Imperial College
London

Centre for Bio-Inspired Technology

Annual Report 2015

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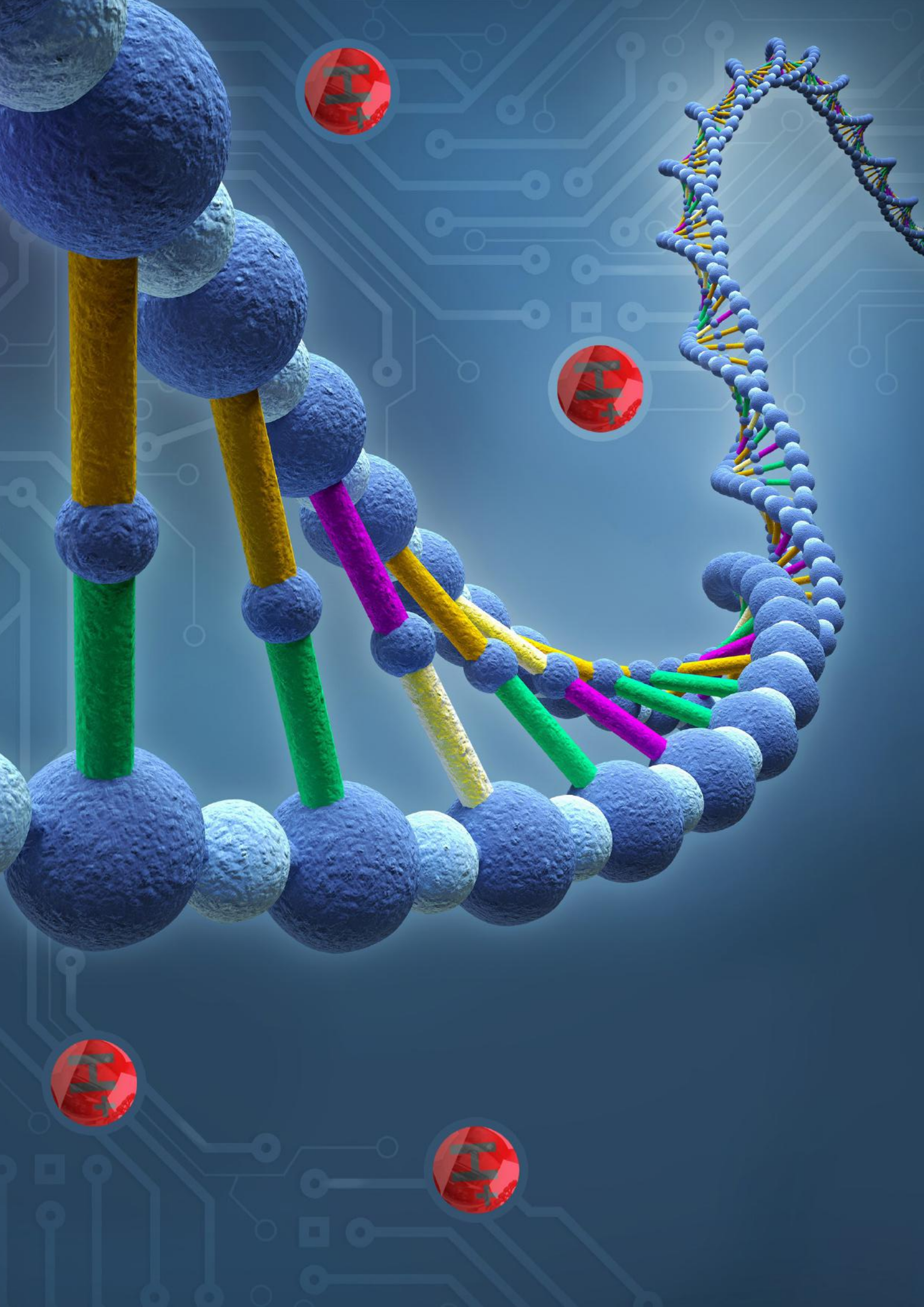


Director’s foreword

It is my great delight as director, to report that the Centre for Bio-Inspired Technology has enjoyed another successful year of outstanding research through the hard work, dedication and innovation of its members. Our team has developed cutting-edge technology in fields spanning nutrition and cosmetics, with a continued strength in biomedical engineering and healthcare.

This year, I am especially proud to say that our Department was rated top in the UK’s 2014 Research Excellence Framework (REF) for Electrical and Electronic Engineering (a major assessment of research quality in UK higher education institutions, occurring once every five years). For the first time, it included “Impact Case Studies” which assess the impact of the submitted research. Of the five case studies submitted by our department, one focussed particularly on this centre, all were ranked 4* – “quality that is world-leading in terms of originality, significance and rigour”. Notably, our department was the only one in our subject panel (UoA13 – Electrical and Electronic Engineering, Metallurgy and Materials) to be honoured with such a flawless assessment.

It is also particularly encouraging to reflect upon the successes the centre has enjoyed in our grant applications. In particular, we were awarded two grants for tackling Anti-Microbial Resistance (AMR) – a pressing issue for hospitals struggling to maintain the effectiveness of antibiotics. These are highly interdisciplinary research programmes, drawing together expertise from multiple departments to “bridge the gaps” between engineering, medicine and the natural sciences in order to tackle one of society’s great challenges for the 21st Century.
We were also successful in our application for an EPSRC Platform Grant – a highly coveted award which gives very flexible funding to retain key members of our team, foster new talent and pursue high-risk feasibility studies. The broad remit of this reward is rare and will be instrumental in enabling us to maintain our position as a world-leading centre in biomedical engineering.

Continuing our commitment to developing impactful technology-transfer through clinical engagement, our biomedical projects have continued to progress. Dr Pantelis Georgiou and Dr Pau Herrero Viñas have advanced their clinical trials with the artificial pancreas for treating diabetes. Meanwhile, Dr Nicoletta Nicolaou’s has commenced clinical trials for the AnaeWARE project at Hammersmith Hospital, which will soon be extended to Chelsea and Westminster Hospital. Lastly, the I2MOVE trials are demonstrating the potential for regulating appetite by stimulation of the vagus nerve, leading the way for novel “electroceutical” therapies for the treatment of obesity.

Besides biomedical devices, we are also poised to release open-source computational tools from Dr Benjamin Evans and Dr Konstantin Nikolic called “PyRhO”, which will bring modelling abilities to experimentalists and accelerate progress in optogenetics. The centre plans to produce more such public-domain resources, both software and hardware, for the good of the scientific community in the near future. Additionally, several of our groups have continued our commitment to public engagement with special events at the Science Museum and the Imperial Festival.

It is always pleasing to witness our “home-grown” talent achieve recognition for their contributions and this year is no exception. We would like to congratulate Dr Pantelis Georgiou on his promotion to Senior Lecturer and Dr Tim Constandinou for being awarded a prestigious EPSRC Fellowship. Finally, this year I was also honoured with the IEEE Biomedical Engineering Award, for which I am deeply grateful to the CBIT members whose labours have facilitated this accolade.

Finally, we are also particularly pleased to see the Queen recognise our co-founder, Professor Winston Wong, with an OBE for his significant contributions to education.

Professor Chris Toumazou
FRS, FREng, FMedSci, Regius Professor of Engineering

Founding Sponsor's foreword

It is most satisfactory to see another year of research development and innovation at the Centre for Bio-inspired Technology. By securing competitive funding steadily the Centre is thriving, it now counts with a growing number of multidisciplinary researchers working in pioneering projects.

It was only four years ago that the Centre was created with the idea of transferring knowledge learned at the laboratory to the market. Something that is not trivial as it usually takes years for cutting edge technology to reach the wider public. With this new Centre we wanted to inspire new research and accelerate the pace and bring innovation closer to the consumer.

The Centre is leader in merging electronic and medical industry, by bringing together multidisciplinary teams to find solutions for health care such as satiety control implants, breast cancer detection and insulin intelligent pumps.
Innovation comes from learning how to think outside the box, and by finding new applications to the electronics developed at the Centre we realised that our technology can be even more versatile and that we could do something that nobody from the electronic industry has done before: bringing medical grade technology to the consumer.
The lab-on-chip technology, developed at the Centre, which currently is being applied to health

care conditions such as sepsis and breast cancer, could also used for skincare in the cosmetic industry.

I was pleased to receive this year the Order of the British Empire (OBE) from her Majesty the Queen for contributing to education. I thank their Centre for the great support.

Professor Winston Wong OBE, BSc, DIC, PhD, DSc

People

Academic and senior research staff

Professor Chris Toumazou FRS, FREng, FMedSci
Regius Professor of Engineering;
Director, Centre for Bio-Inspired Technology;
Chief Scientist, Institute of Biomedical Engineering;
Winston Wong
Chair in Biomedical Circuits
Department of Electrical and Electronic Engineering

Dr Timothy G Constandinou
Senior Lecturer, Department of Electrical and Electronic Engineering;
Deputy Director, Centre for Bio-Inspired Technology

Dr Pantelis Georgiou
Senior Lecturer, Department of Electrical and Electronic Engineering;
Head of Bio-Inspired Metabolic Technology Laboratory

Professor Chris N McLeod
Principal Research Fellow

Dr Konstantin Nikolic
Senior Research Fellow

Research staff

FELLOWS

Reza Bahmanyar, PhD

Andrea Alenda González, PhD

Amir Eftekhar, PhD

Nir Grossman, PhD

Pau Herrero Vinas,PhD

Nishanth Kulasekeram,PhD

Yan Liu, PhD

Yufei Liu, PhD

Belinda Nedjai, PhD

Nicoletta Nicolaou, PhD

Nour Shublaq, DPhil

ASSOCIATES

Benjamin Evans, DPhil

Sara Ghoreishizadeh, PhD

Melpomeni Kalofonou, PhD

Song Luan, PhD

Mohammadreza Sohbati, PhD

Irina Spulber, PhD

Szostak, Katarzyna

Huan Wang, PhD

Ian Williams, PhD

Longfang Zou, PhD

Claudio Zuliani, PhD

ASSISTANTS

Mohamed El-Sharkawy

Dorian Haci

Bernard Hernandez

Khalid Mirza

Peter Pesl

Research students

Deren Barsakcioglu

Onur Guven

Ermis Koutsos

Timo Lauteslager

Lorena Gonçalves de Alcântara e Freitas

Lieuwe Leene

Dora Ma

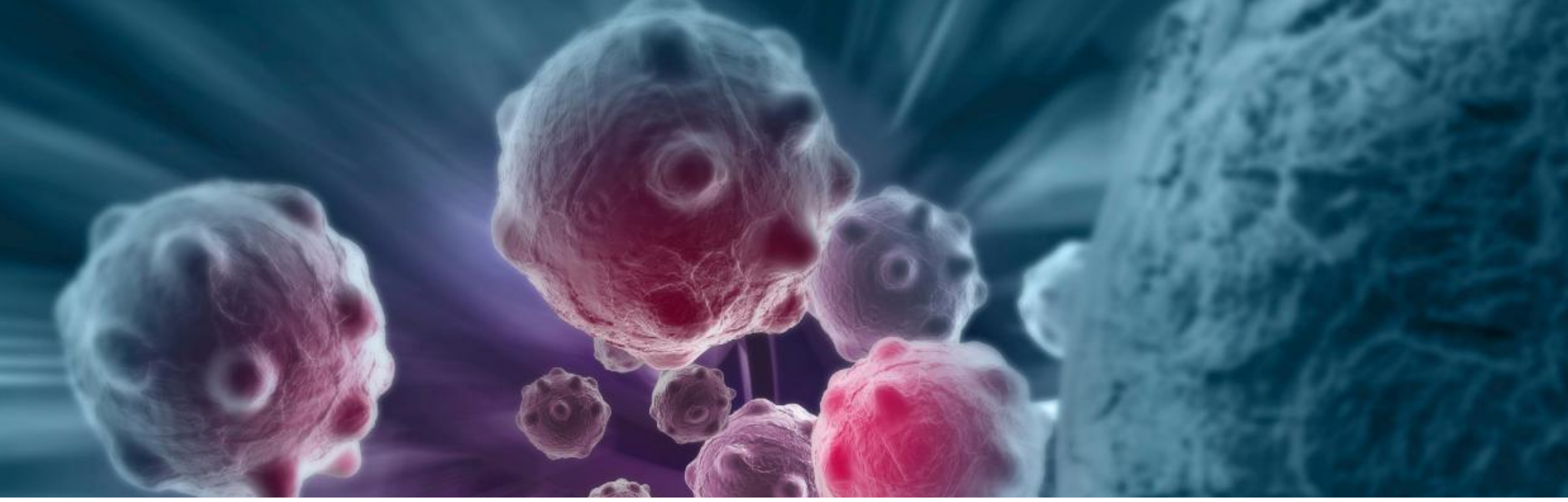
Nicholaos Miscourides

Nicolas Moser

Adrien Rapeaux

Francesca Troiani

Stephen Woods



Administrative staff

Sarah Agarwal
Project Administrator (Part time)

Wiesia Hsissen
Senior Group Administrator (CAS)

Gifty Kugblenu
PA to Professor Toumazou

Izabela Wojcicka-Grzesiak
Research Group Administrator (CBIT)

Consultants

Raymond Thompson
Rapid Prototyping Design Consultant

Visiting academics

PROFESSORS

Professor Tor Sverre Lande
University of Oslo

Professor Andrew Mason
Michigan State University

Professor Bhusana Premanode

Professor David Skellern
Formerly Macquarie University, Australia

Professor Peter Wells FRS
Cardiff University

Professor Winston Wong OBE
Grace THW, Taiwan

Professor Sir Magdi Yacoub FRS
National Heart & Lung Institute, Harefield Hospital

Professor Patrick Soon-Shiong
Chairman of the National Coalition of Health Integration (USA)

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National Heart & Lung Institute, Harefield Hospital

Professor Patrick Soon-Shiong
Chairman of the National Coalition of Health Integration (USA)

RESEARCHERS

Dr Alison Burdett
Toumaz Group, UK

Dr Jamil El-Imad
W Investments, UK

Dr Julio Georgiou
University of Cyprus

Dr Kiichi Niitsu
Nagoya University, Japan

Dr Miguel Silveira
Sensium Healthcare Ltd., UK

Dr Themis Prodromakis
University of Southampton

Graduates in 2014-2015

Mr Yuanqi Hu
Cirrus Logic International (UK) Ltd

Mr Mohammadreza Sohbati
Research Associate, Centre for Bio-Inspired Technology

Researchers who have taken up appointments elsewhere

Dr Sivylla Paraskevopoulou
Imperial College London

Dr William Spinner

Mr Satoshi Yoshizaki
Brookman Technology, Japan

News: Staff and events

FEBRUARY 2015

The i2MOVE team's work was showcased at the Science Museum's Cravings exhibition. An exhibition showcasing the science around cravings and appetite and the future technology to aid in controlling it. The exhibition is open until January 2016.

MARCH 2015

You Have Been Upgraded

The Centre for Bio-Inspired Technology was invited to contribute to "You Have Been Upgraded" festival at Science Museum that ran from 25th to 29th March 2015. Bringing together over more than 50 scientists, engineers ethicists and artists; the festival showcased an expo of human enhancement centred on a theatrical experience that aimed to provoke ethical considerations of human enhancement, as well as informing the public of current state of the technology and science.

Two groups presented their work on technologies for the restoration and enhancement of human sensory function then spent the sessions answering questions from attendees, demonstrating their research and discussing future directions of the technology. Dr. Timothy G. Constandinou, Dr. Ian Williams and Deren Barsakcioglu, presented their work on neural recording for improving prosthetic limbs with proprioceptive feedback while Dr. Konstantin Nikolic, Dr. Benjamin Evans and Nora Gaspar exhibited a prototype bio-inspired retinal prostheses for restoring vision. The work was greeted by the public with almost as much enthusiasm as for Deren and Ian's dramatic performance!

Dr Timothy Constandinou awarded EPSRC Early Career Fellowship

The Deputy Director of the Centre has been awarded the five-year fellowship of £1.054M from the Engineering and Physical Sciences Research Council (EPSRC).

This award will provide Tim the opportunity to dedicate himself to his research hands-on and take the driving seat to lead this forward. The extra resources and flexibility will allow his team to grow and consolidate capability to pursue a very exciting and ambitious vision.

Tim and his team will investigate 3 key themes aligned to the grand challenges that neural implant technology currently faces. They will develop chip-scale (millimetre sized) implantable devices that are fully autonomous, distributed and highly scalable. The research outcomes will directly feed into ongoing research and applications in brain machine interfaces within the experimental neuroscience community. This Fellowship will also enable us to work together with key partners in both the UK and US across the ICT, engineering and neuroscience communities.

The Fellowship formally started on 1st August 2015. See further details in the "Featured Research" section.

MAY 2015

Dr Pantelis Georgiou promoted to Senior Lecturer

The Director of Metabolic Technology in the Centre has been promoted to Senior Lecturer in the Department of Electrical and Electronic Engineering. Pantelis originally joined the department as an undergraduate student in 2000. After completing his PhD in 2008, he then moved to the Institute of Biomedical Engineering and in 2009 he was appointed as a research fellow with a focus in diabetes technology. In 2010, he became director of metabolic technology within the Centre for Bio-Inspired Technology and then re-joined the EEE Department as academic faculty in 2011, as a Lecturer in the Circuits & Systems Research group. He continues to maintain his role in the Centre and also leads the research theme in Metabolic Technology.

June 2015

Women in Engineering

Research staff from the Centre (Dr Irina Spulber, Dr Andrea Alenda Gonzalez, Dr Melpomeni Kalofonou and Dr Sara Ghoreishizadeh Seyedeh) joined by other female academic, research and administrative staff across the Faculty of Engineering, celebrated the Annual National Women in Engineering Day, June 23rd 2015.

President of Imperial College London, Professor Alice Gast, gave an inspiring speech, recognising the year's achievements, encouraging all female staff to actively share their passion for engineering, enhancing the visibility of their work while motivating future generations to study and be creative in the field.

Professor Chris Toumazou Awarded IEEE Field Medal in Biomedical Engineering for Outstanding Contributions to Biomedical Circuit Technology

The award was presented by IEEE President and CEO, Howard E. Michel at a ceremony during the 2015 International Symposium on Circuits and Systems (ISCAS) in Lisbon. It recognises Professor Toumazou's contributions to biomedical circuit technology which includes the invention of semiconductor DNA analysis and its ability to revolutionise healthcare and save lives.

Commenting on the award Professor Toumazou said: "My research is driven by an acute awareness of areas of unmet medical need, and in identifying how electronic inventions can help. The ability to reduce time to diagnosis in serious blood infections from days to just a few hours using our semiconductor DNA analysis platform can mean the difference between life and death for some patients. I am honoured that the IEEE has recognised my work.

Gabor lecture

This year Gabor lecture was deleivered by the Centre's director, Regius Professor Chris Toumazouwith the title "U+ life: the era of microchip Medicine". The Gabor lecture is named after Denis Gabor, an Imperial electrical engineer who won the Nobel Prize for Physics in 1971 for his invention of holography, a system of lens-less, three-dimensional photography.

Professor Toumazou praised the Nobel laureate's legacy, which influences his own work, particularly the way that 'Gabor saw the link between life science and engineering'.
Professor Toumazou acknowledged the contributions of Imperial alumnus Professor Winston Wong in driving forward the College's position at the forefront of biomedical engineering. In 2009, Professor Wong, a renowned Taiwanese businessman, funded the creation of the Winston Wong Centre for Bio-Inspired Technology, which is directed by Professor Toumazou.

Others distinguished guests at the event included the Duke of York, former Thai prime minister Thaksin Shinawatra, McLaren F1 founder Ron Dennis, and Duran Duran star Nick Rhodes.

The team at the IEEE BioCAS 2014 conference in Lausanne, Switzerland.

OCTOBER 2014 - SEPTEMBER 2015

Researchers prominent at international conferences

Researchers from the Centre have attended several international conferences this year and delivered papers.

Society for Neuroscience Conference, Washington DC

Konstantin Nikolic and Benjamin Evans attended (total number of attendees was close to 30,000). A poster presentation: “Multiscale computational tools for optogenetics” very well received.

2014 IEEE Biomedical Circuits and System (BioCAS) conference

The BioCAS conference held in Lausanne, Switzerland in November 2014 was attended by Nicoletta Nicolaou,Mohamed El sharkawy, Peter Pesl, Tim Constandiniu, Onur Guven, Pantelis Georgiou and Sara Ghoreishizadeh (above).
Both the bio-inspired artificial pancreas and advanced bolus calculator for diabetes were showcased in the live demonstrations session.

2014 Brain forum

The Brain Forum 2015 (March 30 – April 1) took place at Swisstech Convention Centre in Lausanne. From neurodegeneration and neuroprosthesis to founding and ethics, different topics of interest for the neuroscientific area were explored. Over 1000 people from different backgrounds participated to the Forum, creating an extremely stimulating environment.

International Conference on Advanced Technologies & Treatments for Diabetes

On February 18-21, 2015, a team of 5 members from CBIT attended in Paris (France) the 8th International Conference on Advanced Technologies & Treatments for Diabetes (ATTD 2015) where they presented the latest results on diabetes-related technology developed in our group. A total of 2 oral presentations and 4 posters were presented by members of our team.

ATTD has become synonymous with top calibre scientific programs that have provided participants with cutting edge research and analysis into the latest developments in diabetes-related technology. ATTD brings the world’s leading researchers and clinicians together for a lively exchange of ideas and information related to the technology, treatment and prevention of diabetes and related illnesses.

2015 IEEE International Symposium on Circuits and system (ISCAS)

The ISCAS Conference held in Lisbon, Portugal in June 2015 was attended by Adrien Rapeaux, Nicholaos Miscourides, Lieuwe Leene, Dorian Haci, Pantelis Georgiou, Tim Constandinou, Tor Sverre Lande, Nicolas Mosier, Irina Spulber and Konstantin Nikolic.

Organization for Computational Neuroscience, July 2015, Prague

In the summer, Benjamin Evans attended the annual Organization for Computational Neuroscience conference in the Czech Republic’s capital to present the poster “PyRhO: A Virtual Optogenetics Laboratory”. The poster unveiled PyRhO, the computational tools for optogenetics developed in CBIT and was roundly met with enthusiasm, especially for the accompanying GUI. Whilst there, he also attended satellite workshops and tutorials on open collaboration in computational neuroscience and modelling with the Brian simulator run by Dan Goodman, a recent addition to our department.

Reflections from Alumni

SIVYLLA-ELENI PARASKEVOPOULOU, PHD

Research Associate
2014-2015

I completed my PhD at Imperial College, in the Centre of Bio-Inspired Technology (CBIT), in 2013. My research proposed and developed key electronic circuits and algorithms to interface intra-cortical microelectrode arrays. By implementing nano-power circuits and hardware-efficient algorithms, my research has extended current neural recording capabilities by an order of magnitude (100s to 1000s of channels). From January 2014 until July 2015, I worked as a Research Associate at the CBIT developing electro-chemical prosthesis and unsupervised algorithms for interfacing peripheral nerves and working towards a closed-loop system for appetite control. My vision is that next-generation neuroprostheses will be multi-channel, autonomous, adaptive and robust.

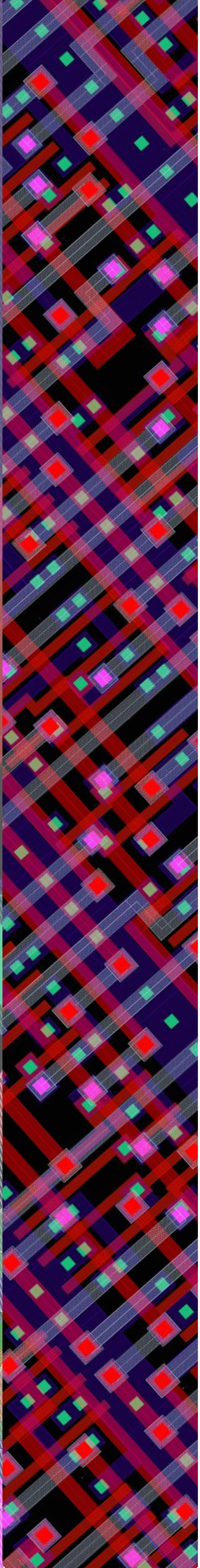
I have been fortunate to study and work in this leading research centre in the UK, developing devices to emulate and supplement biology. The high standards of the group are reflected in the impact of the research, quality of publications, state-of-the-art facilities and of course, the brilliant staff and students. As a leaving note, I would like to urge my former colleagues to continue to pursue excellence.

SATOSHI YOSHIZAKI

Research Assistant
2014

I worked at the Centre for Bio-Inspired Technology (CBIT) for one year as a research assistant. During this period, I was involved in the design of a CMOS image sensor (CIS) chip for capsule endoscopy. The aim of my project was to implement new features including narrowband sensing and a new octagonal pixel array. Additionally, I worked on a Lab-on-chip (LOC) micro-heater (μHeater) project. My role here was to design the system board to control the μHeater chip. The objective was to utilise multiple tiny coil-type heaters on the chip to stimulate cells thermally with high spatial resolution. The platform would measure the response of these stimulated cells by recording the biopotentials through electrodes on the μHeater array surface. This LOC system is currently being applied to analyse thermal mechanisms in electrically excitable cells.

Throughout these projects, I had the opportunity to be involved with exciting cutting edge research. Being in such a great multidisciplinary environment with colleagues from many different backgrounds including electronic engineering, biomedical engineering, chemistry and physics, always motivated me to learn new fields and broaden my horizons. Also, the close interaction and high-level discussion with colleagues inspired me a lot, and motivated me to further develop my career. After leaving CBIT, I returned to Japan and joined industry where I currently work as an analogue circuit designer. The work and experience gained at CBIT influenced my career, specifically continuing to work in the CIS field. Certainly spending so much time with people in CBIT as co-workers and friends was a truly invaluable experience for me.



Our mission: Inspired by life-style aspirations and biological systems, the Centre is inventing, developing and demonstrating devices to meet global challenges in healthcare and well-being, by mimicking living systems effectively and efficiently to create innovative and advanced technologies.

Research strategy

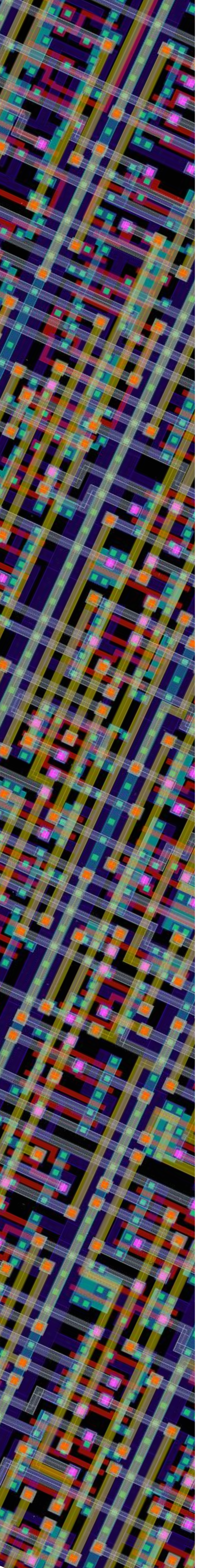
The Centre's research programme involves a strong combination of integrated miniature sensing with biologically inspired, intelligent processing, leveraging on state-of-the-art semiconductor technology. We aim to make small healthcare devices, which combine electronics with biological processes. By applying conventional silicon microchip technology in new ways, we are creating new opportunities for medical device innovation.

We have pioneered next generation semiconductor sequencing (spun out and licensed internationally), developed and trailed the worlds first bio-inspired artificial pancreas for Type I diabetes, invented and commercialized the disposable digital plaster for healthcare monitoring (now both FDA-approved and CE-marked), and are continuing to push the envelope of how semiconductor technology is being applied to biomedicine.

Such advances mean that there can be a shift in care away from a centralised model that puts the physician at its core to a smarter, more decentralised approach centred on the patient – known as personalised healthcare. They also open up new ways of coping with the huge problems of ageing populations and surges in chronic ailments such as diabetes and heart disease.

We believe this shift in the model will result in a more portable, precise and personal way to deliver healthcare using user-friendly devices such as wearable computing and smart phones. The design of these devices can 'hide' the processes of monitoring physiological conditions but allows data to be displayed in ways that patients can see results and act on the information. We also believe this shift has the potential to reduce the costs of healthcare by removing the need for onsite clinic visits for monitoring and shorter stays in hospital beds because patients can be diagnosed and monitored more quickly and in many cases remotely.

Researchers within the Centre for Bio-Inspired Technology work together with scientists and engineers from across Imperial College as well as in collaboration with partner institutions and industry. Project teams include medical researchers and clinicians to ensure the focus remains on the medical needs we aim to address. The Centre's Research Strategy is based on applying engineering technologies in innovative ways to provide personalised healthcare devices for chronic disease management. This is organized into five application-aligned technology themes: Genetic, Metabolic, Neural, Cardiovascular and Cancer.



Genetic technology

Research is focused on the development of semiconductor based genetic and epigenetic detection platforms for early diagnosis and monitoring of disease progression.

HEAD OF RESEARCH
Professor Chris Toumazou FRS, FREng, FMedSci

We are living in an era that has experienced significant technological revolutions as well as advances in medicine and health management, improving our quality of life, giving us the opportunity to be the protagonists of a trend in personalised medicine. Significant advances in the field of genetic technology have been made, with the development of semiconductor based platforms for point-of-need diagnostics, on-the-spot genetic testing and next-generation DNA sequencing to provide lab-free, fast, robust, easy-to-use and cost-effective solutions for healthcare. This realisation has been enabled with the use of CMOS technology, which brings with it the capability of integration of millions of sensors per microchip, enabled by the relentless scaling according to Moore's law.

CMOS based detection systems are expected to revolutionise medical practice, with multiple areas benefiting from these, from genetic analysis of infectious agents and bacterial genome sequencing to early screening of cancer markers and monitoring of chronic disease progression. In addition to genetic changes, epigenetic events play a significant role in multiple stages of disease development. Epigenetic profiles of genes can be used to distinguish diseased from normal cells, and are a powerful tool for risk markers used in early detection strategies.
Our research at the Centre for Bio-Inspired Technology involves the development of 'lab-on-chip' platforms for detection of genetic and epigenetic biomarkers, by integrating CMOS based ISFET sensors with application-specific biochemical assays. Emphasis is given in the areas of genotyping, genetic/epigenetic detection and monitoring of cancer as well as epigenetic monitoring of chronic kidney disease.

Genetic testing has been conventionally based on complex chemical, lab-based methods to detect DNA sequences. With the use of standard CMOS microchip technology, this can be simplified to a lab-free, sample-to-result answer, a YES or NO output as a result of a 'match' or 'mismatch' of DNA base pairs, translated into an ON or OFF state of a chemically sensitive transistor. Research in the Centre led to the development of the Genalysis® technology platform, a low cost microchip based platform built into a USB-sized device, capable of delivering fast and accurate on-the-spot tests for detection of any target nucleic acid sequence in either DNA or RNA as well as nucleotide insertions. Disposable 'lab-on-chip' cartridges housing biochemical reagents, advanced microfluidics and low-power silicon biosensors are key to this novel technology, with each cartridge to be customised to a variety of applications and markets. Built on the reliability, scalability and processing power of silicon microchip technology, this platform technology is mass-producible and highly portable. The commercialisation of this technology is being undertaken by DNA Electronics Ltd., a spinout company from the Centre.

RESEARCH IN GENETIC TECHNOLOGY CONTINUES IN THE CENTRE WITH A SPECIFIC FOCUS ON:

Epigenetic testing and monitoring of biomarkers involved in the initiation and progression of tumour development could provide valuable information in the clinical monitoring of cancer and the assessment of treatment efficacy. The role of DNA methylation in several stages of tumour development has shown great potential in detection, diagnosis, prognosis and monitoring of disease, through disruptions in gene expression leading to aberrant gene inactivation.
We have developed a semiconductor based platform with integrated chemical sensors, able to detect DNA methylation based biomarkers in real-time, avoiding the use of fluorescent dyes or labels. This will be used in cancer risk identification and early diagnosis by measuring simultaneously multiple epigenetic targets on a single microchip.

Epigenetics also plays an important role during the progression of chronic kidney disease (CKD), a condition resulting from chronic kidney damage and prolonged renal dysfunction, often leading to renal replacement therapy. We are applying the same technology to chronic kidney disease monitoring using DNA methylation based biomarkers. The implementation of an efficient detection system aids developments in related epigenetic therapy for typically irreversible kidney damage, preventing the need for dialysis and renal transplantation.

Semiconductor based DNA sequencing has revolutionised the cost of sequencing of the human genome making it more affordable and therefore accessible for healthcare applications where rapid diagnostics is strongly needed for the right treatment to be provided at the right time. This is possible due to pH based DNA detection using Ion-sensitive Field Effect Transistors (patented by our group), which are implemented in CMOS and therefore scale according to Moore's law. This research focuses on creating CMOS based systems with local intelligence, which can efficiently sequence the human genome for a variety of diseases including sepsis, cancer and diabetes.

Metabolic technology

Research is developing technologies for application in early detection, diagnosis and therapy of metabolic disease with the main focus on treating diabetes and its complications.

HEAD OF RESEARCH
Dr Pantelis Georgiou

Recent trends in daily lifestyle and poor diet have led to an increase in metabolic disorders which are affecting millions of people worldwide. A metabolic disorder develops when organs responsible for regulating metabolism fail to carry out their operation. Diabetes mellitus, currently the most severe metabolic disease and the leading cause of mortality and morbidity in the developed world, is caused by an absolute, or relative, lack of the hormone insulin which is responsible for homeostasis of glucose concentrations. Insulin deficiency leads to elevated glucose concentrations which, in turn, cause organ damage including retinopathy leading to blindness, nephropathy leading to kidney failure and neuropathy which is irreversible nerve damage. At least 3% of the world's population today is diagnosed with diabetes and this number is doubling every 15 years.

Current research includes:

The bio-inspired artificial pancreas – a fully closed loop system, which mimics the functionality of a healthy pancreas. The core of the system contains a silicon integrated circuit, which behaves in the same way as biological alpha and beta cells of the pancreas. In doing so, it aims to offer more physiological control to subjects with type 1 diabetes, using insulin to control hyperglycaemic events and glucagon to prevent hypoglycaemia.

We are pleased to announce that to date we have successfully validated the bio-inspired artificial pancreas in adult participants with type 1 diabetes acquiring over 800 hours of clinical data with the system, and proving it's safety and efficacy. Clinical trials were conducted at the NIHR/Wellcome Trust Imperial Clinical Research Facility, Hammersmith Hospital. Studies conducted so far include a 6-hour fasting closed-loop (CL) study (n=20), 13-hour overnight/post breakfast closed-loop study (n=17), 24-hour Randomised controlled crossover study (n=12), 24- hour CL study without meal announcement (n=8) and a 6-hour bi-hormonal study (n=6).

We are delighted to report that our results to date have proven the safety and efficacy of the Bio-inspired Artificial Pancreas and we are now moving forwards to conduct 3 month ambulatory trials on type 1 diabetic subjects in their home environment.

Diabetes management systems – an integrated system of wireless sensors (glucose, heart rate and motion), decision support systems and smart-phones to create a telemedicine platform capable of continually monitoring, recording vital parameters and providing advice on insulin dosing which is required for treatment of diabetes. Additionally, the smart-phone provides a constant link to a clinicians database to allow constant monitoring from the hospital.

We are delighted to report that our smart-phone based Advanced Bolus Calculator for Diabetes (ABC4D) is currently undergoing clinical trials in people with Type 1 diabetes and results to date are promising.

Sensory systems for continuous monitoring of metabolites - which includes devices which fully integrate chemical sensors and low power processing algorithms to provide cheap, disposable and intelligent chemical monitoring systems with long battery lifetimes. These are currently being used to make reliable and robust continuous glucose sensors by integrating glucose sensing micro-spikes with CMOS technology, making the sensor more robust, intelligent and adaptive. These will be expanded to sense other metabolites as well relevant to diabetes management. Lab-on-chip diagnostics for diabetes – which includes devices that fully integrate a number of electrochemical sensors in CMOS to provide cheap and disposable diagnostics, which can be used at the point of need. These are diagnostic systems for potential genetic screening of type 1 and type 2 diabetes and their associated variants and complications such as MODY (Maturity Onset Diabetes of the Young).

Metabolic Algorithms and Models – which includes developing in silico models describing the interaction between glucose, insulin, glucagon and other metabolites within the body to allow reliable simulation and validation of algorithms used for diabetes management. We also develop fault detection systems to account for glucose sensor and insulin pump failures and variability within our closed loop system.

Neural interfaces and neuroprosthetics

Improvements in medical care and quality of life for individuals with neurological conditions such as epilepsy, spinal cord injury, paralysis and sensory impairment by developing implantable or wearable assistive technologies.

HEAD OF RESEARCH
Dr Timothy Constandinou
www.imperial.ac.uk/neural-interfaces

We are now entering a tremendously exciting phase in our quest to understand the human brain. With large-scale programmes like the US Presidential BRAIN Initiative and the EU Human Brain Project, there is currently a huge appetite for new neurotechnologies and applications. We have already witnessed the impact made by devices such as cochlear implants and deep brain stimulators, with hundreds of thousands of individuals that have and are benefitting every day.

Soon, similar assistive technology will emerge for the blind, those suffering from epilepsy, and many others.

With the current capability in microtechnology, never before have there been so many opportunities to develop devices that effectively interface with the nervous system. Such devices are often referred to as neural interfaces or brain-machine interfaces and range from wearable surface-electrode systems to fully implantable devices. The interface typically uses an electrical connection (i.e. electrodes) to achieve the neural recording and/or stimulation utilising a variety of techniques, including: electroencephalography (EEG), electromyography (EMG), electrocorticography (ECoG) and direct interfacing using cuff electrodes or penetrating microelectrode arrays (MEAs). Neural prostheses use such interfaces to bypass dysfunctional pathways in the nervous system, by applying electronics to replace lost function. Our research at the Centre for Bio-Inspired Technology is aimed, ultimately at developing such devices to provide neural rehabilitation by exploiting the integration capability and scalability of modern semiconductor technology.

ONGOING NEUROPROSTHETICS RESEARCH

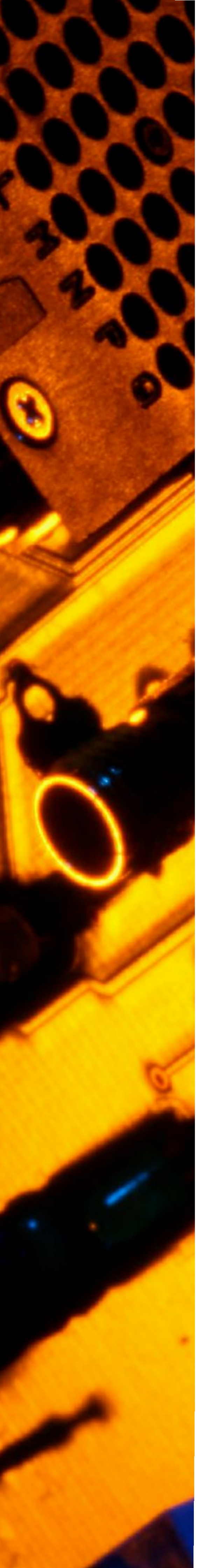
AnaeWARE (Monitoring awareness during anaesthesia – a multi-modal approach). The project will involve the collection of anonymous multi-modal signals from patients undergoing elective surgery at Hammersmith Hospital, London. The data will be analysed in order to identify how anesthetic administration affects the relationships between the different modalities and investigate whether such changes provide increased discriminatory power between wakefulness and anesthesia, or even prediction of wakefulness.
www.imperial.ac.uk/neural-interfaces/research/projects/anaeware/

CANDO (Controlling Abnormal Network Dynamics using Optogenetics). A world-class, multi-site, cross-disciplinary project to develop a cortical implant for optogenetic neural control. Over seven years the project will progress through several phases. Initial phases focus on technology design and development, followed by rigorous testing of performance and safety. The aim is to create a first-in-human-trial in the seventh year in patients with focal epilepsy.
www.cando.ac.uk

I2MOVE (Intelligent implantable modulator of Vagus nerve function for treatment of obesity). The i2MOVE project is about tackling obesity. In this project, we are designing a bio-inspired implant that will serve as a novel treatment for obesity. The aim is to target the vagus nerve which transmits information between the gut and the brain. By stimulating the vagus nerve with electrical impulses, the implant will mimic the natural satiety signals produced after a meal, providing the patient with a means of appetite control.
www.imperial.ac.uk/a-z-research/i2move/

iPROBE (in-vivo Platform for the Real-time Observation of Brain Extracellular activity). We are developing a methodology to record simultaneously from thousands of neurons spread over multiple structures of the living brain, and deliver a next generation neural recording platform to the international scientific community. This platform will exceed the current state-of-the-art by over an order of magnitude, providing a completely unprecedented understanding of how huge networks of individual neurons interact in time and space to support brain functions.
www.imperial.ac.uk/neural-interfaces/research/projects/iprobe/

SenseBack (Enabling Technologies for Sensory Feedback in Next-Generation Assistive Devices). The goal of this project is to develop technologies that will enable the next generation of assistive devices to provide truly natural control through enhanced sensory feedback. To enable this level of feedback, we must meet two clear objectives: to generate artificial signals that mimic those of the natural arm and hand, and to provide a means of delivering those signals to the nervous system of a prosthesis user.
www.senseback.com



Cardiovascular technology

Research is focussed on real time monitoring of vital cardiovascular parameters to enable patients to move out of hospital into the home and provide early warning systems for serious cardiovascular conditions.

HEAD OF RESEARCH
Professor Chris McLeod

Recent statistics from the American Heart Association states that over 80 million adults (one in three) have one or more types of cardiovascular disease. In the UK, the British Heart Foundation states that nearly 200,000 deaths result every year from cardiovascular disease, which accounts for more than one third of all deaths in the UK. Coupling these stark statistics with an ageing population and the already burdened health service, the cardiovascular technology research in the Centre is striving to apply cutting edge innovation to help reduce the incidence.

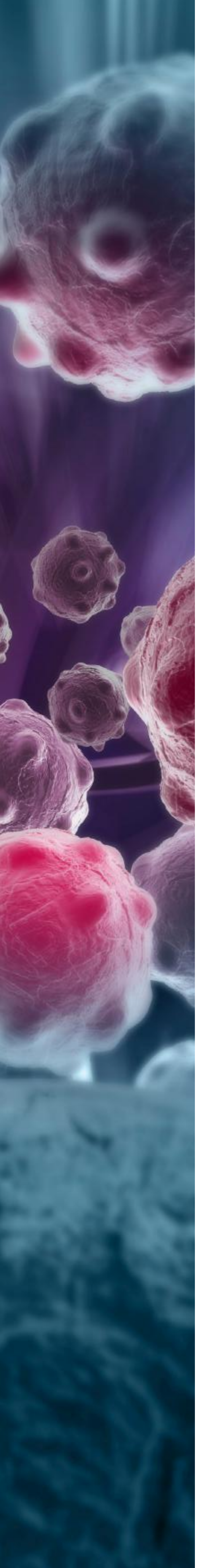
The research involves the design and characterisation of both external and implanted sensors along with the non-trivial issues surrounding wireless communication and bio-signal analysis. The centre has the capability for in vitro experimentation and access to excellent laboratories for in vivo verification. These facilities, along with many experienced collaborators, both clinical academic and industrial, provide a closed-loop development cycle for current and future cardiovascular technology projects within the Centre.

CURRENT RESEARCH INCLUDES:

Implanted blood pressure sensors to measure pressure continuously and requiring no procedure by the patient will enable doctors to detect 'events' which are almost always missed by traditional once-a-day or once-a-month checks. Using SAW technology, we aim to offer an alternative type of transducer with inherent characteristics suited to very long-term monitoring. We expect to achieve an implant capable of continuous monitoring for 10 or more years in ambulatory patients. Our wireless pressure sensor is designed to be implantable in any of the major cardiovascular vessels and to be adaptable for implantation within the heart. The application to heart failure is one example of the intended use of the sensor. Others are for pulmonary arterial hypertension and systemic hypertension. The capability of continuous BPM enables the development of complex software to extract significant events and to reduce the data to manageable quantities for practical realisations but also to aid research into the effects of treatments by providing hitherto unobtainable measurements.

Research is continuing to refine the design of the sensor, its delivery to the pulmonary and systemic circulations and the portable reader worn by the patient which links the sensor data to a wide-area network for remote monitoring – this will be in a computer server in a GP's surgery or hospital clinic where software will generate both patient and clinician messages in the event of abnormal data. The device is designed to improve the diagnostic and progression information available to clinicians to optimise pharmacological therapy for patients living at home with heart failure. The system includes full mHealth connection with means for 24/7 monitoring.

Research is underway to take the implantable pressure sensors through manufacture for regulatory approval and through a Phase 1 safety trial by 2017. The implants and system will be applied to other indications following a successful Phase 1 trial.



Cancer technology

Research is focused on the development of semiconductor based point of care technology for early diagnosis and monitoring of cancer.

HEAD OF RESEARCH
Prof Chris Toumazou FRS, FREng, FMedSci

Our research in the Centre for Bio-Inspired Technology is focused on the application of sensor technologies for early screening, detection and monitoring of cancer markers, with the ultimate goal being the development of Point-of-Care devices for the personalisation of cancer therapy. Primary focus is on the areas of:

Breath analysis for oesophago-gastric cancer detection: Only 35% of patients with oesophago-gastric cancer are currently treated with curative intent, whereas 15% of those operable patients have Stage I cancer. The five-year survival for oesophageal and gastric cancer is 13% and 18% respectively in the UK, among the worst in Europe, demonstrating the clinical consequences of this diagnostic challenge. Our ultimate goal is to develop a hand-held, Point-of-Care device that can detect and analyse Volatile Organic Components (VOCs) in breath, to evaluate the risk of oesophago-gastric cancer and suggest the need for further endoscopic investigation. This project is part of an ongoing collaboration with Prof George Hanna from St Mary's Hospital and his group, world leading experts in breathomics for oesophago-gastric cancer. A series of studies have already been conducted, which have identified statistically significant differences in the concentration of twelve VOCs from three chemical groups (aldehydes, fatty acids and phenols) from the exhaled breath of patients with oesophago-gastric cancer compared with a control group. Our research in the Centre for Bio-Inspired Technology involves the development of a prototype for VOC breath profiling, providing thus information necessary to determine and quantify the risk of oesophago-gastric cancer. Final diagnostic recommendation will be determined using an information theory based machine learning algorithm developed in our group by Dr Nikolic and his research team, which has been successfully implemented on other biological problems, e.g. identification of receptive field vectors (RFVs) for retinal ganglion cell types.

Early detection of endocrine resistance in breast cancer: In the UK, the majority of patients with breast cancer have no evidence of distant spread (metastases) at the time of diagnosis. Surgery is capable of removing the primary cancer, but evidence has now shown that small numbers of cancer cells seed throughout the body (micrometastases), while remaining undetectable by diagnostic scans. These often persist despite medical treatment given after surgery and can grow and spread over time if left unchecked. It is thus apparent that monitoring of residual disease in breast cancer could provide maximum benefit to the patient, through an easily accessible test that could survey the evolving tumour genetic profile and could guide more targeted treatment decisions. To date, the methods used for prediction of risk of metastasis do not monitor residual disease or provide a good lead interval before the development of metastases, require tumour samples collected at surgery or at biopsy, delivered to pathology labs, analysed by specialized equipment with results to take up to several days to become available. The aim is therefore the development of a Point-of-Care system, capable of measuring early signs of breast cancer in blood circulation that could enable monitoring of early signs of residual disease and prediction of relapse in operated and treated primary breast cancer patients.

This project is in collaboration with Prof Charles Coombes (Department of Surgery and Cancer, Imperial College London) and Prof Jacqui Shaw (Department of Cancer Studies, University of Leicester) whose research has shown that tumour specific mutations in circulating free DNA (cfDNA) found in blood plasma, can be used as biomarkers for detection and monitoring of breast cancer progression (from first diagnosis to follow-up), with the potential to differentiate between the period of cancer dormancy and of minimal residual disease.

Both applications will require the utilization of sensory based systems for screening of cancer markers. Utilising the group's expertise in the development of Lab-on-Chip platforms, integrating arrays of silicon chip-based chemical sensors also known as Ion-Sensitive Field Effect Transistors (ISFETs), combined with microelectronics in CMOS, we can identify changes in chemical reactions related to biomedical applications in a way which gives robustness to sensor characteristics while improving accuracy of detection. Specifically in the area of diagnostics and disease prevention, where the emergence of smart sensory systems is evident, the capability for these integrated systems to perform intelligent sensing and actuation would improve significantly the speed for decision making at the point of need.

Research Funding

We are grateful to receive research funding from government, the EU, charities, donors and industry. Our current funding Portfolio includes the following:

Project	Sponsor	Start Date	Duration
Enabling technologies for sensory feedback in next-generation assistive devices	EPSRC	March 2015	3 years
EMBRACE	EPSRC	Auguest 2015	2 years
Controlling Abnormal Network Dynamics with Optogenetics (CANDO)	Wellcome Trust / EPSRC	August 2014	7 years
"AnaeWARE" Monitoring awareness during anaesthesia	Commission of the European Communities	August 2014	2 years
i4i EPOC IMPACT	National Institute for Health Research	August 2015	3 years
Implantable Empowering Next Generation Neural Interfaces	EPSRC	August 2015	5 years
iPROBE: in-vivo Platform for the Real-time Observation of Brain Extracellular Activity	EPSRC	September 2013	3 years
A Bio-Inspired Artificial Pancreas for Control of Type 1 Diabetes in the Home	Wellcome Trust	August 2013	2 years
Real-Time Neural Chemical Sensing in the Peripheral Nervous System	EPSRC	July 2013	3 years
An Intelligent and Implantable Modulator of Vagus Nerve Function Treatment of Obesity	Commission of the European Communities	April 2013	5 years
Automated Blood Pressure Monitoring	Wellcome Trust	March 2012	3.5 years
Disruptive Semiconductor Technologies for Advanced Healthcare System	EPSRC	August 2015	5 years
Centre for Bio-Inspired Technology	Winston Wong	October 2009	ongoing

Transforming Diabetes Management with Bio-inspired Technology

Pantelis Georgiou, PhD
Research Team: Christofer Toumazou, Desmond Johnston, Nick Oliver, Pau Herrero Vinas, Monika Reddy, Mohamed El-Sharkawy, Peter Pesl, Shivshankar Seechurn, Narvada Jungee, Hazel Thomson, Darrell Pavitt.
Funding: The Wellcome trust
http://www.imperial.ac.uk/bioinspiredtechnology/research/bionicpancreas

Diabetes is an emerging global epidemic currently affecting 347 million people worldwide and increasing rapidly in prevalence. Soaring numbers have put a huge strain on the healthcare system and on individuals with the disease, as elevated blood glucose levels can cause macro-vascular and micro-vascular complications such as blindness, kidney failure, heart disease and nerve damage.
Type 1 diabetes, which accounts for 10% of the diabetes population, is an autoimmune disease that results in destruction of the insulin producing beta-cells of the pancreas. It directly affects 1.25 million people in the US and 300,000 people in the United Kingdom. There are 15,000 new diagnoses in the US annually and the total cost of managing type 1 diabetes and its complications in the US is $14.9 billion per year. In the UK diabetes currently consumes more than 10% of the National Health Service budget.

The most common form of treatment currently available for type 1 diabetes is self-management through multiple daily insulin injections using an insulin pen. Though this can reduce the risk of micro- and macrovascular complications, optimal management remains challenging with frequent hypo- and hyperglycaemia. As a result diabetes remains the most common cause of chronic kidney disease requiring renal replacement therapy (accounting for 44% of US cases in 2011) and blindness (diabetic retinopathy affects 28.5% of people with diabetes). While intensive glucose control mitigates some of the increased vascular risk, it is often at the expense of an increased frequency and severity of hypo-glycaemia. This has profound effects on quality of life and may have serious physical consequences including coma and death.

Diabetes technology is an increasingly important component of type 1 diabetes management with continuous subcutaneous insulin infusion (CSII, pump therapy) supported by a NICE technology appraisal and evidence supporting subcutaneous continuous glucose sensor usage. The next step in diabetes technology is the artificial pancreas, a closed-loop insulin delivery system comprising a subcutaneous glucose sensor, a control algorithm to calculate insulin infusion from dynamic glucose changes, and an insulin pump. The primary focus of the artificial pancreas is to reduce hypoglycaemia, especially overnight, and to increase percentage time spent in target. Improvements in glycaemic control have the potential to reduce the frequency and severity of hypoglycaemia, to improve HbA1c, and quality of life.

Within the Centre for Bio-inspired Technology, and in collaboration with expert diabetes specialists within the Imperial College NHS trust and support from the Wellcome Trust, we have developed a Bio-inspired Artificial Pancreas for control of type 1 diabetes. Our system utilises a cellular model of insulin secretion obtained from physiological data for the controller [1]. This cellular model of insulin release is able to replicate the majority of the experimental data seen in the physiology of beta-cells, including biphasic insulin secretion, staircase modulation of insulin secretion, the potentiation effect of glucose, and kiss-and-run secretion by insulin granules. The bio-inspired controller has been implemented in a miniature silicon microchip and integrated into a small handheld device as illustrated in Figure 1 [2]. This form of semiconductor microchip technology offers unique advantages of miniaturisation and low power. We have designed the whole system to consume less than 2mW of power guaranteeing two days of use on a single charge. The handheld unit is small (approximately 100mm x 60mm x 25mm) and lightweight (less than 100 grams) intended to allow comfortable and inconspicuous ambulatory monitoring and control of glucose. The module casing houses a printed circuit board (PCB) with the controller and all the necessary electronic components to measure, process, display and save measured glucose and calculated insulin, plus a rechargeable battery and wireless radio. It has also been designed to be robust and withstand being dropped and contains capability to attach to belts and clothing.

The Bio-inspired Artificial Pancreas (BiAP). Shown is the BiAP handheld unit which interfaces to a Dexcom G5 continuous glucose monitor and a Cellnovo Insulin Patch pump.

Clinical Validation: We are pleased to announce that to date we have successfully validated the bio-inspired artificial pancreas in adult participants with type 1 diabetes acquiring over 800 hours of clinical data with the system, and proving it's safety and efficacy. Clinical trials were conducted at the NIHR/ Wellcome Trust Imperial Clinical Research Facility, Hammersmith Hospital. Studies conducted so far include a 6-hour fasting closed-loop (CL) study (n=20), 13-hour overnight/post breakfast closed-loop study (n=17), 24-hour Randomised controlled crossover study (n=12), 24- hour CL study without meal announcement (n=8) and a 6-hour bi-hormonal study (n=6).

Clinical data with the bio-inspired artificial pancreas system during the fasting and overnight periods, and following breakfast (the most challenging meal for glucose control algorithms), have been published [3]. These have demonstrated feasible, safe glucose control without hypoglycaemia. Results are comparable to initial clinical studies of other systems. Results from the randomised controlled study of closed loop control against standard pump therapy over 24 hours in the clinical research facility have been presented internationally and are accepted for publication [4]. 12 adults with type 1 diabetes completed the study (58% female, mean (SD) age 45(10) years, BMI 25(4) kg/m2, duration of diabetes 22(12) years and HbA1c 7.4 (0.7)% (58 (8) mmol/mol)). The overall percentage time in target did not differ between closed-loop and open-loop (71% vs 66.9%, p=0.9). However, closed-loop insulin delivery reduced time spent in hypoglycaemia from 17.9% to 3.0% (p‹0.01), and reduced time in hypoglycaemia defined by any biochemical cut-off (3.9mmol/L, 3.3mmol/L and 2.8mmol/L). The reduction in hypoglycaemia was particularly marked overnight with no difference in total insulin delivered between the two groups during this time period. Increased time was spent in hyperglycaemia (10% vs 28.9%, p=0.01);

The Bio-inspired Artificial Pancreas is currently being evaluated in a 24-hour randomised controlled crossover study, using a bi-hormonal configuration (insulin and glucagon) versus closed-loop with insulin alone versus open-loop (standard pump therapy), during and after exercise, Figure 2. Use of glucagon has benefits as within the body the pancreas secretes glucagon as a counter-regulatory hormone to insulin preventing hypoglycemia.

Results so far have proven improved control can also be achieved using a bi-hormonal system.

Our Bio-inspired Artificial Pancreas has been proven to safely control blood glucose in yype 1 diabetes and shown significant improvement in reducing hypoglycaemia overnight. We are now in a position to send the technology home with subjects to evaluate it's performance in a free-living environment. In 2016 we will be looking to conduct the first 3-month home trial with the technology. This important milestone is one more step towards commercialising this first Bio-inspired Artificial Pancreas.

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2. Herrero, P.; El Sharkawy, M.; Pesl, P.; Reddy, M.; Oliver, N.; Johnston, D.; Toumazou, C.; Georgiou, P., "Live demonstration: A handheld Bio-inspired Artificial pancreas for treatment of diabetes," Biomedical Circuits and Systems Conference (BioCAS), 2014 IEEE , vol., no., pp.172,172, 22-24 Oct. 2014
3. Reddy M, Herrero P, El Sharkawy M, Pesl P, Jugnee N, Thomson H, Pavitt D, Toumazou C, Johnston DG, Georgiou P, Oliver N. Feasibility Study of a Bio–inspired Artificial Pancreas in Adults with Type 1 Diabetes. Diabetes Technology and Therapeutics 2014;16:550-557
4. Reddy M, Herrero P, El Sharkawy M, Pesl P, Jugnee N, Pavitt D, Godsland I, Alberti GA, Toumazou C, Johnston DG, Georgiou P, Oliver N. Metabolic Control with the Bio-inspired Artificial Pancreas (BiAP) in Adults with Type 1 Diabetes: A 24-hour Randomised Controlled Crossover Study. JDST 2015 Oct-accepted.

Bi-hormonal Clinical Trials of the Bio-inspired Artificial Pancreas.

The i2MOVE Project: A Research Update

https://www.imperial.ac.uk/a-z-research/i2move/

In our 2013 Annual Report, we announced a new project, i2MOVE, an Intelligent Implantable Modulator of Vagus Nerve function for the treatment of Obesity. Our aim – to tap into the Vagus nerve, understand its role in regulating appetite and develop a device to modulate its behavior thus providing a novel solution to Obesity.

The Vagus Nerve

The Vagus nerve, from the Latin "wanderer" is the principal communication link between the brain and our vital organs: heart, lungs, stomach liver, etc. First identified as far back as Roman times (Galen, 130-210AD) and later by Leonardo Da Vinci, it forms part of a large communication network of nerves that controls motor and sensory behavior in our limbs and organs.

Yet, centuries later, our knowledge of the Vagus nerve and its many functions is still at its infancy. Only in the last few decades have we been able to link it healthcare problems, such as obesity, epilepsy, arthritis and cancer. It has even been implicated in stress and anxiety, with studies linking vagal activity to our attentiveness, organization and ability to handle stress. Only just this year it has been shown to play a role directly in inflammatory processes. This has implications for several inflammatory disorders, including cancer, arthritis and asthma.

It is little surprise then that well-being and medical devices have emerged over the last 25 years which target the Vagus Nerve. Termed Vagus Nerve Stimulation, or VNS, these invasive and non-invasive devices stimulate the nerve with an electrical impulse, aiming to modulate its behavior. VNS now represents 10% of a growing neuromodulation market worth around $4billion.

A Knowledge Gap

Although the technology is mature, there exists a large knowledge gap in exactly how the Vagus nerve plays such an important role in the wide range of disorders it is linked to. How does the Vagus nerve modulate physiological behavior? Can this be replicated by VNS and if so how do parameters of VNS alter this behavior?

To answer these questions requires a multi-disciplinary approach. There are technological and experimental hurdles that need to be overcome in order to access and decipher the large volume of signaling within a nerve. To put this in perspective: the human Vagus nerve, where it innervates the stomach, is less than 2mm in diameter, containing in excess of 10,000 communication channels, or axons, with signals one-millionth the size of your standard battery surrounded by noise source 100s of times larger, a needle in the haystack. The challenge is substantial, but not impossible.

The i2MOVE Project

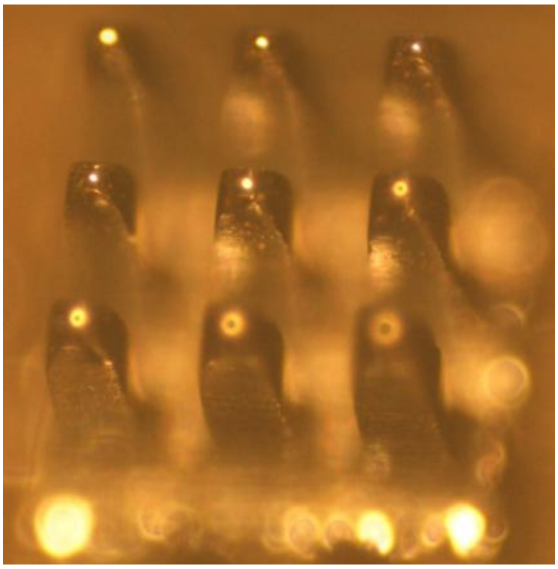
These questions and challenges are what the i2MOVE project aims to address, with appetite, and obesity, as a central theme. Obesity, now affects nearly 1/3rd of the World's population, with a total estimated cost of over $1trillion. Surgical re-wiring of the gut and stomach has been the only effective the solution to date, yet it is irreversible and has surgical risks. The i2MOVE project aims to provide a novel solution that is based on our own body's control mechanisms.

Appetite is regulated by a complex integrated hormonal response mediated by the Vagus nerve. The initial goal of our studies has been to derive the electro-chemical signatures of the Vagus nerve in response to food intake and hormone release. Subsequently, we can close the loop and modulate vagal behavior once we know hunger signaling has been initiated.

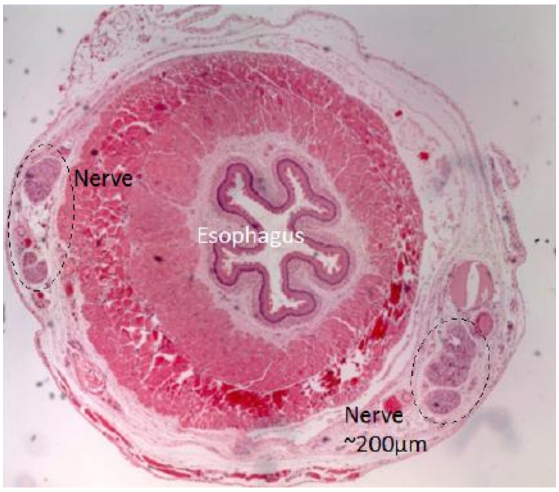
To do this we have combined the engineering labs of Prof. Toumazou with the metabolic labs of Prof. Sir Stephen Bloom. We have built a multi-disciplinary team. These include neurophysiologists, chemical, microfabrication and electronics engineers, physiologists and biologists. Our unique approach is the monitoring of electrical and chemical activity of the nerve.

We have developed in-house microspikes that penetrate the nerve, and are unique in that they are made to be both electrically and chemically sensitive. Thus we can monitor traditional electrical signalling of the nerve, but also the chemical changes that drive the electrical. Being chemical, we are not plagued by large amounts of noise.

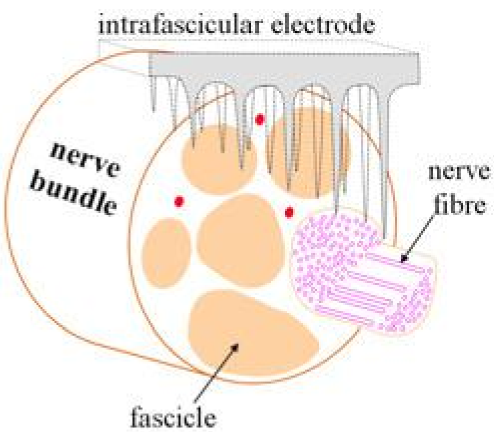
Our work in the last few years has been to set up the lab, design these microelectrodes, develop low-noise electronic instrumentation and state-of-the-art signal processing paradigms with electrophysiological techniques to extract hormonal patterns of the Vagus nerve. As the literature on the Vagus nerve has been so limited we have also spent time understanding and characterizing the behavior of the nerve (cross section Figure 1, middle). We have been able to capture signaling from the nerve (Figure 2), correlated to various behavior of the gut. We have also been able to capture profiles of pH activity that correlate with hormone infusions (GLP1 and CCK).



In-house microspikes, 100um pitch, 300um high, total 0.3x0.3mm



A typical left and right Vagus nerve, where the it innervates the stomach



The microspikes placed inside the nerve.

The Future

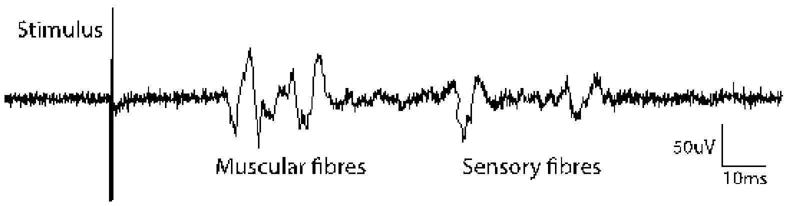
Where do we go from here? Our experiments to-date have been acute, in a controlled experimental environment. We have been able to take the first steps to deciphering the Vagus nerve's signaling correlated to the hormones that regulate our appetite. As we gather more data towards this, we will also be focusing on two further paths.

The first is working towards chronic experiments, wherein we will be able to analyse vagal signals during real-time activity and eating habits. We can then analyse, and correlate with blood samples, how vagal activity varies throughout the day in relation to the hormones naturally released around appetite. Secondly, we are also investigating how VNS itself affects the hormone release in our system such that we can design selective stimulation parameters for closed-loop appetite controls.

To further our goals, we are have also formed several collaborations and projects with other academic groups looking at the Vagus nerve's role in other diseases including liver disease and cancer. All of these paths will lead us to the novel closed-loop implantable device we envision.

Research Team:

- Prof. Chris Toumazou (PI)
- Dr. Amir Eftekhar
- Dr. Claudio Zuliani
- Dr. Yufei Liu
- Dr. Andrea Alenda-Gonzalez
- Nishanth Kulasekeram
- Khalid Mirza (electronics)
- Prof. Sir Steve Bloom (Co-PI)
- Dr. James Gardiner
- Dr. Agnieszka Falinska
- Dr. Simon Cork
- Prof. Gary Frost
- Dr. Waljit Dhillo



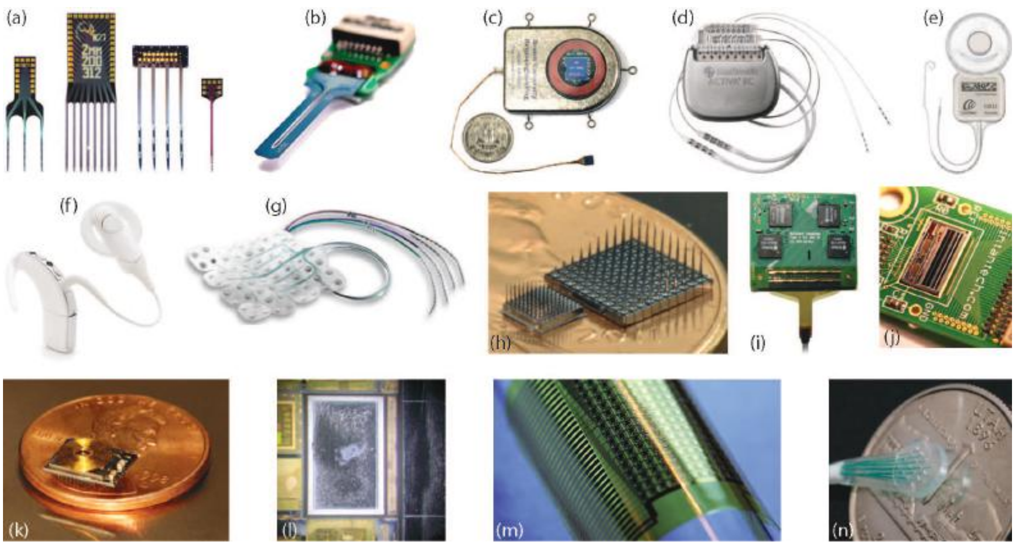
Fast (muscular) and slow (sensory) fibre responses to an electrical stimulation on the Vagus nerve.

ENGINI: Empowering Next Generation Implantable Neural Interfaces

Timothy Constandinou, PhD
Research Team: Katarzyna Szostak, Deren Barsakcioglu
Project Partners: Dr Andrew Jackson (Newcastle University), Professor Nick Donaldson (UCL), Professor Andrew Mason (Michigan State University), Professor Maysam Ghovanloo (Georgia Institute of Technology)
Funding: Engineering and Physical Sciences Research Council – Early Career Fellowship
www.imperial.ac.uk/neural-interfaces

Being able to control devices with our thoughts is a concept that has for long captured the imagination. Neural Interfaces or Brain Machine Interfaces (BMIs) are devices that aim to do precisely this. Next generation devices will be distributed like the brain itself. It is currently estimated that if we were able to record electrical activity simultaneously from between 1,000 and 10,000 neurons, this would enable useful prosthetic control (e.g. of a prosthetic arm).

However, rather than relying on a single, highly complex implant and trying to cram more and more channels in this (the current paradigm), the idea here is to develop a simpler, smaller, well-engineered primitive and deploy multiple such devices. It is essential these are each compact, autonomous, calibration-free, and completely wireless. It is envisaged that each device will be mm-scale, and be capable of recording only a few channels (i.e. up to 20), but also perform real-time signal processing.



Current state-of-the-art neural interface technology. (a) Neuronexus (Michigan) probes; (b) IMEC probe; (c) 100-ch. hermetically sealed BMI; (d) Medtronics Aptiva DBS; (e) Cochlear Nucleus CI512 implant; (f) Cochlear Nucleus 5 Sound Processor; (g) Blackrock ECoG grid; (h) Blackrock Utah array; (i) Amplipex HS4 256-ch. module; (j) Intan Tech. 64-ch. front-end; (k) Utah microsystem; (l) implantable IC micro-package (developed by UCL); (m) Flexible electronics/electrodes (Viventi et al); (n) Utah Micro-ECoG. For next generation devices to integrate (orders of magnitude) more channels, they must address the three grand challenges: biocompatibility, power efficiency and connectivity.

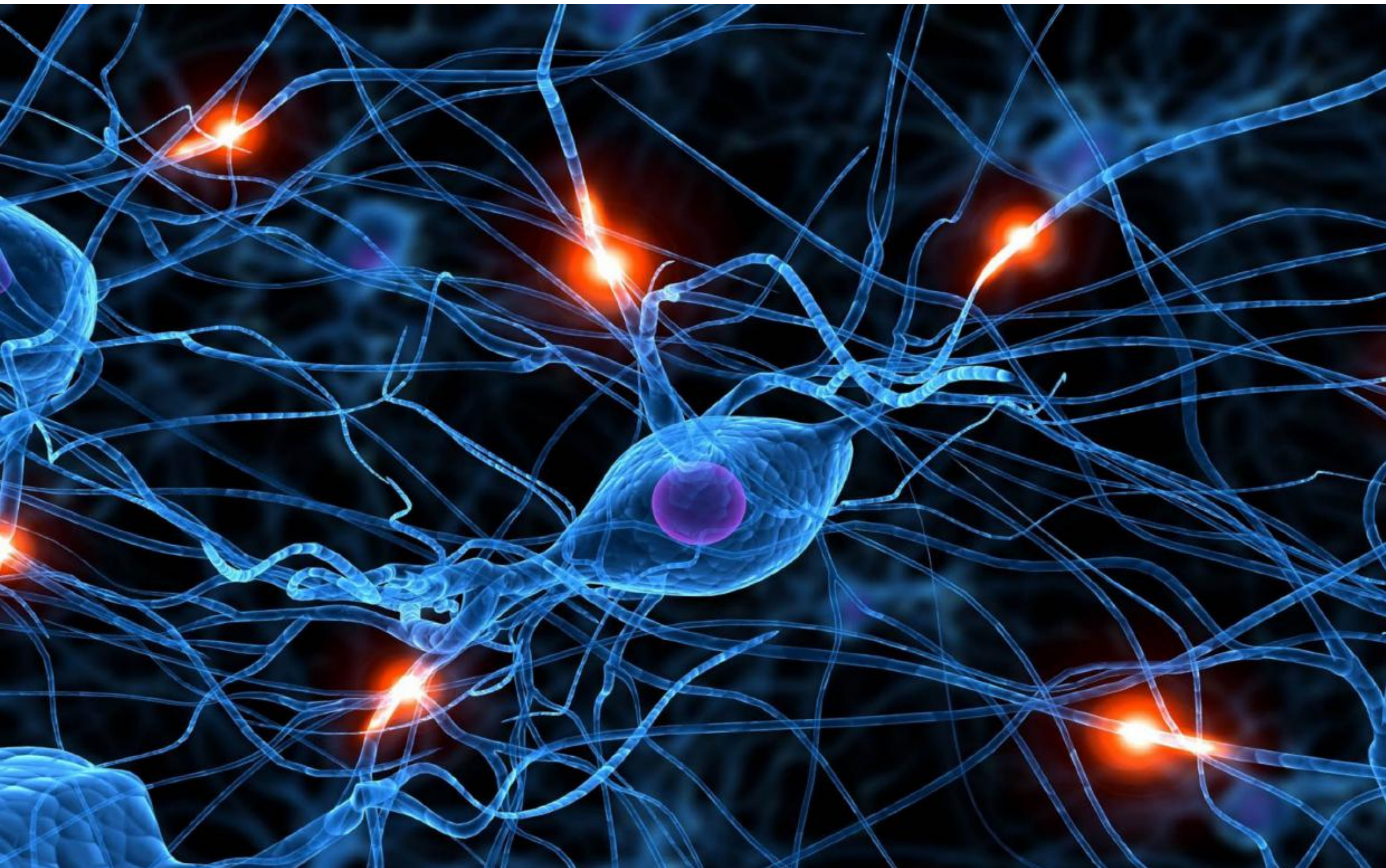
This processing will achieve data reduction so as to wirelessly communicate only useful information, rather than raw data, which can most often be just noise and of no use. Making these underlying devices "simpler" will overcome many of the common challenges that are associated with scaling of neural interfaces, for example, wires breaking, biocompatibility of the packaging, thermal dissipation and yield.

By distributing tens to hundreds of these in a "grid" of neural interfaces, many of the desirable features of distributed networks come into play; for example, redundancy and robustness to single component failure. A first tangible application for this platform will see these devices embedded in a uniform array within a flexible substrate for electrocorticography (i.e. recording from the surface of the brain).

It will however, also be investigated how the underlying devices can be made applicable to other formats, for instance, in penetrating intracortical devices (recording from within the cortex). Such devices will communicate the neural "control signals" to an external prosthetic device. These can then, for example, be used for: an amputee to control a robotic prosthetic; a paraplegic to control a mobility aid; or an individual with locked in syndrome to communicate with the outside world.

This Fellowship will consolidate expertise and build a core capability that can deliver such devices. This will be achieved by working together with researchers and professionals across multiple disciplines including ICT, engineering, healthcare technologies, medical devices and neuroscience. The research is extremely well aligned with the current quest to understand the brain; for example, US presidential BRAIN initiative, and the EU human brain project. It will impact neuroscience research, by extending current capabilities by at least an order of magnitude, but also medical devices by inventing and demonstrating a radically new approach.

Interfacing with neural tissue. For next generation devices to be viable, they must address the three grand challenges: biocompatibility, power efficiency and connectivity.



The Centre for Bio-Inspired Technology:

The Centre has been fortunate to attract internationally noted researchers to spend time working with its staff and students and adding to the collaborative and entrepreneurial mix which is fundamental to its success. Here, two of its Visiting Professors give their views of the Centre and discuss the contribution the research is making to the future direction of healthcare.

Professor Tor Sverre (Bassen) Lande

University of Oslo

The amazing computational power of microelectronics systems has given us tools we did not imagine just a decade ago. Nanoscale microelectronics is appearing in all sorts of gadgets around us. With minimal power, complete sensory systems including wireless connectivity will soon be embedded in many of the objects and devices around us. The notion of "Internet-of-Things (IoT)" has emerged although somewhat misleading, since the term Internet implies communication using TCP/IP. Maybe the notion of a "Sensory Swarm" as coined by J. Rabaey is more adequate. Here, most research efforts have focused on the infrastructure itself (or implementing the "swarm"), whilst in my opinion, the real challenge is achieving good sensory function. However good the infrastructure available, this can never compensate for low-quality sensors (crap-in = crap-out). The envisaged and desired framework for IoT sensing devices is that they are miniature, highly integrated, portable, with long-term reliable operation in harsh environments, and all be integrated in a low-cost gadget. This means the sensor must have good sensitivity and precision, be compact, reliable, inexpensive, battery-powered and preferably integrated on the silicon chip itself together with other electronics. These challenges alone are tough to achieve for devices operating in normal living conditions collecting environmental information. Applying this to the sensory swarm or even into/onto the human body for personalized healthcare is even more challenging on power, size and reliability. The application of remote health monitoring is particularly beneficial for chronic disease management. Continuous monitoring can even provide life saving capability through emergency functions. Body sensors and actuators can also increase expected lifetime through, for example, improved medication (insulin dosage) in diabetes treatment/management. The fundamental challenge however remains; currently there exists no long-term blood glucose sensor, despite major research and development efforts. Blood sample based techniques are limited by "clogging" and reagent lifetimes while transcutaneous glucose sensors are currently not good enough. This is just one example of body sensing that demonstrates this fundamental challenge of requiring good sensors.

For more than two decades I have enjoyed the privilege of working with both staff and students at the Centre of Bio-inspired Technology. I have spent two sabbatical years (2003 and 2013) at the centre and keep coming back on regular visits to an attractive research environment. Several brave research efforts towards bridging technology and biology for quality-of-life improvement has brought forward novel solutions founded on solid science and engineering. Serious and sustained efforts towards body sensing have brought forward important, new sensor technologies like chemical sensor devices (ISFET) integrated in standard technology that has already demonstrated significant impact. Ongoing research efforts on ISFETs is looking at further improving performance as well as the spatial sensor density toward "chemical imaging" suitable for high-quality and fast diagnosis. Furthermore, there are exciting new efforts for interfacing with the nervous system with localized and distributed processing that aim to provide improved spatiotemporal response. Novel brain-imaging technology using microwave may enable functional brain imaging with "live" monitoring of brain activity using portable devices. In implementing such systems, a number of new circuit methods (both analogue and digital) have been developed including new integrated data-converters and specialized signal processing solutions combining both analogue and digital technology. These are just a few examples of many ongoing efforts at the centre that I am convinced will provide impact to the viability of new biomedical sensory systems in the near future.

I believe however, that one of the most important characteristics of this Centre is the particularly strong friendly environment that is made up of people from all over the world. It is especially unique how this multidisciplinary, multinational and multicultural group of researchers work together so closely, sharing both their successes and failures. Even outside of work, colleagues here are close friends, bringing back "goodies" to the group whenever someone visits home, going to the pub together every Friday, and even celebrating personal occasions such as weddings together with colleagues (several in 2015!). Who would want to let go of such an environment, when there is also room for visiting Professors?

Two visiting professors share their views

Professor Andrew Mason

Michigan State University

When Marty and Doc went "Back to the Future" in 1989, we all caught a glimpse of what 2015 would be like, at least in the eyes of Hollywood. For those of us growing up in the generation of Marty and Doc, it is hard to believe that the real 2015 has arrived and nearly passed into history. Although our science and engineering talents have failed to deliver on the hovering skateboards and self-fitting clothes promised by movies, as one who has devoted a career to advancing technology I must say that we have accomplished amazing feats since the days we imagined a DeLorean flying through time.

Empowered by nearly immediate access to a nearly infinite information collective via the internet, and by the myriad of technologies that have combined to make smart phones a powerful resource for mobile computing, the astounding feats of science and engineering have been especially profound in the area of bioelectronics for healthcare. In 2015 we find ourselves with an amazing capability to diagnose and treat a spectrum of diseases and disorders that were not long ago mysteries in medicine. We have established many new technologies, such as rapid and inexpensive DNA sequencing, that have enabled a much-needed shift toward personalized medicine, to focus on specific conditions of individual patients and prescribe precise treatments matched to an individual's physiology and living environment. Through advances in electronics and biomedical signal processing we have wearable devices that can track physical activity and others that can record key cardiovascular metrics. In the area of neuroscience, we continue to make great strides toward chronic recording of brain activity, prosthetics with high degrees of freedom, and closed-loop feedback systems to control tremors and seizures.

As the semiconductor industry continues its slide into the More than Moore era, biomedical electronics is in a prime position for explosive growth in adapting modern technology to solve real-world healthcare challenges. We are developing new circuits structures and packaging techniques like lab-on-CMOS to interface silicon technologies with subcellular processes. New materials and methods are enabling next-generation wearable and implantable electronic system with flexible/conformal and even dissolvable technologies. A fascinating diversity of new microsensors and diagnostic methods are being developed for medical and environmental awareness that may someday soon enable mobile phones to serve as a portable field medic, ala the Star Trek tricorder.

While we strive toward the visions of science fiction, and of the scientists, engineers and doctors with the imagination and skill to realize them, we find great opportunity to build on past successes and face new challenges. Personalized medicine, which spans from genomics and metabolics to wearable instrumentation and social data mining, has tremendous potential for growth and profound impact on human health. New imaging and diagnostic systems, new smart devices for assisted living including health and weight management, and new tools to assess environmental impact of pharmaceuticals and other byproducts of human consumption, are all great opportunities for innovation into the future of healthcare bioelectronics.

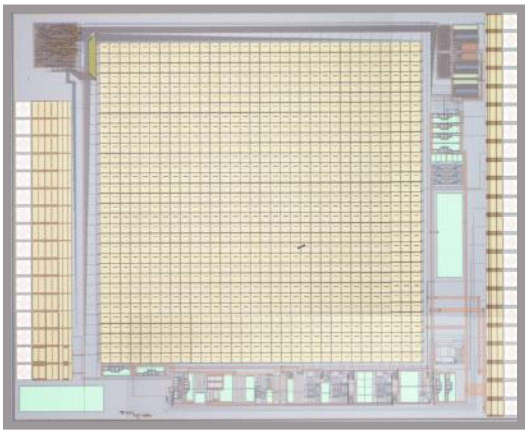
Around the globe, and throughout the past, present, and future of healthcare bioelectronics, few research groups have shown the innovation, productivity and potential of Imperial's Centre for Bio-Inspired Technology. From pioneering work in silicon based chemical sensing technology to futuristic goals for chronically implanted brain-machine-interfaces, the Centre is a world-recognized leader in biomedical circuits and systems. Having the honor to spend my 2015 sabbatical working with this group, I realize that one of the most outstanding characteristics of the institute is its focus on transferring technology from the laboratory into industry, amplifying the accessible and impact of research innovation. Ongoing projects including DNA-based antimicrobial resistance, implantable treatments for epilepsy, bio-inspired artificial pancreas, and genetic biomarkers testing tools represent a new wave of technology from the Centre that will further expand its worldwide visibility. I am excited to be working with the team at the Centre for Bio-Inspired Technology to engineering healthy minds and able bodies and deliver revolutionary biomedical technologies "Back to the Future".

Chip gallery

The Centre's researchers have produced six new chips this year making a total production so far of 41 chips in a variety of CMOS technologies.

The Centre's focus is primarily the application of modern semiconductor technology to develop new bio-inspired systems and medical devices. This has in part been made possible through the EU-subsidised multi-project wafer (MPW) brokerage service provided by Europractice, which provides our design tools via STFC (UK) and technology access via IMEC (Belgium) and Franhofer (Germany).

The 'Chip Gallery' is also available online at: http://www.imperial.ac.uk/bio-inspired-technology/resources/chip-gallery/

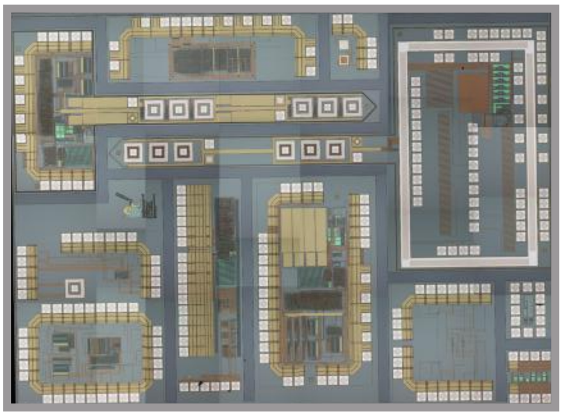


BE14K02 (Dolphin) - Nov 2014

Technology: Austriamicrosystems 0.35µm 2P4M CMOS

Purpose: A 32x32 ISFET chemical sensing array for DNA sequencing

Designer: Yuanqi Hu, Pantelis Georgiou



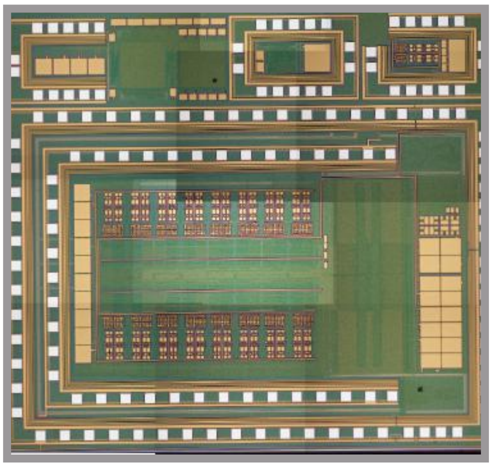
IBE14L01 (Yoda) – DEC 2014

Technology: Austriamicrosystems 0.35um 2P4M CMOS

Purpose: Neural implant probes with embedded recording and stimulation circuits.

Designers: Imperial College: Yan Liu, Song Luan, Timothy Constandinou

Newcastle University: Hubin Zhao, Reza Ramezani, Fahimeh Dehkhoda, Ahmed Ali, Patrick Degeenar.

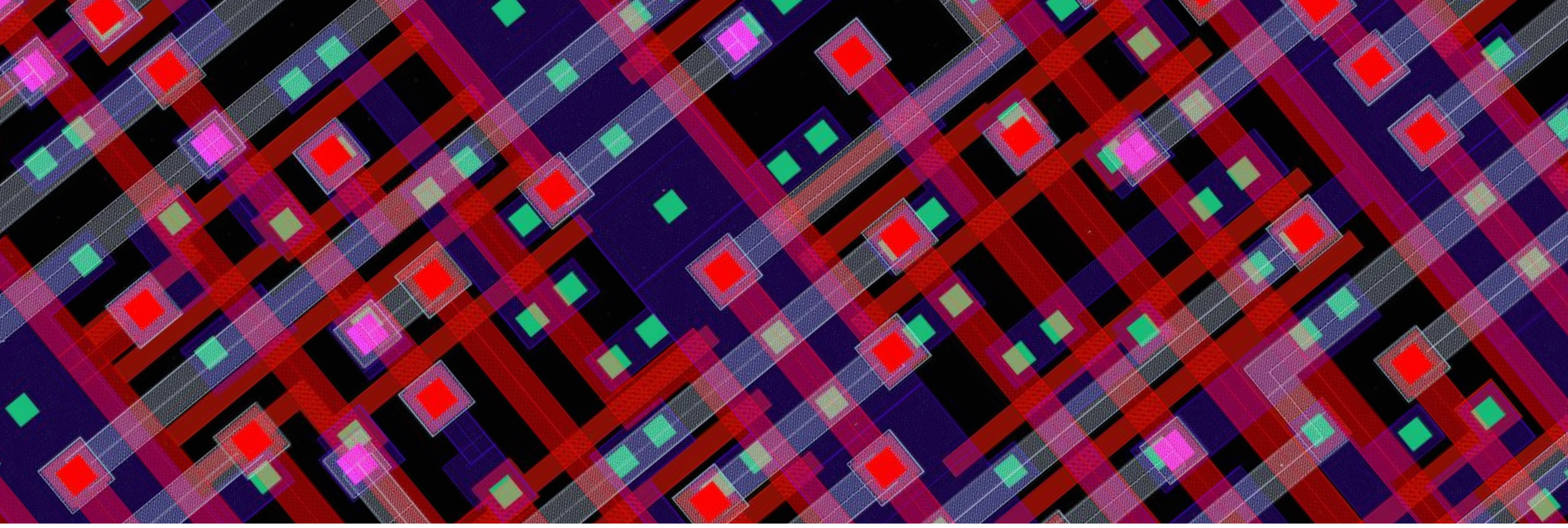


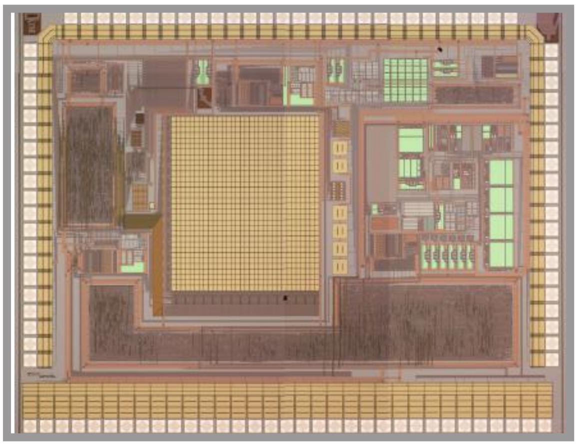
IBE15B01 (Gollum) - Feb 2015

Technology: Austriamicrosystems 0.18um 1P6M CMOS

Purpose: A 64 Channel 12b recording system with fully embedded 16 parallel micro controller structure, and test circuits including a 13b DAC

Designers: Lieuwe Leene, Yan Liu, Timothy Constandinou



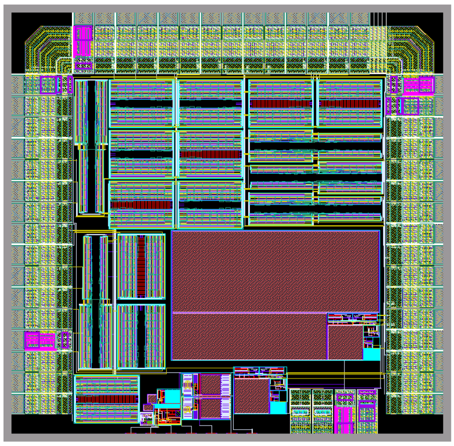


IBE15G01 (Batman) Jul 2015

Technology: Austriamicrosystems 0.35um 2P4M CMOS

Purpose: Multiproject chip including several ISFET arrays and a sEMG fatigue monitor and processor.

Designers: Ermis Koutsos, Nicolas Moser, Dora Ma, Nicholaos Miscourides, Guenole Lallement, Pantelis Georgiou,

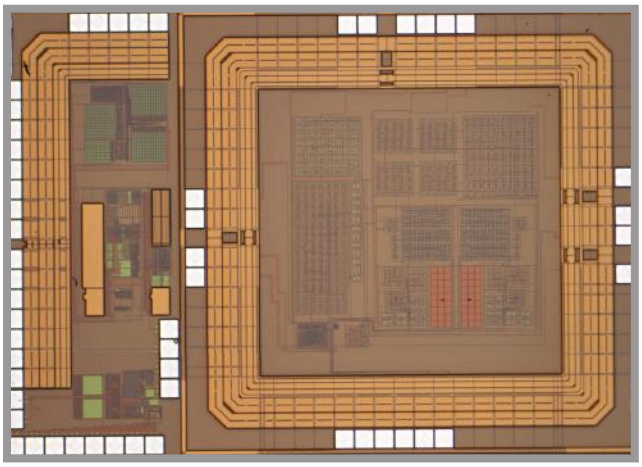


IBE15K01 (Fireworks) – Nov 2015

Technology: Austriamicrosystems 0.35um 2P4M CMOS

Purpose: Power recovery and data transmission system for neural implants.

Designers: Sara Ghoreishizadeh, Timothy Constandinou

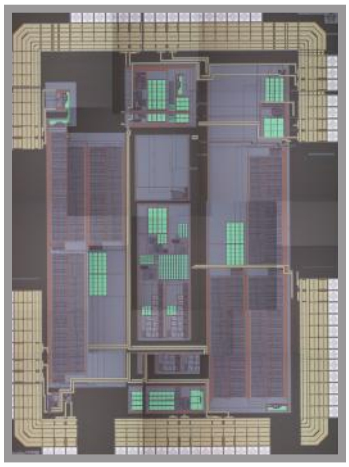


IBE15H01 (I2MOVE_TC2) Aug 2015

Technology: Austriamicrosystems HV 0.35um 2P4M CMOS

Purpose: Neural stimulation circuits, neural amplifier, power recovery, and Logarithmic ADC

Designers: Nishanth Kulasekeram, Amir Eftekhar, Sara Ghoreishizadeh, Yuwadee Sundarasaradula, Yan Liu, Timothy Constandinou



IBE15N01 (I2MOVE_TC1) - Feb 2015

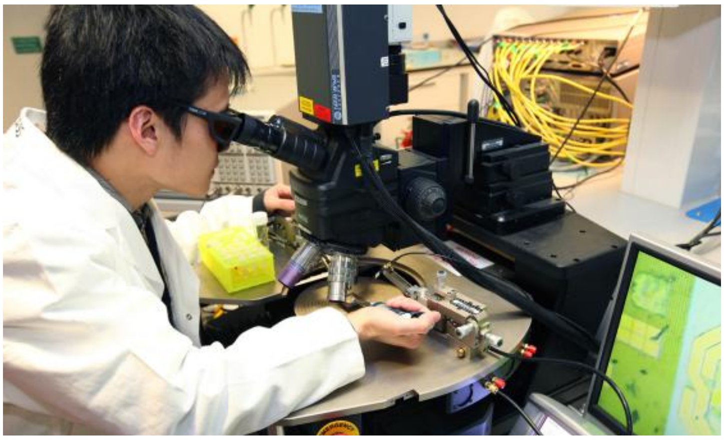
Technology: Austriamicrosystems 0.35μm 2P4M CMOS

Purpose: Testchip for obesity

Designers: Nishanth Kulasekeram, Sivylla Paraskevopoulou, Yan Liu

Research facilities

The laboratory areas have been designed to meet the needs of the four main application areas within the Centre's research strategy. Researchers have been able to undertake a large number of high-quality research projects in the Centre by leveraging on the multidisciplinary expertise of their colleagues and collaborators and the employment of the facilities. The main thrust of the research strategy is not to further advance the performance of existing electronic systems but to enable entirely new applications by utilising well-established technologies in new, innovative ways. All members of the Centre have access to the full range of facilities and equipment and some researchers have developed a high level of expertise in specific areas to ensure that these are exploited to the full.

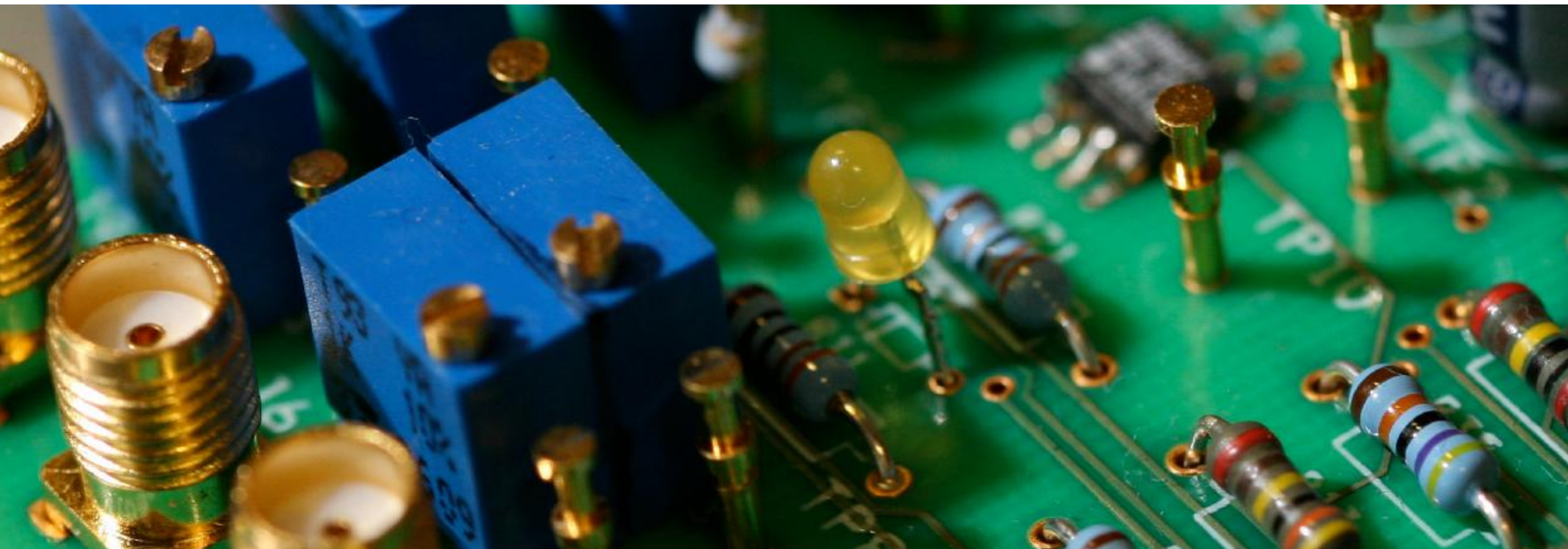


EDA and CAD Laboratory

CAD is an indispensable process in any modern engineering design. This laboratory is equipped with high performance workstations and servers to support high-end tools for microelectronic design, microsystems (including MEMS, microfluidics), RF/microwave devices, mechanical design, etc. For example, researchers here develop application-specific integrated circuits (ASICs) that are then sent for fabrication at CMOS foundries. The facility has licensed all industry standard tools including Cadence, Mentor Graphics, Synopsys, Ansys, Solidworks, and several others, and a range of modern process technologies down to the 45nm node. All servers can be remotely connected from anywhere around the world via the internet enabling designers to work remotely and multiple chip designs can be carried out in parallel.

Microelectronics Test Laboratory

This laboratory is comprehensively equipped for the development, testing and measurement of biomedical circuits and systems. Such devices often require low noise instrumentation operating at relatively low frequency and have ultra low power requirements. This facility includes instruments for semiconductor characterisation, equipment for time, frequency and impedance characterisation (e.g. oscilloscopes, spectrum analysers, CV), instruments for low noise transimpedance and voltage amplification, signal generation, a semi-automatic probe station with laser for trimming and failure analysis, a temperature chamber, PCB rapid prototyping facility (LPKF-based), and all standard electronic test & measurement equipment.

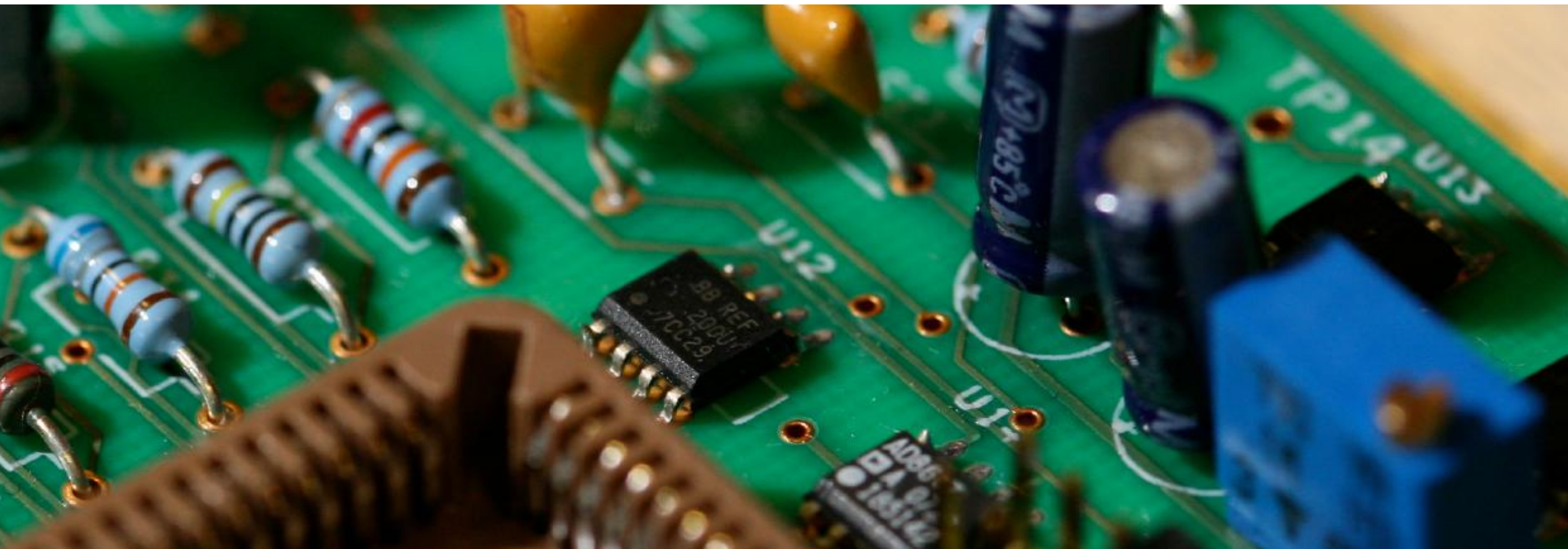


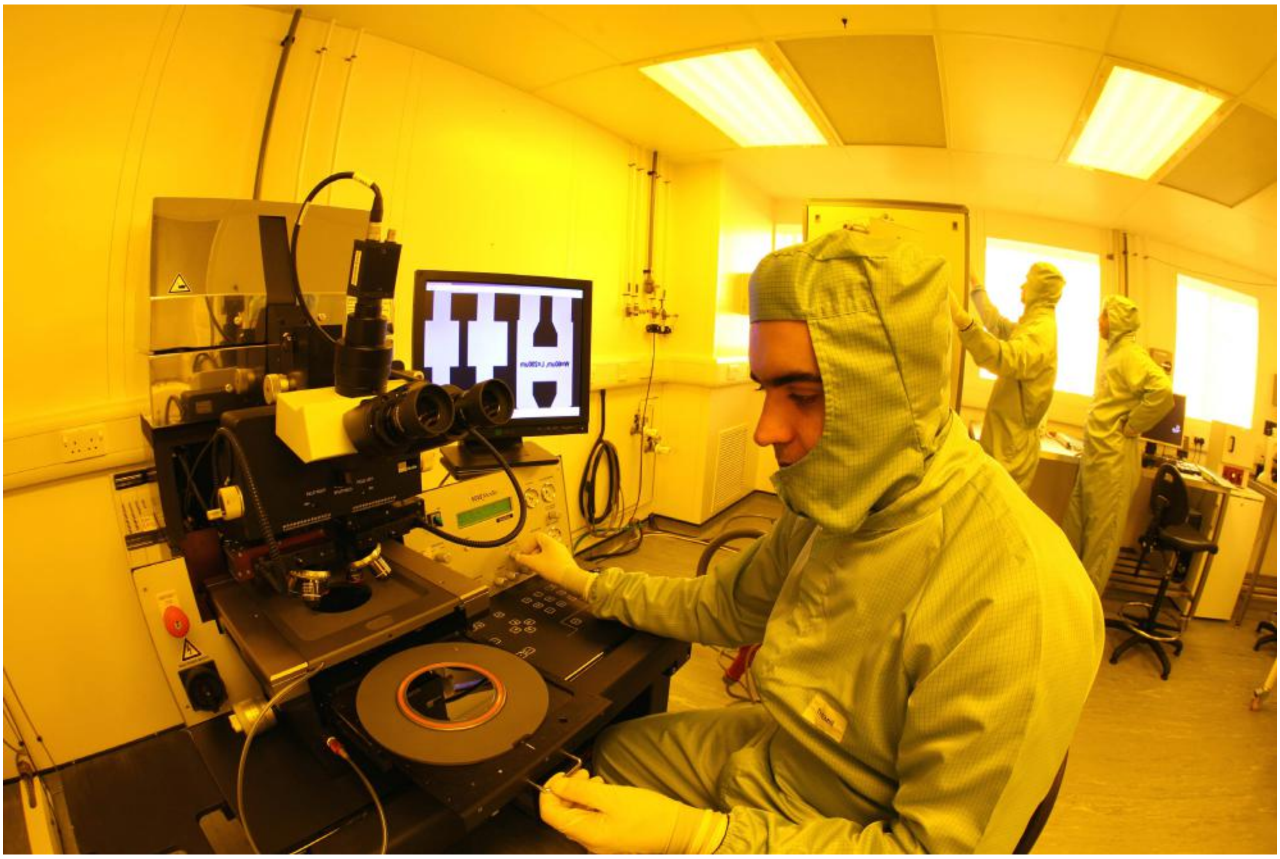
Electromagnetics Test Laboratory

Within this facility is a large, shielded, certified anechoic chamber, valid up to 34GHz, a 67GHz Agilent PNA with Cascade manual probe station and E-CAL automatic calibration for discrete SMA socketed use (up to 26.5GHz), an 8GHz 40Gs/s Agilent oscilloscope and a Picosecond pulse generator, as well as a host of other miscellaneous instruments. It is unique for the Centre to have access to such a chamber and it provides an ideal test facility for any project involving on-body or in-body antennas and indeed the communication between both. This, in conjunction with equipment such as the Agilent PNA and Dielectric Probe facilitates the use of anatomically and electromagnetically correct bio-phantoms to replicate the losses incurred when sensors and antennas are implanted in the body, leading to quicker prototype development and proof of concept.

Anechoic (RF and Acoustic) Test Chambers

State-of-the-art soundproof and electromagnetic radiation proof chambers for ultra-low noise sensing. The acoustic facility includes a large (5m x 5m x 2m) anechoic shielded chamber providing an extremely low-noise environment suitable for all low frequency acoustic, optical and mechanical device/sensor characterisation. The RF facility includes a large (4m x 3m x 2m) anechoic shielded chamber suitable for a wide range of low noise measurements with significantly attenuated electromagnetic levels. This has been calibrated for uninterrupted use between 10MHz and 34GHz.



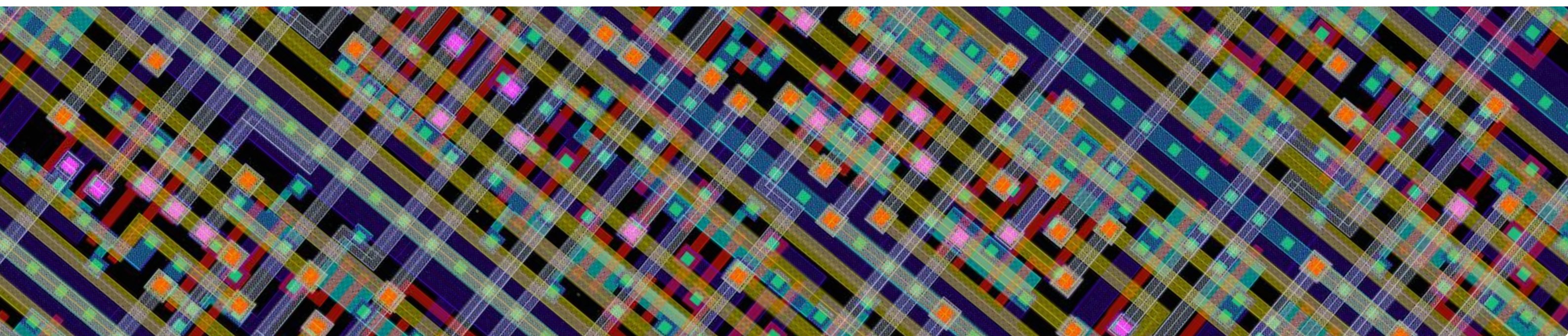


Application Specific Technology Laboratories

In addition to the state-of-the-art “general use” laboratories, the Centre additionally has three specialist laboratories that are application-specific to: Neural interfaces and Neuroprosthetics, Metabolic Technology and Genetic Technology. These laboratories provide application-specific facilities that are research-specific. For example, biosensor characterisation for metabolic technology, low noise biopotential recording for neural interfaces, etc.

Cleanroom Suite

The Centre has a suite of two ISO class 6 cleanrooms (equivalent to US standards class 1000). These have been designed to support CE Marking/FDA approvals, to class 100/1000 to develop biosensor devices, electrode and microfluidic fabrication and packaging/post-processing of CMOS chips. The largest room, the ‘yellow’ room, houses most of the fabrication tools/processes and all relevant inspection and measurement facilities. This includes photolithography (SUSS MA6/BA6), sputtering/evaporation for film deposition of metals/oxides (BOC Edwards Auto 500), surface characterisation (Veeco Dektak 6M stylus profiler), plasma chamber, wet and dry benches, parylene conformal coating (SCS parylene deposition), microscopy and wirebonding.



Who we are

ACADEMIC STAFF PROFILE

Professor Chris Toumazou

Regius Professor of Engineering
Director, Centre for Bio-Inspired Technology
Chief Scientist, Institute of Biomedical Engineering
Winston Wong Chair in Biomedical Circuits, Department of Electrical and Electronic Engineering

www.imperial.ac.uk/people/c.toumazou

Toumazou's life work has been dedicated to saving and improving lives through the invention of revolutionary, innovative and disruptive technology and the creation of a leading edge medical research institute and three commercial ventures to commercialize his research.

Toumazou is a Professor of Analog Circuit Design, Chief Scientist and Founder of Imperial's first Institute of Biomedical Engineering, Research Director of the Centre for Bio-inspired Technology, and Winston Wong Chair in Biomedical Circuits at the Electrical and Electronic Engineering Department at Imperial College London. He was made a Professor at Imperial College London at 33, one of the youngest ever to achieve this distinction. In 2013 he was appointed the first Regius Professor of Engineering, an award made to Imperial College London to celebrate the Diamond Jubilee of Her Majesty The Queen.

In addition to being involved with a number of commercial ventures, Toumazou is Founder and Non-Executive Director of Toumaz Holdings Ltd, UK; Chairman, CEO and Founder of DNA Electronics Ltd, UK; and Chief Scientific Advisor to GENEU Ltd, UK.

These technology-based companies have interests spanning ultra-low-power mobile technology, DNA Sequencing and DNA testing to create personalised skin health products.

Toumazou's career began with the invention and development of entirely novel concept of current-mode analogue circuitry for ultra-low-power electronic devices. Since then, he has been involved in inventing, developing and demonstrating new technologies to meet a range of healthcare challenges – mainly applying silicon chip technology to biomedical and life-science applications, most recently to DNA analysis. In particular Toumazou invented and licensed Portable and Rapid Semiconductor Genome Sequencing which has now become a multi-million dollar industry. One of his motivators was the diagnosis of his 13-year old son with end-stage kidney failure through a rare genetic mutation.

In 2003 he raised a total of £26m to create the Institute of Biomedical Engineering at Imperial College London, a multidisciplinary research institute and hub focusing on personalised medicine and bionanotechnology.http://en.wikipedia.org/wiki/Chris_Toumazou - cite_note-ingenia-6 He became its first Director (2014) and Chief Scientist (2011). His own specialism is in the field of personalised healthcare, providing wearable or implantable devices for early diagnosis and detection of disease.

Toumazou's visionary research and entrepreneurial actions have shown how natural analogue physics of silicon semiconductor technology can be used to mimic and replace biological functions. These include cochlear implants for born-deaf children, a bio-inspired artificial pancreas for type 1 diabetes, wireless heart monitors for personalised ambulatory health monitoring pre- and post-operatively, semiconductor-based DNA sequencing platform with applications in pharmacogenomics and recreational genetics, and an intelligent neural stimulator as a drug alternative to tackle obesity.

He was elected Fellow of the Royal Society (2008), Fellow of the Royal Academy of Engineering (2008) and Fellow of the Academy of Medical Sciences (2013), making him one of a handful in the UK who are fellows of all three premier societies. Toumazou has received numerous awards and prizes for his innovative research including the 2009 World Technology Award for Health and Medicine, the Silver Medal of the Royal Academy of Engineering in 2007 and in 2010 Honorary DEng from Oxford Brookes University. In 2009 he gave the Keynote Lecture to mark the IEEE 125th Anniversary celebrations in Europe at the Royal Institution. He has given numerous public lectures and keynote addresses at a national and international level. In 2011 he was invited to speak at the TEDMED conference in San Diego; his lecture entitled 'When Will Wireless Medicine Change Healthcare'. Other notable lectures include the G8 Summit (2013) and Royal Society public talk (2011).

In June 2014 Professor Toumazou's technology was also recognised by the European Patent Office when he was awarded the prestigious 2014 European Inventor of the Year Award for Research making him the first British winner since 2008. Toumazou has also been awarded by Cardiff University with Honorary Fellowship in 2014 and later that year - in November 2014 – the Faraday Medal, the highest honour of the UK's Institution of Engineering and Technology (IET) for the invention of semiconductor sequencing and pioneering work that has led to disposable semiconductor healthcare.

To date Chris has published over 750 research papers and holds more than 50 patents in the field of semiconductors and healthcare, for which he has received many awards and honours.

Timothy Constandinou, PhD

Senior Lecturer – Department of Electrical & Electronic Engineering
Deputy Director – Centre for Bio-Inspired Technology

www.imperial.ac.uk/people/t.constandinou

Timothy Constandinou is currently a Senior Lecturer and EPSRC Early Career Fellow within the Department of Electrical & Electronic Engineering at Imperial College London. He received both his BEng and PhD degrees in Electrical and Electronic Engineering from Imperial College London, in 2001 and 2005 respectively. He then joined the Institute of Biomedical Engineering as Research Officer until 2009, when he was appointed Deputy Director of the newly formed Centre for Bio-Inspired Technology. In 2010, continuing as Deputy Director, he joined the Department of Electrical & Electronic Engineering, where he currently holds an academic faculty position within the Circuits & Systems research group.

His research utilises integrated circuit and microsystem technologies to create advanced neural interfaces that enable 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.

During his career he has contributed to several projects from concept through to working demonstrator. This includes developing a fully implantable cochlear prosthesis for the profoundly deaf (2001-2), biologically inspired vision chips (2003-5) and an implantable vestibular prosthesis for balance restoration (2006-9). His recent research (2010 onwards) has focused on developing efficient (low power/area/communication bandwidth) real-time systems for neural interfacing that combine recording, processing, stimulation and communication. He leads the neural interfaces group (www.imperial.ac.uk/neural-interfaces) at Imperial within the Centre for Bio-Inspired Technology. Current projects include:

- **EPSRC Early Career Fellowship (ENGINI)** – Empowering Next Generation Implantable Neural Interfaces: creating truly wireless, autonomous, chip-scale implants for distributed sensing.

- **iPROBE – in-vivo Platform for the Real-time Observation of Brain Extracellular activity** (supported by the EPSRC): a digital 1k+ channel scalable neural recording interface for neuroscience research (in collaboration with Newcastle University, University of Leicester and UCL).
- **CANDO – Controlling Abnormal Network Dynamics with Optogenetics** (supported by the Wellcome Trust and EPSRC): a next generation brain pacemaker for the treatment of drug-insensitive epilepsy (in collaboration with Newcastle University and UCL).

- **Enabling Technologies for Sensory Feedback in Next Generation Assistive Devices** (supported by the EPSRC): a platform for providing sensory feedback via a PNS interface in upper-limb prosthetics (in collaboration with the Universities of Newcastle, Southampton, Leeds, Keele, and Essex).

- **AnaeWARE:** (supported by EU FP7): Monitoring awareness during anaesthesia – a multi-modal approach (in collaboration with the Hammersmith Hospital, Imperial College Healthcare NHS Trust).

- **Investigating new modalities for observing neural activity** (supported by EPSRC DTAs and platform), including: “functional neuroimaging using ultra-wideband impulse radar” and “optical neural recording (without optogenetics) for large-scale activity monitoring”.

Dr. Constandinou is a Senior Member of the IEEE, a Fellow of the IET, a Chartered Engineer and Member of the IoP. He is an associate editor of the IEEE Transactions on Biomedical Circuits & Systems (TBioCAS), chair-elect of the IEEE Sensory Systems Technical Committee (SSTC), and member of IEEE Biomedical Circuits & Systems Technical Committee (BioCAS-TC). He is currently chair of the IET Awards & Prizes committee and also serves on the IET Knowledge Services Board (KSB).

ACADEMIC STAFF PROFILE

Pantelis Georgiou, PhD

Senior Lecturer in Circuits and Systems – Department of Electrical and Electronic Engineering
Director – Bio-Inspired Metabolic Technology Laboratory, Centre for Bio-Inspired Technology

www.imperial.ac.uk/people/pantelis

Pantelis Georgiou is a Senior Lecturer within the Department of Electrical and Electronic Engineering and is the head of the Bio-inspired Metabolic Technology Laboratory in the Centre for Bio-Inspired Technology; He received the MEng (Hons) degree in Electrical and Electronic Engineering in 2004 and a PhD degree in 2008 both from Imperial College London. During his PhD he conducted pioneering work on the silicon beta cell leading towards the development of the first bio-inspired artificial pancreas for type I diabetes. He then moved to the Institute of Biomedical Engineering where he was appointed as a research fellow and head of the Bio-inspired Metabolic Technology lab. In 2011, continuing his role in the centre, he joined the Department of Electrical & Electronic Engineering, where he currently holds an academic faculty position within the Circuits & Systems research group.

His current research includes low-power microelectronics, bio-inspired design, integrated sensing systems, Lab-on-CMOS and development of novel medical devices. One of his key research focuses is on new technologies for treatment of Diabetes such as the artificial pancreas but also develops novel lab-on-chip technology with application in genomics, diagnostics in antimicrobial resistance (AMR), in addition to wearable technologies for rehabilitation of conditions such as Osteoarthritis. He has also has been involved in the creation of several commercial technologies such as a point-of- care portable platform technology for genetic detection (DNA Electronics Ltd). In 2004 he was awarded the Imperial College Governors' Prize for Electrical and Electronic Engineering and in 2013 he was awarded the IET Mike Sergeant award for outstanding achievement in engineering and his work on the Bio-inspired Artificial pancreas.

Some of his current research projects include:

- **The bio-inspired artificial pancreas** – Type 1 diabetes results in the inability to produce insulin resulting in extremely high blood sugar. Current methods of control lead to many secondary complications such as blindness, nerve damage and heart disease. This project aims to create a closed-loop system for tight glycaemic control inspired by the biology of the pancreas. The bio-inspired artificial pancreas controls blood sugar continually through intensive insulin infusion improving quality of life and reducing adverse effects of diabetes.

- **Bio-inspired glucose sensing** – This project aims to investigate the sensing mechanisms commonly found in metabolic cells in an effort to engineer more reliable and robust chemical sensing systems in CMOS. Specifically we aim to create glucose-sensing arrays inspired by biological function to improve accuracy and functionality in ambulatory applications for diabetes.

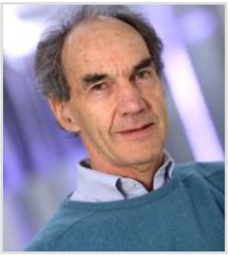
- **Decision support systems for diabetes** – Diabetes, Type 1 & 2 results in extremely high blood sugar. To minimise the adverse effects good control through intensive insulin infusion is required for insulin dependent diabetes and controlled exercise and diet for no-insulin dependent diabetes. This project aims to create a novel decision support system based on artificial intelligence to help guide the control of blood sugar in diabetes through guided supervision in a similar way to what a clinician would recommend. It is capable of factoring in multiple parameters such as blood glucose, exercise, meals and stress, all of which effect outcome.

- **Next generation ISFET** arrays for ion-imaging and point-of-care diagnostics– Semiconductor based chemical sensing using Lab-on-CMOS platforms is becoming an attractive alternative to conventional optical sensing due to the capability to integrate millions of sensors on a single substrate to create sensing arrays, ability to create small form factor point-of care diagnostics, and low cost associated with the economies of scale of silicon. My lab is developing next generation chemical sensing arrays using Ion-sensitive Field Effect transistors. Our applications include semi-conductor based DNA sequencing, diagnostics for bacterial genotyping and pathogen detection to combat Antimicrobial Resistance and Infection in the hospitals, and ion-imaging to create point-of-care systems for multiple metabolite monitoring.

- **Smart clothing for rehabilitation of osteoarthritis**– This project aims to integrate intelligent sensing capability in clothing for smart rehabilitation of osteoarthritis. Through monitoring of joint function through a variety of sensors (flexible impedance, sEMG, motion) and integration of wireless capability a low-power wearable platform will be developed to help guide rehabilitation after intervention such as knee replacement surgery.

- **Real time muscle fatigue detection for smart rehabilitation** – This project will create a real-time method for tracking muscle fatigue for applications in rehabilitation and sport physiotherapy. Through specific continuous time techniques, an energy efficient, miniaturised system will be developed in CMOS that extracts muscle fatigue through monitoring of EMG. More importantly this system will be information driven rather than conventionally data driven, reducing requirements on data transmission and thus saving power.

Dr Georgiou is a member of the IEEE (Institution of Electrical and Electronic Engineers), a member of the IET (The Institution of Engineering and Technology) and a Chartered Engineer (CEng). He serves on the BioCAS (Biomedical Circuits and Systems) and Sensory Systems technical committees of the IEEE CAS Society. He is also the CAS representative on the IEEE sensors council. He also sits on the IET Awards and Prizes committee.



Professor Chris McLeod

Principal Research Fellow- Centre for Bio-inspired technology, Institute of Biomedical Engineering

Chris McLeod was appointed Principal Research Fellow in Cardiovascular Instrumentation in 2009 after joining the IBE at its inception in 2005 as a Visiting Professor. Until 2008 he had been a Professor of Electronic Engineering at Oxford Brookes University where he led research in Medical Devices in collaboration with the clinical departments of Anaesthetics, Neurophysiology and Paediatrics, holding an Honorary Research Fellowship in the Department of Anaesthetics. The research activities were mainly funded by the Wellcome Trust and EPSRC. Prior to joining Oxford Brookes he worked with clinical research groups in Paediatrics and the Nuffield Institute for Medical Research in Oxford. He received an MA degree in Engineering from Cambridge, an MSc in Bioengineering from Strathclyde and a D.Phil in Bioengineering from Oxford.

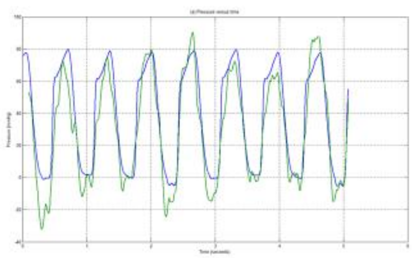
His research has, in the past, been based on minimally-invasive sensing of physiological data for patients in intensive care, both adult and neonatal, to improve the quality of signals, to increase the value of recorded signals and to decrease the obtrusiveness of recording apparatus. He currently leads the research group developing permanently implantable sensors for monitoring the cardiovascular system in ambulatory patients at home with long-term conditions and piloting implantable sensors for other medical applications. The monitoring system delivers objective data to a clinician or server through a wide-area network. The sensors are based on acoustic resonators which can be powered and interrogated wirelessly from the body surface.

Motivation for current research
There is a hypothesis that objective measurements of Pulmonary Arterial Pressure can be used to determine the optimal pharmaceutical therapy for patients with progressive heart failure. If optimal, patients will have the minimum morbidity (i.e. best achievable quality of life) and disease progression will be retarded. Early indications from permanently implanted sensors measured once daily in an American trial (CHAMPION) show a significantly reduced re-hospitalisation rate in patients. We believe that an ambulatory monitoring regime will further improve the data available to optimise therapy, with the added potential of being a clinical alarm system.

His current research and development programme is funded by the Wellcome Trust and Department of Health for which he is extremely grateful. The IBE at Imperial has been an excellent base for this activity, so thanks also to Chris Toumazou for making him welcome here.

Recent publications:

- **C.N.McLeod**, R.Harding, P.Johnson, M.E.McClelland, P.L.Whyte Studies on the Control of Respiration and Behaviour during Development in Ewe reared Lambs. Biotelemetry (1978) 4:63 68.
- A.B.Baker and **C.N.McLeod.** Oesophageal Multipurpose Monitoring Probe. Anaesthesia (1983) 38:892 897.
- K. Paulson, S. Jouravleva, **CN. McLeod** “Dielectric Relaxation Time Spectroscopy” IEEE-BME Vol 47 no.11 pp1510-7, (2000)
- Kerrouche N, **McLeod CN** & Lionheart WRB ‘ Time series of EIT chest images using singular value decomposition and Fourier transform’. Physiol Meas 22(1) pp 147-158. (2001)



Simultaneous recordings of porcine left ventricular pressure from a catheter-tip transducer (green) and SAW sensor (blue)

ACADEMIC STAFF PROFILE

Konstantin Nikolic, PhD

Senior Research Fellow

www.imperial.ac.uk/people/k.nikolic

Konstantin received a DiplEng and Masters from the Department of Electrical Engineering, Belgrade University, Serbia and a PhD in Condensed Matter Physics from Imperial College London. He was a Lecturer and Associate Professor at the Faculty of Electrical Engineering, Belgrade University (teaching Physics, Quantum Mechanics and Semiconductor Devices) in the period 1994-1999. Then he moved to UCL (Department of Physics and Astronomy, Image Processing Group) until he joined the Institute of Biomedical Engineering, Imperial College London in 2005. In 2006 he became Corrigan Research Fellow and in 2012 Senior Research Fellow. His papers currently have 1269 citations, h-index=17, g-index=34 (27/Sep/2015).

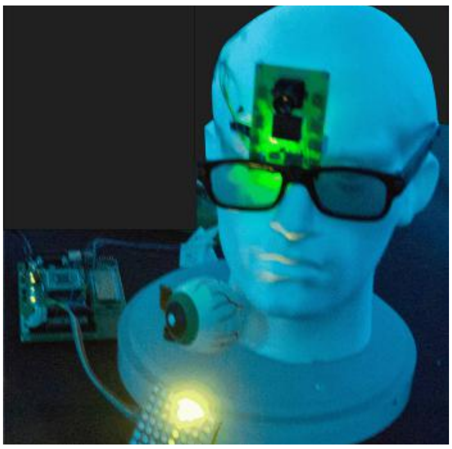
Living cells receive information from their surroundings, process that information and communicate between themselves. They perform information processing tasks using noisy components in noisy environment and with limited energy resources, but still they achieve very complex computation. This is achieved by using very sophisticated molecular machinery. Then, on the next level, these cells form living organisms which are capable of even more impressive information processing and communication. Capturing all this complexity in our simplistic models doesn't seem possible. Still, our models and simulations provide useful insights, and represent a fundamental basis in understanding how to design new bio-inspired devices.

My group develops methods and computational tools for understanding, modelling and simulating various biological and physiological processes and their applications in bio-inspired electronic systems. Current projects include:

- **PyRhO – Multiscale Computational Platform for Optogenetics** (BBSRC funding, PI).
- **Characterisation of functional properties of retinal ganglion cells using information theory** (EU project SeeBetter, PI).
- **Development of a machine learning algorithm for a breathalyser device for cancer detection** (Wellcome-Imperial Strategic Support, Co-I).
- **New types of thermal neural stimulation and optical stimulation and recordings** (EPSRC-Imperial Impact Acceleration Fund, Co-I).
- **Platform Grant for Disruptive Semiconductor Technologies for Advanced Healthcare Devices** (EPSRC, CoI).

Recent Publications:

- Z. Mou, I. F. Triantis, V. M. Woods, C. Toumazou, **K. Nikolic**, "A simulation study of the combined thermoelectric extracellular stimulation of the sciatic nerve of the Xenopus laevis: the localized transient heat block", IEEE Trans. Biomedical Engineering, vol. 59, pp. 1758-1769, 2012.
- **K. Nikolic**, J. Loizu, P. Degenaar, and C. Toumazou, "A stochastic model of the single photon response in Drosophila photoreceptors", Integrative Biology, vol. 2, pp. 354-370, 2010.
- N. Grossman, V. Poher, M. S. Grubb, G. T. Kennedy, **K. Nikolic**, B. McGovern, et al. "Multi-site optical excitation using ChR2 and micro-LED array", Journal of Neural Engineering, vol. 7, p. 016004, 2010. (119 citations).
- **K. Nikolic**, N. Grossman, M. S. Grubb, J. Burrone, C. Toumazou, and P. Degenaar, "Photocycles of Channelrhodopsin-2," Photochemistry and Photobiology, vol. 85, pp. 400-411, 2009. (82 citations).



Retinal Prosthesis prototype, consisting of a event-based camera (Dynamic Vision Sensor), Microcontroller processing unit and a Stimulator (LED matrix).

Sarah Agarwal

Project Administrator (part time)

Sarah is the Project Administrator for the EPSRC project, ‘Engineering, Physical, Natural Sciences and Medicine; Bridging Research in Antimicrobial Resistance; Collaboration and Exchange (EMBRACE)’. Her role is to support the EMBRACE Fellows and multidisciplinary collaborations around antimicrobial resistance.

Wiesia Hsissen

Senior Group Administrator, Circuits and Systems Research Group, Department of Electrical and Electronic Engineering

Wiesia is the senior group administrator of the Circuit and Systems (CAS) research group of which the Centre of Bio-inspired Technology is part of. She joined the Department of Electrical and Electronic Engineering in 1990 and has kept a key role in supporting the CAS group ever since.

Gifty Kugblenu

PA to Professor Chris Toumazou

Gifty joined the Centre in 2010 as PA to Professor Toumazou. She provides the essential support he needs to fulfil his various roles including as Director of the Centre, Professor of Biomedical Circuits in the Department of Electrical and Electronic Engineering,chairman to Toumaz Ltd and CEO to DNA Electronics Ltd.

Izabela Wojcicka-Grzesiak

Research Group Administrator, Centre for Bio-Inspired Technology

Iza is the group administrator for the Centre for Bio-Inspired Technology. She originally joined Imperial in 2006 as an administrator within the Institute of Biomedical Engineering and was appointed group administrator of the Centre in 2009 when it was formed. Iza now plays a key role within the Centre supporting staff, students, research and facilities. Within her role she deals with all matters relating to finance, HR, health and safety and general administration.

Mohammad Reza Bahmanyar, PhD

Research focus: Wireless Medical Implants and Devices

Funding: Wellcome Trust

Motivation:

Implantable medical devices play an important role in improving the quality of life of patients across the world. These devices are often the result of multidisciplinary research, where different technologies are used and work together. Rapid advancement of technology in different areas and ever increasing need for new medical devices (e.g. due to the aging population) means that the future of healthcare will rely on efficient convergence of multiple disciplines. Understanding and utilizing science and technology in a creative way to develop novel medical devices that can potentially help patients is the main drive in my research.

Objectives:

Measuring physical (e.g. pressure) and biochemical (e.g. glucose concentration) quantities inside the human body can assist in managing relevant medical conditions and assessing the efficiency of treatments. This requires biocompatible miniature implants of high longevity that can be interrogated wirelessly. Producing such devices is challenging and demands creative use of existing, and developing novel, technologies to achieve:

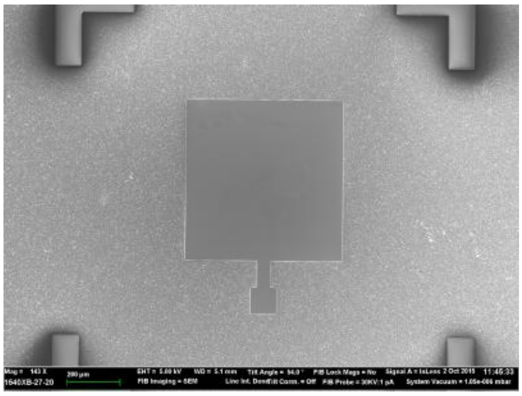
- Miniaturisation without compromising the functionality.
- Increasing the longevity without compromising safety and biocompatibility.
- No cross-interference with other wireless systems.
- Devising ways of using the acquired data to maximise the benefit to the patient and minimise the cost to the healthcare system.

Short Bio:

I have been doing research at the interface of engineering/physics with medicine for 15 years, developing experience in medical devices including working with manufactures and regulators. I have worked on the development of instruments, algorithms, sensors and devices for cardiovascular and ocular applications and DNA analysis. I joined the Institute of Biomedical Engineering in 2009. I am the PI on two projects on cardiovascular devices; also part of a team, funded by the Wellcome Trust and the Department of Health to develop a complete implant system for a phase I clinical trial for pulmonary artery blood pressure monitoring.

Recent Publications:

- O. H. Murphy, A. Borghi, **M. R. Bahmanyar**, C. N. McLeod, M. Navaratnarajah. M. Yacoub, C. Toumazou, “RF communication with implantable wireless device: effects of beating heart on performance of miniature antenna”, Healthcare Technology Letters, vol. 1, no. 2, pp. 51-55, 2014.
- M. Zolgharni, N. M. Dhutia, G. D. Cole, **M. R. Bahmanyar,** S. Jones, S. M. A. Sohaib, S. B. Tai, K. Willson, J. A. Finegold, D. P. Francis, “Automated Aortic Doppler Flow Tracing for Reproducible Research and Clinical Measurements”, IEEE Transactions on Medical Imaging, vol. 33, no.5, pp. 1071-1082, 2014.
- A. Borghi, O. H. Murphy, **R. Bahmanyar,** C. McLeod, “Effect of Stent Radial Force on Stress Pattern After Deployment: A Finite Element Study”, Journal of Materials Engineering and Performance, 2014.
- Olive H. Murphy, **Mohammad Reza Bahmanyar,** Alessandro Borghi, Christopher N. McLeod, Manoraj Navaratnarajah, Magdi H. Yacoub, Christofer Toumazou, “Continuous in vivo blood pressure measurements using a fully implantable wireless SAW sensor”, Biomedical Microdevices, April 2013; DOI 10.1007/s10544-013-9759-7.



A film bulk acoustic wave resonator for IOP measurement.

SAW pressure sensing implant for pulmonary artery.

Andrea Alenda González, PhD

Research Focus: Bio-inspire implant to treat obsesity

Funding: ERC Synergy (i2MOVE)

Motivation:
Obesity is one of the biggest health challenges of the century. According to the World Health Organization it is a pandemic. Being obese and overweight increases the risk of suffering from cancer, diabetes, and heart disease. It is the major cause of preventable death with few effective treatments.

The Vagus nerve communicates between the brain and gut, regulating satiety. By stimulating the Vagus it is possible to make a person feel full. Although Vagus Nerve Stimulation (VNS) is being used for weight loss it gives limited performance when compared to bariatric surgery. These devices lack intelligence, as they consist of a pacemaker-like periodic pulse generator, with no biological feedback.

Objectives:
The i2MOVE project is designed to integrate state of the art technology and physiological research together to produce a new generation of implant to treat obesity. This pioneering VNS treatment will be capable of stimulating and simultaneously record electrical and chemical activity from the Vagus, unlike any other VNS on the market.

As patients vary, no two VNS programs should be the same. This intelligent VNS would enable a dynamic and tailor-made program specific to each patient. True personalised medicine.

As a neuroscientist my role is to understand the physiology and anatomy of the Vagus nerve and liaise with the engineering team to find optimal nerve-implant interface solutions.

Short Bio:
I have been a Research Fellow in Medical Devices at the Centre for Bio-Inspired Technology since 2013. My field of expertise is systems neuroscience; how connections of different brain regions coordinate to produce neural responses that underlie cognition. I have worked on how the brain perceives touch and how it constructs a map of its environment.

After more than a decade doing research in basic neuroscience, it is exciting to participate in a project on applied biomedicine. In the i2MOVE project the prospect of joining the dots between the nervous system and the rest of the body is an exciting challenge that no systems neuroscience physiologist is able to resist.

Recent Publications:

- E. Marozzi, L. L. Ginzberg, **A. Alenda**, K. J. Jeffery, “Purely Traslational Realigment in Grid Cell Firing Patterns Following Nonmetric Context Change”, Cereb Cortex, 2015.
- **A. Alenda**, M. Maravall, M. R. Bale, R. S. Petersen, “Transformation of Adaptation and Gain Rescaling along the Whisker Sensory Pathway”, PlosOne, 2013.
- **A. Alenda**, M. Molano-Mazon, S. Panzeri, M. Maravall, “Sensory Input Drives Multiple Intracellular Information Streams in the Somatosensory Cortex”, J Neurosci, 2010.
- R. S. Petersen, M. Brambilla, **A. Alenda**, S. Panzeri, M. A. Montemurro, M. Maravall, “Diverse and temporally precise kinetic feature selectivity in the VPm thalamic nucleus”, Neuron, 2008.

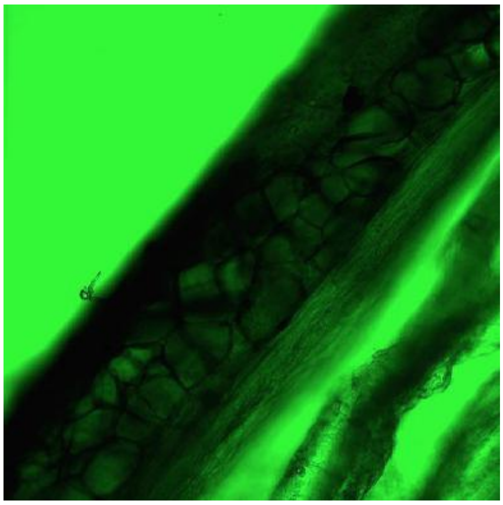


Image taken by a two photon confocal microscope and corresponds to a subdiaphraghmatic vagus nerve stained with evans blue.

Amir Eftekhar, PhD

Research Focus: The Research & Development of Intelligent Medical Devices to monitor, assist and treat Neurological Disorders

Funding: ERC Synergy (i2MOVE)

www.imperial.ac.uk/people/a.eftekhar

Motivation:
We live in a world where the incidence of some of the most devastating diseases has no definitive cure. Obesity, for example, has a worldwide cost of $1.3trillion, affecting at least one third of the world's population. Neurological disorders such as dementia, epilepsy and Alzheimer's are increasingly prevalent, with new insights constantly emerging. Technology is playing a key part in providing efficient therapeutic paths. My motivation is to research and develop such technology in order to facilitate treatment of these, and other, healthcare problems.

Objectives:
I am engineer by trade, but with a broad depth of knowledge in application areas of medical devices. Thus, as a problem solver, I apply existing technology to applications where they can be integrated well, or develop new technology and paradigms, sometimes disruptive, towards the same end. With a strong background in signal processing and electronics, I work with multi-disciplinary teams, on a few select projects, with the objective to integrate intelligent, real-time algorithms and technology into medical devices.

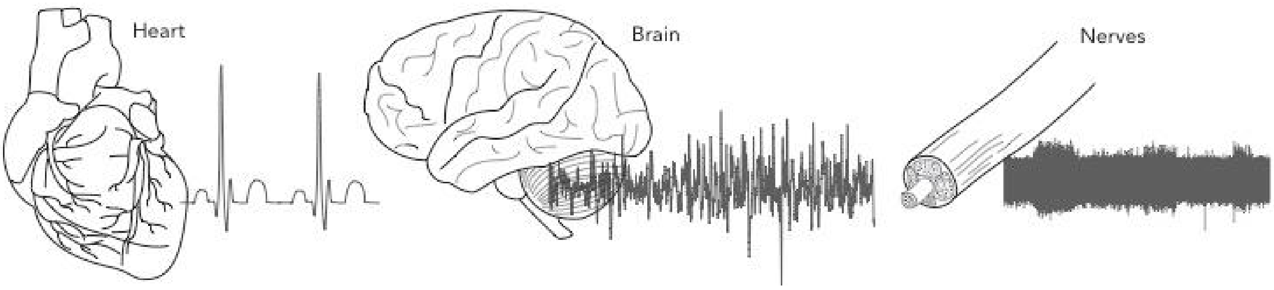
Short Bio:
I completed my PhD at Imperial College London in 2010. Since then I have taken on the role of Research Associate then Fellow at the CBIT, focusing my research on applications of technology to neurological studies. Primarily this involves electrode technology for interfacing with the Central and Peripheral Nervous System, front-end electronics (analog/digital) for implantable or portable systems to interface with these electrodes and advanced signal processing methods for extracting and quantifying the dynamics of biosignals. I currently lead the technological development of a €7million ERC project, targeting the Vagus nerve as a means of deciphering its role in appetite.

Recent Publications:

- S. E. Paraskevopoulou, D. Wu, **A. Eftekhar,** T. G. Constandinou, "Hierarchical Adaptive Means (HAM) clustering for hardware-efficient, unsupervised and real-time spike sorting", Journal of Neuroscience Methods, vol. 235, pp. 145–156, 2014.
- S. E. Paraskevopoulou, **A. Eftekhar**, N. Kulasekeram, C. Toumazou, "A Low-Noise Instrumentation Amplifier with DC Suppression forRecording ENG Signals", Proc. IEEE EMBS Conference, 2015.

Key References:

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



An illustration of my main research areas: (left) heart activity (electrocardiogram or ECG), (middle) brain signaling (electroencephalogram or EEG) and (right) peripheral nerves (electroneurogram or ENG).

Fellow

STAFF RESEARCH REPORT

Nir Grossman, PhD

Research Focus: Noninvasive Human Neuromodulation

Funding: Wellcome Trust MIT Postdoctoral Fellowship

http://www.imperial.ac.uk/people/nir.grossman06

Motivation:

Neuromodulation is widely used to study and treat the brain, presenting an attractive alternative for pharmacology treatment. Transcranial alternate current stimulation (TACS) is a new neural modulation method that uses weak, exogenous and periodic electric fields for synchronising neural activity. TACS has been showing already very interesting neurobiological and behavioral effects despite a lack of exact understanding of the mechanism by which the mesoscopic neural oscillatory dynamics is modulated. The concept of remote modulation of the brain's oscillations - a hallmark of physiological and pathological functions, is very new and bears exciting engineering and clinical challenges and opportunities.

Objectives:

Nir's research is aim to develop mechanistic principles to achieve targeted and individualised noninvasive modulation of human brain oscillations.

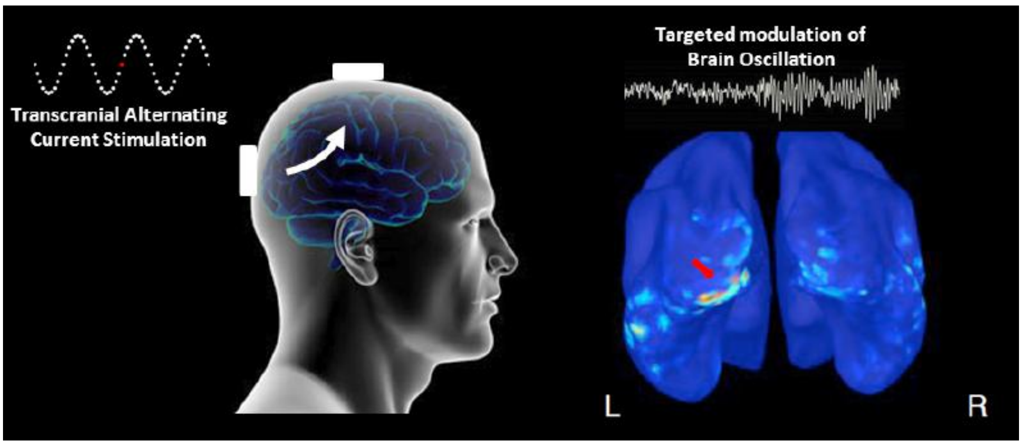
Short Bio:

Nir is a Wellcome Trust MIT Fellow with Prof. Chris Toumazou, working with Prof. Ed Boyden (MIT) and Prof. Alvaro Pascual-Leone (Harvard) on a neuromodulation technology that uses electric fields to entrain, non-invasively, oscillatory neural activity.

Nir has a PhD in Neuroscience from Imperial College London. In his PhD Nir and his co-workers, were developing a new type of retinal prosthesis that was based on a genetic expression of a microbial light sensitive ion channel. Nir has MSc in Electromagnetic Engineering from the Technical University of Hamburg-Harburg (TUHH), Germany and BSc in Physics from the Israeli Institute of Technology.

Recent Publications:

- **N. Grossman**, K. Nikolic, C. Toumazou, P. Degenaar, "Modeling Study of the Light Stimulation of a Neuron Cell with Channelrhodopsin-2 Mutants", IEEE Transactions on Biomedical Engineering, vol. 58, no. 6, pp. 1742-51, 2011.
- **N. Grossman**, V. Pohrer, M. Grubb, G. T. Kennedy, K. Nikolic, M. A. A. Neil, M. D. Dawson, J. Burrone, P. Degenaar, "Multi-site optical excitation using ChR2 and micro-LED array", J. Neural Eng., vol. 7, 2010.
- P. Degenaar, **N. Grossman**, M. A. Memon, J. Burrone, M. Dawson, E. Drakakis, M. Neil, K. Nikolic, "Optobionic vision – a new genetically enhanced light on retinal prosthesis", J. Neural Eng., vol. 6, no. 3, 2009.
- **N. Grossman**, A. Ovsianikov, A. Petrov, M. Eich, B. Chichkov, "Investigation of optical properties of spiral photonic crystals", Optic Express, vol. 15, no. 20, pp. 13236-43, 2007.



Pau Herrero-Viñas, PhD

Research focus: Applying Engineering Solutions To Diabetes Management and to Reduce Antimicrobial Resistance

Funding: Wellcome Trust

www.imperial.ac.uk/people/p.herrero-vinias

Motivation:
Diabetes describes a group of metabolic diseases in which the person has high blood glucose, either because insulin production is inadequate, or because the body's cells do not respond properly to insulin. Around 385 million people throughout the world have diabetes. Optimal glucose management is crucial to reduce the risk of complications such as blindness, kidney disease and amputations.

Antimicrobial resistance is now a major threat to patient safety and increasingly we are seeing patients infected with bacteria for which there are very few antimicrobials that remain effective. To conserve the effectiveness of antimicrobials we need to develop ways to use them more sensibly.

Objectives:
In field of diabetes management, my main objective is to develop a closed-loop insulin delivery system for tight glycemic control in type 1 diabetes. This system has already been validated in clinic and further trials to test this technology in a home environment are ready to commence.

Another diabetes-related project I am involved with consists of developing an intelligent decision support system for meal insulin dosing. This system is aimed at providing superior glycemic control with respect to existing insulin bolus calculators.

In the field of antimicrobial resistance, my main focus of research is on developing of a point-of-care decision support system to optimise antimicrobial therapy in intensive and secondary care. Such technology is currently being tested at the Imperial College Healthcare NHS Trust.

Short Bio:
Pau Herrero-Viñas received the MEng degree in industrial engineering from the University of Girona (Spain) in 2001, and the PhD degree in control engineering from University of Angers (France) in 2006. He then spent one year as a Research Fellow at the University of California Santa Barbara (USA), working on an artificial pancreas project. After his stay in California, he spent two years at Sant Pau Hospital in Barcelona (Spain) leading different eHealth projects for the prevention and management of diabetes. He is currently a Research Fellow within the Centre for Bio-inspired Technology at Imperial College London.

Recent Publications:

- **P Herrero**, P Pesl, J Bondia, M Reddy, N Oliver, P Georgiou, C Toumazou, "Method for automatic adjustment of an insulin bolus calculator: In silico robustness evaluation under intra-day variability", Computer Methods And Programs In Biomedicine, vol. 119, no. 1, pp. 1-8, 2015.
- **P Herrero**, P Pesl, M Reddy, N Oliver, P Georgiou, C Toumazou, "Advanced Insulin Bolus Advisor based on Run-To-Run Control and Case-Based Reasoning", IEEE J Biomed Health Inform, vol. 19, no. 3, pp. 1087-1096, 2015.
- P Pesl, **P Herrero**, M Reddy, M Xenou, N Oliver, D Johnston, C Toumazou, P Georgiou, "An Advanced Bolus Calculator for Type 1 Diabetes: System Architecture and Usability Results", IEEE J Biomed Health Inform, vol. --, no. --, pp. --, 2015 (in press).
- M Reddy, **P Herrero**, M El-Sharkawy, P Pesl, N Jugnee, H Thomson, D Pavitt, C Toumazou, D Johnston, P Georgiou, N Oliver, "Feasibility Study of a Bio-inspired Artificial Pancreas in Adults with Type 1 Diabetes". Diabetes Technology and Therapeutics, vol. 16, no. 9, pp. 550–557, 2014.

The Advanced Bolus Calculator for Diabetes Management System (ABC4D).

Intelligent point-of-care decision support system for antimicrobial prescribing.

Fellow

Nishanth Kulasekeram

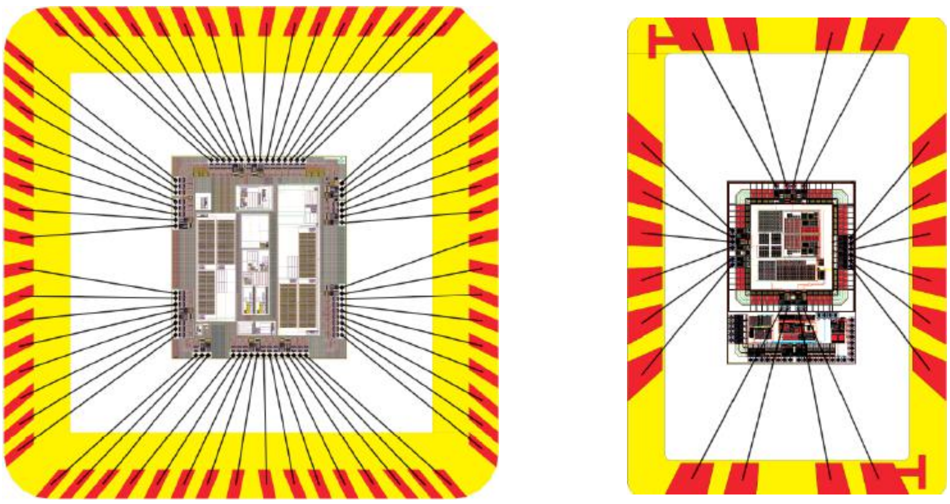
Research focus: To develop low-power microelectronics for a fully implantable peripheral nerve interface for the monitoring and treatment of obesity

Funding: ERC Synergy (i2MOVE)

Motivation:
At this present day, there are key challenges that need to be addressed to design a fully implantable solution. The biggest and most important challenge is the ability to design a recording channel capable of amplifying bio-potentials, nerve signals with maximum amplitudes of 15μV in a noise floor of 1-3μVrms within a bandwidth of up to 10KHz. We also need to detect mass activity that has amplitudes between 1-10μV, which is very close to the noise floor of the front-end amplifiers and sensor electrodes. This is coupled with low-power requirements of the complete solution to extend the battery life for the implanted system.

Objectives:
My objective is to develop a multichannel recording and stimulating integrated solution by the end of 2016, To date most front-end low-noise amplifiers used within our single channel systems have noise optimized differential input stages that increases the physical dimensions of the amplifiers. I have considered a technique to suppress the flicker noise contribution of individual transistors, thus reducing the physical dimensions, and overall silicon area. My present research and achievements to date, would pave the way towards achieving these goals.

Short Bio:
I have spent the last 12 years in the semiconductor industry prior to joining the Centre of Bio Inspired Technology, here at Imperial College London, in July 2014. Over the past 12 months, since joining, I have developed integrated circuit (IC) solutions to aid the detection of compound action potentials, and mass activity off the subdiaphragmatic Vagus nerve. The IC on the left, houses a variety of single channel electrical and pH recording solutions, along with a novel flicker noise cancellation circuit. The IC on the right is intended as a current stimulator to stimulate the cervical Vagus.



Integrated circuits developed for single channel recording and stimulation

Fellow

Yan Liu, PhD

Research Focus: Integrated Neural Microsystems and Neural Interfaces

Funding: Wellcome Trust/EPSRC (CANDO Project)

www.imperial.ac.uk/people/yan.liu06

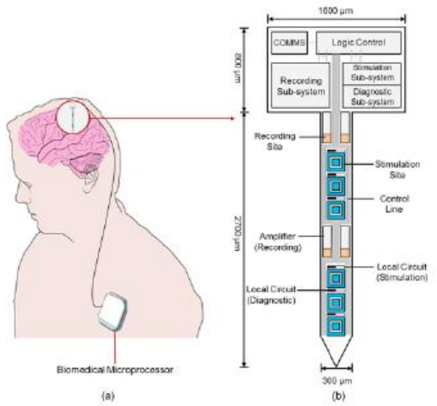
Motivation:
My work is in part motivated by the current quest to understand the human brain, developing new tools and applying these to create both next generation brain machine interfaces and therapeutic neural network regulation. Such devices will need to observe the activity of multiple neurons in real time, feedback to apply control mechanism with low latency, be chronically stable and be adaptive over time.

Objectives:
My work is mainly focusing on neural recording systems, and integrating neural instrumentation into more general platforms. Several challenges remain in implementing such systems, such as how can they be made to be compact, low power, low noise, high interference immunity, high channel count, be suitable for chronic operation and generate high quality, low data rate information with minimum latency. Furthermore, the physical embodiment of such microsystems often poses a reliability challenge, for example, how to provide chip with stable power supply and high speed data interface with minimized impact from and to adjacent tissues in long term. In CANDO project for instance, a CMOS based integrated implant will monitor the brain activity and provide pulses of light to prevent the build of abnormal activity. High quality, compact neural recording systems immune to optical and electrical interface are essential for real-time control and diagnosis.

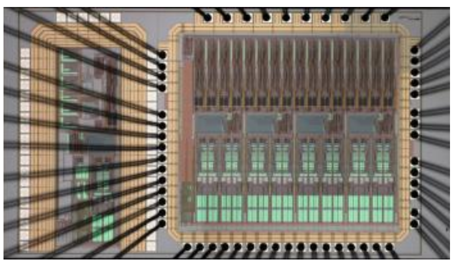
Short Bio:
Yan Liu received the B.Eng. degree in process equipment and control engineering from Zhejiang University, Zhejiang, China, in 2006, and the M.Sc. and Ph.D. degrees, both in electronic engineering, from Imperial College London, London, U.K., in 2007 and 2012, respectively. Currently, he is a Research Fellow at the Centre for Bio-inspired Technology, Department of Electrical and Electronic Engineering, Imperial College London. His research interests include CMOS lab-on-chip devices, brain machine interfaces, and novel mixed-signal circuits for biomedical applications.

Recent Publications:

- H. Zhao, F. Dehkhoda, R. Ramezani, D. Sokolov, **Y. Liu**, T. G. Constandinou, P. Degenaar, "A CMOS-based Neural Implantable Optrode for Optogenetic Stimulation and Electrical Recording", Proc. IEEE BioCAS Conference, 2015.
- F. Dehkhoda, A. Soltan, R. Ramezani, H. Zhao, **Y. Liu,** T. G. Constandinou, P. Degenaar, "Smart Optrode for Neural Stimulation and Sensing", Proc. IEEE Sensors Conference, 2015.
- D. Y. Barsakcioglu, **Y. Liu**, P. Bhunjun, J. Navajas, A. Eftekhar, A. Jackson, R. Quian Quiroga, T. G. Constandinou, "An Analogue Front-End Model for Developing Neural Spike Sorting Systems", IEEE. Trans. BioCAS, vol. 8, no. 2, pp. 216-227, 2014
- L. Zheng, L. B. Leene, **Y. Liu**, T. G. Constandinou, "An adaptive 16/64 kHz, 9-bit SAR ADC with peak-aligned sampling for neural spike recording", Proc. IEEE ISCAS, pp. 2385-2388, 2014.



Device concept for CANDO project. Shown are: (a) overall device architecture; (b) optrode floorplan illustrating the internal organization.



Microphotograph of a recent "smart" recording chip for brain machine interfaces.

Fellow

Yufei Liu, PhD

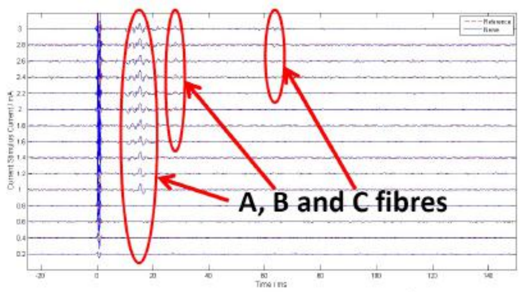
Research focus: Advanced micro/nano fabrication and Smart microsystem for point of care applications

Funding: ERC Synergy (i2MOVE)

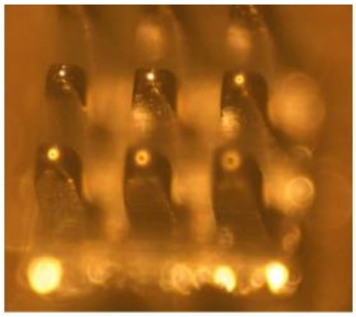
Motivation:
One of the biggest challenge and objective of the Intelligent Implantable MOdulator of Vagus nervE function for treatment of Obesity (i2MOVE) project is to access the vagus nerve with high-resolution microelectrodes. Cuff electrodes are excellent for recording and stimulation of the whole nerve. However, although some directional and fibre-type selectivity is possible, fascicle selectivity is not. To interface selectively within fascicles, we are developing nerve cuff electrodes integrated with penetrating interfascicular electrodes, which penetrate the nerve to be positioned between fascicles.

Objectives:
In a state-of-the-art cleanroom of Centre for Bio-Inspired Technology, my first objective was to develop our own microfabricated cuff electrodes. Cuff electrodes have been successfully fabricated with photolithography, metal deposition and lift off technologies. Bipolar and tripolar electrode arrays are successfully made of Chromium-Gold, which were designed for matching the requirements of impedance and recording signal-to-noise ratio. In-vivo tests have shown we can record A, B, and C fibres on the vagus nerve. Microspike array have also successfully fabricated, which would subsequently be functionalised to be pH and ion sensitive.

Short Bio:
Dr. Yufei Liu joint Imperial College London, as a Research Fellow in Centre for Bio-Inspired Technology, in Nov 2013. He worked previously as a Research Officer in Swansea University, between Jan 2010 and Nov 2013. Yufei has over 20 peer reviewed publications and over 10 patents worldwide. He was the nominee of The Technology Strategy Board 2013 Business Leaders of Tomorrow Award and The 2015 TATA Steel Award for Outstanding Impact in Commerce, Industry and Enterprise. Yufei is also the winner for 2012 Wales Early Stage Development Fund, 2013 EPSRC Bridge the Gap Fund and 2014 EPSRC Techealth Innovation Fund.



In-vivo test reults using sucessfully made cuff electrodes



Fabricated microspike array

Belinda Nedjai, PhD

Research focus : The Neuro-Immuno Modulation of gastric cancer: Investigation of the vagal immune pathways in gastric cancer tumorgenesis, progression and treatment.

Funding: EPSRC

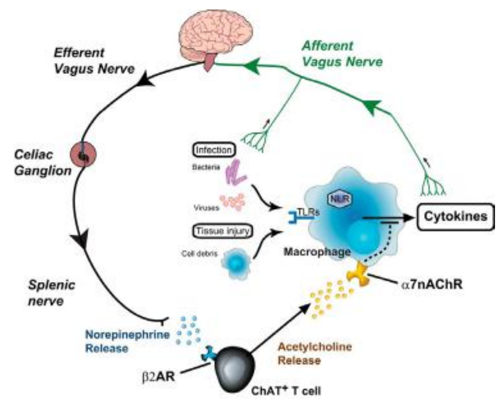
Motivation:
The aim of this research project is to characterise the bi-directional communications of the vagal-immune pathway in gastric cancer tumor genesis, tumor progression and treatment. Gastric cancer is the fifth most common cancer and the third leading cause of cancer mortality worldwide, with a 5-year survival rate of less than 25%. Surgery remains the only potentially curative treatment. It has been shown that vagotomy improves the success rate of post-operative chemotherapy suggesting a key role of vagus nerve in tumor growth and progression. This project addresses whether neural recording of the vagus nerve can be used for early detection of tumor growth? and if vagus nerve stimulation can inhibit the development and/or progression of cancer via its anti-inflammatory effects.

Objectives:
There is a need to develop a novel intelligent chemical recording platform on cuff electrode technology to allow better specificity of neural recording and stimulation, that can do 1) Selective activation of the cholinergic anti-inflammatory pathway in-vivo on rat's models of gastric cancer, to investigate the effect on tumor growth and 2) Monitoring continuous activity of afferent vagus activity in-vivo to identify patterns of neural activity relating to the inflammatory and tumorigenic processes in the viscera. Ultimately, this research will lead to the development of a novel intelligent, implantable cuff technology for monitoring and regulating vagal activity related to inflammation and cancer.

Short Bio:
Belinda has developed a strong interest in the inflammation and innate immunity studying cytokines and chemokines networks and their relevance to diseases. She holds a PhD in immunology and functional genomics from Queen Mary, Bart's and The London School of Medicine. She has expertise in inflammation, acquired during her Master's degree in Cellular and Molecular Physiopathology, University Pierre et Marie Curie, Paris and postdocs. Her last research project in the Centre of Bio-inspired technology has successfully contributed to a start up company, GeneU and two clinical trials of DNA technology applied to skin care.

Recent Publications:

- **B Nedjai,** JM Viney, Hull, H Li, C Anderson, CA Horie, R Horuk, N Vaidehi, JE Pease. CXCR3 antagonist VUF10085 binds to an intrahelical site distinct from that of the broad spectrum antagonist TAK-779. Br J Pharmacol. 2015 Apr;172 (7):1822-1833.
- MD Turner, **B Nedjai,** T Hurst, DJ Pennington. Cytokines and chemokines: At the crossroads of cell signalling and inflammatory disease. Biochim Biophys Acta. 2014 Nov;1843(11):2563-2582.
- **B Nedjai,** H Li, IL Stroke, EL Wise, ML Webb, JR Merritt, I Henderson, AE Klon, AG Cole, R Horuk, N Vaidehi, JE Pease. Small molecule chemokine mimetics suggest a molecular basis for the observation that CXCL10 and CXCL11 are allosteric ligands of CXCR3. Br J Pharmacol. 2012 Jun; 166(3):912-23.
- **B Nedjai,** N Quillinan, RJ Coughlan, L Church, MF McDermott, GA Hitman, MD Turner. Lessons from anti-TNF biologics: infliximab failure in a TRAPS family with the T50M mutation in TNFRSF1A. Adv Exp Med Biol. 2011;691:409-19.



Microphotograph of a recent "smart" recording chip for brain machine interfaces.

Nicoletta Nicolaou, PhD

Research Focus: "AnaeWARE". Monitoring awareness during surgery: a multi-modal approach

Funding: EU FP7 Marie-Curie

www.imperial.ac.uk/people/n.nicolaou

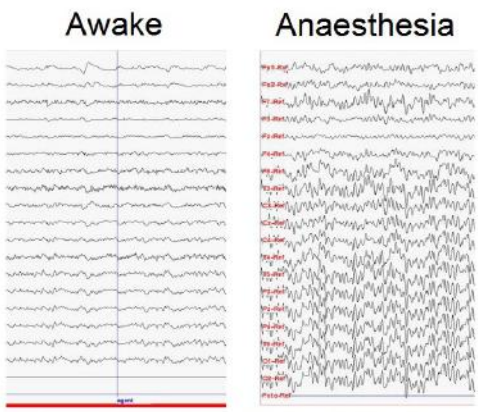
Motivation:
Regaining consciousness during surgery is a rare, but traumatic event that could have long-term consequences (e.g. post-traumatic stress disorder). Available technology often lacks the capability of identifying the return of consciousness. An important reason for this is that we still do not understand how anesthetics exactly act. In order to improve current technology to alert, and even predict, the return of consciousness, we need to understand and study the changes to our body (brain, heart, respiration etc) caused by anesthetic administration. Only then can we utilize this information into a single index of anesthetic depth and improve anesthetic practice.

Objectives:
In order to improve current technology we must, first, understand how activity from different body systems interacts and how this interaction is affected by anesthetic administration. Secondly, the observed changes will be linked to theoretical models of anesthetic effect on different body systems in order to identify particular model parameters that could act as markers of returning consciousness. A combined index that can be used to monitor the underlying state of hypnosis can then be developed. Our long-term vision is a system that uses theoretical modeling to compliment experimental observations; such a system could show improved performance in identifying impending consciousness.

Short Bio:
After a 7-year postdoctoral appointment at the University of Cyprus, I moved to Imperial College London in August 2014 as part of a Marie-Curie Intra-European Fellowship (Grant no. 623767). Even though my background is a BSc and PhD in Cybernetics and Control Engineering (University of Reading – UK), I soon discovered a strong interest towards the fascinating aspects of the brain – one of the most complex biological control systems – and how our brain activity can be used to reveal the intrinsic mechanisms behind our conscious, and even unconscious, actions. My main research interests focus on changes in brain activity under anesthesia.

Recent Publications:

- **N. Nicolaou**, J. Georgiou, "Spatial Analytic Phase Difference of EEG activity during anesthetic-induced unconsciousness., Clin Neurophysiol, vol. 125, no. 10, pp. 2122-31, 2014.
- **N. Nicolaou**, J. Georgiou, "Global field synchrony during general anaesthesia", Br J Anaesth, vol. 112, no. 3, pp. 529-39, 2014.
- **N. Nicolaou**, J. Georgiou, "Neural network-based classification of anesthesia/awareness using Granger causality features", Clin EEG Neurosci, vol. 45, no. 2, pp. 77-88, 2014.
- **N. Nicolaou**, S. Hourris, P. Alexandrou, J. Georgiou, "EEG-based automatic classification of 'awake' versus 'anesthetized' state in general anesthesia using Granger causality", PLoS One, vol. 7, no. 3, pp. e33869, 2012.



EEG activity during wakefulness (left) and anaesthesia (right

Nour Shublaq, DPhil

Research focus (title): Molecular diagnostics at the point of need to identify drug-resistant pathogens from whole blood specimens

Funding: Winston Wong Centre for Bio-Inspired Technology

Motivation:
Patients with sepsis, a severe bloodstream infection associated with organ dysfunction, constitutes a large proportion of the critically ill population and, although outcomes have improved, mortality remains higher than 25–30%, and even 40–50% when shock is present [1]. No effective specific anti-sepsis treatments exist; therefore management of patients relies mainly on early recognition allowing correct therapeutic measures to be started rapidly [2]. Early, effective antibiotic therapy is essential, but this need is confounded by the problem of slow time-to-result with current standard-of-care diagnostic tests as well as multidrug-resistant organisms. Physicians are faced with the dilemma of trying to restrict the routine use of third-line so-called reserve drugs versus the need to ensure early adequate coverage of potentially multidrug-resistant organisms. The time window for the administration of an appropriate therapy is ‹ 6 hours once symptoms are recognised, and it is optimal to administer broad-range antibiotics within the first hour, preferably after obtaining a blood culture for microbiological diagnosis [3] which usually takes 1 to 3 days. In order to diagnose sepsis early, tests with high specificities and positive predictive values are required [2].

Objectives
AMR is publicly recognised as a global threat as important as climate change and international terrorism, mainly owing to the indiscriminate use of antibiotics. The global issue and need for One Health approach have been recognised by UK CMO's Strategy Reports (Sept 2011 and 11 March 2013), UK's £10M Longitude Prize (18th November 2014), Obama's Executive Order (18th September 2014) and the subsequent five year roadmap, National Action Plan for Antibiotic Resistant Bacteria (March 2015), and cooperation of various funders in leveraging monies by putting joint AMR calls.

On 25th September 2015, the Antimicrobial Research Collaborative (ARC) launched under the auspices of Imperial College London and joint leadership of Profs Alison Holmes and Chris Toumazou. In relation to this, my objectives are wide ranging but mainly concentrate on the success of the AMR initiative- including but not restricted to:

- Understanding the market problem and opportunity from a variety of sources including literature reviews, Key Opinion Leaders at Imperial College and beyond, etc.

- Assimilating and analysing knowledge gathered and preparing reports, proposals etc. as appropriate.

- Working with various stakeholders around AMR

Short Bio:
Since February 2014, Nour provides technical knowledge and expertise in business organisation and development towards successful translation of CBIT activities in close collaboration with Imperial Spinouts – particularly in the areas of AMR, Cancer, and recreational consumer electronics. Prior to joining Imperial, she served as 'Senior Research Associate' at University College London (UCL) with responsibility to coordinate and drive major R&D initiatives in the Computational Life and Medical Sciences Domain at UCL, UCL Partners (16 UK NHS Trusts) and beyond, via competitive proposals; act as the industry point-of-act; and serving on committees to inform the direction of e-infrastructure policy at UK and EU level. Nour is an Electrical Engineer with an M.Sc. (2007) and a D.Phil. (2011) in Biomedical Engineering from the University of Oxford.

Key References:

- Vincent, J.L, et al, Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. Lancet Respir Med, 2014. 2(5): p. 380-6.
- Cohen, J., et al., Sepsis: a roadmap for future research. Lancet Infect Dis, 2015. 15(5): p. 581-614.
- Dellinger, R.P., et al., Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med, 2013. 41(2): p. 580-637.

[Photo credit: DNA Electronics]

Benjamin Evans, DPhil

Research focus: PyRhO: Multiscale Computational Tools for Optogenetics
Funding: EPSRC

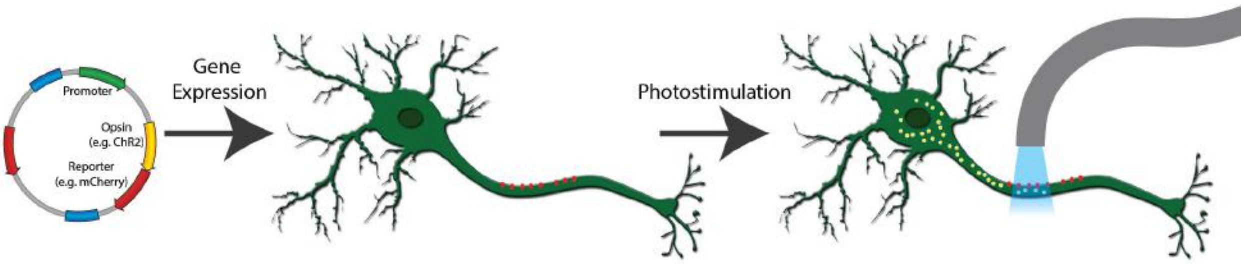
Motivation:
Since joining CBIT in June 2014 my focus has been on computational optogenetics. Optogenetics is a powerful technique for modulating the responses of neurons with millisecond precision, through inserting genes which express photosensitive proteins (rhodopsins) in their membranes. With many opsins and cell types to partner with, investigating the multitude of combinations experimentally is practically impossible, drastically limiting the technique's usefulness. Computationally characterising the photocurrent arising from optical stimulation of opsins and predicting its effect on individual or networks of transfected cells would therefore greatly enhance the effectiveness of optogenetics as a tool for transforming the biological and medical sciences.

Objectives:
My research aims to produce an integrated suite of computational tools for parameterising, simulating and analysing models of rhodopsins at multiple scales. These tools are being developed in Python as an open-source module dubbed PyRhO. The software will allow neuroscientists to automatically select and parameterise an appropriate computational model from minimal experimental data, allowing research questions to be more easily addressed in silico. It is hoped that PyRhO will help with, not only neuroscience research but also eventual medical applications, including deep brain stimulation for Parkinson's disease, closed-loop neural inhibition for epilepsy and sight restoration through sensitising retinal ganglion cells.

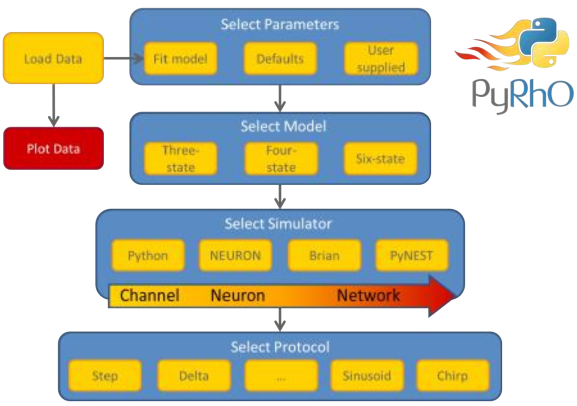
Short Bio:
I am interested in many areas of science and have enjoyed an unusually multi-disciplinary background, including degrees in Experimental Psychology, Intelligent Systems and a DPhil in Computational Neuroscience. Prior to joining Imperial, I built self-organising spiking neural networks to model the learning processes of object recognition in the ventral visual system. Having spent my doctorate reverse engineering part of the brain, moving from a psychology to an engineering department was a more natural step than it may at first seem. Besides computational modelling, I am also interested in neuromorphic hardware, machine learning, bouldering, playing the guitar and Jack Russell Terriers.

Recent Publications:

- **BD Evans**, S Jarvis, SR Schultz, K Nikolic, "PyRhO: A Multiscale Optogenetics Simulation Platform", Frontiers in Neuroinformatics, Submitted.
- ES Boyden, F Zhang, E Bamberg, G Nagel, K Deisseroth, "Millisecond-timescale, genetically targeted optical control of neural activity", Nature Neuroscience, vol. 8 no. 9, pp. 1263–1268, 2005.
- K Nikolic, N Grossman, MS Grubb, J Burrone, C Toumazou, P Degenaar, "Photocycles of Channelrhodopsin-2", Photochemistry and Photobiology, vol. 85, pp. 400–411, 2009.
- O Yizhar, LE Fenno, TJ Davidson, M Mogri, K Deisseroth, "Optogenetics in Neural Systems", Neuron, vol. 71 no. 1, pp. 9–34, 2011.



Experimental procedures of Optogenetics leading to neural excitation (or inhibition) (from www.addgene.org).



Schematic of PyRhO illustrating the layers of abstraction and modelling scales.

Associate

STAFF RESEARCH REPORT

Sara S. Ghoreishizadeh, PhD

Research Focus: Integrated Circuit and System Design for Next-Generation Implantable Medical Devices

Funding: Wellcome Trust/EPSRC (CANDO Project)

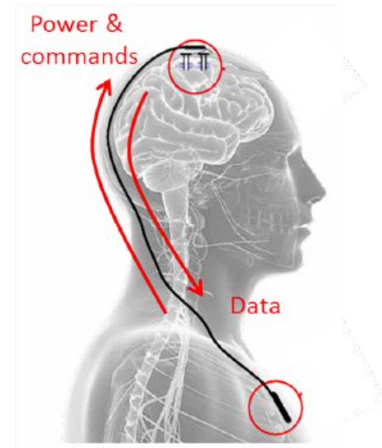
Motivation:
Implantable medical devices (IMDs) such as Pacemakers and deep-brain-stimulators have helped millions of patients with fatal conditions to have a better or even normal life. New breed of IMDs are emerging based on new technologies. An example is the cortical implant powered by Optogenetics to control abnormal network dynamics (CANDO). CANDO is a world-class, cross-disciplinary project to develop such a cortical implant. The goal is to create a first-in-human trial in patients with focal epilepsy. Implantable multi-metabolite sensors (IMTB) are another example of emerging IMDs. IMTB detects specific group of key metabolites to accurately monitor the health-condition of the patient.

Objectives:
Existing IMTBs are not fully-integrated and they also suffer from limited life-time of the biosensors and their constant need for calibration with external references. My objective is to design fully-integrated microelectronics to provide autonomy and auto-calibration for multi-metabolite sensors. CANDO includes a single controller with multiple satellite units. Achieving reliable Data communication and efficient power transmission between CANDO implants is very challenging as both the energy and implant size are limited, and the communication medium is very noisy. My objective in CANDO is to design algorithms, systems, and circuits to enable high data-rate communication and efficient power transmission between implants.

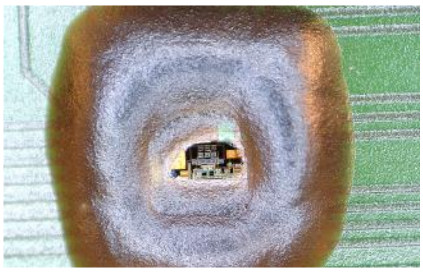
Short Bio:
I received BSc degree in electrical engineering and MSc degree in microelectronics from Sharif University of Technology, Iran, in 2007 and 2009, respectively. From September 2010 to March 2015 I was research assistant and doctoral candidate at EPFL, Switzerland. My PhD thesis was focused on designing dedicated circuits for health-care monitoring and personalized-therapy within highly-integrated implantable medical devices (IMD), and IMD integration. I joined CBIT in April 2015 as a post-doctoral research associate and since December I am a Junior Research Fellow. My main research interests are circuits and systems design for IMDs as well as IMD automation and calibration.

Recent Publications:

- **S. S. Ghoreishizadeh**, C. Baj-Rossi, A. Cavallini, S. Carrara, G. De Micheli, "An Integrated Control and Readout Circuit for Implantable Multi-Target Electrochemical Biosensing", IEEE Trans. BioCAS, vol. 8, no. 6, pp. 891-898, 2014.
- **S. S. Ghoreishizadeh**, C. Boero, A. Pullini, C. Baj-Rossi, S. Carrara, G. De Micheli, "Sub-mW reconfigurable interface IC for electrochemical sensing", Proc. IEEE BioCAS Conference, pp. 232-235, 2014.
- E. G. Kilinc, C. Baj-Rossi, **S. S. Ghoreishizadeh**, S. Riario, F. Stradolini, C. Boero, G. De Micheli, F. Maloberti, S. Carrara, C. Dehollain, "A System for Wireless Power Transfer and Data Communication of Long-Term Bio-Monitoring", IEEE Sensors Journal, vol.15, no.11, pp. 6559-6569, 2015.



Power/data communication in CANDO



Biosensors and circuits integrated on mm-size silicon chip

Associate

Melpomeni Kalofonou, PhD

Research focus: Semiconductor technologies for early detection and monitoring of cancer

Funding: EPSRC

Motivation:
Cancer is undoubtedly among the leading causes of morbidity and mortality worldwide, with the development of new methods for prevention and early detection to be at the forefront of cancer research, aiming for more targeted treatments that could prolong survival and minimise risk of relapse.

It has been shown that cancer specific genetic changes (mutations) can evolve in parallel to the phases of cancer progression, reflecting the original tumour and can thus be used as biomarkers for monitoring disease dormancy, of signs of minimal residual disease and of response to treatment. Tumour development has also been associated with epigenetic changes, such as DNA methylation, a chemical modification that can affect the regulation of gene expression without altering the genetic sequences, responsible for turning genes “on” or “off”. Especially in the event of cancer recurrence or metastasis, monitoring tumour-specific DNA methylation based changes could be of great value in stratifying the risk per patient case, contributing in a more individualised clinical assessment, thus providing a better detection efficacy, while reducing the economical burden on the healthcare services.

Objectives:
Common types of cancer, such as breast cancer (with a lifetime risk of 1 in 8 women and more than 30% of treated cases to lead most likely to a metastasis) could considerably benefit from a reshaped model of early cancer screening at a both genetic and epigenetic level of monitoring, avoiding the use of imaging methods and the inherent risks of false-positive readings which could result in further unnecessary testing such as biopsies/further imaging tests.

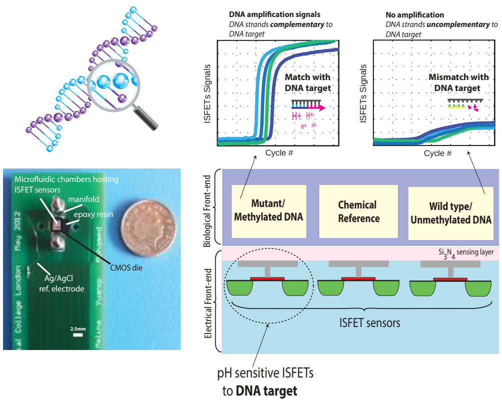
Semiconductor technology has been proven to be a very promising approach for rapid and label-free detection of genetic changes using CMOS integrated ISFET sensors, without the need for optics. We have also demonstrated that DNA methylation can be detected in gene targets using semiconductor technology in a CMOS based System-on-Chip (SoC) platform consisting of fully integrated ISFETs.

The objectives of my research include the development of Point-of-Care systems using this technology for continuous monitoring of cancer specific gene targets in a minimally invasive way. The applications can vary across a spectrum of cancer specific biomarkers, aiming to show the great potential of integration of clinical factors with microchip based lab-on-chip sensing and diagnostic platforms.

Short Bio:
Melpomeni received the Dipl.-Eng. degree in Electrical and Computer Engineering from the University of Patras, Greece in 2007 followed by an MSc (Dept. of Bioengineering) and PhD (Dept. of Electrical and Electronic Engineering, Centre for Bio-Inspired Technology) in 2009 and 2013 respectively from Imperial College London, both in the field of Biomedical Engineering. Her PhD research targeted the use of semiconductor technology and specifically the integration of microchip based sensors (ISFETs) with current mode circuits, to develop Lab-on-Chip platforms for applications related to early screening of cancer. Her work led to the demonstration of the first proof-of-concept method of using System-on-Chip semiconductor based platforms for real-time amplification and detection of DNA methylation, an epigenetic biomarker present in tumour suppressor genes, contributing significantly in the development and progression of cancer. With the completion of her studies, she was appointed a postdoctoral position at the Centre to continue her research in the field, with primary focus of her current research being the development of cancer technologies for early detection and monitoring of breast cancer, the most common cancer in women worldwide.

Recent Publications:

- **M. Kalofonou**, C. Toumazou, “Early screening of breast cancer recurrence by monitoring DNA methylation based biomarkers using semiconductor technology”, MEC Annual Meeting and Bioengineering14, Cancer Engineering and Technologies, 2014.
- **M. Kalofonou**, C. Toumazou, “An ISFET based analogue ratiometric method for DNA methylation detection”, IEEE International Symposium on Circuits and Systems (ISCAS), 1832-1835, 2014.
- **M. Kalofonou**, C. Toumazou, “A low power sub-μW Chemical Gilbert Cell for ISFET differential reaction monitoring”, IEEE Transactions on Biomedical Circuits and Systems, vol. 8, no. 4, 565-574, 2013.
- **M. Kalofonou**, C. Toumazou, “Semiconductor technology for early detection of DNA methylation for cancer: From concept to practice”, Sensors and Actuators B: Chemical, vol. 178, 572-580, 2013.



pH-based detection of DNA targets using ISFETs in CMOS. The picture shows a novel System-on-Chip utilising ratiometric detection of DNA methylation in cancer-specific gene targets

Song Luan, PhD

Research Focus: Integrated neural microsystems and neural interfaces

Funding: EPSRC (iPROBE project)

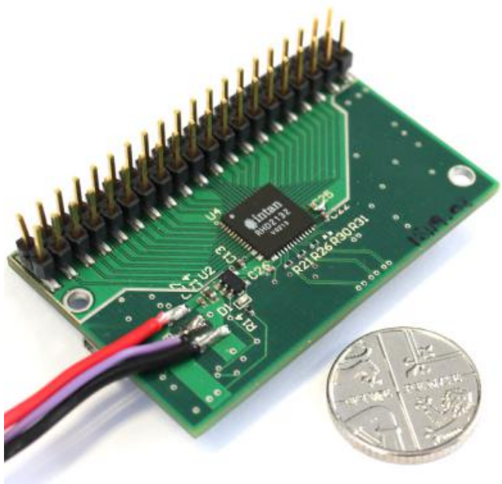
Motivation:
As electronic systems keep shrinking in size and improving in functionality, more and more applications are now focusing on vital sign monitoring. E.g. heart rate, blood pressure, etc. There is currently a tremendous drive to develop new enabling technologies for neuroscience. This will pave the way to a new breed of neural interfaces and prosthetic devices that will restore natural function. The underlying, ultimate motivation is however to improve the quality of life of individuals with neural damage and dysfunction.

Objectives:
To make a successful neural interface requires collaboration between the biosciences and engineering. My key objectives are predominantly engineering focused: to make devices more compact (particularly for implantables, wearables), versatile and energy efficient (battery lifetime, improving biocompatibility due to dissipation), The main projects I am involved aim to: (1) build a scalable miniature system that is capable of real-time FPGA based spike sorting thus reducing data-rate reduction for wireless communication and other real-time applications; (2) record at least 1k channels of neural signals. My role in these projects is designing the scalable system arch/mechanical and back-end data acquisition module and software. The prototype has been successfully verified in-vivo and a lighter and more versatile version has been in fabrication. The system has been demoed BioCAS 2015.

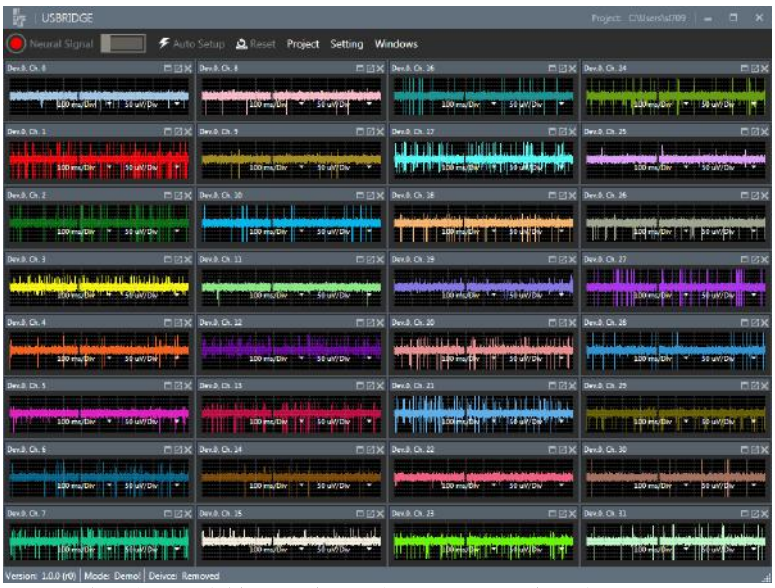
Short Bio:
Song Luan received the M.Sc. in analogue and digital integrated circuit design and Ph.D. degrees in biomedical microelectronics engineering from Imperial College London in 2010 and 2014 respectively.
In 2014, he works as a research associate in the Next Generation Neural Interfaces Lab. He has designed different types of integrated neural stimulation circuits and systems with 0.35 and 0.18 um process. He is also an advanced engineer in PCB, firmware and software development for in-house custom hardware. His main research interests include neural interfaces and its applications, low power microelectronics and wireless power/data link.

Recent Publications:

- **S. Luan**, I. Williams, K. Nikolic, and G. Timothy, “Live Demonstration: a Scalable 32-Channel Neural Recording and Real-Time FPGA Based Spike Sorting System,” Proc. IEEE BioCAS Conference, Atlanta, GA, 2015.
- **S. Luan**, I. Williams, K. Nikolic, and G. Timothy, “Neuromodulation: present and emerging methods”, Frontiers in Neuroengineering, vol. 7, no. 27, 2014.



Prototype Headstage Developed for Scalable Neural Recording Interface with Realtime Spike Sorting.



GUI Developed for Scalable Neural Recording Interface with Realtime Spike Sorting.

Mohammadreza Sohbati, PhD

Research focus: Semiconductor-based DNA Sequencing and Genotyping

Funding: EPSRC

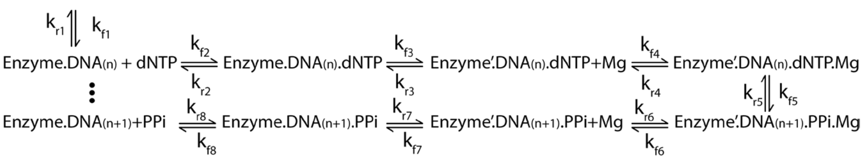
Motivation:
Molecular biology has been remarkably redirecting life sciences by studying cellular functions at a molecular level. Understanding the genetic codes and mutations is reshaping the approach to disorders and malfunctions, from diagnostics to prognostics and early detection. However, applying its significant achievements at the point of need and achieving a role to shape human lifestyle requires the companionship of instruments that can accelerate both its progress in the labs and its ease of use. Timeliness, accuracy, throughput, and cost are vital in their merit. The advent of ion-sensitive transistors has made the semiconductor microchips an exceptional platform in this industry.

Objectives:
The main focus of my research has been on circuits and systems for pH-based DNA detection. A key part of my work has been dedicated to ion-sensitive field-effect transistors (ISFETs), which form the building block of our technology. In particular, I investigated on their shape and dimension effects. On the other hand, to understand the parameters influencing the signal (eventually the accuracy, limit of detection, throughput and processing speed), I worked on modeling the reactions and the signals in DNA detection. We managed to produce a basic, but the first, model of DNA amplification (replication) signal.

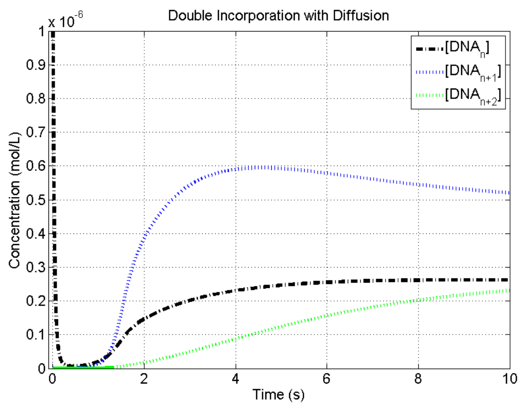
Short Bio:
I received my BSc in Electrical Engineering with focus on Telecommunications from the University of Tehran, Iran, in 2009. Then I graduated in 2010 from Imperial College London with MSc on Integrated Circuit Design. Staying at Imperial, in 2015 I finished my PhD under Prof. Toumazou's supervision on Circuits and Systems for pH-based DNA Detection. Currently, I am staying at the centre as a post-doctoral research associate.

Recent Publications:

- **M. Sohbati,** "Circuits and Systems for DNA Detection by Ion-Sensitive Field Effect Transistor", PhD Thesis, Imperial College London, 2015
- **M. Sohbati,** C. Toumazou. "Dimension and Shape Effects on the ISFET Performance", IEEE Sensors Journal, vol. 15, no. 3, pp. 1670-1679, 2015.



Chain of reactions involved in DNA synthesis.



An example of the modelling result, showing extension of a DNA for two bases.

Irina Spulber, PhD

Research focus: Wearable Electronics for Functional Rehabilitation

Funding: EPSRC

Motivation:
The UK's current demographic shift towards an increasingly aging population urgently brings on the agenda the need for new approaches to healthcare and innovative supportive technologies. The society at large would hugely benefit from new, low cost, wearable technology that can address specific long-term rehabilitation needs, empowering the patients with self-management tools, while alleviating the burden on the health services. A particular motivation for this research was osteoarthritis (OA) – a debilitating condition affecting over 8.5 sufferers in the UK alone. OA currently has no cure with treatment ranging from conservative rehabilitation interventions to surgical joint replacement.

Objectives:
In its early stages OA requires active management through correct exercise and physiotherapeutic interventions, and our main aim was to develop a wearable system tailored for functional monitoring and rehabilitation.

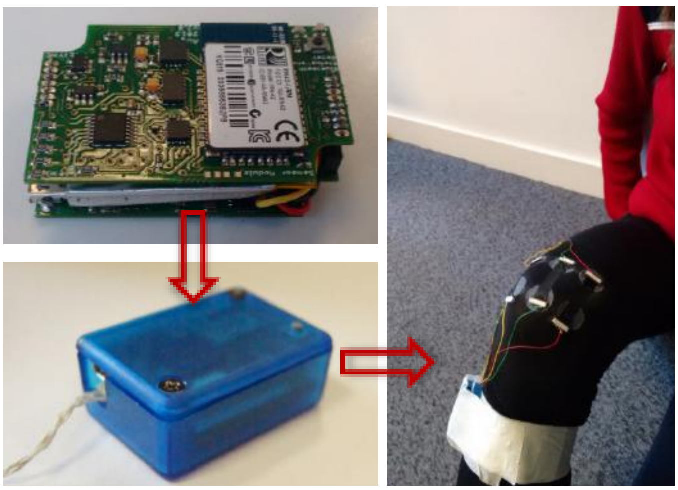
We designed a patient-centred, multi-sensor wireless platform that is versatile in its functionality and can be integrated into a sensorised smart garment. The garment is intended as a take at home support tool for patients to wear it while exercising, so that their physiotherapist can remotely monitor their motions and joint function in real-life settings. Access to such data will enable practitioners to devise customised rehabilitation and management strategies. It is envisaged that monitoring progress via a wireless smart garment will motivate patients, promote physical activity, as well as increase compliance with rehabilitation regimes.

Short Bio:
Irina Spulber received the Dipl.-Ing. in Electrical Engineering from the Gh. Asachi Technical University of Iasi, Romania, specializing in instrumentation and measurement systems. Subsequently she continued her postgraduate studies in the UK with an M.Sc. in Advanced Electronic Engineering and a Ph.D. degree both from University of Warwick. She worked at the University College London before joining the Centre for Bio-Inspired Technology at Imperial College in 2011 to conduct research for the Medical Engineering Solutions in Osteoarthritis Centre of Excellence. Her current interest are medical measurement systems, medical devices, wireless sensing platforms, body-worn sensors, smart garments and wearable electronics for healthcare applications.

Recent Publications:

- **I. Spulber**, Y.-M. Chen, E. Papi, S. Anastasova-Ivanova, J. Bergmann, A.H. McGregor, P. Georgiouβ, "Live Demonstration: Wearable Electronics for a Smart Garment Aiding Rehabilitation", presented at the IEEE International Symposium on Circuits and Systems (ISCAS), p. 912, 2015.
- E. Papi, **I. Spulber,** M. Kotti, P. Georgiou, A.H. McGregor, "Smart Sensing System for Combined Activity Classification and Estimation of Knee Range of Motion", IEEE Sensors Journal, vol. 15, issue 10, pp. 5535 – 5544, 2015.
- **I. Spulber,** E.Papi, Y.M. Chen, S. Anastasova-Ivanova, J. Bergmann, P. Georgiou, A.H. McGregor, "Development of a Wireless Multi-Functional Body Sensing Platform for Smart Garment Integration", IEEE Biomedical Circuits and Systems, p. 157, 2014.
- Y.-M. Chen, **I. Spulber,** E. Papi, S. Anastasova-Ivanova, J. Bergmann, P. Georgiou , A.H. McGregor, "An investigation of body worn sensors for lower limb monitoring and rehabilitation management", MecBioeng14, London, 2014.

a. *b.* *c.*



Wireless sensing node: electronic boards (a) and packaged device (b); Subject wearing the smart garment while exercising (c)

Katarzyna Szostak

Research focus: Microengineering Next Generation Implantable Neural Interfaces

Funding: EPSRC

www.imperial.ac.uk/people/k.szostak

Motivation:

Until recently, implants that would be capable of interacting directly with the nervous system were considered a rather unlikely possibility. This is no longer the case. With growing development in the area of brain machine interface technology (BMI), being able to implant such a device opens new possibilities not only to study brain but also to help people with neurological conditions such as tetraplegia, Alzheimer's disease, epilepsy or schizophrenia.

Objectives:

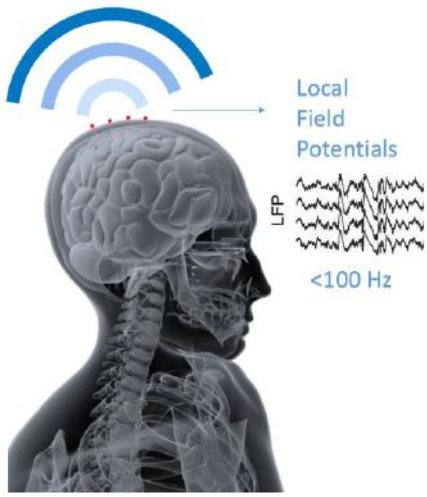
The main objective of my research is to design and engineer microscale components for an entirely new type of neural implant. Specifically, we are targeting ultra miniature chip-scale, fully autonomous, implantable devices. My work involves the design, fabrication and characterisation of bespoke micro-devices, in addition to the system integration of electrodes, interconnects, circuits, micropackages, etc. The envisaged "final" implant devices will be simple, small, calibration-free and will connect within a brain area network to work seamlessly and reliably in chronic applications.

Short Bio:

Kasia obtained both her BSc. (Hons) in Electronics and Telecommunication (2011) and Masters (Distinction) in Microsystems, Electronics and Photonics (2012) from Wroclaw University of Technology, Poland. Both her dissertations were focused on different aspects of microfabrication- silicon etching processes and wafer bonding. Katarzyna's research interests are focused on microfabrication technologies. She worked for research institutes and private companies across Europe (Poland, Germany, Belgium, Finland) developing new processes, sensors and clean-room based solutions. In August 2015, Katarzyna joined the Neural Interfaces team at Imperial College London where she is currently working on developing a new generation of the implantable neural interfaces within ENGINI project.

Key references:

- I. Stevenson, K. Kording, "How advances in neural recording affect data analysis", Nature Neuroscience, vol. 14, pp. 139-142, 2011
- G. Baranauskas, "What limits the performance of current invasive brain machine interfaces?", Frontiers Syst Neurosci, vol. 8, 2014.
- M. Jorfi, J. L. Skousen, C. Weder et al., Progress towards biocompatible intracortical microelectrodes for neural interfacing applications", Journal Neural Eng, vol. 12, 2015.



The concept of ENGINI microelectrodes system

Huan Wang, PhD

Research focus: Microfabrication of Acoustic Wave Sensors

Funding: MRC

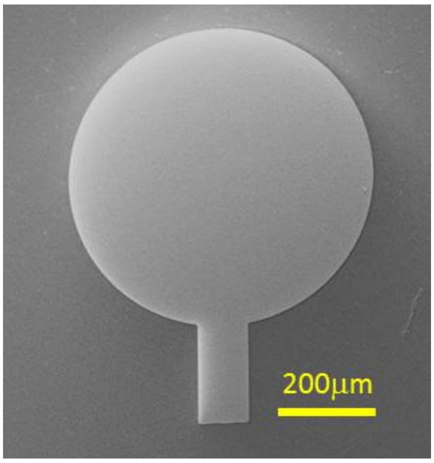
Motivation:
Regular eye-pressure monitoring is critical to detect glaucoma at its early stage, as it is a progressive disease and can cause permanent blindness if the eye pressure is not controlled. Globally 60.5 million people suffered glaucoma in 2010 and the number may increase to 80 million by 2020. Since current clinical devices do not provide continuous pressure monitoring, it is a case for developing implantable pressure sensors. Due to the implant size requirements and operating frequencies at GHz range, traditional sensors are difficult to be used. Film bulk acoustic wave resonators can be used to meet such requirements.

Objectives:
The focus of the project I am currently working on is to develop highly sensitive sandwich-structured thin film bulk acoustic wave AlN sensors for pressure sensing. High quality factor is an essential parameter for resonator-based sensors and results in better signal quality, low energy loss and higher pressure sensitivity. In order to produce high quality factor resonators in GHz range, highly c-axis oriented crystalline of AlN thin films of should be grown on silicon substrates followed by various characterization. Then cleanroom fabrication processing will be investigated to fabrication highly sensitive AlN based FBAR.

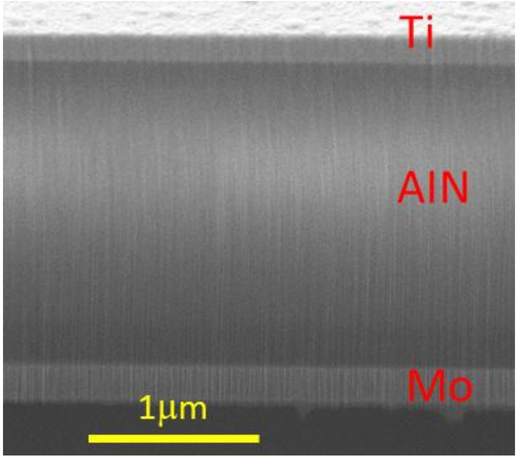
Short Bio:
I have done my PhD researches in nanofabrication and characterisation at London Centre for Nanotechnology in University College London in the area of nanowires based NEMES, especially nanomechanical resonators for mass sensing application. Then I joined Imperial College London in early 2014 to work on fabrication and characterisation of ultra-sensitive thin film acoustic wave sensors for medical applications. During this time, I have been broadening my skills in microfabrication as well as implantable medical devices field of pressure sensing.

Recent Publications:

- **H. Wang**, J. C. Fenton and P. A. Warburton, et al., Model-independent Quantitative Measurement of Nanomechanical Oscillator Vibrations using electron-microscope line-scans, Review of Scientific Instruments, 84, 7, 075002(1-7), 2013



SEM image of top-view of the AlN thin film acoustic wave sensor



SEM image of cross-section of the AlN thin film acoustic wave sensor

Ian Williams, PhD

Research Focus: Sensory Feedback for Upper Limb Prosthetics
Funding: EPSRC (SenseBack project)

www.imperial.ac.uk/people/i.williams10

Motivation:
Advanced upper limb prosthetics are becoming increasingly capable and prevalent, however, amputees struggle to utilise even a fraction of that capability in the real world and must constantly look at the prosthesis in order to use it effectively. A key reason for this limited control and the need for visual monitoring is that the prosthesis is insensate – providing no tactile or proprioceptive feedback. This means that the control is open loop and the prosthesis will always remain a tool attached to the body rather than becoming an extension of the body itself.

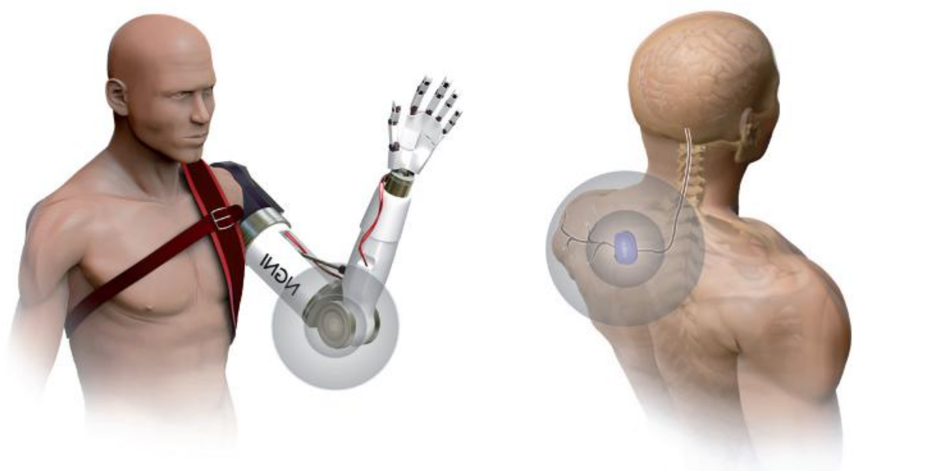
Objectives:
Our research aims to improve prosthetic limb control by providing artificial proprioceptive and tactile neural feedback from an upper limb prosthesis. By selectively stimulating sensory neurons remaining in the peripheral nerves of the limb stump we aim to enable closed loop control of the limb (mirroring normal limb function). This should ultimately enable the limb to be operated with greater dexterity and without visually monitoring it.

To achieve this we are collaborating with a number of other UK universities (as part of the Senseback project) to develop flexible intraneural electrodes, miniaturised high performance stimulation & recording electronics, and models of neural signals in the human hand.

Short Bio:
Ian Williams received the M.Eng. degree in electronic engineering from Edinburgh University, UK, in 2004. From 2004 to 2010 he worked in a number of project management and research related roles for the UK Ministry of Defence. In 2014 he completed his Ph.D. in Electronic Engineering at Imperial College London, UK. His research interests include brain-machine interfaces and his doctoral research focused on developing a neural proprioceptive prosthesis for upper limb amputees.

Recent Publications:

- **Williams I,** S. Luan, A. Jackson, T.G. Constandinou. "A Scalable 32 Channel Neural Recording and Real-time FPGA Based Spike Sorting System", Proc. IEEE BioCAS Conference, 2015.
- S. Luan, **I. Williams,** T. G. Constandinou, and K. Nikolic. "Neuromodulation: present and emerging methods". Frontiers in Neuroengineering, vol. 7, pp. 27-, 2014.
- **I. Williams,** T. G. Constandinou,"Computationally Efficient Modelling of Proprioceptive Signals in the Upper Limb for Prostheses: a Simulation Study". Frontiers in Neuroscience, vol. 8, pp. 181-, 2014.
- **I. Williams,** T. G. Constandinou. "An energy-efficient, dynamic voltage scaling neural stimulator for a proprioceptive prosthesis". IEEE Trans. BioCAS, vol. 7, 2013.



Concept of a proprioceptive neural prosthesis. Signals from joint angle and torque sensors (fitted to a prosthetic limb) are processed to generate estimates of normal neural feedback patterns, these are wirelessly transmitted to an implant which stimulates nerves associated with the amputated limb.

Longfang Zou, PhD

Research focus: Antennas for Wireless Implanted Medical Devices
Funding: Wellcome Trust

Motivation:
Wireless implanted medical devices show promising characteristics in continuous monitoring of physiological indicators and possibly raising an alert in case of need, while preserving the mobility and lifestyle of patients. They allow early detection of any degradation in patients' condition, without frequently visiting or remaining in the hospital. In addition to the clear benefits to the patients, it would be advantageous for healthcare provider by reducing recurrent expensive invasive measurements and hospitalization periods.

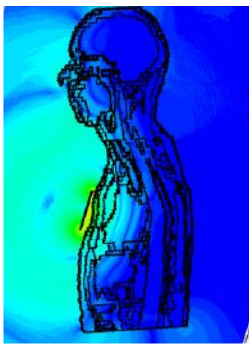
Objectives:
My role within the wider project is the development of implantable and wearable antennas to provide robust and bidirectional link between the implanted medical devices and external instruments. Along with the mandatory requirements of biocompatibility and electromagnetic compatibility, the research is focused on the design, package, optimization and in vitro/ in vivo testing of implanted and body worn antennas. Various antennas have been designed and optimized to satisfy required specifications. For example, in the current blood pressure monitoring project, the implant depth of the passive sensor is larger than 6 cm. The complex, dispersive and highly lossy characteristics of human body put more emphasis on high gain and high efficiency antennas. On the contrary, subcutaneous antennas have less requirement on efficiency but more on the size. The designed antennas have met the necessary standards in phantom testing. The continuing study is devoted to improving comfort of patients and preparing animal and human trials. Meanwhile, effective inductive coupling is under investigation to reduce the exposure level of body under electromagnetic for superficially implanted medical devices.

Short Bio:
Longfang Zou received the Ph.D. degree in electrical engineering (with Dean's Commendation for Doctoral Thesis Excellence) from the University of Adelaide, Australia in 2013. From 2013 to 2014, he worked at the University of Bristol on the project of Optical Nano-Antennas. He joined the Centre for Bio-Inspired Technology, Imperial College London in June 2014. His research interests include Implantable and Wearable Antennas, Optical Nano-Antennas, Dielectric Resonator Antennas, Antenna Array & Reflect Arrays.

Recent Publications:

- **L. Zou**, W. Withayachumnankul, C.M. Shah, A. Mitchell, M. Klemm, M. Bhaskaran, S. Sriram and C. Fumeaux, "Efficiency and Scalability of Dielectric Resonator Antennas at Optical Frequencies," in IEEE Photonics Journal, vol. 6, no. 4, pp. 1-10, Aug. 2014.
- **L. Zou**, M. López-García, W. Withayachumnankul, C.M. Shah, A. Mitchell, M. Klemm, M. Bhaskaran, S. Sriram, R. Oulton, M. Klemm, and C. Fumeaux, "Spectral and angular characteristics of dielectric resonator metasurface at optical frequencies", Applied Physics Letters, vol. 105, 2014.
- **L. Zou**, M. Cryan and M Klemm, "Phase change material based tunable reflectarray for free-space optical inter/intra chip interconnects", Optics express, vol. 22, no. 20, 24142-24148, 2014.

Antennas and sensor for Intracranial pressure monitoring.



Electromagnetic excitation of deep implanted medical devices.

Claudio Zuliani, PhD

Research focus: Sensing technology for real-time monitoring of chemicals and bio-markers within neural interfaces.

Funding: ERC Synergy (i2MOVE)

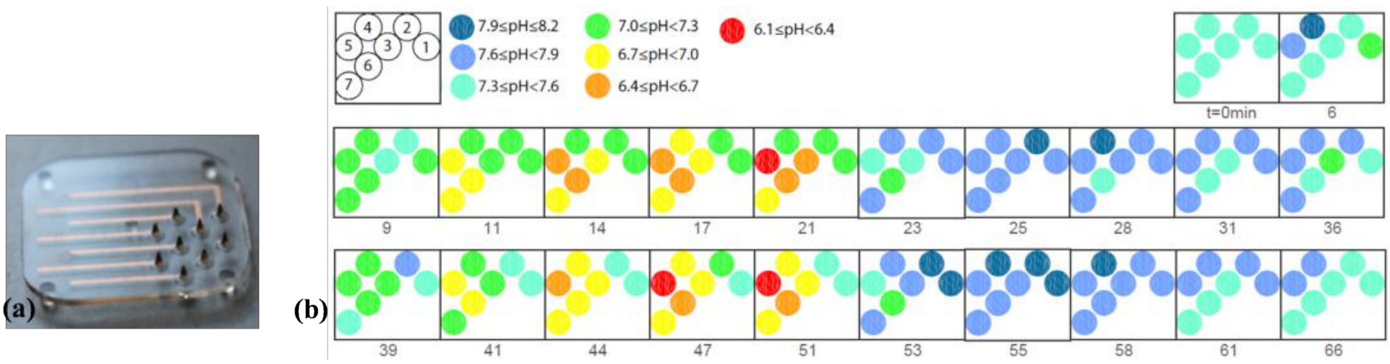
Motivation:
Metabolic and neural disorders have been on the rise in the past 30 years. These disorders have a huge physiological and societal impact and represent a financial burden to our healthcare systems. Our societies are desperately in need of new therapeutic methods which can offer minimally invasive, refined and personalized treatments in order to relieve these issues.

Objectives:
My main objective is the research and development of chemical sensing technology to map the chemical fingerprints associated with appetite signals. This is in order to engineer a closed-loop neural interface able of modulating intelligently the gut-brain communication. This interface offers novel means of treating obesity and holds the promise of a less-invasive alternative to bariatric surgery.

Short Bio:
I studied Industrial Chemistry at the University of Padua completing a master on the electron transfer in peptide bridges. After an experience in the R&D of batteries in the private sector, I joined the University of Newcastle for an internship dealing with photoelectrocatalysis. I completed my PhD at Dublin City University applying nano- and micro-electrodes in the sensing field. After two postdoctoral positions at the University of Liverpool working on molecular wires and at Dublin City University on environmental and wearable sensing applications, I joined Imperial College as research associate.

Recent Publications:

- **C.Zuliani**,V. Curto, G. Matzeu, K.J.Fraser, D.Diamond,Properties andCustomization of Sensor Materials for Biomedical Applications. In Comprehensive Materials Processing; Hashmi, S., Ed.; Vol. 13; Elsevier Ltd: Elsevier, 2014; pp 221–243.
- **C. Zuliani,** A Potentiometric Disposable Strip for Measuring pH in Saliva. Electrochimica Acta, 2014, 132, 292
- **C. Zuliani**, et al. A liquid-junction-free reference electrode based on a PEDOT solid-contact and ionogel capping membrane. Talanta, 2014, 125, 58
- **C. Zuliani,** et al. Formation and Growth of Oxide Layers at Platinum and Gold Nano-and Microelectrodes. Analytical Chemistry, 2010, 82, 7135.



(a) Array of individually addressable microneedles which were coated with iridium oxide in order to sense pH changes. (b) Colour map of the pH distribution obtained with the microneedles device inserted into an ex-vivo perfused rat heart. Snapshots taken at the minutes indicated below each frame. The rat heart underwent two cycles of global heart ischemia/reperfusion. Ischemia occurred at t=8 min and 38 min while reperfusion at t=22 min and 52 min.

Deren Y. Barsakcioglu

Research Focus: Resource Efficient On-node Spike Sorting

Supervisor: Dr Timothy Constandinou

Funding: EPSRC DTA and EEE Departmental Scholarship

Motivation:
The ability to interface neurons using electronics is presenting new opportunities for basic neuroscience research and neural rehabilitation with prosthetic devices. Commonly referred as neuroprosthetics, such devices aim to restore the lost sensory and/or motor abilities by tapping into sensory or motor pathways via a neural interface.

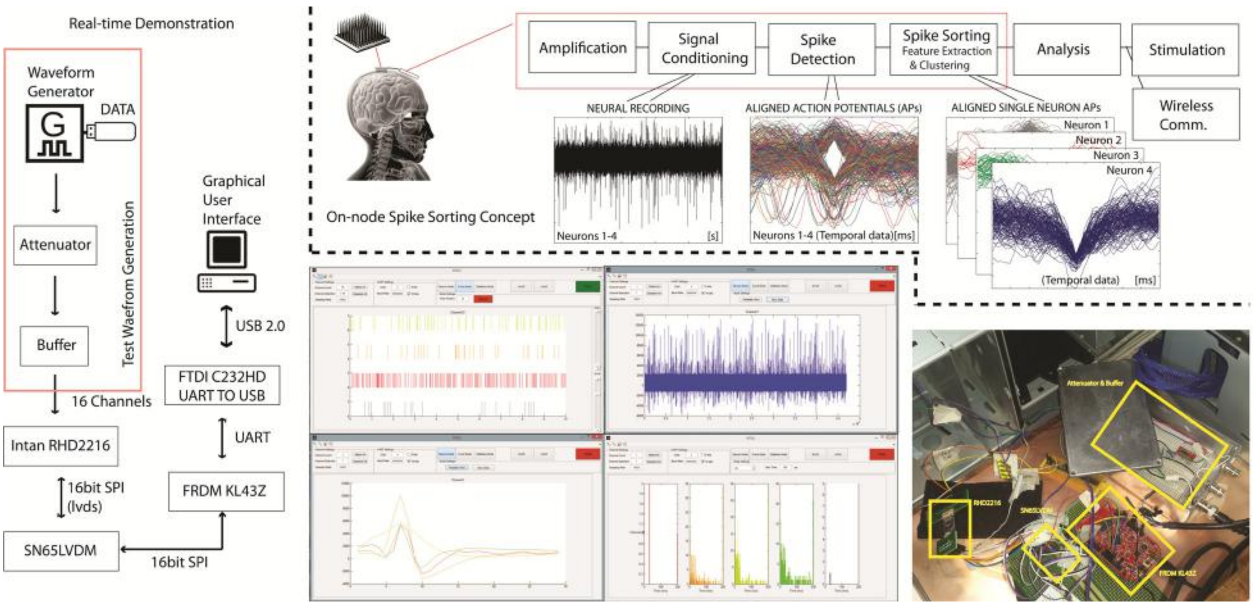
The improvement in micro-fabrication techniques and technology has resulted in a significant increase in recording capability. However, wireless transcutaneous telemetries that are crucial for both the clinical systems and prosthetic devices have fundamental limitations as to the amount of data that can be transmitted within safe limits for thermal dissipation. In order to overcome this bandwidth and power consumption bottleneck, the required data reduction prior to transmission can be achieved by on-chip spike sorting, which is the classification of extracellular action potentials recorded over a recording channel. My PhD research over the past four years has focused on investigating the impact of both analogue front end and spike sorting related parameters in terms of sorting accuracy and hardware resource (i.e. power and area), as well as developing novel feature extraction and spike sorting methods.

Objectives:
One of the objectives of my current research - funded by EPSRC Doctoral Prize Fellowship – focuses on adaptive spike sorting and translation of the systems I developed during my PhD into a compact neuroscience tool. Another objective of my current research involves a novel method to ensure long-term, stable, efficient and accurate monitoring of large neuronal ensembles for next generation neural prosthetic devices.

Short Bio:
Deren Y. Barsakcioglu obtained his B.Sc. degree in Electrical and Computer Engineering from University of Texas at Austin in 2010. He then received his M.Sc. degree in Analogue and Digital IC Design in 2011, and his PhD degree in 2015 from Imperial College London, London, UK. He has recently been awarded EPSRC Doctoral Prize Fellowship, and is currently a post-doctoral researcher at Centre for Bio-Inspired Technology, Department of Electrical and Electronic Engineering at Imperial College London, UK.

Recent Publications:

- **D. Y. Barsakcioglu,** et al. “Design Optimisation of Front-End Neural Interfaces for Spike Sorting Systems”. Proc. IEEE ISCAS, pp. 2501-2504, 2013.
- S. E. Paraskevopoulou, **D. Y. Barsakcioglu,** et al. “Feature Extraction using First and Second Derivative Extrema (FSDE), for Real-time and Hardware-Efficient Spike Sorting.” Journal of Neuroscience Methods, vol. 215, no. 1, pp. 29-37, 2013.
- J. Navajas, **D. Y. Barsakcioglu,** et al. (2014). Minimum requirements for accurate and efficient real-time on-chip spike sorting. Journal of neuroscience methods, vol. 230, pp. 51-64, 2013.
- **D. Y. Barsakcioglu,** et al “An Analogue Front-End Model for Developing Neural Spike Sorting Systems” IFEEE TBioCAS, vol. 8, no. 2, pp. 216-227, 2014.



Demonstration of real-time on-node spike sorting system consisting of an MCU-based spike sorting implementation, Intan RHD2216 analogue front-end, and a graphical user interface (GUI)

Radu Berdan

Research Focus: Applications of Memristors in Conventional Analogue Circuits

Supervisor: Dr. Christos Papavassiliou

Funding: EPSRC

Motivation:
Resistive Random Access Memories (RRAM), also known as memristors, have demonstrated all prerequisites in terms of performance and scalability for becoming a strong contender for the post-FLASH storage medium. At its core, a RRAM device is an electronically programmable variable resistor which also has potential uses in conventional analogue electronics (replacing configurable resistive arrays), logic circuits (unifying computation and storage) and neuromorphic engineering (as artificial synapses). With a simple two terminal nanoscale MIM structure and a plethora of materials from which memristors can be manufactured, this technology provides immense potential for unorthodox and exciting applications in the future.

Objectives:
An ideal memristor should have a predictable and repeatable response to a known input stimulus. Unfortunately before this can happen, manufacturing processes of memristors require tuning in order to provide high yield devices that guarantee good performance in future applications. My research has focused on designing and manufacturing of a measuring system (hardware and software), which allows the user to characterize pristine manufactured devices and describe their behavior. This process provides quick and quantified information on the quality of the solid-state devices, which can then be used by fabrication experts to manufacture superior devices in the next iteration.

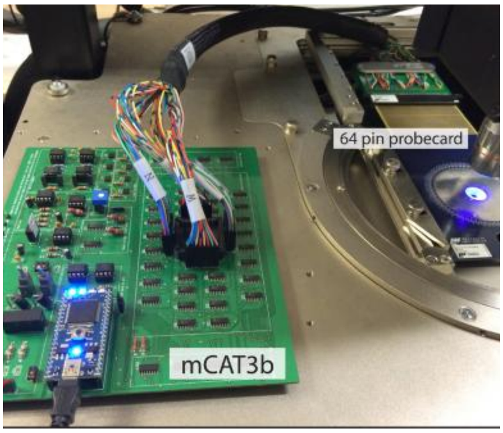
Short Bio:
Radu received a Bachelor of Science (Hons) from University of Sheffield, UK in 2012 where his final year project focused on measuring instruments for noise in avalanche photodiodes. He then went on to study MSc in Analogue and Digital IC Design at Imperial College London, where he finished with Distinction and an Award. He is currently continuing his MSc project on memristors towards his PhD.

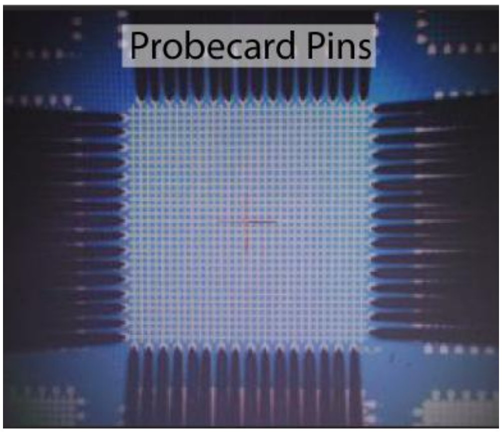
Key References:

- D.B. Strukov, G. S. Snider, D. R. Stewart, R. S. Stanley, "The missing memristor found", Nature, vol. 453, pp. 80-83, 2008.

Recent Publications:

- **R. Berdan**, A. Serb, A. Khiat, A. Regoutz, C. Papavassiliou, T. Prodromakis, "A u-Controller-Based System for Interfacing Selectorless RRAM Crossbar Arrays," IEEE Trans. on Electron Devices, vol.62, no.7, pp. 2190-2196, 2015.





Lorena Gonçalves de Alcântara e Freitas

Research focus: AnaeWARE - Monitoring awareness during anaesthesia – a multi-modal approach.
Supervisor: Dr Tim Constandinou and Dr Nicoletta Nicolaou

Motivation:
Modern anaesthesia consists of a cocktail of drugs targeting different components (i.e. analgesia, immobility, hypnosis, amnesia). It is crucial to deliver the correct doses to avoid serious consequences such as cardiovascular depression (overdose) or intra-operative awareness (underdose). However, the chemical amounts required to address each aspect of anaesthesia vary between patients, making dosage calculation a challenging task. Monitoring devices that measure brain activity to estimate awareness levels have failed to consistently provide accurate information. AnaeWARE investigates whether a multi-modal approach (combining brain activity with cardiovascular and respiratory information) may offer more reliable monitoring without imposing additional costs to healthcare funds.

Objectives:
The final aim of the project is to devise an index of awareness that is consistent and subject-independent. My contribution involves three main tasks: 1) recruiting patients and collecting their data during surgeries that require general anaesthesia; 2) analysing how anaesthesia changes the relationships between the different data modalities and whether these changes increase the discriminatory power between wakefulness and unconsciousness; 3) implementing theoretical models that describe the effects of anesthetics on the body.

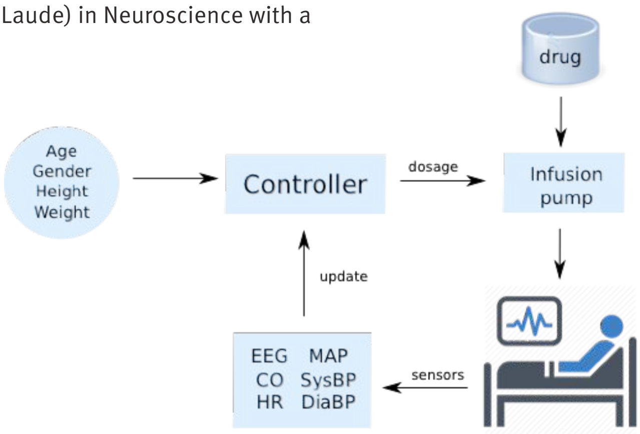
Short Bio:
Lorena joined the Centre for Bio-Inspired Technology in August 2015 as an Erasmus Mundus project student. She received her MSc (Cum Laude) in Neuroscience with a double diploma from the Vrije Universiteit Amsterdam (Netherlands) and the Charité Universitätsmedizin Berlin (Germany). Before starting her adventure in Europe Lorena obtained her BSc in Computer Science from the Federal University of Uberlândia (Brazil). During this time she spent a year at the ENSIMAG (France), where she followed a specialization course in Information Systems Engineering and worked at INRIA Grenoble. She has also worked as a Software Developer and Deployment Analyst for two years.

Recent Publications:

- **L Freitas**, B Blankertz, J Höhne , "Online EEG Artifact Rejection Based on Automatic Dimensionality Reduction", 37th Annual International Conference of the IEEE Engineering in Biology and Medicine Society, Milan, 2015

Key References:

- N Nicolaou, J Georgiou, "Neural network-based classification of anesthesia/ awareness using Granger causality features", Clin EEG Neurosci, vol. 45, pp. 77-88, 2014
- N Nicolaou, J Georgiou, "Global field synchrony during general anaesthesia", Br J Anaesth, vol. 112, pp. 529-539, 2014
- N Nicolaou, J Georgiou, "Spatial Analytic Phase Difference of EEG activity during anesthetic-induced unconsciousness", Clin Neurophysiol, vol. 125, pp. 2122-2131, 2014



An awareness monitor based on a combination of brain and cardiovascular data used for feedback on a Closed Loop System for automatic anaesthesia delivery.

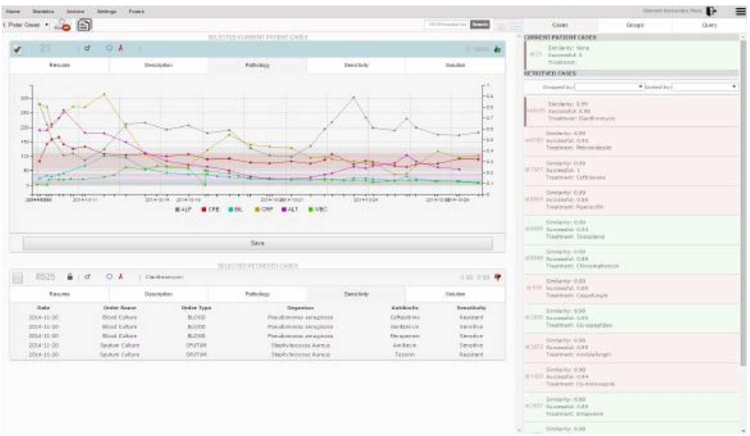
Bernard Hernandez

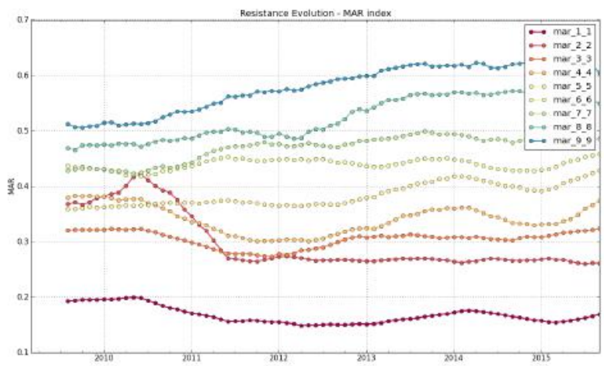
Research focus: Enhanced, Personalized and Integrated Care for Infection Management at Point of Care (EPIC IMPOC)
Supervisor: Dr Pantelis Georgiou
Funding: NiHR i4i

Motivation:
Bacteria and other microorganisms are a common cause of infections. The antimicrobials are drugs that kill or stop the growth of microorganisms, thereby are commonly used to treat infections. Continuous evolution of microbial organisms and unnecessary antibiotic prescription, particularly within infection diseases, are a common concern in critical care, infection management and antimicrobial stewardship; which are observing an increased rate of antimicrobial resistance. Antibiotic resistance is most likely to develop in areas with a considerable concentration of sick patients and high risk of infection where antimicrobials are used extensively. Failure to recognize and respond to the early stage infections is considered a major cause of avoidable mortality.

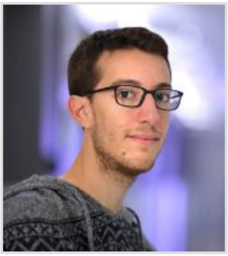
Objectives:
We postulated that an appropriately designed clinical information technology (IT) system could improve reliability and consistency of collecting vital signs; their visualization, interpretation and analysis; and the delivery of a more sophisticated decision support system (DSS) that suggests an optimal solution at the point of care (POC). This application not only attempts to resolve antimicrobial resistance and increase the successful outcomes. It will suppose a potential reduction in infection specialist time spent consulting and a powerful source of knowledge to educate new specialists.

Short Bio:
Bernard Hernandez is research associate at Imperial College London and is currently pursuing his PhD in Antimicrobial Resistance. He received his B.S in Telecommunications and Computer Science from URJC, Madrid and his M.Sc. in Machine Learning from KTH, Stockholm.





Decision support system used for antibiotic prescribing and data visualisation.



Mohamed El Sharkawy

Research focus: Bio-inspired Systems for Treatment of Diabetes
Supervisor: Dr Pantelis Georgiou
Funding: Wellcome Trust

Motivation:
The world health organization (WHO) estimates that more than 180 million people have diabetes worldwide. It predicts that this number will double by 2030.In the year 2005 almost 1.1 million people died from diabetes. If left uncontrolled, diabetes can lead to a number of serious consequences. The Diabetes Control and Complications Trial (DCCT) was a major clinical study that took place in 1993 and showed the benefits of tight glycaemic control [2]. The study involved 1,441 volunteers, ages 13 to 39, with type 1 diabetes and showed that intensive glucose control leads to 76% and 50% risk reduction in eye disease and kidney disease respectively. These results make it clear that technologies that help diabetics manage their blood glucose levels more effectively are of paramount importance.

Objectives :
My research focuses on the development of a bio-inspired artificial pancreas for tight glycaemic control of blood glucose. The ultimate aim is to have a system that is low power, user friendly and improves on current open loop pump therapy. Sensor accuracy is a major challenge that needs to be addressed for successful realisation of an artificial pancreas.

Using the beta-cell and exploiting the noise improving capability due to gap-junction coupling of multiple cells, my research has shown how glucose sensor accuracy can be improved through a bio-inspired method. Following on from this finding, it is additionally proven that similar robustness due to noise is also achievable when fabricating beta-cells in CMOS through reduction in variation due to mismatch.

Short Bio:
Mohamed graduated in 2008 from the German University in Cairo, Egypt with Bachelors in Electronics Engineering (BE). Following that in 2009 he graduated from Imperial College London with an MSc in Analogue and Digital Integrated Circuit Design. From 2010 to present he has been involved in the bio-inspired artificial pancreas project as a research assistant and a part time phd student. His interest is mainly focused on developing technologies for type 1 diabetes management.

Recent Publications:

- **M. El Sharkawy**, P. Georgiou, “A study of pancreatic cell coupling for improved glucose sensing” Biomedical Circuits and Systems Conference (BioCAS), vol. 16, pp. 556—559, 2014
- M. Reddy et al., “Feasibility study of a bio-inspired artificial pancreas in adults with type 1 diabetes”, Diabetes technology & therapeutics, vol. 16, no. 9, pp. 550—557, 2014.

Key References:

- Jama , “Lifetime benefits and costs of intensive therapy as practiced in the diabetes control and complications trial”, B. DCCT, vol. 276, pp. 1409—1415, 1996.

The Bio-inspired Artificial Pancreas

Onur Guven

Research Focus: Ultra Low Power Microelectronics for Robust ECG Signal Conditioning
Supervisor: Dr. Timothy Constandinou
Funding: Texas Instruments Corporation

Motivation:
Electrocardiography (ECG) is the main diagnostic tool for detecting cardiac disorders . This non-invasive procedure can provide crucial information for clinicians. According to the World Health Organization (WHO), cardiovascular related diseases (CVDs) are still the main cause of deaths globally [1] Therefore, the need to improve modern healthcare systems for the reliable diagnosis and early detection of CVDs is certainly a priority.

With the advent of medical device technology, mobile and ambulatory applications prove to be the new advancement in pre-detection of coronary heart diseases and many others. Therefore, there is an increasing demand by both professionals and patients in shifting from hospitalised care solutions to home care detection systems in order to act before heart disorders reach critical levels. Once critical levels are detected via ambulatory devices, further tests can be held in hospitals by keeping the electrode irritation to a minimum level.

Objectives:
ECG's non-invasiveness coupled with the growing trend in wearable, ambulatory systems still carries critical challenges for accuracy, noise and artefact removal. A closed loop system approach for maintaining the ECG signal integrity has been investigated throughout this work. The main focus is to estimate the baseline wander, electrode offset and motion artefacts in the digital domain and to subtract from the original signal through a feedback mechanism. This feedback operation of the overall system avoids conventional high pass filtering as in low resolution ECG solutions, and eliminates low frequency distortion to the ECG signal and provides real time ECG measurements. While maintaining these requirements, computationally efficient baseline detection algorithm and a hybrid interpolation algorithm minimizes the number of operations and the power requirements of the overall system without requiring bulky computerised systems.

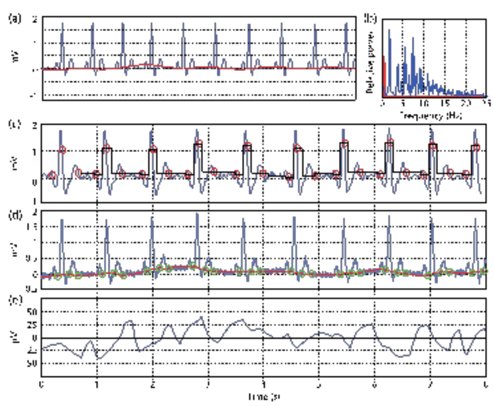
Short Bio:
Onur Guven received the B.Sc. degree in electrical and electronic engineering from the Bosphorus University at Istanbul, Turkey, and the M.Sc. degree in analogue and digital IC design from Imperial College London, U.K., in 2008 and 2009, respectively. Currently, he is working toward for the Ph.D. degree at the Centre for Bio-Inspired Technology, Imperial College London. His main interests are biomedical signal processing, embedded system design and IC circuit design.

Recent Publications:

- **O. Guven**, A. Eftekhar, R. Hoshyar, G. Frattini, W. Kindt, T. G. Constandinou, "Realtime ECG Baseline Removal: An Isoelectric Point Estimation Approach" Proc. IEEE BioCAS Conference, pp. 29-32, 2014.

Key References:

- M. Dai, S. Lian, "Removal of baseline wander from dynamic electrocardiogram signals", Proc. IEEE CISP Conference, pp. 1-4, 2009.
- G. Friesen, T. Jannett, M. Jadallah, S. Yates, S. Quint, and H. Nagle, "A comparison of the noise sensitivity of nine QRS detection algorithms," IEEE Trans. Biomedical Engineering, vol. 37, no. 1, pp. 85-98, 1990.



Operation of baseline wander estimation algorithm using an 8 second synthetic ECG waveform and noise artefacts.

Dorian Haci

Research Focus: Embedded Platforms for the Realtime Evaluation of Implantable Neural Interfaces

Supervisor: Dr Timothy Constandinou

Funding: Wellcome Trust/EPSRC (CANDO project)

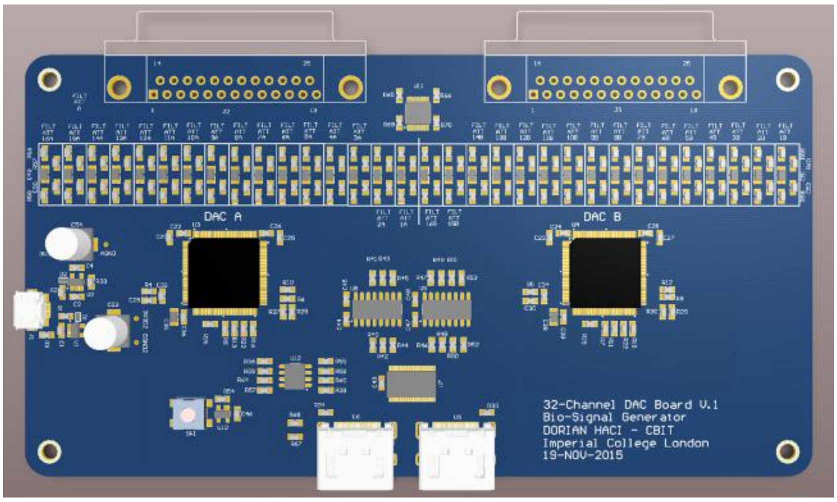
Motivation:
One of the greatest challenges of today's science is to understand how the cell-to-cell connections between neurons generate our perception of the world, our thoughts and actions. Many neurological and psychiatric diseases cause abnormal activity patterns of this network. The sensing and comprehension of this disruption is extremely important to prevent the effects of the diseases to manifest and to develop and perform empirically based treatments. New technologies have recently developed implantable devices that effectively monitor these activities. However, a common and time-consuming issue for these devices is the electrical and biological testing necessary before experimental in-vivo validation.

Objectives:
In order to accelerate the development of implantable neural interfaces, my work (at the first instance) aims to create instrumentation to emulate biological tissue for purposes of evaluating electronic hardware (i.e. biosignal generation). Key challenges include ultra low noise performance, the generation of multichannel data (i.e. high overall datarate), portability, robustness in a noisy lab environment. It is intended this hardware be used to substitute the recording electrodes for lab-based test. Specifically, the platform will replicate bio-potential signals that would be observed in extracellular neural recordings.

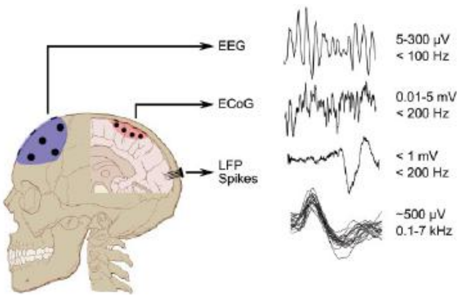
Short Bio:
In 2012 I received a BSc in Electronic Engineering at the Polytechnic University of Turin, Italy. My final year project involved designing and testing proximity sensors and sensor amplifiers for BDC Electronic Company. I continued my studies with an MSc in electronic engineering, specialising in Wireless Systems Design and Communication Systems. I was awarded a scholarship for developing my MSc thesis project at Imperial College London, where I designed and implemented an innovative thermally controlled system for bio-applications using low cost PCB technology. I received my MSc in Turin in December 2014. I joined the Neural Interfaces group at the Centre for Bio-inspired Technology as a Research Assistant in June 2015.

Key references:

- Buzsáki, G., Anastassiou, C. A., & Koch, C. (2012). The origin of extracellular fields and currents—EEG, ECoG, LFP and spikes. Nature reviews neuroscience, 13(6), 407-420.
- Webster, J. (2009). Medical instrumentation: application and design. John Wiley & Sons.



Printed Circuit Board (PCB) design of a 32-channel ultra low noise Bio-signal Generator.



Different neural signals we aim to emulate and their range in frequency and electric potential.

Ermis Koutsos

Research focus: Low-power real-time sEMG fatigue monitoring ASICs for rehabilitation of osteoarthritis.
Supervisor: Dr Pantelis Georgiou
Funding: EPSRC DTA

Motivation:
Electromyography (EMG) is a technique used to evaluate the electrical activity of muscle. Muscle fatigue tracking can be a helpful tool for the rehabilitation of osteoarthritis in the knee, a chronic condition affecting 8.5 million people in the UK causing pain and loss of mobility. Knee rehabilitation focuses on maintaining a balance between the two large muscles that hold the patella (knee cap) in place. Careful tracking of muscle fatigue of these two muscles can provide essential adjustments to the rehabilitation procedure. Furthermore, fatigue monitoring can be applied in the field of spots science, medical research and ergonomics in an effort to better understand the muscle fatigue manifestations.

Objectives:
The aim of this project is to create a real time sEMG based muscle fatigue monitoring device using low power integrated circuits. Our latest fabricated IC capable of real-time estimation of Muscle fibre conduction velocity is embedded in a compact, energy efficient, wearable prototype device that extracts muscle fatigue through monitoring of surface EMG. This wearable node can be applied to any muscle of the body, thus providing a tool to aid in rehabilitation or muscle research. Processing of the EMG takes place locally, resulting to information driven system rather than a conventionally data driven system, reducing requirements on data transmission and power.

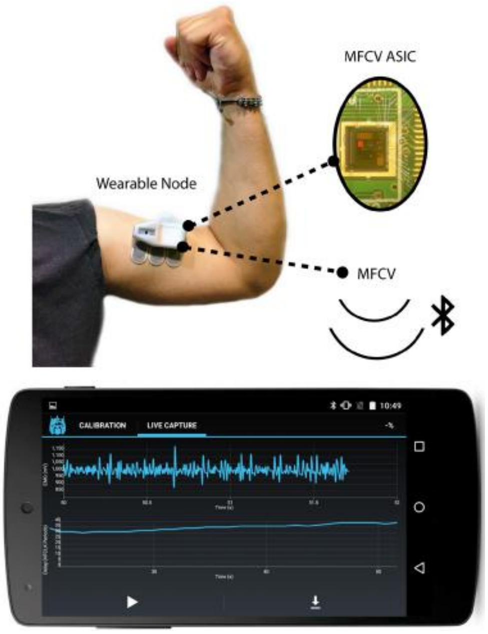
Short Bio:
Ermis Koutsos received his BSc degree in Electrical and Electronic Engineering from University of Surrey - U.K., in 2011 and his MSc in analogue and digital integrated circuit design from the Dept. of Electrical and Electronic Engineering of Imperial College London - U.K., in 2012. Since 2012 he is a PhD candidate in the Centre of Bio-Inspired Technology, Institute of Biomedical Engineering, Imperial College London, under the supervision of Dr. Pantelis Georgiou. His research interest focuses on the design of low power mixed signal electronics for biomedical applications. Mr. Koutsos is a scholar of EPSRC.

Key References:

- M. Cifrek, V. Medved, S. Tonkoviβ, S. Ostoji, " Surface EMG based muscle fatigue evaluation in biomechanics", Clinical Biomechanics, vol. 24(4), pp. 327-340, 2009.
- M. B. I. Reaz, M. S. Hussain, F. Mohd-Yasin, "Techniques of EMG signal analysis: detection, processing, classification and applications", Biological procedures online , vol. 8(1), pp. 11-35, 2006.

Recent Publications:

- **E. Koutsos**, V. Cretu, P. Georgiou, 'A Muscle Fibre Conduction Velocity Tracking ASIC for Local Fatigue Monitoring', Submitted to IEEE Transactions on Biomedical Circuits and Systems, 2015.
- J. Heaffey, **E. Koutsos**, P. Georgiou, 'Wearable Device for Remote EMG and Muscle Fatigue Monitoring', Submitted to IEEE Biomedical Circuits and Systems Conference (BioCAS), 2015.



Developed wearable node with dedicated muscle fatigue tracking ASIC and custom Android monitoring application.

Timo Lauteslager

Research Focus: Functional neuroimaging using ultra-wideband impulse radar
Supervisor: Dr. Timothy Constandinou
Funding: EPSRC DTA and EEE Departmental Scholarship

Motivation:
A newly emerging technique that has lately received a lot of attention in the biomedical field, is microwave imaging. Electromagnetic waves in the microwave frequency band are non-ionizing and have tissue-penetrating abilities, making them very suitable for diagnostic applications. Using radar techniques, a volume of blood in the brain can be detected, which is known to be an indicator for neural activity. In the current project we will investigate the feasibility of using radar for imaging brain activity. Being able to image the brain non-invasively is paramount for our ability to study and diagnose neurological disorders, and evaluate their treatment.

Objectives:
Other neuroimaging modalities suffer from high cost, low mobility and a low temporal resolution. By using a new single chip implementation of an ultra-wideband impulse radar, we intend to overcome these problems. We are still facing a number of challenges. Currently we are characterizing the radar module and testing different signal processing techniques. In collaboration with researchers from the University of Oslo, we are developing antennas that are optimal for coupling with the human body. Eventually we will construct an imaging device, containing an array of antennas, to perform multistatic radar. We intend to provide the first evidence that neural activity can be measured non-invasively using microwave technology.

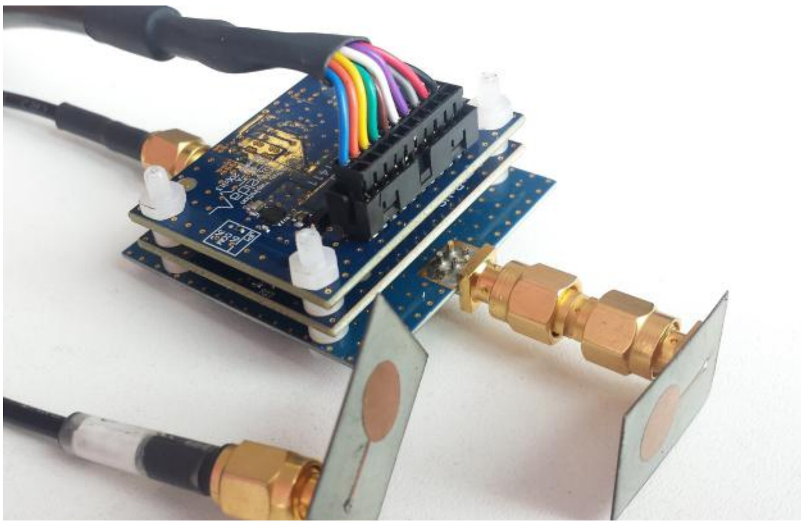
Short Bio:
Timo Lauteslager followed his undergrad in Biomedical Engineering at the University of Twente, The Netherlands, where he received his BSc degree in 2012. Subsequently he was awarded with a 2 year Erasmus Mundus scholarship from the European Committee. This scholarship allowed him to follow a joint degree master program in Biomedical Engineering, at Czech Technical University and Trinity College Dublin. He specialized in biosignal processing and neural engineering. In 2014 he received his MSc with distinction from both universities. Timo has joined the Neural Interfaces group at the Centre for Bio-inspired Technology as a PhD candidate in January 2015.

Recent Publications:

- **T. Lauteslager,** N. Nicolaou, T. S. Lande, T. G. Constandinou, "Functional neuroimaging using UWB impulse radar: A feasibility study", Proc. IEEE BioCAS Conference, 2015.

Key References:

- M. Persson et al., "Microwave-based stroke diagnosis making global prehospital thrombolytic treatment possible," IEEE Trans. on Biomedical Engineering, vol. 61, no. 11, pp. 2806-2817, 2014.
- H. Hjortland, T. S. Lande, "CTBV integrated impulse radio design for biomedical applications," IEEE Trans. BioCAS, vol. 3, no. 2, pp. 79-88, 2009.



Novelda ultra-wideband radar chip with wideband patch antennas.

Lieuwe B. Leene

Research Focus: Scaling Neural Interfaces into the Gigabit Domain

Supervisor: Dr. Timothy Constandinou

Funding: EPSRC Prize Studentship

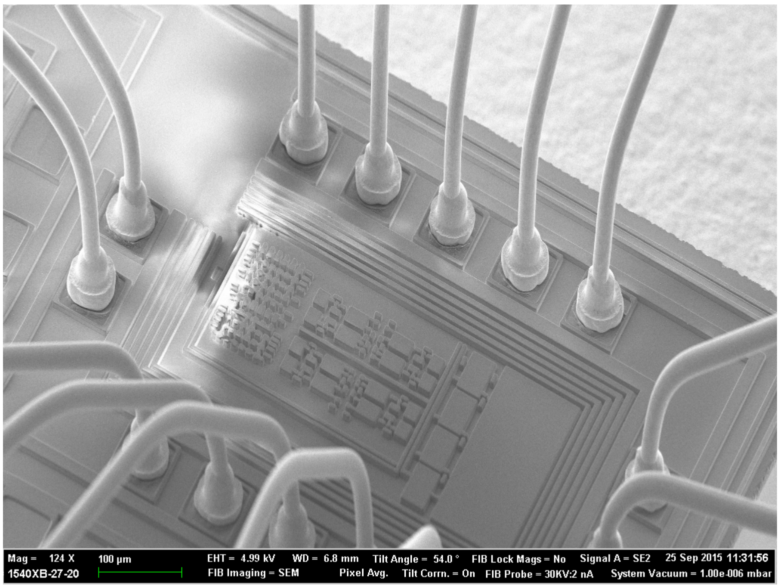
Motivation:
Current trends in Neuroscience and commercially available biomedical electronics have demonstrated great promise for better health care. But moreover there is a growing need to address viable system on chip (SOC) integration for large scale neural recording platforms that can be implanted.
This effort raises new challenges beside the conventional focus power and noise. In addition design effort is rapidly increasing with the complexity of these systems. Bringing the software abstraction closer to the interface mitigates this concern but also opens new opportunities for different processing modalities on chip.

Objectives:
This work builds on identifying high level characteristics, trends, and limitations related to scaling system topology. Where the focus lies with developing circuit level instrumentation that specifically target massively scaled SOCs recording from thousands of neurons. Key aspects will lie with exploring hardware efficient processing modalities and allow processing abstraction pertinent to mechanism at the recording the interface.

Short Bio:
Lieuwe Leene is currently finishing his final year Electronic Engineering PhD at Imperial College London specialized in developing integrated electronics for healthcare implantable devices. He received his BEng. Electronic Engineering (Honors Research Option - Microelectronics and VLSI Stream) from the Hong Kong University of Science and Technology and his MSc Analogue and Digital Integrated Circuit Design from Imperial College London. Lieuwe then joined the NGNI Neural Interfaces group at the Center for Bio-Inspired Technology as PhD student.

Recent Publications:

- **L. B. Leene**, Y. Liu, T. G. Constandinou, "A compact recording array for neural interfaces", IEEE BioCAS Conference, pp. 97-100, 2013.
- **L. B. Leene**, T. G. Constandinou, "Ultra-low power design strategy for two-stage amplifier topologies", IET Electronics Letters, vol. 50, no. 8, pp. 583-585, 2014.
- K. Faliagkas, **L. B. Leene**, T. G. Constandinou, "A novel neural recording system utilising continuous time energy based compression", Proc. IEEE ISCAS, pp. 3000-3003, 2015.
- L. Zheng, **L. B. Leene**, Y. Liu, T. G. Constandinou, "An adaptive 16/64 kHz, 9-bit SAR ADC with peak-aligned sampling for neural spike recording", Proc. IEEE ISCAS, pp. 2385-2388, 2014.



SEM Image of 4 channel recording 0.18 CMOS ASIC. [Credit to Sugou Huo for his assistance at Nano-technology Center London].

Dora Ma

Research focus: Early detection and monitor progression using epigenetic biomarkers for chronic kidney disease
Supervisor: Prof Chris Toumazou
Funding: EEE Departmental Scholarship

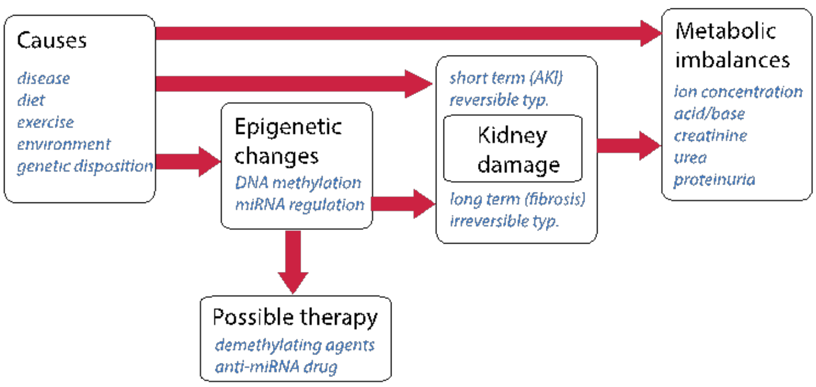
Motivation:
Chronic kidney disease (CKD) is one of the most common diseases affecting many people, with 1.8 million confirmed diagnoses in the UK alone. With the number increasing, the emphasis when treating CKD is to prevent patients from reaching end-stage renal failure, which results in the need for dialysis or kidney transplant. The chances of kidney failure decreases with early detection and adequate management. Recently, there has been strong evidence showing the role of epigenetics in the development and progression of chronic kidney disease. This implies the potential for more accurate biomarkers by detecting the epigenetic mechanism that causes the kidney damage directly.

Objectives:
My research aims to apply semiconductor technology to detect DNA methylation and quantify microRNA for early diagnosis and monitor progression for chronic kidney disease. The Lab-on-chip systems are based on ion sensitive field effect transistors (ISFETs), which allows for label free epigenetic detection in CMOS technology. The project has two main focuses, namely point of care diagnostics and laboratory analysis. The point of care system provides fast and simple results and does not require laboratory technicians, whilst the laboratory analysis system gives more detailed information on the epigenetic marker in question. The objective is to develop signal-processing circuits that will make these systems possible.

Short Bio:
Dora is a second year PhD student. She graduated from Imperial College in 2013 with a MEng from the department of Electrical and Electronic Engineering. Having done her final year project on analogue signal processing for DNA sequencing with Professor Toumazou, she continued to pursue a PhD in a similar area.

References:

- L. J. Smyth, G. J. McKay, A. P. Maxwell, and A. J. McKnight, "DNA hypermethylation and DNA hypomethylation is present at different loci in chronic kidney disease.," Epigenetics, vol. 9, no. 3, pp. 366–76, Mar. 2014.
- W. Bechtel, S. McGoohan, E. M. Zeisberg, G. A. Muller, H. Kalbacher, D. J. Salant, C. A. Muller, R. Kalluri, and M. Zeisberg, "Methylation determines fibroblast activation and fibrogenesis in the kidney," Nat Med, vol. 16, no. 5, pp. 544–550, 2010.
- T. Sakurait and Y. Husimi, "Real-Time Monitoring of DNA Polymerase Reactions by a Micro ISFET pH Sensor," no. 3, pp. 1996–1997, 1997.



An illustration of the difference paths and mechanisms of kidney damage

Nicholas Miscourides

Research focus: Intelligent and fully autonomous CMOS-based chemical sensing platforms.

Supervisor: Dr Pantelis Georgiou

Funding: EPSRC CDT in HiPEDS

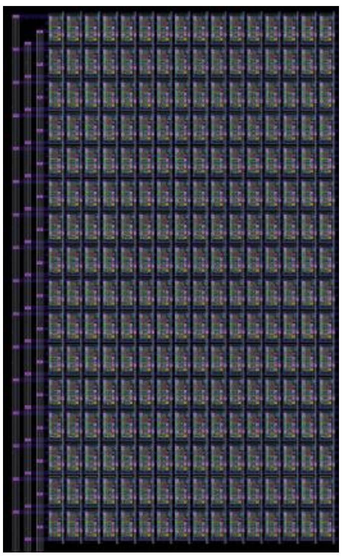
Motivation:
Chemical sensing platforms will play a major role in the future through numerous applications in areas such as medical diagnosis and screening, rapid tests, genomics and environmental monitoring. Currently, chemical sensors being used for continuous measurements are prone to faults and performance degradation thus requiring human intervention for frequent recalibration. For example, CMOS-based pH sensors primarily used for DNA detection, suffer from chemical drift manifesting as a reduction in sensitivity over time whereas blood glucose sensors which represent the largest commercial application of portable chemical sensors to-date, require calibration once per day to ensure reliable results.

Objectives:
My research aims to develop a framework and the methodology to ensure that chemical sensors are always accurate and reliable, minimizing any human intervention. Focusing on the case of CMOS-based, pH-sensitive chemical sensors, this work proposes a 3-tier solution including (1) designing the sensor front-end comprising large-scale ISFET arrays (2) investigating suitable methods for sensor health check and ways to extract useful sensor features and (3) developing a closed-loop adaptive algorithm to compensate for the sensor's non-ideal performance. This is a multidisciplinary project, drawing upon the fields of IC design, signal processing and machine learning to produce the first self-aware and fully autonomous chemical sensing system. Recent work has focused on investigating different architectures regarding the ISFET front-end sensing as well as exploring additional features that can be used to assess the condition of the sensor such as the impedance of the electrolyte-silicon interface.

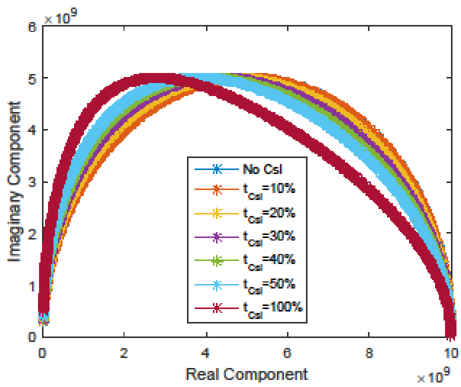
Short Bio:
Nicholas received the M.Eng. degree (Hons) in Electrical and Electronic Engineering in July 2014 and the M.Res. degree (Distinction) in High-Performance Embedded and Distributed Systems (HiPEDS) in September 2015 both from Imperial College London. During his studies, he was awarded the Sir Bruce White Prize for the best MEng thesis of my year. Currently he is pursuing the Ph.D. degree at the Centre for Bioinspired Technology jointly with HiPEDS Centre for Doctoral Training. Nicholas is a A. G. Leventis Foundation scholar.

Recent Publications:

- **N. Miscourides**, P. Georgiou, "Impact of Technology Scaling on ISFET Performance for Genetic Sequencing," in IEEE Sensors J., vol.15, no.4, pp. 2219-2226, 2015.



A 16x16 ISFET array used for chemical sensing of hydrogen ions.



Nyquist diagram showing how the equivalent impedance of an ISFET-electrolyte interface changes when the device is in operation. A surface charge layer is gradually growing causing the sensitivity of the sensor to deteriorate.

Khalid Baig Mirza

Research focus: Research and Development of stimulation technology for non-invasive obesity management.

Supervisor: Prof Chris Toumazou/Dr Amir Eftekhar

Funding: EPSRC

Motivation:

WHO statistics indicates obesity as the second largest preventable cause of death after tobacco consumption. Current estimates put the cost of obesity management at $ 47 billion, $ 6 billion of which is shared by NHS alone. Gastric Bypass Surgery is the most effective technique to manage morbid obesity[1] . However, surgery is expensive and accompanied by many complications. Therefore, it is necessary to explore suitable alternatives such as non-invasive Vagus Nerve Stimulation (VNS) since the vagus nerve plays a major role in appetite regulation and food intake[2] .

Objectives:

The preferred stimulation modality for VNS is electrical, which involves surgery to implant a stimulation device. My research and objective investigates noninvasive methods of VNS and to explore the feasibility and trade-offs of an emerging non-invasive ultrasonic technique for stimulation. As a step towards designing an ultrasonic VNS system, I have demonstrated that pulsed ultrasonic waves have a higher focus and less spatial energy distribution, hence are preferable over continuous ultrasonic waves (Fig. 1). I also aim to understand and quantify the effect of ultrasonic VNS by combining non-invasive stimulation with recording of responses on the Vagus nerve using a low noise recording system (Fig. 2).

Short Bio:

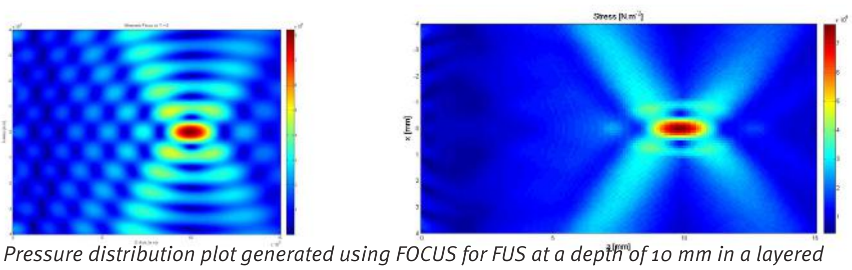
I completed my MSc in Analogue and Digital IC Design from Dept. of Electrical and Electronic Engineering, Imperial College London and started working as an Electronics Engineer for Ingenia Technology, in a product design team to implement a novel authentication technology called Laser Surface Authentication (LSA). After 2 years at Ingenia, I returned to work and pursue a PhD at the Institute of Biomedical Engineering, Imperial College London.

Recent Publications:

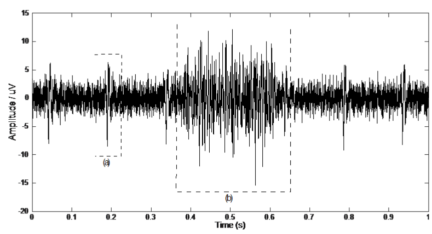
- **K B Mirza**, S Paraskevopoulou, A Eftekhar, C Toumazou, " Focussed Pulsed Ultrasonic Waves for Non-Invasive Neural Stimulation" , 3rd European Symposium on Focused Ultrasound Therapy, 2015, European Focused Ultrasound Society (EUFUS) , 2015.
- **K B Mirza,** S Luan, A Eftekhar, T G. Constandinou "Towards a fully-integrated solution for capacitor-based neural stimulation", Circuits and Systems (ISCAS), 2012 IEEE International Symposium on (pp. 2243–2246). IEEE, 2015

References:

- K. Behrns, "Bariatric Surgery and Long-term Cardiovascular Events," Yearbook of Surgery, vol. 2012, pp. 236{238, 2012}.
- H. R. Berthoud, "The vagus nerve, food intake and obesity," Regulatory Peptides, vol. 149 pp. 15{25, 2008}.



Pressure distribution plot generated using FOCUS for FUS at a depth of 10 mm in a layered media for continuous (top), pulsed (middle) ultrasonic waves in a 64 element linear array.



Neural mass activity recording on the vagus nerve coinciding with (a) heart rate and (b) breathing.

Nicolas Moser

Research focus: Distributed sensing platforms for ion-imaging and diagnostics

Supervisor: Dr Pantelis Georgiou

Funding: EPSRC HiPEDS CDT

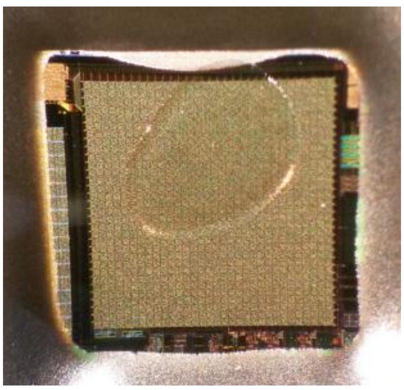
Motivation:
ISFETs have been used extensively in the past as floating gate transistors exhibiting inherent sensitivity to pH and simple integration in CMOS technology. These sensors ultimately allow for efficient and low-cost DNA sequencing platforms, which serve for numerous applications, ranging from the diagnostics of genetic anomalies to the detection of genes which indicate microbial resistance inside the whole genome of bacteria. The deposition of special membranes also allow such a platform to yield sensitivity to other ions such as Potassium, which, if monitored, could help prevent collapse during exercise for athletes or soldiers.

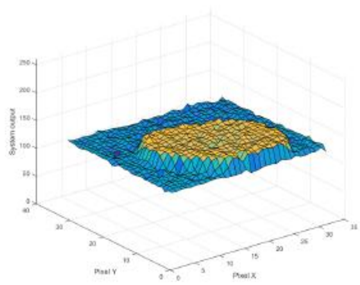
Objectives:
The main objective of this research is to develop a new architecture for ISFET sensing arrays with in-pixel processing and storing capabilities, exhibiting scalability across all CMOS processes. The architecture must in a compact form implement an auto-calibration algorithm to reduce pixel variation and compensate for common non-idealities of the sensor, such as trapped charge and drift. Although this platform was originally aimed for DNA sequencing, novel applications are being investigated. These include RNA sequencing as well as the conception of a multi-ion sensing platform, targeting Potassium, Sodium, Magnesium, Calcium and other essential ions inside our body.

Short Bio:
Nicolas obtained his Bachelor's Degree in Electronics and Chemical Engineering at the Université Catholique de Louvain (UCL) in Belgium in 2013. He then graduated in 2014 with an MSc Degree at Imperial College London in Analogue & Digital Integrated Circuit Design, where he received the Award for the best MSc project with significant original contribution to the topic area and the MSc Outstanding Achievement Prize. He is now part of the Centre for Doctoral Training programme in High Performance Embedded and Integrated Systems (HiPEDS) and in the first year of his PhD.

Recent Publications:

- **N. Moser,** T. S. Lande, and P. Georgiou, A novel pH-to-time ISFET pixel architecture with offset compensation, in Circuits and Systems (ISCAS), 2015 IEEE International Symposium on, May 2015, pp. 481-484.





ISFET sensing platform using an existing prototype designed by Dr Yuanqi Hu. Left : the chip was partially coated with a special membrane allowing certain pixels to exhibit sensitivity to Potassium. Right : Only these pixels respond to a variation of one decade in K+ concentration.

Peter Pesl

Research focus: Advanced Decision Support Systems for treatment of Type 1 Diabetes

Supervisor: Dr Pantelis Georgiou

Funding: Wellcome Trust

Motivation:
For many people with type 1 diabetes (T1DM), achieving good glucose control is a challenge. Simplistic toolswhich currently exist, such as insulin bolus calculators, aim to help people with T1DM to manage their condition by calculating the insulin dose needed in order to cover a meal. However, until now, these tools are neither intelligent nor personalised and often need to be refined and re-adjusted by clinical experts. As a result current treatment is sub-optimal leading to many complications.

Objectives:
The objective of my work is to develop and evaluate the performance of a decision support tool for people with diabetes called the 'Advanced Bolus Calculator for Diabetes (ABC4D)'. ABC4D displays real-time insulin advice on smartphones of people with T1DM and learns based on the glucose outcome of the advice. Over time, ABC4D recognises patterns in the user's life with an artificial intelligence technique called 'Case-based Reasoning', where daily life scenarios, such as exercise or meals with alcohol, are stored within cases. The insulin therapy is then automatically adapted for each 'case', thus providing personalised advice based on the life style of the individual. We have completed a pilot study where 10 people with diabetes used ABC4D continuously for 6 weeks in their home environment.

Short Bio:
Peter received the engineer's degree at the College of Electronics in Leonding/Austria specialising in technical computer science in 2005 before completing his undergraduate degree in Medical Device Technologies at the University of Applied Sciences Linz in 2010. Since then he has been working at the Centre for Bio-Inspired Technologies at Imperial College London on novel technologies for diabetes management. Currently he is working towards the PhD degree focusing on intelligent decision support systems for people with Type 1 diabetes.

Recent Publications:

- **P. Pesl**, P. Herrero, M. Reddy, M. Xenou, N. Oliver, D. Johnston, C. Toumazou, P. Georgiou, 'An Advanced Bolus Calculator for Type 1 Diabetes: System Architecture and Usability Results',IEEE Journal of Biomedical and Health Informatics, pp. 1-1, 2015.
- **P. Pesl**, P. Herrero, M. Reddy, M. Xenou, N. Oliver, D. Johnston, C. Toumazou, P. Georgiou 'Acceptability of a Patient and Clinical Platform of an Advanced Bolus Calculator for Diabetes (ABC4D)', Advanced Technologies and Treatments for Diabetes (Poster at Conference), 2015
- P. Herrero, **P. Pesl,** J. Bondia, M. Reddy, N. Oliver, P. Georgiou and C. Toumazou, 'Method for automatic adjustment of an insulin bolus calculator: In silico robustness evaluation under intra-day variability', Computer Methods and Programs in Biomedicine, vol. 119, no. 1, pp. 1-8, 2015
- P. Herrero , **P. Pesl** P, M. Reddy, N. Oliver, P. Georgiou, C. Toumazou 'Advanced Insulin Bolus Advisor based on Run-To-Run Control and Case-Based Reasoning', IEEE Journal of Biomedical and Health Informatics, vol.19, no.3, pp.1087-1096, May 2015.

Smartphone application, which was used during our clinical trials, showing a personalised insulin bolus advice.

Adrien Rapeaux

Research focus: Algorithms and Systems for Highly-Selective Neural Stimulation and Recording

Supervisor: Dr. Timothy Constandinou

Funding: EPSRC CDT in HiPEDS

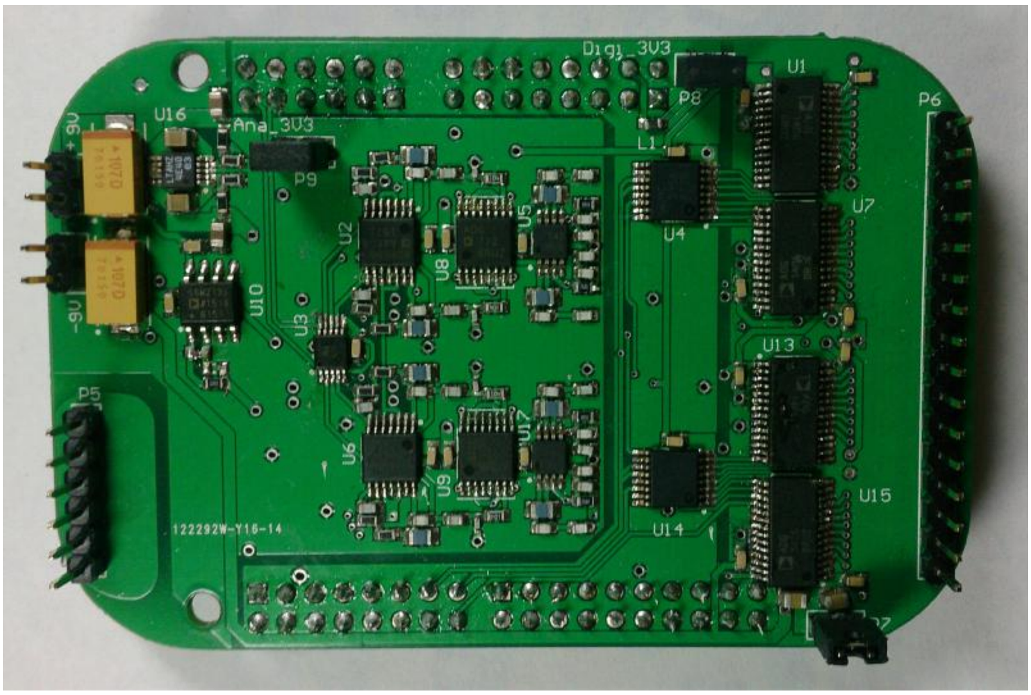
Motivation:
Neuroprosthetics research develops devices to restore lost neural function, requiring precise stimulation and recording from micron-scale neural fibers. Clinically-used electrodes lack selectivity and stimulate entire nerves, leading to side-effects when using them. Many novel electrodes have been designed with an aim to improve selectivity however there exists a tradeoff between selectivity and invasiveness that makes chronic use of these designs difficult. Boosting the selectivity of existing low-invasiveness, FDA-approved electrodes could lead to direct improvements in prosthetic control, artificial sensory feedback, and nerve stimulation therapies.

Objectives:
My research focuses on the development of algorithms to improve the selectivity of existing clinically-used electrodes such as cuff electrodes on the one hand, and development of systems and implants to test and validate these algorithms in real nervous tissue on the other hand. The goal is to bring electronic engineering and computation neuroscience together to create better implants that work with existing electrode technologies.

Short Bio:
I initially came to Imperial in 2013-2014 for the final year of an Electronic Engineering Master at Phelma School of Engineering, during which I developed a nerve fiber size-selective stimulation algorithm with an application in bladder control, leading to a publication this year. I was supervised by Dr. Constandinou who subsequently offered me a place in the new Centre for Doctoral Training in High-Performance Embedded and Distributed Systems (HiPEDS). I am now entering the PhD phase of the program after one year of Master in Research, during which I developed a microcontroller-powered multichannel neural interface (see Fig. 1).

Recent Publications:

- **A. Rapeaux**, K. Nikolic, I. Williams, A. Eftekhar, and T. Constandinou, “Fiber size-selective stimulation using action potential filtering for a peripheral nerve interface: a simulation study”, Proc. IEEE EMBS Conference, pp. 3411–3414, 2015.



Multichannel neural interface PCB

Francesca Troiani

Research Focus: Optical Neural Recording for large scale activity monitoring

Supervisors: Dr. Timothy Constandinou and Dr Konstantin Nikolic

Funding: EPSRC DTA and EEE Departmental Scholarship

Motivation:

At the current stage of research it is not possible to record neural activity without having to choose between a non-invasive setup and a good resolution. This creates the need for a new methodology that would act like a bridge between non invasive (and low resolution) and invasive (and high resolution) techniques.

In the 60s neuroscientists have discovered changes in light scattered from a neuron during action potential and, since then, optical properties of neurons have been extensively studied. Thus the use of light, with its characteristic to travel through matter, seems to be the best chance to detect neural activity non invasively.

Objectives:

The main objective of my project is to detect neural activity optically without the use of fluorescent dyes or genetically encoded indicators. By using optical coherence tomography (a low coherence optical technique whose basic principle is similar to the one of ultrasonography), I want to detect the small changes in the refractive index that occur in neurons during action potential and correlate them to neurons electrical activity. Working on peripheral nervous system (i.e. Xenopus Laevis's sciatic nerve), I aim to be able to target specific fibers inside the nerve.

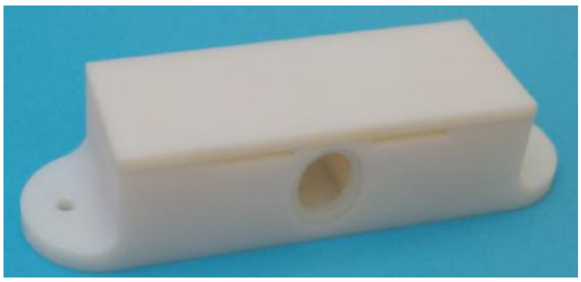
Short Bio:

I received my BSc in Physics in 2011 and my MSc in nuclear and subnuclear physics (cum laude) in 2013 from University of Trieste, Italy. My MSc project was done in collaboration with a group of physicists at SISSA (International School for Advanced Studies) on a computational model for grid cells. After graduation I was awarded a six months postgraduate fellowship from SISSA to continue my work on the formation of spatial representations on hyperbolic surfaces. I have joined the Neural Interfaces group at the Centre for Bio-inspired Technology as a PhD candidate in August 2014.

Key References:

- L. B. Cohen, R. D. Keynes, B. Hille, "Light scattering and birefringence changes during nerve activity", Nature, vol. 218, pp. 438–441,1968.
- D. Huang, E. A. Swanson, C. P. Lin, J. S. Schuman, W. G. Stinson, W. Chang, M. R. Hee, T. Flotte, P. Kenton, A. Carmen & J. G. Fujimoto, "Optical coherence tomography", Science, vol. 254, no. 5035, pp. 1178–1181, 1991.

The experimental setup



A close up of the bath chamber.

Stephen Woods

Research Focus: Wireless Capsule Endoscope for Targeted Drug Delivery
Supervisor: Dr. Timothy Constandinou

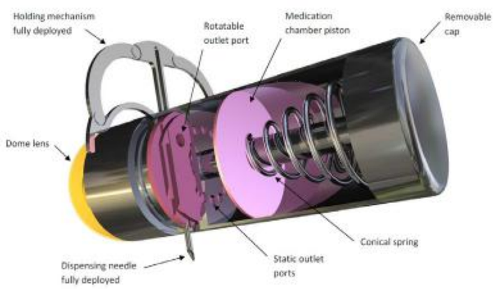
Motivation:
Endoscopes and colonoscopies are used routinely by gastroenterologists to diagnose and treat pathologies such as Crohn's disease in the gastrointestinal (GI) tract. However the small intestine poses a problem for these conventional methods as it is very difficult to access. One method employed to overcome this problem is the use of wireless capsule endoscopes (WCE). These pill-sized cameras take pictures of the intestinal wall which are then used to diagnose pathologies. The problem with this method is that it does not offer the ability to administer therapy to an affected area.

Objectives:
The aim of my research is to design and analyse mechanisms, which will give additional functionality to WCE to allow them to diagnose and treat pathologies of the GI tract, specifically in the small intestine. Three highly novel sub-systems will be explored for their suitability, when combined, to deliver a targeted dose of medication to a site of interest in the small intestine. The particular challenge with designing a microrobotic system which can perform a surgical procedure such as targeted drug delivery is in the allowable working envelope for the microrobot. As it is to be swallowed the microrobot requires a small package size of approximately 12.0mm diameter by 25.0mm long.

Short Bio:
I received the BEng (Honours) degree in 2008 and the MEng in 2013. I am currently employed as Head of Design for Duckworth & Kent Ltd. where, for the past 16 years, I have been designing titanium surgical instruments for ophthalmology. I hold a number of patents in the fields of: LASEK, lens delivery systems and implant systems. I am a Fellow of the Institute of Engineering Designers and hold the position of Chartered Engineer. I am currently working towards the PhD degree at the Centre for Bio-Inspired Technology (Institute of Biomedical Engineering and Department of Electrical and Electronic Engineering) at Imperial College London. My current research interests include microactuators and medical robotic systems.

Recent Publications:

- **S. P. Woods,** T. G. Constandinou, "A Novel Holding Mechanism for Next Generation Active Wireless Capsule Endoscopy", Proc. IEEE EMBS Conference, pp. 1181-1185, 2015.
- **S. P. Woods,** T. G. Constandinou, "Engineering Micro Mechanical Systems for the Next Generation Wireless Capsule Endoscopy," Biomedical Research International, vol. 2015, Article ID 741867, pp. 1-14, 2015.
- **S. P. Woods,** T. G. Constandinou, "Wireless Capsule Endoscope for Targeted Drug Delivery: Mechanics and Design Considerations," IEEE Transactions on Biomedical Engineering, vol. 60, no. 4, pp. 945-953, 2013.
- **S. P. Woods,** T. G. Constandinou, "Towards a Micropositioning System for Targeted Drug Delivery in Wireless Capsule Endoscopy," Proc. IEEE EMBS Conference, pp. 7372-7375, 2011.



Swallowable microrobot capable of delivering 1 ml of targeted medication. Needle shown fully extended and the medication partially deployed.

Imperial College
London

Centre for Bio-inspired Technology
Department of Electrical and Electronic Engineering
Imperial College London
South Kensington
London SW7 2AZ

T +44 (0) 20 7594 0701
F +44 (0) 20 7594 0704

bioinspired@imperial.ac.uk

www.imperial.ac.uk/bioinspiredtechnology

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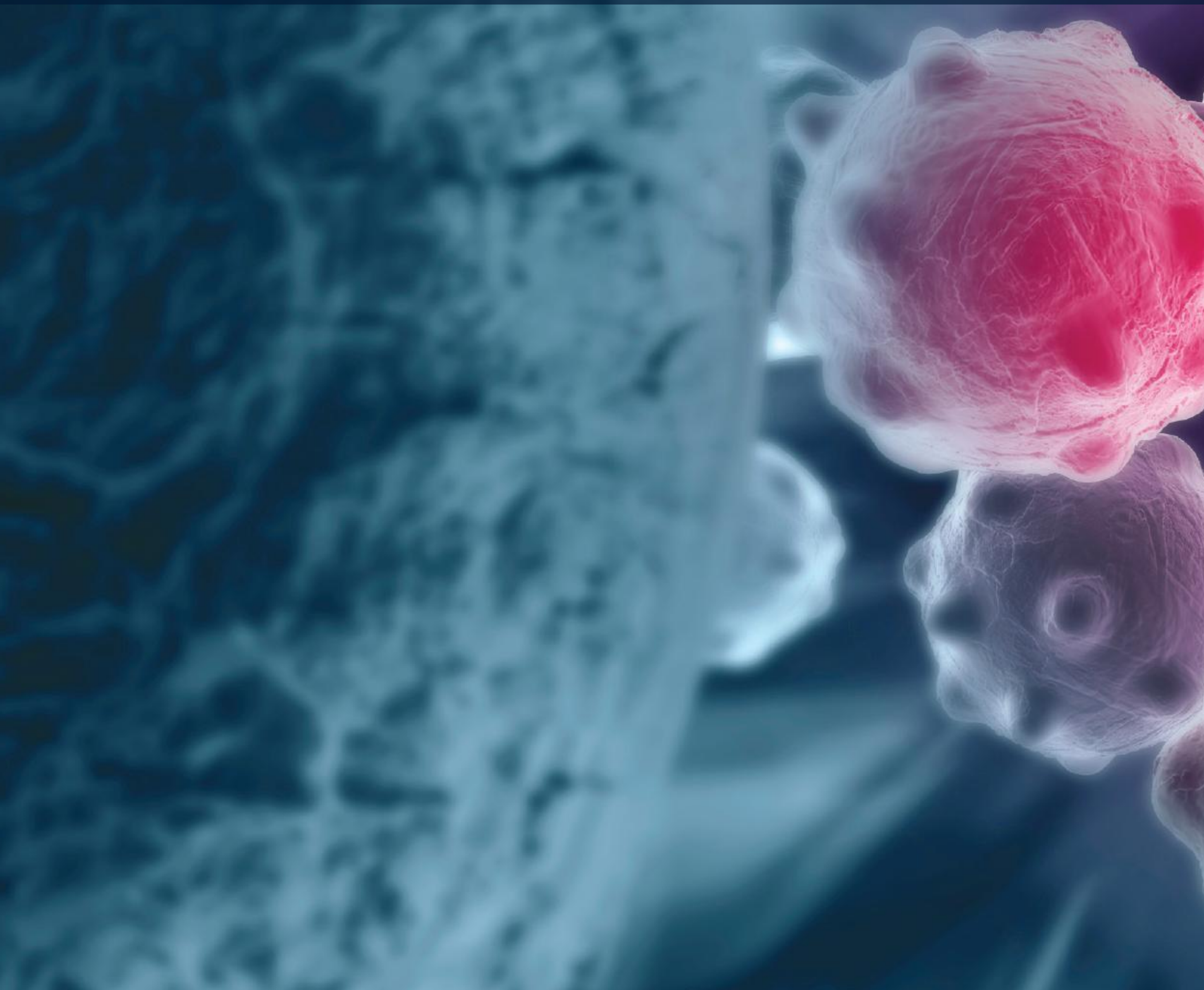

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