain for Imperial College Team. Current diagnostic include developing machine learning algorithms for adaptive personalized treatment and diagnostic and longitudinal monitoring capability in a) genetic Neurodegenerative disorders and b) Parkinsons, funded by NIHR clinical testing grants.

Giorgio Gilestro

Department of Life Sciences

Sleep is a mysterious activity. All animals that have been tested so far, from the simplest invertebrates to the highest mammals, have shown to possess – and to require – the fundamental characteristics of sleep, independently of the size or the complexity of their nervous systems. In all animals sleep is a vital necessity, as chronic sleep deprivation leads to a still unexplained death. Most animals sleep for a considerable fraction of their life and also the molecular basis of sleep regulation seem to be strongly conserved as most species respond in the same way to many hypnotic drugs or wake-stimulants. This remarkable conservation across evolution suggests that the core function of sleep has to be sought at the basic cell biological level of neuronal function, namely that sleep is an intrinsic requirement of any neuronal network and, possibly, every neuron (or even cell?). We take advantage of this striking evolutionary conservation and use simpler animal models to understand 1) what sleep is and 2) what it does. Combining state of the art genetics, neuronal manipulation and bioinformatics, we investigate how sleep changes behaviour in simple animals and how behaviour consequently affects sleep needs. The laboratory employs a very multidisciplinary strategy, ranging from optogenetics to machine learning and video tracking. Current projects include: understand how sleep consolidates memory; understand how sleep deprivation affects decision making; characterise the conserved traits of sleep in evolution, from Drosophila to mammals.



The brain of Drosophila melanogaster is composed of 200 thousands genetically traceable neurons. Above, in green, the neurons of the olfactory system highlighted using a fluorescent protein.

Dan Goodman

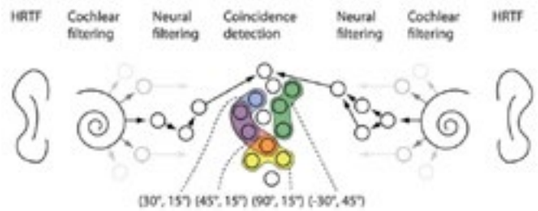
Department of Electrical & Electronic Engineering

The brain processes information using highly connected parallel networks of neurons communicating via precisely timed, discrete neural impulses (called "spikes"). This spike-based form of computation is specific to the brain, being radically different to conventional digital and analogue computation. Despite several interesting hypotheses and specific models, there is as yet not comprehensive theory of this form of computation. The aim of my research is to uncover the principles underlying spike-based neuronal computation, both as a fundamental research problem and with an eye to applications in intelligent systems and neural prosthetics (as we know that brains massively outperform state of the art algorithms).

Specifically, I work in two main domains: neuroinformatics and sensory neuroscience.

Neuroinformatics is concerned with developing computational techniques for understanding the brain. Specifically, processing and analysing experimental data, and simulating models. This work is becoming increasingly important as neuroscientists study larger and more detailed systems, requiring the use of high performance computational techniques which are not, as yet, easily accessible for non-experts. My research is about leveraging modern, heterogeneous forms of computing such as GPUs, FPGAs, and the SpiNNaker spiking neural network supercomputer, but making them accessible to neuroscience researchers. I currently work in two main areas of neuroinformatics with associated software packages: simulating spiking neural networks (the Brian simulator); and, analysing data recorded from multi-channel electrodes in the brain (KlustaSuite).

Sensory neuroscience is the study of how the brain processes sensory information, such as sight, sound, touch, etc. I work primarily in the auditory system as the role of precise temporal information is so well established there. I am interested in how sensory processing is done in realistic rather than laboratory environments. Specifically, rather than using simplified stimuli such as pure tones, I prefer to analyse the processing of complex stimuli such as natural sounds in a noisy background. I am also interested in the problem of processing a continuous stream of sensory data rather than the typical laboratory problem of responding to a brief, precisely delineated stimulus.



Model of how sound localisation could be performed in a complex listening environment using the behaviour of ensembles of spiking neurons

Adam Hampshire

Division of Brain Sciences

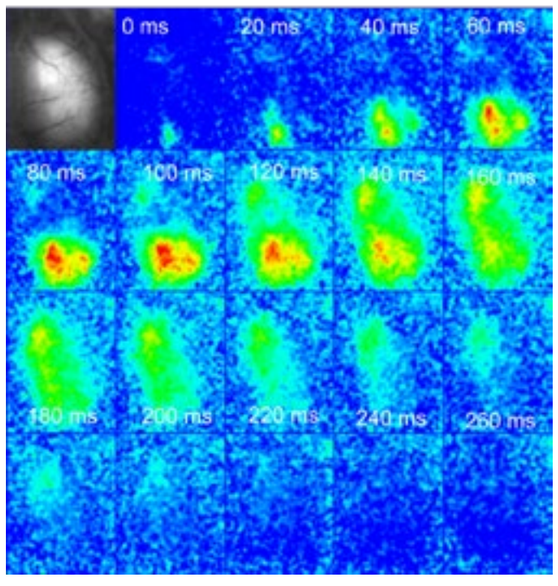
The overarching aim of my research is to derive a better understanding of how the human brain supports higher cognition and how the different aspects of higher cognition are affected in the pathological brain. This is with a particular focus on understanding how 'domain general' functional networks, which have nodes within the lateral frontal cortices, support 'cognitive control' processes, this being the set of cognitive processes that enable us to think and act in a controlled manner. I apply an interdisciplinary set of methods in pursuit of this aim. For example, I use connectivity methods to determine how lateral frontal cortex sub-regions interact in functional networks with other areas of the brain when supporting cognitive tasks. I also examine how these networks are impacted in the clinical populations that suffer from impaired cognitive control. I develop Internet and App based technology for remotely assessing and cognitively training large-scale cohorts of individuals. This technology enables me to study the population distribution of cognitive abilities and is being used to deliver remote assessment and cognitive training for a variety of clinical populations. I am also developing computational models of lateral frontal cortex networks. These models are particularly useful, because they integrate multimodal findings about human brain systems into working simulations, which can then be used to explore the relationship between local neural processes, large-scale network dynamics and cognitive control behaviours.

Thomas Knöpfel
Division of Brain Sciences

My lab specializes on light and genetics-based functional imaging approaches to better understand how behaviour emerges from the electrical activities of neuronal circuits. Using genetically encoded indicators, we pursue a mesoscopic scale imaging approach that bridges cellular and system levels of understanding.
One of the key challenges in current neurosciences is to understand how the brain generates behaviour and cognition out of the collective electrical activity of cortical nerve cells. Elucidation of these mechanisms is a prerequisite of the development of causal treatments of brain dysfunctions. We approach this problem by imaging cortical activity during cortex-dependent behaviours in murine models.

This laboratory has pioneered work over the last 15 years that has led to the development of genetically encoded calcium and voltage indicators that enable cell class specific mapping of neuronal activities with coverage across multiple brain areas.

This imaging technology allows for relatively non-invasive (through the skull) imaging of the brain's electrical activities at the temporal and spatial scales the brain processes neuronal information and generates behavioural output.



Cortex wide voltage imaging. Spread of neuronal activation from sensory to motor areas. A voltage sensitive fluorescent protein (vsfp) was expressed in layer 2/3 pyramidal cells over a large cortical area including motor cortex (m), primary somato-sensory cortex (s1) and primary visual cortex (v1). A light flash at t=0 triggered a response in primary visual cortex and higher visual areas from where it spread over the large portion of the hemisphere, triggering a response in the motor cortex.

Specific research topics include: Development and tuning of genetically-encoded, voltage-sensitive fluorescent proteins; Linking cortex-wide patters of electrical activity with goal-directed behaviour.

Andre Kovloz
Department of Bioengineering

Our research, broadly speaking, focuses on how the auditory system, a keystone of human communication, achieves its remarkable sensitivity, selectivity, and invariance. We investigate 1) how the inner ear converts sounds into electrical signals, and 2) how auditory cortex interprets these signals.

In the classical theory of hearing developed in the 19th Century, von Helmholtz recognized that the ear contains an array of resonators like a piano that contains an array of strings tuned to particular frequencies. A hundred years later, Thomas Gold realized that viscous friction in the liquid that fills the inner ear prohibits any passive resonance. Like the strings of a piano in honey, the ear's mechanotransduction elements are over-damped and will not resonate passively. In this paper (doi:10.1038/nature10073), my colleagues and I demonstrated that a balance of the elastic, viscous, and inertial forces in a hair bundle, the inner ear's mechanosensitive organelle, minimizes viscous friction in the ear and thus makes the sensitive hearing possible.

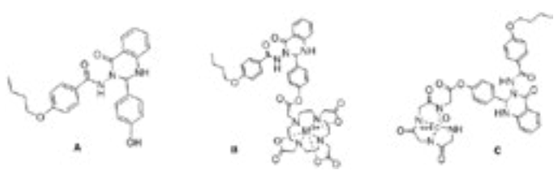
1. To understand hearing, we must understand how sounds perform work on mechano-electrical transduction (MET) ion channels, i.e. the nature of the movement that transforms a sound's mechanical energy into the channel opening. This transformation must be efficient, for the ear's sensitivity is great. For example, a bat can hear footsteps of a cricket walking on sand, and a grain of rice dropped from a height of 1cm contains enough kinetic energy to open all MET channels of all the humans on Earth. We develop new methods to apply mechanical forces to open single MET channels and to measure currents through them, in order to understand how sensitive hearing works. This knowledge will help us to cure deafness rationally and effectively.

2. Like any successful pattern-recognition system, the auditory system must achieve selectivity and invariance in natural sound recognition. Selectivity is important because it allows the system to distinguish different stimuli; invariance is essential because a signal's physical content can vary greatly, but not all variations are always informative. For instance, we can recognize our name spoken by a man or a woman, slowly or rapidly, in a quiet room or on a busy street. Because combining selectivity with invariance is in general a hard problem, no speech-recognition algorithm today can match this performance of the human auditory system. How the brain solves this problem is a second research topic in my laboratory. We explore it in the central auditory system of songbirds and mice, investigating the structure of a neuron's receptive field and computations performed within the receptive field. Characterizing these mechanisms is both fundamentally interesting and required to understand the neurobiological nature of many brain disorders.

Nick Long
Department of Chemistry

Inflammation is central to maintaining a functional, healthy state within a host system. However, dysregulation of the inflammatory response results in tissue damage, as observed in pathological conditions such as stroke. In order to address clinical issues and improve therapeutic means, it is important to visualise biological processes on a molecular and cellular level. Design of medically relevant molecular imaging agents that incorporate targeting motifs, provides diagnostic markers and a means to mechanistically probe cellular processes. Research in the Long group aims to design and prepare versatile inflammation-targeted ligand frameworks that can be functionalised with metal components. Depending on the choice of metal, the compounds can function as imaging probes for Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) or optical (fluorescence) imaging. Dual-modality probes are also a focus, providing a set of compounds that allow modality-specific limitations such as resolution or sensitivity to be circumvented.

Specifically for projects within the Centre for Neurotechnology, and in collaboration with Dr. Felicity Gavins, the formyl peptide receptors 1 & 2 (termed FPR1 and FPR2), located on neutrophils are being targeted to enable visualisation of inflammation. Indications that the FPR2 receptor could act as a therapeutic target for neurodegenerative disorders have led to a screening of potential binding frameworks. For example, a non-peptidic, small-molecule based FPR2 antagonist, quin C7 (A in the above figure) is being utilised within the Long group, with this targeting vector being coupled to an imaging moiety i.e. a europium or gadolinium metal centre for optical and MRI respectively (labelled B) or radiolabelled with 99mTc (labelled C).

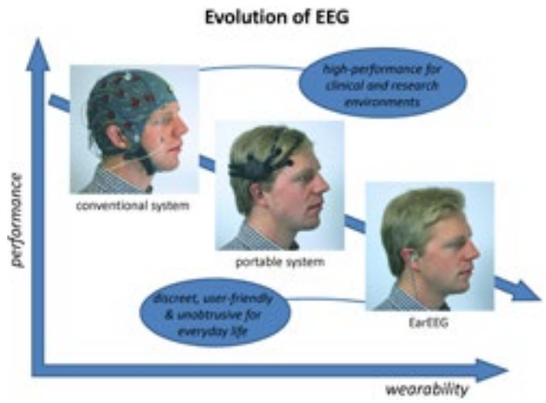


Target molecules quin c7 (a), quin c7-do3a with m denoting potential metals (b) and quin c7-tetraglycine (c)

The research features synthetic chemistry methodology and imaging probe design, complemented by biological analysis and biomedical imaging, and will provide a range of novel diagnostic probes to be tested under in vitro and in vivo conditions.

Danilo Mandic
Department of Electrical & Electronic Engineering

Prof Danilo Mandic specialises in statistical signal processing, brain computer interface, and ultra-wearable physiological sensing. His ear-EEG technology is the first to make possible the recording of both EEG and vital signs from within the ear canal, with applications in continuous 24/7 monitoring of brain and body function outside the clinic. Danilo has won five best paper awards in the area of neurotechnology, and is a recipient of President's Award for excellent in postgraduate supervision



The Ear-EEG provides unobtrusive, discreet, and comfortable means for the recording of EEG and vital signs in the community

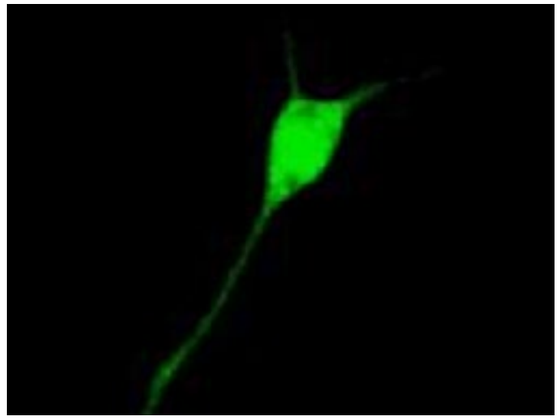
Paul Matthews
Division of Brain Sciences

Our research is directed towards novel approaches for human therapeutic target validation, low cost clinical trial design and stratified medicine. All of these problems share challenges of providing greater depth of patient characterisation, longitudinally, and integrating large amounts of data into predictive models. A core area for the lab involves the integration of molecular and physiological imaging to define the relationships between

target engagement assessed through positron emission tomography, systems level pharmacodynamic responses assessed using MR imaging and 'omics and patient behaviour. Imaging efforts, including the evaluation of novel radioligand technology, is being pursued in a collaboration with Imanova Ltd and the Imperial Neuropsychopharmacology Unit. A major application area is in neurodegenerative disease as part of the portfolio of the Dementias Platform UK, through whom the lab has resourced a state of the art, time of flight, integrated clinical MRI-PET system for future studies. In a collaboration with Biogen and the Imperial Data Science Institute, a new data management platform for integration of clinician- and patient-centred data, large scale omics and imaging is being created as part of a UK-wide consortium for care of people with multiple sclerosis. The Progressive MS Alliance and the Data Science Institute are collaborating in work to develop remote sensing for quantitative indices of movement and automated, home based detection of sleep pathology. An EPSRC –funded effort is linking researchers in Oxford, Imperial and the Farr Institute for development of improved mathematical approaches to mining such data for defining patient trajectories as an informative. New work intends to extend these studies in applications for neurodegenerative disease studies in the 500,000 person large UK Biobank

Kenji Okuse
Department of Life Sciences

Our research focus is the molecular mechanisms of pain pathways, and our expertise includes primary culture of sensory neurons and macrophages, live cell Ca2+ imaging, and molecular biology. Currently we are studying the role of VGF in pain pathways. VGF is a neuropeptide precursor generated by nociceptive sensory neurons upon nerve damage, and may play a crucial role in the development of chronic pain. We have shown that one of the VGF-derived peptides, TLQP-21, activates macrophages using live cell Ca2+ imaging. Inoculation of macrophages activated by TLQP-21 into rat hind paws causes mechanical hypersensitivity. This activation of macrophages by TLQP-21 is mediated via TLQP-21 receptor gC1qR, a complement system protein, and knocking down gC1qR renders TLQP-21 unable to activate macrophages. Furthermore, neutralising anti-gC1qR antibody delays the onset of pain behaviour in nerve damage pain model rats (J. Biol. Chem. 288, 34638-46, 2013). Our current aim is to discover the molecular mechanism involved in the sensitisation of sensory neurons upon nerve injury. Sensory neurons do not show intracellular Ca2+ increase when low concentration of KCl (1 mM) is applied, however, incubation with the conditioned media of macrophages stimulated with TLQP-21 leads to the excitation of sensory neurons by low KCl. Gene expression analysis of TLQP-21 stimulated macrophages using qRT-PCR revealed upregulation of several cytokine genes including IL-1β. Preincubation with IL-1β also sensitizes sensory neurons in a manner similar to the macrophage conditioned media. These phenomena of sensitisation of sensory neurons may explain how allodynia, pain due to a stimulus that does not normally provoke pain, occurs in neuropathic pain condition.



Visualising excitation of sensory neurons

Tobias Reichenbach
Department of Bioengineering

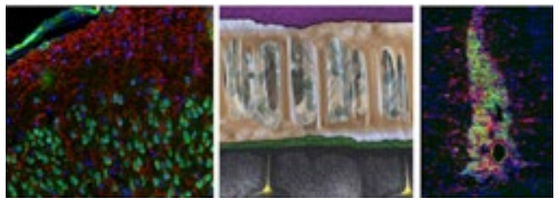
Hearing and communication impairments affect more than 16% of the adult population in the UK, and an afflicted individual experiences major problems with her or his social and professional life. Hearing and communication

impairments are a particular problem in the elderly and hence in the UK's aging society. They involve a range of neural disorders, but their understanding, diagnosis and treatment remain open problems.

In my research with the Centre for Neurotechnology at Imperial College London I aim to develop novel ways for diagnosing and treating hearing and communication disorders. To this end I research on the neural mechanisms by which the brain processes complex real-world acoustic stimuli such as speech. I then aim to assess these neural mechanisms through novel, wearable devices for non-invasive brain measurements such as electroencephalography (EEG). My group currently focuses on three different types of hearing and communication impairments, namely mild to moderate sensorineural hearing loss, auditory processing disorder and aphasia.

Richard Reynolds
Division of Brain Sciences

The Multiple Sclerosis research group at Imperial College carries out studies of the cellular and molecular events that lead to the pathological changes in the human brain that are characteristic of this condition. We are particular interested in the failure of repair processes and the progressive neurodegeneration that underlie the accumulation of clinical deficit. This work uses a combination of human post-mortem tissues, experimental models and cell culture systems to dissect and manipulate these pathological processes. In collaboration with other members of the Centre for Neurotechnology, we are carrying out computer modelling some of these processes in order to understand how they affect electrical signalling within the brain and to model ways of reversing the deficits. Other work in the group is investigating the use of functional biomaterials in the long term delivery of novel therapeutics to the damaged brain.



Left image shows how neurons (green) lie closely under the surface of the brain, which is surrounded by a matrix of tissue (modelled in the centre image). Right image demonstrates how we can inject hollow nanoshells (green) into the space surrounding the brain, which could then be used to deliver molecules to protect neurons

Esther Rodriguez-Villegas
Department of Electrical & Electronic Engineering

One of my areas of research has as objective to create high performance, size record breaking physiological monitoring systems to both improve the welfare of animals in pharmacological research, and also to be able to carry out experiments that could not be done before due to the characteristics of existing systems. More specifically, we are creating miniature (<1.5g with battery), high performance, wireless systems that can be comfortably worn for long periods of time by even very small animals (including mice), with the aim to better study their brain activity in order to understand disorders such as schizophrenia and Alzheimer's disease. Use of these very small implants will allow even the smallest animals to move around freely and be housed in groups, improving their welfare when compared to current methods which require the animals to be frequently handled causing stress and affecting their performance in the test.

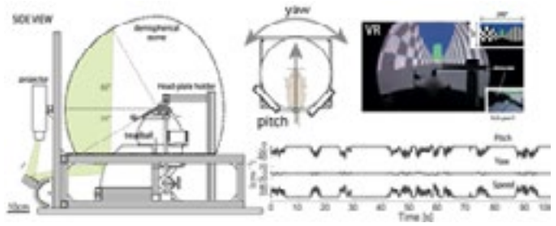
Another area of my research focuses on creating novel, customized signal processing algorithms and ultra low power implementations of these algorithms for wireless miniaturized wearable brainwave monitoring systems for humans. We specifically target systems for epilepsy and sleep monitoring/diagnosis due to the huge human and economic impact of these areas, but our work also provide a framework of algorithms and low power consumption circuits for the real-time analysis of EEG signals which can be readily mapped to brain computer interfaces (BCIs) and, more blue-sky, augmented cognition applications, as these fields mature.

Simon Schultz
Department of Bioengineering

Simon Schultz is Reader in Neurotechnology, Royal Society Industry Fellow, and Director of the Centre for Neurotechnology. He is a Fellow of the Institute of Engineering & Technology (FIET).

His research group, the Neural Coding Laboratory, develops and applies photonic, electrophysiological and information technology to "reverse engineer" the operating principles cortical circuits. As well as advancing our understanding of how the brain works, this helps us to understand how cortical circuits dysfunction in brain disorders. Specific recent interests include how networks of neurons in the visual and somatosensory cortices process sensory information for perceptual decisions, and how the cerebellar cortical circuit uses sensory information to control locomotion. The group has a particular interest in the role of cortical circuits in neurodegenerative disorders such as Alzheimer's Disease. To investigate these questions, the group has been developing novel two-photon laser scanning technology for acquiring functional signals from many neuronal locations simultaneously, "virtual reality" technology for studying sensorimotor behaviour, and information theoretic data analysis tools that scale to the study of

large neuronal populations.



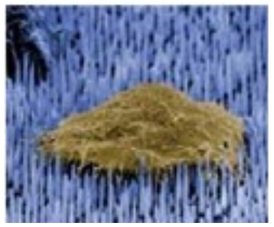
Behavioural apparatus for studying sensorimotor control

Barry Seemungal
Division of Brain Sciences

Barry Seemungal is a neurologist with expertise in vestibular neuroscience, clinical neuro-otology and related fields of neurotechnology. He has provided expert review for the European Union FET programme (Future and Emerging Technologies) specifically for the CLONS programme, a neurotechnology programme with the aim of developing a vestibular prosthesis. He has received funding from the Academy of Medical Sciences and The Medical Research Council. Barry has pioneered the use of non-invasive brain stimulation in elucidating the loci and mechanisms of cerebrocortical vestibular functioning. He has neurotechnology collaborations at Imperial with: (1) Danilo Mandic (EEE) – Pathways to Impact grant (EPSRC); (2) Simon Schultz – (BioEng) – Information theory analysis of human visual perception with outputs: Seemungal et al. Vestibular activation differentially modulates human early visual cortex and V5/MT excitability and response entropy. Cereb Cortex. 2013;23(1):12-9 and Yousif et al. Dopamine D1 receptor activation preserves visual motion perceptual performance despite increased neural noise – a double-blinded, placebo-controlled study involving human V5/MT transcranial magnetic stimulation (in preparation – Journal of Neuroscience); (3) Aldo Faisal (BioEng) – FoM and FoE kickstart grant; (4) Marco Aurosicchio (MechEng) – Health Innovation Challenge Fund grant application (in process) for device to quantify concussion

Molly Stevens
Department of Materials/
Department of Bioengineering

Molly Stevens is Professor of Biomedical Materials and Regenerative Medicine and the Research Director for Biomedical Material Sciences in the Department of Materials, Department of Bioengineering and the Institute of Biomedical Engineering at Imperial College London. Prof Stevens' group comprises an extremely multidisciplinary research programme focusing on designing and developing materials-based approaches for applications in regenerative medicine and tissue engineering. The research group has been recognised with over 20 major awards, including the EU40 Prize for best material scientists in Europe from the Materials Research Society and the 2014 Research Group of the Year from the European Life Sciences Awards, amongst many others. Within the EPRSC CDT in Neuro-technology the Stevens Group is developing a materials-based nanotechnological approach comprising a model neuronal interfacing system to investigate human pluripotent stem cells (hPSCs), in partnership with Prof Simone Di Giovanni (co-PI). The Stevens Group is expanding upon their nanoneedle-based platform technology, which is capable of interfacing with and delivering cargoes to cells efficiently and non-destructively (Nature Materials, Front Cover, 2015, ACS Nano 2015 and Adv Mater 2015). We are targeting a first-in-field demonstration of an optimised neuronal interfacing system based on aligned in vitro cortical neuronal networks derived from hPSCs and porous silicon nanoneedles.



We propose to upgrade and optimise a neuronal interfacing system based on aligned in vitro cortical neuronal networks derived from hPSCs and porous silicon nanoneedles (Nature Mater 2015 (pictured), ACS Nano 2015 and Adv Mater 2015). This will enable localised intracellular stimulation and recording and it will provide a nano-sensing platform to non-invasively detect activity-dependent gene expression changes

Richard Syms
Department of Electrical & Electronic Engineering

Richard Syms has been developing miniaturized dual numerical aperture confocal scanning microscope systems for applications in optogenetics. The systems are based on piezoelectrically scanned optical waveguides that use excitation of orthogonal bending mode resonances to create a Lissajous scan pattern. Recent work has solved two key problems, namely lack of method of constructing a waveguide cantilever that combines high optical quality with suitable mechanical performance, and lack of a sensor for feedback control of the fibre position. Dip coating of pairs of optical fibres is used to construct waveguide cantilevers with a non-circular cross section and a precise non-unity ratio between the orthogonal resonances that matches the ratio needed for Lissajous

Optical pattern-writing example, from: Mokhtar MHH, PhD thesis, Imperial College, 2015

scans. Over-scanning the fibre onto an aperture reflector is used to provide intermittent optical feedback and correct for residual phase shifts. The result is a highly accurate optical scanning system, with two channels that may be used separately for confocal imaging and neural stimulation.

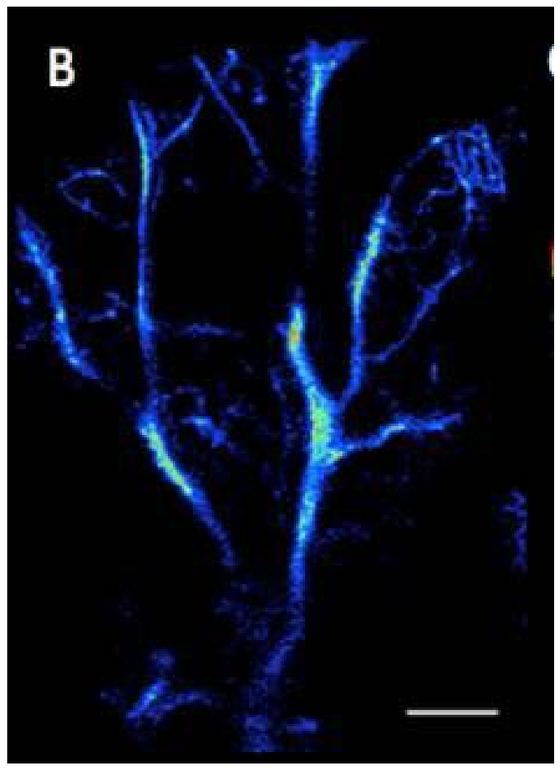
Mengxing Tang
Department of Bioengineering

Dr Tang's current research mainly focuses on developing new imaging and image analysis methodologies using ultrasound and its allied techniques for quantifying physiological flow, tissue perfusion, tissue mechanical properties and molecular information and their applications in a wide range of clinical and pre-clinical applications including cardiovascular diseases, cancer and neurology. In recent EPSRC funded projects his group have investigated various techniques of experimental measurements, modelling, image formation and analysis in order to obtain better understanding of the imaging physics in contrast enhance ultrasound, to push the boundary of imaging performance in terms of spatial and temporal resolution and imaging sensitivity, and to extract physiologically relevant quantitative information from imaging data. Dr Tang has recently started a collaborative project with Dr Chadderton on using high frame-rate ultrasound and microbubble contrast agents for brain functional imaging. To date Dr Tang has authored over 60 peer reviewed journal papers.

Ravi Vaidyanathan
Department of Mechanical Engineering

Mechatronics is the synergistic combination of precision engineering, electronic control, and systems thinking in the design of products and manufacturing processes. Bio-Mechatronics may be viewed as its extension fused with influence from biological systems; i.e. mechatronic systems designed based on inspiration from neural and physiological systems. In animals, for example, intrinsic properties of the musculoskeletal system augment the neural stabilization of the organism for an array of critical of functions. Modelling this hierarchical coupling for implementation in robotic systems has spurred innovation in medicine, cybernetics, and mobile robots.

Our research focuses on mechanisms of sensory-motor control, specifically with respect to systems-level coupling between mechanics and neurophysiology. The core hypothesis is the idea that complex behaviour emerges from the interaction of an entity with its environment as a result of sensory-motor activity; interactions among a breadth of subsystems must be tuned and adapted to achieve this objective. Our vision is to contribute to the formulation of theoretical and computational frameworks to elucidate how the dynamics of the morphology of the



A high resolution in vivo vascular ultrasound image. Bar is 1mm. (christensen-jeffries et al. IEEE trans med imaging. 2015 feb;34(2):433-40)

structural subsystem (mechatronic or biological) play a computational role in the entire entity, and in effect subsume portions of the control architecture. We view this formulation from a hierarchical systems perspective, where the mapping of motor commands to sensory signals involves a transformation based on the non-linear dynamics of the system. The computational complexity of the transformation pertains directly to the dynamic coupling in the system; the more coupling, the greater the complexity of the transformation. Our current research in this area is founded upon a combination of systems engineering, adaptive control, pattern recognition, dynamic systems theory, and analytic mechanics to address theoretical and experimental challenges posed by the application of robotic and electro-mechanical systems to real-world issued faced in medicine and biology.

Biomechatronics Lab activity summary

Ramon Vilar

Department of Chemistry

Our research focuses in developing novel molecular tools and technologies to study living organisms. This includes optical probes for cellular imaging, responsive contrast agents for Magnetic Resonance Imaging (MRI) and targeted DNA binders with anticancer properties. In the context of the CDT in Neurotechnology, we are developing novel theranostic agents targeted at malignant brain tumours.

Further information about our research can be found at: http://www.imperial.ac.uk/people/r.vilar and http://www3.imperial.ac.uk/medinchem

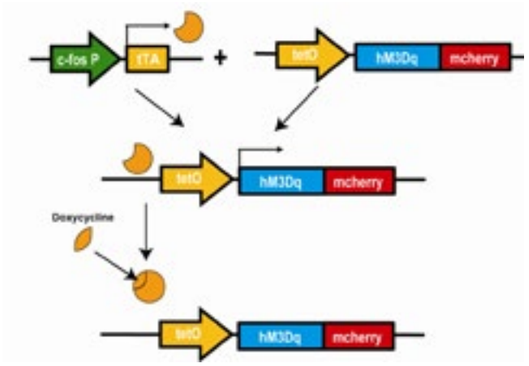
Bill Wisden

Department of Life Sciences

My work is done collaboratively with Prof Nick Franks (Life Sciences) and Dr Stephen Brickley (Life Sciences). Why we spend about 30% of our lives in a state of vulnerable inactivity, sleep, is an enduring mystery. Like hunger, thirst and sex, the urge to sleep the longer we stay awake is a primal biological drive. It builds during waking and then dissipates during sleep. But what exactly the drive to sleep is remains unsolved. Understanding this drive is important both for fundamental neuroscience and medicine. In fact the drive to "recovery sleep" after prolonged sleep deprivation seems so strong, that it is similar to taking a sleeping pill. We are investigating the mechanism for the sleep drive and ask if certain sedatives produce unconsciousness by activating the same mechanisms. We use mice because their brain wiring and the way they sleep is similar to humans, and genetically manipulate and trace the hypothalamic neural circuits that we have recently shown are sufficient for inducing recovery sleep. Using a genetic approach that "tags" the neurons involved (see Figure), we hope to find out how these circuits function. A deeper knowledge of how sedatives work could lead to drugs with fewer side effects and that might even give the restorative benefits of natural sleep. Our work involves experiments at the biophysical, molecular, cellular, anatomical and whole animal levels. We are working with bio-engineers to develop better EEG monitoring devices and light probes. Wisden and Franks hold a Welcome Trust Joint-Investigator Award. Key recent publications:

Yu X et al., (2105) Wakefulness is governed by GABA and Histamine Co-transmission. Neuron 87:164-78
Zhang Z et al., (2015) Neuronal ensembles sufficient for recovery sleep and the sedative actions of α2 adrenergic agonists. Nat Neurosci. 18:553-61.

Figure 34: Regulating neuronal activity by Activity Tagging (Zhang et al., 2015)



Regulating neuronal activity by Activity Tagging (Zhang et al., 2015)

SATELLITE MEMBERS

MRC Brain Network Dynamics Unit

University of Oxford

Peter Brown, Director
Pete McGill, Deputy Director

The ultimate goal of the MRC Brain Networks Dynamics Unit at the University of Oxford is to develop recurrent Brain Computer Interfaces that selectively and strategically target circuit malfunctions in neurological and psychiatric disorders. To realise this, the unit defines the cellular basis of network dynamics and their disturbance at the levels of microcircuits, scales up from these insights to explain systems behaviour and phenotype, and develops and implements spatiotemporally-patterned neuronal manipulations for therapy. The unit is remarkable in its investigation of pathological neuronal network dynamics in two key and related brain circuits, - the neocortical-hippocampal-amygdala system and the basal ganglia-thalamocortical system, and integrates clinical, computational and animal model studies.

Francis Crick Institute

Denis Burdakov

Neural processing, energy sensing and control, adaptive behaviour

Burdakov lab researches how neural circuits estimate vital environmental variables (e.g. energy levels) to create efficient and appropriate behaviour (eating, arousal/exploration, sleep). Our experimental focus is on widely-projecting neural modules responsible for global brain control (e.g. orexin/hypocretin neurons, and other "brain orchestrators").

Mismatching appetite and arousal to the environment causes some of the most frequent diseases today, such as obesity and sleep disorders that affect around 1:4 people worldwide.

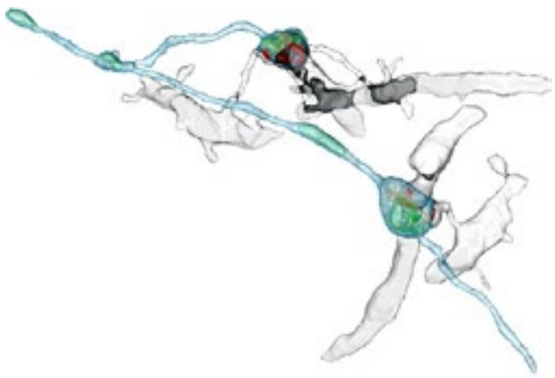
We are more broadly – experimentally and theoretically – interested in "reverse engineering" brain strategies for neural computation and adaptive behaviour.

Andreas Schaefer

Understanding how complex behaviour emerges from the properties of molecules, cells and ensembles of cells is one of the key challenges in neuroscience. We try to tackle this question employing the olfactory system of mice as a model system. We perform whole-cell, extracellular and imaging recordings in the olfactory bulb of awake, behaving mice. Light- and electron-microscopic analysis of the anatomy guides our efforts to perturb the system using genetic, optogenetic and pharmacological tools. To obtain higher-throughput behavioural and electrophysiological analysis we develop new methods for automatized behavioural training and pursue more scalable approaches to electrical neuronal recording.

Ede Rancz

We are interested in the functional and structural underpinnings of how internally generated and external, sensory information interact in cortex to guide behaviour. We specifically study the visual and vestibular systems and their interaction with the best-studied internal representation: that of space. To dissect and interrogate inherently complex cortical networks, we use a multi-scale approach and take advantage of recent technical developments in genetical tools in mice. With the use of cre-driver lines and virally mediated transsynaptic tracing we can map the synaptic partners of single cells and functionally defined neuronal populations to elucidate the underlying rules of such connectivity. Using genetically encoded biosensors and electrophysiological approaches both in vivo and in vitro we can directly assess the physiological relevance of single cell and network function. We aim to provide detailed and quantitative description of single neuron and microcircuit function, not only to generate new knowledge, but also to build new models and hypotheses about the hows and whys of the brain.



THE CENTRE FOR DOCTORAL TRAINING IN NEUROTECHNOLOGY FOR LIFE AND HEALTH

Introduction

The aim of the Centre for Doctoral Training in Neurotechnology for Life and Health is to train a new generation of researchers to investigate and address the challenge of brain-related illness.

Our training programme is driven by understanding and interacting with the brain, a grand challenge with critical industrial and societal impact. The programme builds upon Imperial College's strengths, fusing technology and neuroscience to make a unique contribution, generating graduates needed by industry and improving the quality of life and health in the UK.

A multidisciplinary approach is core to the activities of the CDT; all research projects involve a team of supervisors, each of whom brings complementary expertise to the training programme, and projects bring one or more technological approaches together with neuroscience expertise to solve an important problem underlying brain disorders. Our supervisory teams are drawn from thirteen departments, spanning three faculties at Imperial College (Engineering, Medicine and Natural Sciences), maximizing the range of perspectives and research infrastructure support available for each project.

EPSRC Centre for Doctoral Training in NEUROTECHNOLOGY for life and health

"Bringing a multi-disciplinary approach into the mix is going to be vital to finding a cure for Parkinson's and other brain disorders – engineering is the missing piece."

Todd Sherer, PhD, CEO, Michael J Fox Foundation

The CDT programme

The CDT training programme has a 1+3 structure, with the first year being a purpose-developed MRes in Neurotechnology, followed by a three-year PhD.

During the MRes year, students take three months of taught courses and then carry out a nine-month research project, which involves laboratory rotations (as part of a single project), with a single thesis submission at the end of the MRes year. The aim of the MRes is to develop all of the technical skills required to carry out the PhD work successfully and provide the student with a foundation in research.

MRes taught modules include custom-developed courses such as *Introduction to Neuroscience*, which provides engineering and physical science graduates with a thorough grounding in neuroscience, and *Ethical and Social Implications of Neurotechnology*, a one-day workshop exploring the ethical aspects of neurotechnology. Students also take laboratory technical skills workshops and modules from the MSc Biomedical Engineering.

All MRes students are housed in the purpose-built EPSRC Centres for Doctoral Training Suite in the South Kensington Campus. This space is shared with seven other ESPRC CDTs and provides space for over eighty desks, three teaching rooms, an administrative office and kitchen facilities.

"We at GSK believe a revolution in disease therapy can be built in the next 1-2 decades at the interface between biology and engineering, and to really advance bioelectronic medicines – which will rely on neurotechnology to bring about clinical effect – we will be seeking a future cadre of multidisciplinary investigators who are equally well-versed in both neuroscience and engineering."

Kristoffer Famm, PhD, VP Bioelectronics R&D, GSK

MRES NEUROTECHNOLOGY PROGRAMME SYLLABUS (2014/15) AT A GLANCE

Taught element (25% of overall MRes mark)

CORE MODULES

- Introduction to Neuroscience (term 1)
- Statistics and Data Analysis (term 1)
- Machine Learning and Neural Computation (term 1)
- Journal Club (terms 1 & 2)
- Ethical & Social Implications of Neurotechnology (term 1)
- Medical Device Entrepreneurship (term 1)
- Computational Methods Training (term 1)

ELECTIVE MODULES

- Technical skills lab workshops (terms 1 & 2)
- Modules from the MSc in Biomedical Eng (terms 1 & 2)

Research element (75% of overall MRes mark)

The following components make up the research element of the MRes:

- Literature review and thesis proposal (due beginning of term 2) — 10% of MRes mark
- Poster/oral presentation (due term 3) — 10% of MRes mark
- MRes project (marks for research conduct & written thesis submitted mid-September) — 45% of MRes mark
- Oral examination (end of year) — 10% of MRes mark

Students must take all core modules plus sufficient elective modules to obtain the required number of credits.

ADDITIONAL TRAINING

In addition to working towards their official research milestones, the CDT student cohorts will come together regularly for additional training opportunities including:

Professional skills training
Imperial College Graduate School runs a comprehensive professional development skills programme with a variety of courses offered in the MRes year and throughout the PhD phase, covering such topics as: personal effectiveness, communication skills, networking and teamworking, career management, and research and presentation skills.

Neurotechnology Colloquia and seminars
The Centre hosts a monthly colloquium series as well as other seminars throughout the year. The MRes student cohort will typically host the colloquium speaker for lunch, giving them the opportunity to talk to the speaker, discuss research and ask questions freely.

Winter School
The CDT, in collaboration with researchers from the EU Marie Curie Initial Training Network Neural Engineering Transformative Technologies (NETT), hosts a biennial winter school comprising 2 days of talks aimed at students and researchers from the CDT and NETT. The first winter school was run successfully in January 2015 and was well attended by the students and researchers from across Imperial College.

Internship/exchange programme
During the course of their PhD, CDT students will undertake either an industrial internship with one of the CDT industrial partners, or an international academic research visit (exchange). The internship/exchange programme aims to broaden the perspective of the CDT student, and help them to build their network both into industry and internationally. Twelve industry partners have agreed to host interns and we are developing an international network of universities that will exchange researchers to develop collaborative research projects in Neurotechnology. Exchange schemes with McGill University and the Bernstein Centre in Freiburg have already been established and we aim to extend this to a multilateral network including other universities with a specific Neurotechnology activity, such as ETH, Georgia

Tech, National University of Singapore, the University of Melbourne and MIT.

Research symposium
CDT students will present their work and participate in the annual Centre for Neurotechnology research symposium. The symposium aims to involve representatives from both academia and industry, to provide students with an industry perspective on topics in neurotechnology research and an opportunity for networking and informal career advice.

Public engagement training
CDT students are encouraged to participate in outreach and public engagement activities, in order to share their research with wider audiences. In order to support them in this area, the CDT provides an annual public engagement workshop for CDT and Centre researchers, which aims to guide the participants in engaging the public with their research, designing a public engagement activity and measuring impact of public engagement.

Imperial Festival
Students from the first cohort of the CDT developed and hosted two well-received exhibits at the 2015 Imperial Festival. The activity provided the students with excellent experience of working together to develop and present a public exhibit as well as discussing and engaging with a public audience about their research. Following the success of this activity, we plan to incorporate this into the CDT programme as an official CDT activity for successive cohorts.

CDT Festival of Science and Engineering
CDT students are encouraged to attend and participate in the organisation of the annual Imperial College CDT Festival of Science. This event allows students to collaborate with the other CDTs at Imperial to demonstrate to the research community of Imperial College the range of current research taking place and to come together to discuss scientific issues.

Conferences
All students will attend at least one major international conference during the PhD, as well as one national conference per year. Students will also be encouraged to join professional societies including the Society for Neuroscience, British Neuroscience Association, IET and/or IEEE. To enable this, CDT students are provided with an annual budget for conferences and travel.

Research projects and students

COHORT 1 | 2014-15

Cher Bachar
Supervisors: Vincenzo De Paola, Claudia Clopath, Anil Bharath

High-throughput Visualization and Computational Consequences of Increased Synaptic Plasticity and Axon Regeneration in the Living Aged Brain

Cognitive decline associated with ageing and brain injury affects millions of people every year but the underlying cellular and synaptic mechanisms are not completely understood. Recent evidence shows that synapses are unstable in the aged brain with higher rates of formation, elimination and strength change associated with long-term memory impairment (Grillo et al., PNAS 2013). In this project we study the computational aspects of increased synaptic dynamics. Our approach makes use of recently established in vivo optical imaging and minimal injury assays in the De Paola lab and new computational methods from the Clopath lab to gain insights into the causal relationship between synaptic remodelling and age-related cognitive decline. In addition, novel high-throughput image analysis algorithms based on steerable wavelet technology will be developed together with the Bharath lab.

Tamara Boltersdorf
Supervisors: Nicholas Long, Felicity Gavins

Designing novel imaging probes for targeting inflammatory lesions in brain disorders

Monocytes are circulating white blood cells that play important roles in the inflammatory response and in brain disease. The ability to detect and quantify monocytic accumulation will enable scientists to locate and identify inflammatory brain lesions but also will facilitate the development and testing of anti-inflammatory agents. This cross-disciplinary project involves an iterative cycle of synthetic inorganic/organic chemistry and biological/imaging validation and analysis, and aims to develop diagnostic probes and tools that can detect both acute and chronic inflammation using biomedical imaging, resulting in improved diagnostic markers for the clinic, aiding assessment of improvement/repair of brain function.

Catriona Egan

Supervisors: Claudia Clopath, Paul Chadderton

Experimental and computational study of auditory receptive field properties and connectivity

Neurons in primary auditory cortex show selectivity to a subset of their inputs, a property called receptive fields. Receptive fields are thought to be developed through synaptic plasticity, i.e. changing the connections between the neurons. However, it is unknown why different neurons have different receptive field properties (i.e. function) and how the function relates to their connectivity.

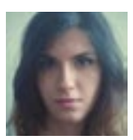
To address these open questions, the project uses experimental tools to measure receptive field diversity, location and connectivity, plus computational modelling of synaptic plasticity to study the link between the connectivity structure and the function.

Rajinder Lotay

Supervisors: Etienne Burdet, Paul Bentley, David Soto, Caroline Alexander

Development of a bedside 'hand-and-brain training' rehabilitation aid for stroke patients

Our project offers unique opportunities to design and investigate compact portable devices, and "addictive" computer games for neurorehabilitation, alongside ~2000 stroke patients cared for annually at Imperial College NHS Trust. The project is supervised by the Human Robotics group (http://www3.imperial.ac.uk/humanrobotics), which has pioneered hand rehabilitation devices, and the Imperial College Division of Brain Sciences, which has expertise in cognitive mechanisms (e.g. attention, motivation) underlying neuro-rehabilitation. This will enable us to develop low-cost, bedside strategies for rehabilitation of hand function, which could be used widely amongst the 150,000 new stroke cases in the UK per annum.



Diana Lucaci

Supervisors: Stephen Brickley, Paul Chadderton, William Wisden

High-resolution mapping of age-related functional changes in cortical connectivity

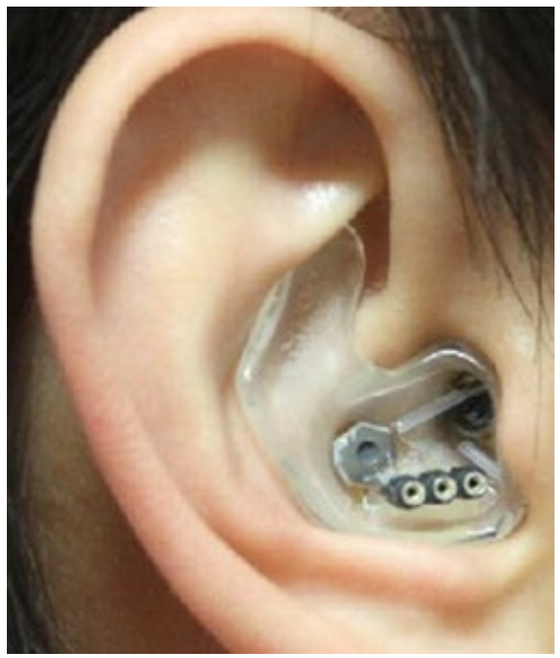
Over a quarter of a million people were diagnosed with dementia in the UK last year but basic scientific information on the nature of this cognitive loss is sadly lacking. Human brain imaging studies have raised the possibility that communication between cortical regions deteriorates with age, but such studies are unable to provide any mechanistic insight into the nature of these changes. However, a number of experimental tools are being developed that should enable high-resolution mapping of age-related changes in cortical connectivity both at the anatomical and functional level. This project applies expertise in novel viral delivery methods (Prof Wisden; Life Sciences), in vivo whole cell recording techniques (Dr Chadderton; Bioengineering), and functional synaptic mapping in vitro (Dr Brickley; Life Sciences) to generate high-quality data that will quantify anatomical and physiological changes in the ageing mouse brain at the level of individual synapses.

Peter Quicke

Supervisors: Simon Schultz, Mark Neil, Thomas Knöpfel

Optical decoding of peripheral nerve signals

Bioelectronic medicines, in which devices connected to groups of individual nerve fibres are used to control the patterns of electrical signals to restore health to organs and biological functions, have been suggested to have the potential to make major advances in the treatment of conditions resistant to drugs, including diabetes, obesity, hypertension and pulmonary diseases. The development of bioelectronic medicines, however, is contingent upon the existence of suitable technology for monitoring and perturbing activity in peripheral nerve fibres, with fine spatial resolution. In this project, we will develop and demonstrate optical technology for decoding physiological signals from patterns of activity across nerve fibres.



Ben Schoenhense

Supervisors: Aldo Faisal, Adam Hampshire

Machine learning and human adaptability: towards a hierarchical model of executive cognition and brain function

The term 'executive cognition' refers to a general class of psychological processes that are closely associated with the frontal lobes and that are fundamental to human adaptability. Executive cognition enables us to rapidly identify the most appropriate set of actions when faced with novel situations, to efficiently organise those actions into complex goal orientated behaviours, and to modify/override established behaviours when environmental conditions change. Impairments of executive cognition are of great clinical relevance because they are a prominent symptom in a raft of neurological and psychiatric patient populations. Despite being the focus of much research, our current theoretical understanding of executive cognition and its relationship to frontal lobe functional organisation is at best rudimentary and operate on proxy measures of executive function.

The aim of this project is to impact on these issues by applying the rigorous mathematical framework of Bayesian Decision theory and Reinforcement learning in the context of behavioural and neuroimaging experiments that probe human executive function. On a practical level, the project will determine the potential utility of these models for providing more sensitive detection and finer-grained classification of cognitive impairments in psychiatric and neurological populations.

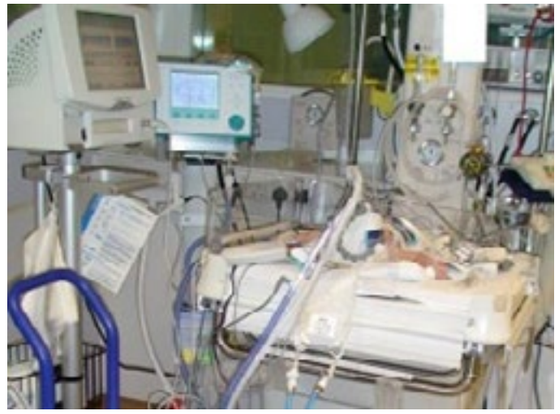
Hugo Weissbart

Supervisors: Tobias Reichenbach, Robert Leech, Etienne Burdet, Richard Wise

EEG assessment of central auditory disorder in patients with brain injury

Our auditory environment is highly complex: different speakers often talk at the same time, music plays in the background, cars drive by. Our central nervous system is highly effective in analyzing such an auditory scene; for example, we can easily understand a speaker despite background noise. A range of neurological disorders can, however, impair the cognitive processes necessary to parse an acoustic scene and hence significantly impair a person's life. Both the brain's auditory processing and the associated disorder remain poorly understood.

The project will develop methods to assess the brain's processing of complex auditory signals such as speech and music through noninvasive electroencephalographic (EEG) recordings. The methods will be used to diagnose patients



with brain injury whose auditory processing is impaired. As an example, the project will study patients with aphasic stroke that affects brain regions for communication and language. The research will help to better understand the neurological basis of such disorder and help to develop novel rehabilitation strategies.

The project involves EEG data acquisition, advanced data analysis, machine learning, computational modelling and clinical research.

Aidan Wickham

Supervisors: Martyn Boutelle, Manos Drakakis. Collaborator: Chris Shaw (KCL)

Wearable wireless sensor arrays to detect the progression of amyotrophic lateral sclerosis (ALS)

Motor Neuron Disease or amyothophic lateral sclerosis (ALS) is a degenerative disorder of motor neurons. Its cause is unknown, and while its incidence is similar to that of multiple sclerosis its progression is much faster, resulting in death within 2-5 years from diagnosis. Research into the underlying causes and possible therapies are hampered by the difficulty in tracking disease progression reliably.

This project is a new collaboration between Bioengineers from Imperial College with expertise in real-time human sensors (Boutelle) and Electronics (Drakakis) and a Clinician and Research expert in ALS from the Institute of Psychiatry (Shaw). Our vision is to use the sensors, instrumentation and signal processing approaches of neurotechnology to design and build comfortable 'smart' clothing to monitor the arms and legs of ALS patients to track disease progression. The new system will be validated against expert clinical assessment scores.

Giorgios Zafeiropoulos

Supervisors: Manos Drakakis, Denis Azzopardi, Amir Eftekhar

Hilbert-Huang Transform (HHT)-based Automated Neonatal EEG Early Warning System

The neonatal period, is one of the most critical in brain development. It is in this period where the process of interconnection development and synchronisation within the brain, which starts in the foetus, continues. Up to 10% of births require intensive neonatal care due to pre-term or at birth complications. These abnormalities can lead to later life brain disorders such as epilepsy. It is a fact that approximately 50% of neonates that have seizures will develop epilepsy. Due to the aforementioned reasons, we decided to use EEG/aEGG signals from the neonatal brain activity, a highly complex signal, together with the Hilbert-Huang Transforms, a powerful tool for complex signals analysis, in order to develop a novel automated analysis platform/modality for the neonatal clinical setting. This will allow advanced seizure/spike and abnormality detection/analysis to be performed, accompanied with a system that can alert clinicians for important changes in neonatal brain activity. Collaborators in addition to supervisors are: Prof. Edwards, Director of the Centre for the Developing Brain (KCL), Prof. Parker (Bioengineering-Imperial) and J.McAvoy (www.cybula.com).

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Tiffany Chan

Supervisors: Ramon Vilar, James Choi, Amin Hajitou, Matt Williams

Ultrasound technology to deliver novel theranostic agents to malignant brain tumours

Glioblastoma multiforme (GBM) is the most aggressive type of malignant brain tumour in humans. Several potential drugs for GBM have been assessed in clinical trials without much success.

One of the problems encountered is the inability of the compounds to cross the blood-brain barrier (BBB). This project aims to address this problem by developing ultrasound technology to disrupt the BBB so that anticancer agents can be delivered to the tumour.

Novel nanomaterials containing anticancer drugs and an MRI probe (for tracking) will be developed and the ultrasound technology applied to deliver them to the brain in an animal model.

James Clarke

Supervisors: Ravi Vaidyanathan, Alison McGregor. Collaborators: Rob Hart, Caroline Hargrove (McLaren Applied Technologies)

Integrated Sensor Suite to Investigate Neurological Dysfunction in Balance

The project will centre on instrumentation for studying mechanisms of sensory-motor control, as applied to human movement and neurological foundations of balance. The goal is to create an integrated, system that will detect, fuse, and transmit sensor data from foot contact force, muscle action, and motion for pervasive monitoring, diagnostic assessment, and treatment of patients with neurological and/or movement dysfunction. Technology innovation in this project will leverage work from the Imperial-McLaren team in:

- Wearable motion tracking: We have developed a range of MARG (Magnetic, Angular Rate, and Gravity) sensor packages and algorithms whose computational efficiency enables use at low power, facilitating integration into the diverse sensor suites targeted in this project
- Pervasive muscle recording: Our team has developed a new sensor for muscle activity for use outside clinical environs; this will be integrated into balance monitoring system in this project.
- Force profile sensing: We have developed a sensor 'sheet' capable of force measurement within clothing, shoes and orthotics. Smart materials are used to create a grid of pressure sensitive areas which can be embedded into a cloth or orthotic liner which will be used to correlate contact forces with balance.
- Biomedical Signal Fusion: This project will extend models we have developed in signal processing to fuse information from multimodal physiological signals from the integrated suite.

Darije Custovic

Supervisors: Adam Hampshire, Claudia Clopath

Neural network mechanisms of inhibitory and attentional control

Many aspects of human cognition, such as response inhibition, working memory and attentional control, have been attributed to the same network of frontal and parietal brain regions. Furthermore, the role of this network in cognition is not static as instead, activities and connectivities diminish as the task at hand transitions from novel to familiar.

The project will examine how frontoparietal networks support such diverse cognitive demands and how local neural plasticity mechanisms (i.e. changes in connections between neurons) underlie the shifting involvement of frontoparietal networks in cognition.

This will be achieved by combining cutting-edge functional neuroimaging and computational modelling methodologies.

Sofia Dall'Orso

Supervisors: Etienne Burdet, Daniel Rueckert, David Edwards
Collaborator: Tomoki Arichi (KCL)

Robot-assisted fMRI investigation of learning in newborn infants

During the first months following birth, brain development is rapid and partly moulded through experience.

We plan to elucidate the neural mechanisms of learning in babies with functional magnetic resonance imaging (fMRI) and a classical conditioning experiment, using a combination of a sound stimulus and a robotic MRI-safe pacifier (which can both provide a gentle stimulus to the infant's mouth and precisely measure their behavioural response through sucking).

This study may answer fundamental questions about how early functional brain development and function is influenced by external experience, and lead to improved treatments for infants at risk of cerebral palsy.

Andrea Fiorentino

Supervisors: Holger Krapp, Mirko Kovac, Reiko Tanaka

Neuronal principles underlying visual flight control in insects applied to autonomous micro air vehicles

During flight an insect has to achieve two fundamental tasks: For one, the insect has to maintain aerodynamic stability - even when caught by gusts of wind - and secondly, it has to void colliding with any obstacles.

Both of these tasks are supported by the animal's visual system which analyse relative motion between its huge compound eyes and objects in the surroundings.
In this project, based on quantitative behavioural data a bio-inspired control architecture will be derived to enable stable flight of an autonomous air vehicle that automatically avoids collisions with objects.

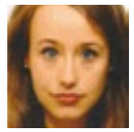
Lewis Formstone

Supervisors: Ravi Vaidyanathan, Paul Bentley, Etienne Burdet, Alison McGregor

Brain lesion-mapping and motion-tracking: How neural trauma impacts motor control

The neural basis of movement is a fundamental question in systems neuroscience and to treat disorders such as stroke, Parkinson's disease, brain injury, etc. Relationships between brain anatomy and motor function, however, remain unknown.

The dissertation will contribute to this gap by mapping sites of brain trauma to arm and arm/hand control. Novel instrumentation will be designed to extract features of motion and muscle activity in stroke patients to correlate brain lesion location to its resulting impact on movement. It will advance knowledge in micro-instrumentation, signal analysis, and brain mapping to answer fundamental questions in neuroanatomy and human movement.



Patricia Gallego

Supervisors: Richard Reynolds, Aldo Faisal, Kambiz Alavian

An integrative approach to studying the functional effects of neuroinflammation in human CNS disease – modelling, imaging & electrophysiology

Neuroinflammation is a feature of all degenerative disorders of the human brain. In multiple sclerosis and Parkinson's disease, diffuse inflammation leads to changes at the nodes of Ranvier, the regions of the nerve fibres where the electrical signals are amplified.

We do not know how these changes give rise to deficits in nerve conduction and how this can be reversed. This project will use computer modelling, human brain tissue studies and electrical recording from brain slices to investigate how the electrical properties of the nerve fibres could be changed to compensate for this neural damage and reverse the neurological deficit.

Katie King

Supervisors: Molly Stevens, Simone di Giovanni

Neuronal Interfacing System for Human Pluripotent Stem Cell Interrogations using Materials-based Nanotechnologies

The generation of competently functional human neurons in vitro is crucial to accurately model degeneration of the nervous system and to provide invaluable insights into fundamental neurobiology.

In this exciting multidisciplinary project, we will combine the latest advancements in nanoengineered technologies, microfabrication at the cell-material interface and restorative neuroscience to develop a platform that will investigate stem cell-derived human neurons for both fundamental neurobiology and regenerative medicine purposes.

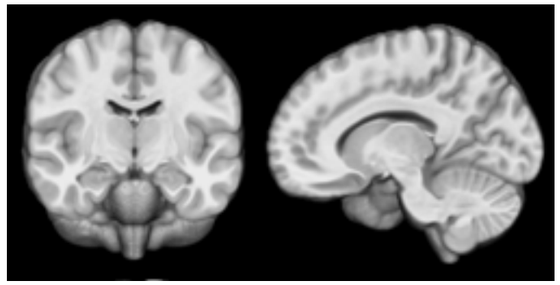
Tim Kirby
Supervisors: Danilo Mandic, David Sharp

Investigating Sports Related Concussion with a Wearable In-Ear System for Continuous Monitoring of Brain and Body Functions

This project aims to develop an in-the-ear (ITE) platform for discreet, unobtrusive, and continuous monitoring of brain function (electroencephalography - EEG) and body functions (pulse, respiration, temperature, movement). Once developed, the system will have many potential applications, from EEG recording in an intensive care setting through to the recording of the immediate effects of sports injuries on brain function. The proposed work will: (i) establish the biophysics behind ITE monitoring of physiological responses, (ii) integrate the EEG and vital sign sensors into a working prototype, (iii) test the ITE system's ability to acutely monitor the acute effects of Sports Related Concussion, in the context of Rugby. There is increasing concern about the effects of sporting head injuries. Repeated minor injuries both cause immediate concussive symptoms, and in some individuals more prolonged effects including dementia. The immediate aftermath of head injuries in sports is currently largely uncharted territory due to the lack of suitable recording devices, yet this stage is critical in the assessment of the injury and eventual recovery. The proposed work will, for the first time, provide a device that allows the immediate effects of sporting concussions to be measured.

Carl Lubba
Supervisors: Simon Schultz, Nick Jones
Collaborator: Victor Pikov (GSK)

Peripheral nerve decoding algorithms for bioelectronic medicines



Bioelectronic medicine, in which devices connected to groups of individual nerve fibres are used to control the patterns of electrical signals to restore health to organs and biological functions, has been suggested to have the potential to make major advances in the treatment of conditions resistant to drugs, including diabetes, obesity, hypertension and pulmonary diseases (Famm et al, Nature 496:159-61, 2013).

The development of bioelectronic medicines, however, is contingent upon the existence of suitable technology for monitoring and perturbing activity in peripheral nerve fibres; in particular, being able to "read out" and interpret signals carried by a peripheral nerve fibre is an essential milestone.

In this project, we will develop decoding algorithms capable of reading out both continuous physiological signals, and discrete "events", from peripheral nervous system (PNS) electrical signals. These algorithms will be applied to a variety of datasets collected by members of a research network in Bioelectronic Medicines that has been established by GlaxoSmithKline, plc.

The project will involve two phases. The first year will comprise an MRes Project, in which the student will gain a deep understanding of the different approaches that can be taken to decoding physiological signals, testing algorithms on simulated data, which will be generated in the course of the project; we expect this computational model of a peripheral nerve to be a major output of the MRes year. In the following years, and exploiting and advancing a new signal processing architecture, the student will develop refined decoding algorithms optimised for use with peripheral nerve signals at several spatial scales, and will work with research groups across the GSK network to apply these algorithms to real PNS datasets.

Gerald Moore
Supervisors: Thomas Knöpfel, Simon Schultz. Collaborator: David Holder (UCL)

Cracking the neuronal code using combined optical imaging and Electrical Impedance Tomography

Understanding of how the brain codes information will be advanced by combining two cutting edge techniques which allow imaging of neuronal activity over milliseconds in the brain. Optical microscopy using dyes or genetically encoded indicators allows imaging of individual neurones within the cortical surface of the brain.
Electrical Impedance Tomography enables imaging of activity of larger groups of neurones everywhere in the brain using mats of tiny electrodes placed on the brain surface. They will be combined using new transparent electrode mats. This will produce a revolutionary new imaging method able to yield new insights into how the brain processes information.

Konstantinos Petkos
Supervisors: Manos Drakakis, Peter Brown. Collaborators: Timothy Denison (Medtronic Neuromodulation [US])

ReBooT: Restoring Brain Operation with Technology; Microelectronics to enable an open source instrument for exploring closed loop neural systems

The project will focus on developing microelectronics for research tools that enable the exploration of neurological disorders. Ultimately, the research tool's hardware and algorithm platforms should set a new performance standard for translational recurrent (bi-directional) brain-computer-interface technology architectures.

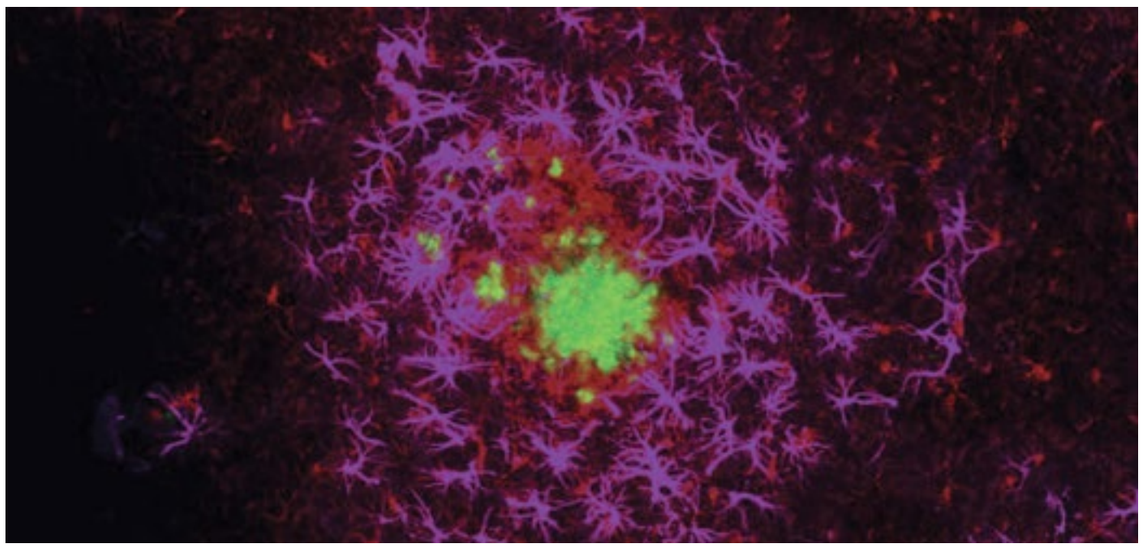
Electronic subsystems will be designed to facilitate the identification and preclinical evaluation of potential biomarkers, classifiers, and control methods using advanced neuromodulation methods. To improve the modulation of neural activity, there is strong interest in improving the actuation capabilities of neural interfaces to more physiologically interact with the nervous system. For example, new microelectronic circuit stimulation designs will allow researchers to generate multiple actuation patterns to investigate neural codes. Additional innovation will be derived from the new methods to apply sensors and sensor fusion. These include exploring biomarkers derived from biopotential amplifiers and impedance sensors. While the microelectronics for the research tool will be designed as general instrument building blocks, feedback from potential users will provide focus for evaluation.

The ultimate goal of the electronics project is to enable research tools that help to translate therapeutic neural control systems to the clinic. However, the initial focus will be on a systems/hardware/chip-focused student for the project.

Tom Robins
Supervisors: Mengxing Tang, Paul Chadderton

Towards whole brain functional imaging in freely moving subjects

The measurement of functional activity in the brain is crucial to understanding how this structure works. Functional ultrasound imaging (fUS) is an exciting new technique that has demonstrated its feasibility in vivo, and has potential for whole brain functional imaging in freely moving subjects.
This project is the first step towards such a portable brain imaging system. The aim is to develop and evaluate an initial fUS system using a customized ultrasound probe within a helmet, in combination with microbubble contrast agents and advanced image reconstruction algorithms for increased imaging sensitivity. Evaluation of the system will be performed by in vitro phantoms and imaging sensory-evoked brain activity



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