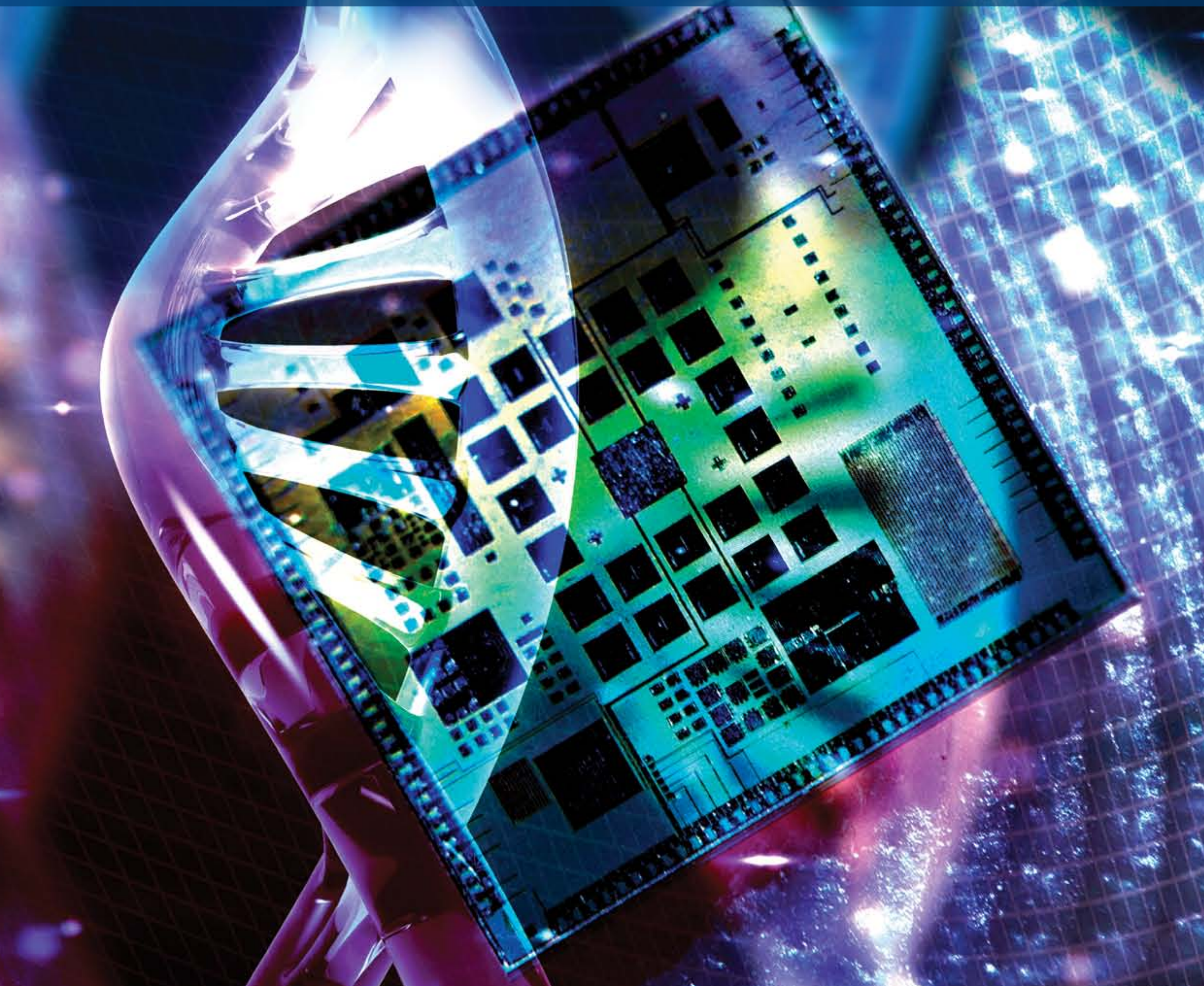
Imperial College
London

Centre for Bio-Inspired Technology

Annual Report 2013



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Centre for Bio-Inspired Technology

Annual Report 2013

Director’s foreword

The Academic Year 2013–2013 has been a most successful year with individual achievements as well as exciting progress in our research. We continue to be successful in attracting funding to the Centre which enables us to develop existing programmes, apply technologies into new fields and to test hypotheses in new areas.

Once again, we celebrate the students who have completed their doctorate degrees in the Centre. The majority choose to remain in research and will continue to be involved in the areas in which the Centre specialises. Whilst it is often very difficult to say farewell to valued colleagues, we recognise it is an exciting time for them and satisfying to know that they continue in research applying what they learnt whilst in the Centre and taking some of our ideas and techniques into new fields. Thus our network of alumni continues to grow and so to do the possibilities for collaboration with new groups or institutions.

We are pleased to update reports on projects in which research has reached an advanced stage and clinical trials are now taking place. As our primary aim is to transfer technology from the laboratory into a commercial environment to ensure it will improve the healthcare and lifestyle of individuals, these trials represent a significant step forward in the process. Once again we also include the latest news from our ‘spin out’ companies through which we commercialise research into marketable products. We have good news to report there too: the Sensium plaster, marketed as Sensium Vitals, is now deployed in the St John’s Health Center in Santa Monica, automatically recording patient vital signs every two minutes. The Health Centre reports a significant improvement in patient care as earlier diagnosis of problems is possible.

Once again, we are able to report success in attracting funding. This includes a major EU grant for research into a device to manage appetite and therefore reduce the risk of obesity and a 3 year grant from the EPSRC to continue the development of neural interface technologies and, specifically, a prosthetic enabling the real-time observation of brain extracellular activity.

This Research Report for 2013 describes the research activities of The Centre for Bio-Inspired Technology as it completes its fourth year of research and I hope you will enjoy reading about our activities over the past year and our achievements . It is a privilege to be Director of the Centre and to work with my colleagues at Imperial and around the world on a range of innovative projects.

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

Founding Sponsor's foreword

It is gratifying to see the Centre complete another year of research and to watch the development not only of the research programmes in bringing devices closer to market but of the staff and students. The number of alumni graduating from the Centre or leaving to start their own research groups is increasing and I am confident that they will continue to pursue their research interests in this most vital of fields.

It has always been the Centre's aim to undertake research which has a direct application to healthcare and to ensure that equal emphasis is given to its transfer from the laboratory to market. I am especially interested in supporting the nurturing and incubation of ideas and technologies and investing in the commercialisation of research to ensure that products reach the healthcare sector. The progress being made in some projects towards clinical trials is particularly encouraging. This year I was able to host a dinner in London at which I brought together researchers and potential investors and where Professor Toumazou was able to talk about his latest application of the DNA sequencing technology, appetite control sensors and an artificial pancreas. It was a lively evening of conversations and discussions around research, ideas and technology transfer. It is a pleasure and a privilege to be able to lend support in this way to the Centre's research programme.

I would like to heartily congratulate Professor Toumazou on being appointed the first Regius Professor at Imperial College London to mark the

Queen's Diamond Jubilee. Only two of the new 12 Regius Professorships were in Engineering. Further congratulations are due on his being elected to a Fellowship of the Academy of Medical Sciences. Chris is one of a very small group who hold fellowships of the three major institutions – the Royal Society, the Royal Academy of Engineering and the Academy of Medical Sciences. These fellowships not only recognise Chris as an innovator and researcher but also his multidisciplinary approach in bringing together science, engineering and medicine to provide solutions to the problems posed by healthcare needs.

I also congratulate all those concerned with the Centre on another successful year and wish the Centre and its researchers continued success.

Professor Winston Wong BSc, PhD, DSc

People

Academic & 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
Lecturer Department of Electrical
and Electronic Engineering

Deputy Director Centre for Bio-Inspired Technology

Dr Pantelis Georgiou
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

Dr Reza Bahmanyar

Dr Alessandro Borghi

Dr Amir Eftekhar

Dr Andrea Alenda González

Dr Pau Herrero Vinas

Dr Yufei Liu

Dr Olive Murphy

Dr Belinda Nedjai

Dr Monika Reddy (Clinical)

Dr Sanjiv Sharma

ASSOCIATES

Dr Yan Liu

Dr William Spinner

Dr Irina Spulber

Dr Claudio Zuliani

Assistants

Mr Mohamed El-Sharkawy

Mr Song Luan

Mr Keshava Murthy

Mr Peter Pesl

Ms Celia Fernandes (Erasmus Student)

Research students

Mr Deren Barsakcioglu

Mr Radu Berdan

Mr Onur Guven

Mr Yuanqi Hu

Mr Ermis Koutsos

Mr Lieuwe Leene

Ms Dora Ma

Mr Mohammadreza Sohbati

Ms Tatiana Trantidou

Mr Ian Williams

Mr Stephen Woods

Administrative staff

Mrs Patricia Chapman
Business Administrator to Professor Toumazou

Mrs Wiesia Hsiessen
Senior Group Administrator

Ms Gifty Kugblenu
PA to Professor Toumazou

Mrs Izabela Wojcicka-Grzesiak
Research Group Administrator

Ms Sandra Lock (March–September 2013)
Research Group Administrator

Visiting academics

* indicates researchers currently based in the Centre

PROFESSORS

Professor Tor Sverre Lande *
University of Oslo

Professor Bhusana Premanode

Professor David Skellern *
Formerly Macquarie University, Australia

Professor Peter Wells FRS
Cardiff University

Professor Winston Wong
Grace THW, Taiwan

Professor Sir Magdi Yacoub FRS *
Imperial College Healthcare NHS Trust

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

RESEARCH FELLOWS

Dr Alison Burdett
Toumaz Technology Ltd

Dr Jamil El-Imad (Honorary Senior Research Fellow)
W Investments, UK

Professor Gareth Jenkins
Nanjing University of Posts and Telecommunications, China

Dr Kiichi Niitsu *
Nagoya University, Japan

Graduates in 2012–2013

Dr Walid Juffali

Dr Melpomeni Kalofonou

Dr Kwok Wa Lui

Dr Christina Morris

Dr Sivylla Paraskevopoulou

Dr Alexander Serb

Researchers who have taken up appointments elsewhere

Dr Ali Khiat
Research Associate, Nanofabrication Centre, University of Southampton

Dr Themis Prodromakis
EPSRC Fellow and member of academic staff, Nano Research Group, Department of Electronics and Computer Science, University of Southampton

Dr Iulia Salaoru
Research Associate, Nanofabrication Centre, University of Southampton

Dr Jakub Trzebinski
Project Manager, Sensor Engineering in Radiometry Basel, Switzerland

Dr Thomas Weissensteiner
Research Associate, Department of Chemistry, Imperial College, London

News

Staff and events

Centre's Director Recognised by major awards

FEBRUARY 2013

EU Grant to find a solution to obesity

A project to create an implant that will reduce appetite in obese patients, led by Professor Chris Toumazou of the Centre and Professor Sir Stephen Bloom of the Faculty of Medicine, has received a major award of over €7,000,000.

Funding is by a new Synergy grant from the European Research Council. Eleven awards have been made across Europe of which two were awarded to Imperial College. Obesity is a growing health concern in countries across the world and this project aims to tackle the disease more effectively than ever before.

The Project, 'Intelligent implantable modulator of Vagus nerve function for treatment of obesity' (i2MOVE) will develop an implant which aims to detect signals in the nerves and instruct the brain and the gut that it is full. Currently there are no treatments for obesity and some of the best methods of coping involve invasive surgery, such as a gastric bypass or fitting a gastric band.

MARCH 2013

Professor Toumazou appointed Regius Professor of Engineering

As part of the celebrations for HM The Queen's Diamond Jubilee, 12 new Regius Professorships were conferred on UK universities.

Imperial College London was awarded one of the new appointments in recognition of the excellence of its research and teaching in the field of engineering. The College appointed Professor Chris Toumazou to be the first recipient of this prestigious position. The title of Regius Professor of Engineering will be bestowed on Professor Toumazou at the Imperial College Commemoration Day Ceremony in October.

JUNE 2013

Centre's Director speaks at G8 Conference on Innovation

Professor Toumazou was one of the speakers at *The Innovation Conference* which brought together leading innovators, from the G8 and beyond.

Openness to ideas and technologies from across the spectrum of business and society is essential in finding solutions to the greatest challenges facing the world. With unique capabilities for taking a broad approach to innovation, the UK's researchers, businesses and social enterprises will have central roles in global initiatives. From public policy to science and technology, the conference facilitated conversations that influenced the dialogue throughout the UK G8 Presidency.

High profile speakers included David Willetts, BIS Minister for Science and Innovation, Sir Richard Branson, who discussed entrepreneurship and innovation, Ron Dennis of McLaren who talked about innovation in F1 and how technologies spin out into other sectors, Zaha Hadid, architect and Thomas Heatherwick, the designer of the new London bus, discussing innovation and creativity. The 250 delegates included leading international entrepreneurs, researchers, scientists, creatives and policy makers from more than 22 different countries.

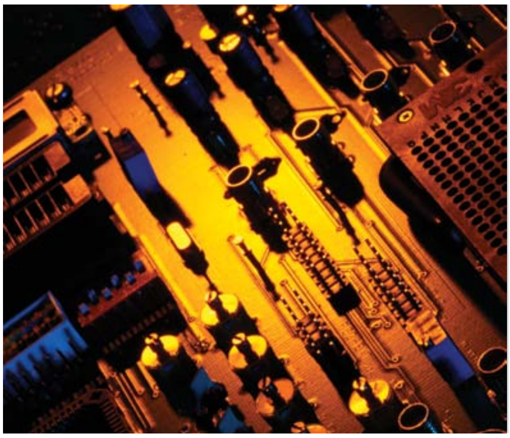
JUNE 2013

Professor Toumazou appointed Fellow of the Academy of Medical Sciences

In recognition of his contribution to research in medicine, Chris Toumazou has been made a Fellow of the Academy of Medical Sciences, one of the UK's five national academies.

The Academy draws its fellows from the fundamental biological sciences, clinical academic medicine, public and population health, health technology implementation, veterinary science, dentistry, medical and nursing care and other professions allied to medical science as well as the essential underpinning disciplines including mathematics, chemistry, physics, engineering, ethics, social science and the law.

Chris Toumazou is one of an elite few to hold fellowships from all 3 major academies: the Royal Society, the Royal Academy of Engineering and the Academy of Medical Sciences.



JULY 2013

Professor Toumazou featured in Nature Methods

In the July issue, Nature Methods focussed on research associated with DNA and RNA. It included a paper entitled 'Simultaneous DNA amplification and detection using a pH-sensing semiconductor system', the results of research carried out by the research teams from the Centre for Bioinspired Technology at Imperial College and the 'spin out' company DNA Electronics Limited.

To accompany the article, the Journal's Author File for July was about Professor Toumazou summarising his academic career and the inspiration for his DNA research.

Toumazou, C. *et al* entitled 'Simultaneous DNA amplification and detection using a pH-sensing semiconductor system'. *Nat Methods* 10, 641–646 2013

www.nature.com/nmeth/index.html

JULY 2013

Professor Toumazou receives Royal Society Gabor Medal

To recognise his engineering solutions for DNA analysis, Chris Toumazou has been awarded the Royal Society Gabor Medal. Throughout his career, which spans over 20 years at Imperial, he has continually explored new opportunities to design semiconductors that can be developed with medical uses in mind.

On hearing of the award, Professor Toumazou said: "This means a lot to me since it recognises interdisciplinary research and how my invention in semiconductors has transformed the way we can now sequence DNA. Today, the fastest growing sequencing technology is based on this invention and a genetic sequencing machine is becoming more like a PC".

The Award is also significant as the Medal 'returns' to the Department of Electrical and Electronic Engineering where Professor Dennis Gabor did his Nobel Prize-winning work on holography.'

JULY 2013

Two Wellcome Trust Institutional Strategic Awards made to Centre Researchers

DEVELOPMENT OF THE ARTIFICIAL PANCREAS FOR HOME CARE

A miniature microchip, which is capable of mimicking the behaviour of the endocrine

pancreas, has been developed at Imperial College and this forms the basis of a bio-inspired artificial pancreas that automatically delivers hormones to control the blood glucose levels in response to changes detected by a glucose sensor. This project builds upon the existing development to create the first bio-inspired artificial pancreas capable of bi-hormonal glucose control to be used in a free-living environment.

Type 1 diabetes is caused by the destruction of insulin-producing beta cells in the pancreas. Current management of type 1 diabetes can lead to prolonged episodes of high and low blood glucose which can have long term side effects such as blindness, kidney failure and heart disease.

This Project, led by Dr Georgiou Pantelis, aims to develop an artificial pancreas for treatment of type 1 diabetes in the home environment and able to manage variations in meal composition and external perturbations such as exercise, physiological stress and intercurrent illness.

NETWORK OF EXCELLENCE FOR OPTOGENETIC MANIPULATION OF NEURAL CIRCUITRY

A collaborative team, led by Dr Konstantin Nikolic, has been awarded funding for a Project which involves multi-disciplinary researchers from across Imperial College.

The team includes, Dr Simon Schultz from Bioengineering, Dr William Wisden from Life Sciences, and Drs Vicenzo De Paola and Daniel Sharp from Medicine.

Optogenetics is the use of gene technology to induce light sensitivity in cells. Using this approach, intracellular signals can be initiated by external optical pulses – this has numerous applications which are only beginning to be explored, such as initiation or suppression of action potentials in excitable cells with millisecond temporal resolution, and modulation of signalling cascades. The network will focus on the development of a novel paradigm for treating brain injury, by optogenetic manipulation of neural circuits to induce neural rewiring.

JULY 2013

Visiting Professor Peter Wells awarded 2013 Royal Medal

The Royal Society has made this award to Professor Wells for pioneering the application of the physical and engineering sciences to the development of ultrasonics as a diagnostic and surgical tool which has revolutionised clinical practice. Peter is a Distinguished Research Professor at the School of Engineering, University of Cardiff.

The three Royal Medals are awarded annually by the Sovereign on the recommendation of the **Council of the Society**. Each year two medals are awarded for the most important contributions 'to the advancement of Natural Knowledge' in the physical and biological sciences respectively. A third medal, the one awarded to Professor Wells, is for distinguished contributions in the applied sciences.

The Royal Medals were founded by HM King George IV in 1825. Between 1826 and 1964 two medals were awarded each year. In 1965 the third medal, covering the applied sciences, was introduced on behalf of HM The Queen.

AUGUST 2013

Dr Pantelis Georgiou receives Mike Sargeant Career Achievement Award

The IET (Institution of Engineering and Technology) award is made annually to a young engineer who is judged to have made the most significant progress in their career over a number of years. For example, they may have shown exceptional leadership in developing a project, have contributed creatively when developing a new product or service, or have demonstrated exceptional commitment to engineering throughout their academic or professional development.

Pantelis Georgiou (3rd from left) with the Bio-Inspired Artificial Pancreas Research Team

Pantelis received his PhD in 2008 and was appointed Lecturer in Circuits and Systems in the Department of Electrical and Electronic Engineering in 2011. He is currently leading the Project to Develop an Artificial Pancreas for Type 1 Diabetes which is currently undergoing clinical trials.

OCTOBER 2012 – SEPTEMBER 2013

Researchers prominent at international conferences

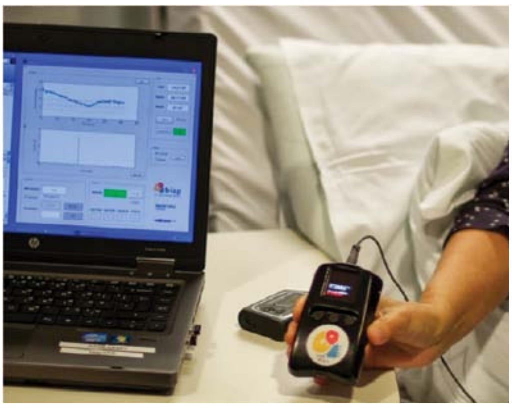
Researchers from the Centre have attended several international conferences this year and delivered papers.

At the IEEE International Symposium on Circuits and Systems (ISCAS) held in Beijing, Deren Barsakcioglu, Amir Eftekhar and Timothy Constandinou received the best paper award (BioCAS track) for their contribution: 'Design optimisation of front-end neural interfaces for spike sorting systems'.

Three other papers were presented and Deren Barsakcioglu, Tim Constandinou, Amir Eftekhar, Pantelis Georgiou, Pau Herrero Vinas, Ermis Koutsos, Lieuwe Leene, Ilias Pagkalos, Sivylla Paraskevopoulou, Mohammedreza Sohbati and Luan Song attended.

The November 2012 IEEE BioCAS Conference in Hsinchu, Taiwan was attended by Radu Berdan, Tim Constandinou, Pantelis Georgiou, Yuanqi Hu, Konstantin Nikolic, Mohammedreza Sohbati and Chris Toumazou.

International presentations of the Bio-Inspired Artificial Pancreas



The Bio-Inspired Artificial Pancreas handheld unit, which holds the control algorithm

The clinical data from the closed-loop studies to date have been presented at the following international conferences:

September 2013 – European Association of the Study of Diabetes Conference in Barcelona

July 2013 – North European Young Diabetologists Meeting in Copenhagen

February 2013 – Advanced Technologies and Treatments for Diabetes Meeting in Paris.

In addition, in **October 2012**, a poster presentation was made at the Diabetes Technology Meeting in Bethesda USA.

News

‘Spin-out’ companies

JULY 2013

Toumaz ‘Sensium Vitals’ helping to save lives

An ongoing task in any hospital is the routine checking of patients’ vital signs. Using traditional methods, these can be intrusive procedures and require skilled health professionals to carry them out but using the Toumaz Group Sensium Vitals ‘plaster’ this can be done more easily and more accurately.

Sensium Vitals is being used in St. John’s Health Center in Santa Monica California, and the hospital is reporting positive results from this new style of monitoring. Recordings are taken automatically every 2 minutes and any deterioration in a patient’s state alerts nurses immediately.

The Sensium Vitals, a disposable ‘plaster’ packed with electrodes and low power wireless technology, is placed on a patient’s chest and vital signs such as changes in temperature, heart rate, and breathing are wirelessly sent to a computer or mobile device for monitoring. For patients it is hardly noticeable and, because patients wearing the device are less likely to experience critical changes hospital costs are likely to be cheaper too.

Sensium Vitals is not limited to use within hospital as each disposable ‘plaster’ has a battery that lasts about three days and patients can continue to wear it after being discharged providing monitoring whilst at home.

Alumni

2012

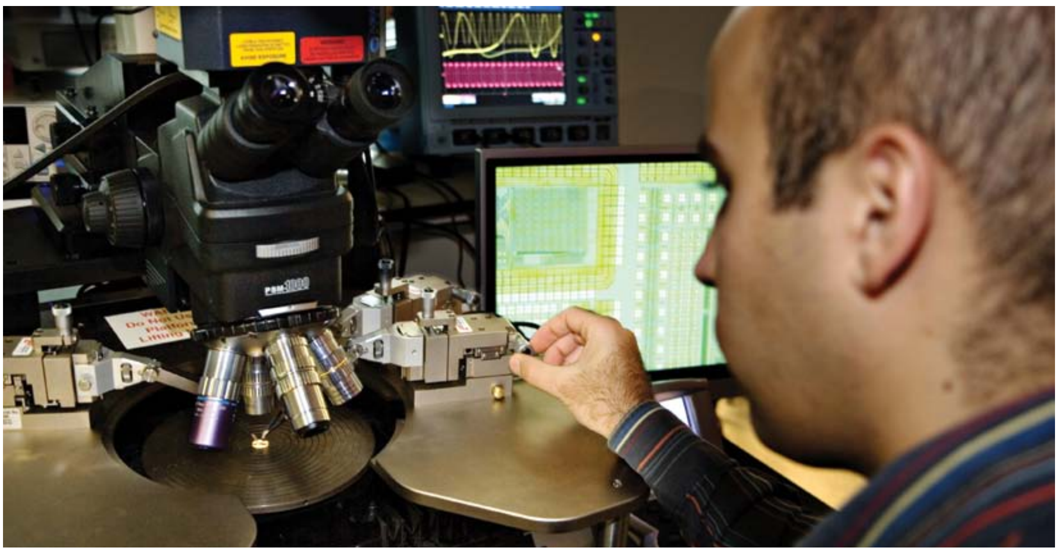
Dr Abdul Al-Ahal; Dr Dylan Banks; Dr Nir Grossman; Mr Bard Haaheim; Dr Gareth Jenkins; Mr Matthew Lubelski Katz; Dr Zhaolei Lang; Dr Yan Liu; Ms Oghenevworhe Omeru; Mr Siavash Saremi-Yarahmadi; Dr Alexander Serb; Dr Surachoke Thanapitak; Dr Virginia Woods

2011

Dr Wai Pan Chan; Dr Belinda Garner; Dr Konstantinos Michelakis; Dr Nick Oliver; Dr Panavy Pookaiyaudom; Dr Manassi Ramanna; Dr Marian Rehak; Dr Dimitrios Sideris; Dr Iasonas Triantis; Dr Anthony Vilches; Dr Winston Wong Jr

2010

Dr Patrick Degenaar



Reflections from Alumni

DR ALEXANDER SERB

PhD graduate 2013

Over the past 4 years, as a PhD student, I have had the pleasure of working for the Centre for Bio-Inspired Technology in the domain of opto-electronics.

Now that this chapter of my life has all but closed I can reflect back on these years and confidently summarise my experiences as a member of the Centre. To begin with, there is no doubt that it is a very professional and organised environment in which to carry out research. This was manifested in the form of the immense support I received over time, primarily from my supervisor but also from colleagues and members of staff, in personal development, technical help and administrative support. At the same time, studying at Imperial, and specifically the Centre, involved no little amount of toil. The combination of challenges pertaining to carrying out good technical work and publishing on time and to a high standard can be a very heavy load, particularly when one's eyes are opened to the competitive world of today. The Centre is acutely aware of the reality of cutting-edge research in today's world and consequently expects, but also helps, its members to perform to a very high standard. As an overall conclusion, the intense and simultaneously supportive environment that I experienced during my time in the Centre precipitated changes in me as a person beyond what I could have ever imagined as an undergraduate seeking a PhD. That in itself was enough to make my time spent at the Centre an effort well-spent.

DR ALI KHIAT

Research Associate 2011–2013

I worked for the Centre for Bio-Inspired Technology for almost two years, as a research associate.

My research was aimed on developing emerging nanodevices for advanced resistive switching mechanisms ReRAM and for imitating synaptic weight modulation that will be used as the enabling block for establishing biophysically realistic neuromorphic systems.

The Centre is one of the best places in the UK, or worldwide, to develop projects that permit progress beyond the state of the art. Excellent cleanroom and characterization facilities helped me and the research group to achieve outstanding outcomes. This wouldn't have been possible without the support received from my supervisor, group members, colleagues and administrative staff. Working for the Centre opens wide varieties of opportunities such as collaborations with other competitive research groups within Imperial College London, the UK and internationally. Personal development is another important aspect in the Centre's policy which is taken with care to prepare group members addressing their career with serenity and professionalism. Personally, I have benefited from various courses I have taken that had a positive impact on my personal and professional projects and improved considerably my track records. As a result of my experience in the Centre, I am currently working within Dr Themis Prodromakis' group at Southampton University.

Research funding

Project	Sponsor	Start Date	Duration
Controlling Abnormal Network Dynamics with Optogenetics	Wellcome Trust / EPSRC	October 2013	7 years
Network of Excellence for the Thermal Micro-Stimulation of Excitable Cells	Wellcome Trust	October 2013	1 year
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
Development of an Easily Deployable Intraocular Wireless Pressure Sensing Implant for Patients with Rapidly Progressing and Blinding Glaucoma	Wellcome Trust ISSF	August 2013	1 year
Real-Time Neural Chemical Sensing in the Peripheral Nervous System	EPSRC	July 2013	3 years
Next Generation Neural Probes for Large-Scale Recording in the Living Brain	efuturesXD (EPSRC)	July 2013	1 year
An Intelligent and Implantable Modulator of Vagus Nerve Function Treatment of Obesity	Commission of the European Communities (EU)	April 2013	5 years
Network of Excellence for Optogenetic Manipulation of Injured Neural Circuits	Wellcome Trust	January 2013	1 year
Automated Blood Pressure Monitoring	Wellcome Trust	March 2012	3 years
Ultra Low Power Biosignal processing	Texas Instruments	May 2011	3 years
'SeeBetter'	Commission of the European Communities	February 2011	3 years
Optimal Insulin Dosing	Imperial College Healthcare NHS Trust-BRC Funding	February 2011	2.5 years
Next Generation Neural Interfaces	EPSRC	October 2010	4 years
Wellcome Medical Engineering Centre	Wellcome Trust / EPSRC	October 2009	5 years
Centre for Bio-Inspired Technology	Winston Wong	October 2009	ongoing

The Centre's Research Strategy is based on applying engineering technologies in innovative ways to provide personalised healthcare devices for chronic disease management. Research, focussed on the three domains of early detection, diagnosis and therapy, is organised into four programmes: Metabolic Technology, Cardiovascular Technology, Genetic Technology and Neural Interfaces and Neuroprosthetics.

Research themes

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 semiconductor technology, we are looking at ways to reduce the power consumption required to operate the devices.

The semiconductor platform technologies being used in current research programmes include:

For early detection: microfluidics, CMOS lab-on-chip devices, biosensors

For diagnostics and monitoring: smart/RF sensors, low power implantable and wearable devices

For therapy – neuroprosthetics: neural interface technology and devices for neurorehabilitation

For monitoring and therapy – metabolic technology: glucose sensing and insulin regulation for diabetes management.

New advances in genomics and information and communications technologies are enabling research in areas of healthcare to progress more rapidly than had previously been possible. These include nanotechnology, robotics, molecular diagnostics and micro-fluidics. These 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 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 personal digital assistants and mobile 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. Patients can be diagnosed and monitored more quickly and in many cases remotely so removing the need for onsite clinic visits for monitoring and shorter stays in hospital beds.

Researchers within the Centre for Bio-Inspired Technology work in collaboration with scientists and engineers from across Imperial College. Project teams include medical researchers and clinicians to ensure the focus remains on the medical needs we aim to address.

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 type 1 diabetics, using insulin to control hyperglycaemic events and glucagon to prevent hypoglycaemia.

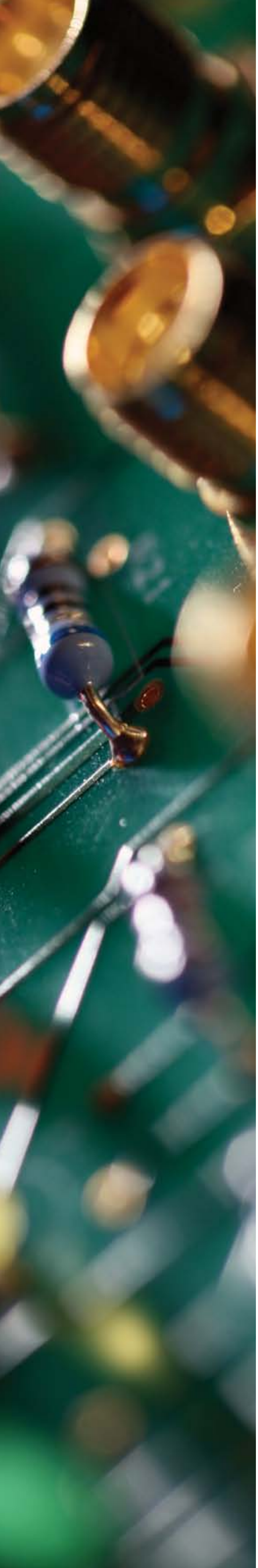
Clinical studies in subjects with type 1 diabetes are currently underway in the Imperial College-Wellcome Trust Sir John McMichael Centre. We are studying 20 subjects with type 1 diabetes aged 18–75 and the trial will assess the safety and efficacy of the bio-inspired artificial pancreas by applying the technology to participants in a variety of scenarios, starting with a fasting test and progressing to overnight control, mealtime control and, finally, an ambulatory test. Initial results evaluated in fasting, overnight and 24-hours studies confirm the device is safe, with good glucose control and no incidence of hypoglycaemia.

We are delighted to report that the Bio-Inspired Artificial Pancreas will be funded over the next two years by the Wellcome Trust to evaluate its performance during exercise, mixed meals and in challenging conditions with the objective to conduct the first trials in the 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, and recording vital parameters and providing advice on insulin dosing which is required for the treatment of diabetes. Additionally, the smart-phone provides a constant link to a clinician's database to allow constant monitoring from the hospital.

Diagnostic lab-on-chips for early detection of disease – which include 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 for the assessment of genetic predisposition to type 1 and type 2 diabetes and their associated complications.

Osteoarthritis – The Group is also part of the Imperial College London Osteoarthritis Centre of Excellence funded by Wellcome Trust and the EPSRC working on the diagnostic systems for early detection of the signs of the disease.



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 these alarming statistics.

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 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 2015. The implants and system will be applied to other indications following a successful Phase 1 trial. In-house expertise is complemented by external industrial production to produce devices meeting the variety of quality assurance, spectral constraint and regulatory directives necessary before applying for first-in-man studies. This approach is designed to ensure that all engineering considerations are engaged in the development and that the resulting devices can be mass-produced in the future.

We are extremely grateful for our support from the HICF (Health Innovation Challenge Fund, a joint Wellcome Trust and Department of Health initiative) which enables full translation of the technology to become a product.

Genetic technology

research is focussed on the development of a genetic detection platform and apparatus for a range of *in vivo* and *in vitro* applications

HEAD OF RESEARCH

Professor Chris Toumazou FRS, FREng, FMedSci

DNA is a biological molecule in the form of chains with millions of nucleic base pairs which 'code' the genetic information which makes us an individual. By investigating this biological code, early detection of hereditary disease or allergies can be realized for individual clients. The complex chemical detection techniques, such as electrophoresis and fluorescent detection, can be simplified to easy YES and NO questions. An analogue of 'match and mismatch' mechanism of base pairs into 'on and off states' of electronic logic gates has been made.

The 'SNP-DR' (a silicon based system for the prediction of drug response) is a low cost microchip based device which can predict drug efficacy or toxicity at the point-of-care. This technology can enable pharmacogenetic testing in personalised medicine, i.e. tailoring drug prescription and dose to a patient's genetic makeup, alongside other factors such as patient history and drug-drug interactions. Predicting drug efficacy will save patient and clinician time, reduce the overall cost of treatment by avoiding the wasteful cycle of trial and error with ineffective prescriptions, and provide improved quality of life.

Research in the Centre led to the development of the 'SNP-DR' platform which is capable of delivering fast, accurate on-the-spot tests for any target nucleic acid sequence, either DNA or RNA. Disposable, low cost, 'lab-on-chip' cartridges housing biochemical reagents, advanced microfluidics and low-power silicon biosensor systems are key to this novel technology for the detection of genetic sequences or mutations.

The micro-volume genetic test reaction-taking place on the fully integrated cartridge is analysed in real-time by a handheld electronic device using custom algorithms to ensure a robust and reliable result. Built on the reliability, scalability and processing power of silicon microchip technology, this platform technology is mass-producible and highly portable. The disposable cartridges can be tailored to any genetic sequence of interest, human or microbial, making this a customisable platform technology amenable to a wide variety of applications and markets, including rapid identification of infections.

The commercialisation of this technology is being undertaken by DNA Electronics Limited, a 'spin out' company from the Centre which is now based in West London.

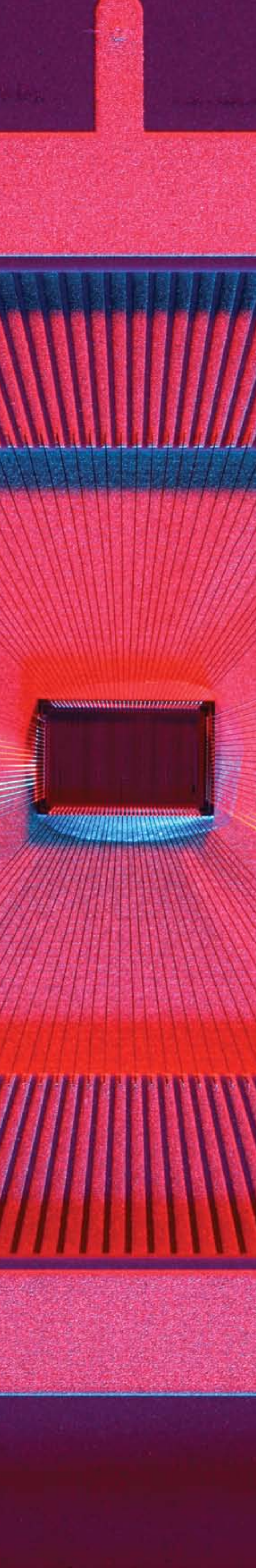
Research into genetic technology continues in the Centre and, in particular, CMOS technology is under investigation to realize fast, robust, biological detection with low-power, high-accuracy, large-scale, integrated processing circuitry. By using the size scaling factor of the semiconductor industry, the detection productivity can be dramatically boosted according to the biological Moore's Law.

CURRENT RESEARCH INCLUDES:

Genetic and epigenetic testing is expected to revolutionize medical practice by allowing early detection of abnormal phenotype as well as by tailoring treatment to individual patients at an unprecedented level. It will require novel devices that are cost-effective, fast, robust and easy to use and we aim to achieve this via a lab-on-chip system integrating sample preparation, biochemical reactions and ISFET based sensors in standard CMOS.

In addition to genetic changes, epigenetic abnormalities such as alterations in DNA methylation patterns are highly associated with multiple cancer types and/or stages of tumorigenesis. The aim of this research is to develop arrays of CMOS based ISFET sensors for the detection of DNA methylation in specific gene markers.

Semiconductor based DNA sequencing has revolutionised the cost of sequencing the human genome making it more affordable and therefore accessible for early detection and therapy of disease. 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 Moores law allowing integration of millions of sensors on one chip. 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.



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 devices for neural rehabilitation

HEAD OF RESEARCH
Dr Timothy Constandinou

Neurotechnology, the application of technology to neuroscience, is a topic that is currently enjoying much interest in the research community. With ever progressing advances in microelectronics and electrode technology, never before have there been so many opportunities to develop advanced devices that effectively interface with neurobiology. 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. For example, cochlear implants use electronics to detect and encode sound and then stimulate the auditory nerve to allow deaf individuals to hear.

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. Our research projects are focused both on developing neural interfacing platforms, in addition to application-specific neuroprosthetic solutions.

NEURAL PROSTHETIC APPLICATIONS

Brain machine interface for motor control – Monitoring cortical activity locally using implanted microelectrodes is demonstrating the ability to achieve multi-dimensional motor control. Current devices record from up to 100 channels and typically stream the raw data to an external processor. Our research is developing next generation devices to record from more channels (1000s), extract information locally (spike sorting) and transmit data (transcutaneous) wirelessly directly to output devices (eg actuators).

Brain activity monitoring for epilepsy prediction – The analysis of brain activity including EEG and ECoG, has led to many algorithms aiming to predict and detect epileptic seizures. This project involves the development of a software and hardware platform for real-time neurological monitoring. Our algorithm extracts neurological patterns and aims to classify them. The vision is of a system with the capability to forewarn a patient, doctor or nurse of an impending seizure or use closed-loop stimulation devices to suppress the seizure before it happens.

Intraspinal microstimulation for SCI – This emerging technique involves directly stimulating motor neurons in the spinal cord. This holds the promise of recruiting better co-ordinated and less fatigue-prone muscle movements with lower stimulation energy than stimulating the muscles directly. Our research is developing a high-channel count platform for achieving highly focused intraspinal microstimulation via a fully wireless link for power and data transfer.

Vagus nerve stimulation for appetite regulation – The vagus nerve is the principal pathway of sensory information passing from gut and other vital organs to brain and spinal cord. Vagus nerve stimulation (VNS) has emerged as an implantable technology to stimulate the pathway and has been used in appetite control, depression and epileptic seizure suppression. Despite this progress and emerging technology, our level of control over it is severely limited. The technology we are developing allows us to selectively stimulate and record from the vagus nerve, and measure intra-nerve chemical activity. This fine level of control will allow us to regulate appetite in obese patients among other important functions.

Proprioceptive feedback for upper-limb prosthetics – Sensory feedback from the body is key to enabling fine motor control, natural (low cognitive load) movement and non-visual awareness of the position of your body. Individuals with prosthetic limbs or suffering from certain types of neural damage lack this proprioceptive feedback in the affected body areas and as such struggle to learn to control them and are unlikely to achieve high levels of coordination. Our research is investigating the provision of artificial proprioceptive feedback from a prosthetic limb by direct electrical stimulation of nerves using a neural implant.

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 Skellern provides his vision of biomedical electronics in 2030 and Professor Wells discusses what makes a world class research centre.

Professor David Skellern

AO Hon DSc (Macquarie) FTSE FIEE HonFIEAust

David Skellern, a former Head of the Department of Electronics at Macquarie University in Sydney and CEO of National ICT Australia, is distinguished for his work on Wireless Local Area Networks which led to a revolution in world communications. He has received many awards including the CSIRO Research Medal and the ATSE Clunies Ross award. He was appointed an Officer of the Order of Australia. for distinguished service to science and engineering.

By 2030, the internet will be the world's communications infrastructure, a single layer of connectivity with wireless access binding us all to each other and to the things in our environment; it will be cheap and fast enough for all our needs. The internet will be woven tightly into the fabric of everyday life. It will be invisible, taken for granted, and heavily relied upon. The pervasive connected world in which everyday objects and the environment interlink has been labelled the 'Internet of Things'. We're seeing it emerge now, with ever more things having embedded sensors, intelligence and wireless communications. Over time, the internet will map our real, physical world onto cyberspace in increasing detail.

The internet of things is fuelling innovation in systems for interacting with and managing our environments. New applications are appearing every day in just about any area you can think of – including the home, retail, business, health, agriculture, energy, infrastructure, transport and government.

You might think that the way we will play in this new system of the world is through our phones, tablets and computers. And you would be right, in part. Yet the remarkable and exciting future is that the activity of the myriad devices on us and inside us will dwarf our active interaction. These wearable and implantable devices are the focus of research in the Centre for Bio-Inspired Technology. Professor Chris Toumazou and colleagues have established the Centre as a leader in the field of devices for personalised medicine.

Following my retirement in 2011 from Australia's National Centre of Research Excellence in Information and Communications Technology (NICTA), and after a year of a little Board work, a lot of leisure travel and frequent stays in London to see children and grandchildren, I was keen to connect with a frontline, innovative research group. The range and excellence of Imperial College's Centre for Bio-Inspired Technology's research drew me to become a part-time visitor here in 2012/13.

It is easy to feel at home in the Centre. With joint goals of research excellence and commercial outcomes, its culture and approach to research are close to what I had worked to achieve at NICTA. The Centre's projects are multidisciplinary and use-inspired, with researchers pursuing deep insights and the advancement of knowledge while also finding genuine, cost-effective solutions to some of the important challenges in medical diagnosis and therapy by inventing breakthrough circuits and systems. The culture is open, collaborative, entrepreneurial and respectful. In combination with the very good facilities and infrastructure, this culture provides an ideal environment in which to nurture some of the world's brightest minds to invent and commercialise new solutions to these challenges.

By 2030, people with health problems will wear or will have implanted small devices that will communicate vital statistics and detailed information to their medical health provider. But we don't have to wait until 2030 to see examples of that future. The Centre for Bio-Inspired Technology's researchers are creating it now. The biomedical devices developed by its researchers over the past decade and now starting to be commercialised will be the exemplars of future biomedical devices. They will generate major impact in the health sector.

The Centre's digital plaster vital signs monitoring technology, the basis of the commercially available SensiumVitals® patch, for example, is an advanced semiconductor-based technology representative of how all routine patient monitoring will be done in the future. The sick will go home from hospital earlier, as they will be monitored remotely. This will give the elderly and the sick greater independence, unclog our hospitals and free up resources for urgent cases. With the current demographic trend towards an aged population, these services will form a critical part of our health system.

Another state-of-the-art semiconductor technology developed at the Centre is a platform for highly targeted, ISFET-based next-generation DNA sequencing. While this is currently being used in revolutionary, rapid diagnosis, point-of-care device applications, it is possible to imagine it being developed in the future for routine remote monitoring of our health.

The many projects currently underway in will produce a stream of innovative personal medicine technologies over the coming years.

What have I personally been doing? A good deal of my time has been taken up in professional service as Vice-President Technical Activities of the IEEE Circuits and Systems Society and as Co-General Chair of the 2014 International Symposium on Circuits and Systems. Beyond that, I have been able to act as a sounding board and offer advice in a small way to several projects, particularly on commercialisation and technology transfer matters, and to contribute generally to the life of the Centre.

In trying to gain a better understanding of Melina Kalofonou's research involving detection of DNA methylation as a marker for certain types of cancer, I came across an intriguing paper suggesting that DNA methylation may be how certain memories are stored in the brain. In continuing to explore that suggestion in the literature, for which there is increasing supporting evidence, I am finding it necessary to widen my knowledge of several disciplines including neurophysiology and biochemistry. It is slow going! My hope, perhaps naïve, is to be able to converge on how we might bring the knowledge, technologies and skills of the Centre to bear on better understanding of how brains store and retrieve memory.

It is inspiring to spend time at the Centre for Bio-Inspired Technology. I thank everyone in the Centre for the privilege of working with and alongside them.

Professor Peter Wells

CBE FRS FREng FMedSci FLSW

Professor Peter Wells is distinguished for pioneering the application of the physical and engineering sciences to the development of ultrasonics as a diagnostic and surgical tool which has revolutionised clinical practice. He has been a Visiting Professor at Imperial College since 2002 and is a regular visitor to the Centre providing advice and support to the research teams. He is Emeritus Professor of Physics and Engineering in Medicine at Bristol University, Distinguished Research Professor at Cardiff University and Visiting Professor at University College London.

The number of UK Universities with truly major world-class medical engineering activities can arguably be counted on the fingers of one hand and, of these, only the Centre for Bio-Inspired Technology at Imperial College London seeks primarily to pursue research into devices which mimic biological processes.

Leadership positions of this kind do not come easily. They depend on having the right people, the right philosophy, the right research, the right collaborations, the right facilities and the right funding. The Centre for Bio-Inspired Technology has existed for only five years but, during this time, it has achieved numerous successes.

These are the ingredients for success, but what does 'success' really mean? Certainly, success has many facets. In healthcare, success begins, of course, with the formulation of a research strategy designed to tackle challenges which are truly important, whether to a small number of people with rare diseases or to a multitude whom science – in its broadest sense – has yet fully to benefit. For instance, profoundly deaf children are thankfully very few. On the other hand, obesity is a modern pandemic. For both of these conditions, the effects on the individual and on society cannot be overstated. The remarkable fact is that both have been tackled, or are being tackled, in the Centre and what in the past might have been expected to be amenable only to surgery, drugs or psychiatry now seems often likely most effectively to be managed by novel and ingenious devices, the products of engineering science.

Bio-inspired technology is essentially interdisciplinary. It epitomises the convergence of the life sciences, engineering and the physical sciences. Further examples of problems being tackled by the Centre include the management of diabetes and the measurement of blood pressure. Two other outstanding developments which originated in the Centre come to mind – the wireless monitoring of vital signs by an unobtrusive 'digital plaster' and the invention the label-free non-optical method for detecting and quantifying target DNA sequences. All this is highly competitive and challenging engineering science in which the Centre leads the world.

The motto of Imperial College is 'Scientia imperii decus et tutamen', which means 'Knowledge is the adornment and protection of the Empire' Certainly this has a patriotic ring but underlying it is the notion that it is the pursuit of knowledge which is the purpose of Imperial College. The pursuit of knowledge is indeed the ethos of the Centre for Bio-Inspired Technology and it is on that foundation that all of the Centre's research is built. The results of research can only be useful if they are published so that others can learn from them and take them forward, or if they are exploited commercially so that they can bring benefits to those who can use them – in the case of bio-inspired technologies, these are ultimately often patients with relevant diseases and those who care for them. But there is more to it than this. The Centre thrives because of the constant stimulation of its young researchers – including those being trained in research methods – who are overflowing with new and exciting ideas, many of which are sure to be the seeds of tomorrow's revolutions in the application of engineering and physics to the life sciences. In healthcare, the traditional silos of science and medicine are giving way to a new era of interdisciplinary research in which the Centre for Bio-Inspired Technology is blazing the trail.

An integrated sensor in clothing: Emerging wireless sensing technology for the management of osteoarthritis

Dr Irina Spulber

Research Associate in integrated sensing systems

Osteoarthritis is a debilitating disease of the joints for which there is currently no 'cure'. Lifestyle management is the only option available to sufferers. Here in the Centre researchers are developing unobtrusive wireless sensors which can be incorporated into clothing to monitor function and enable physiotherapists to devise customised rehabilitation strategies for patients.

Osteoarthritis (OA) is a highly disabling degenerative disease of the joints characterized by damage to the surface of the joint due to progressive disappearance of hyaline articular cartilage, with subsequent sclerosis and formation of cysts and osteophytes, resulting in joint pain, stiffness and reduced range of joint motion. Any synovial joint can develop osteoarthritis but it is often more painful in weight bearing joints such as the knee, hip, and spine than in the wrist, elbow, and shoulder joints. Traditionally considered as a 'wear-and-tear arthritis', OA is often said to be the natural consequence of aging, although younger people may also develop OA as a result of injury or overuse. As age is the strongest predictor of OA, increases in life expectancy and ageing populations will result in a greater occurrence of the disease.

Public health data show that the prevalence, health impact, and economic consequences of OA are expected to increase dramatically during the next couple of decades, predicting to make osteoarthritis the fourth leading cause of disability by the year 2020.

To date, there is no cure for osteoarthritis, the condition is mainly managed through lifestyle modifications complemented by pain-killing treatments. Surgical management is generally reserved for failed medical management where functional disability affects a patient's quality of life. Experts in the field suggest that appropriate therapy for OA combines one or more pharmacological agents with exercise, weight loss and physical therapy.

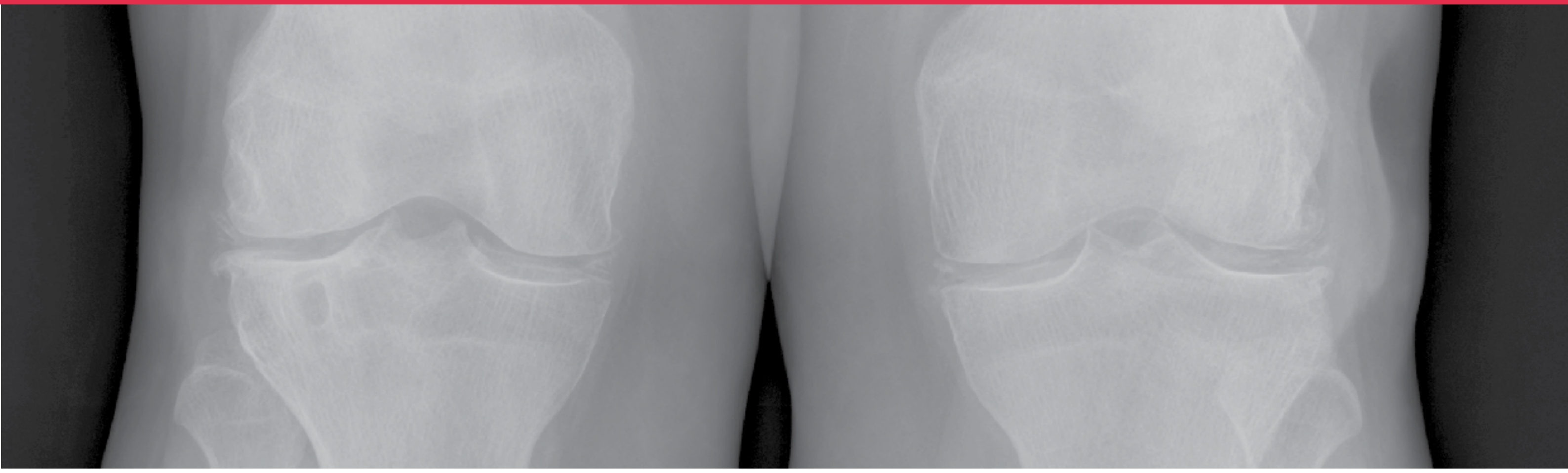
Correct regular exercise along with minor adjustments in the movement patterns, have been shown to significantly improve function, alleviate pain, and delay the need for surgical intervention. 87% of patients who did exercise felt the benefit, thus one way of effectively controlling the growing burden of OA is prioritising conservative approaches.

Here in the Centre we are taking part in a research programme being conducted under the umbrella of the Medical Engineering Solutions in Osteoarthritis, an interdisciplinary Centre of Excellence funded by the Wellcome Trust and the EPSRC.

This collaborative research brings together expertise from Imperial College London's Department of Surgery and Cancer, the MSk Lab (Musculoskeletal Laboratory) at Charing Cross Hospital; the Institute of Biomedical Engineering, Centre for Bio-Inspired Technology, and Toumaz Limited, an ultra-low power wireless technology company.

VISION

The use of innovative technologies is an emerging concept, however the available products on the market present themselves with major limitations in terms of complexity, cost and/or patient acceptability. Our project aims to exploit recent technological advances to develop an unobtrusive, low power, inexpensive, medical wireless sensor system capable of assisting OA patients in their rehabilitation process. Sensors, either body-worn or embedded into smart clothing, will monitor joint motion, muscle activation (EMG) and body movement patterns. The wireless sensor system will monitor function remotely and provide appropriate feedback to both patient and practitioner thus assisting the physiotherapists in devising customised rehabilitation strategies to improve compliance and therapy outcomes as well as motivate the patient to continue exercising.



OUR APPROACH

The group research effort is focused in several directions which include: detecting gait asymmetry with wireless accelerometers and EMG sensors

Gait analysis offers a powerful tool for assessing an individual's biomechanical characteristics for both diagnosis and rehabilitation purposes. However, due to the complexity and high cost of the monitoring equipment, gait analysis is mainly performed in dedicated laboratories. With the recent advances in sensor technology, there is scope to investigate the potential of wireless sensors in assisting clinical practitioners and patients by taking gait analysis outside the laboratory. Small, wearable sensors come to meet this desiderate as they are an inexpensive alternative to the standard gait equipment and can operate in any location, eliminating a number of constraints on the subject.

To this aim, a study was conducted on the combined use of wireless triaxial accelerometers and wireless EMG sensors for monitoring walking patterns. The preliminary trial tests consisted of volunteers wearing the sensors while performing two walking types: 'normal' walking, at a self-selected speed, and an unbalanced, or 'asymmetric' walking, where the subject was requested to limp, the limp being artificially induced by placing a small solid object under the left foot. Data analysis looked at frequency domain differences between normal and asymmetric walking data sets collected simultaneously from triaxial accelerometers and EMG sensors. Frequency and time-frequency analysis of the data provided insights into the spectral content of normal and asymmetric walking. It was found that both acceleration and EMG spectra of asymmetric walking data were shifted when compared with the normal walking data set.

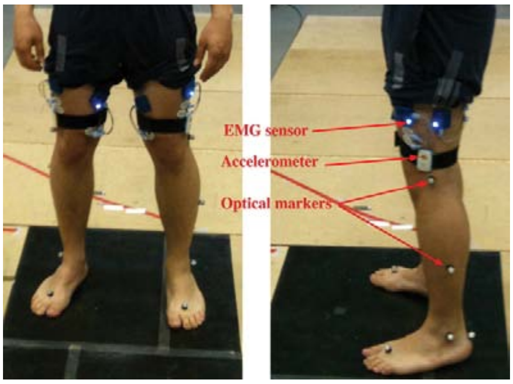


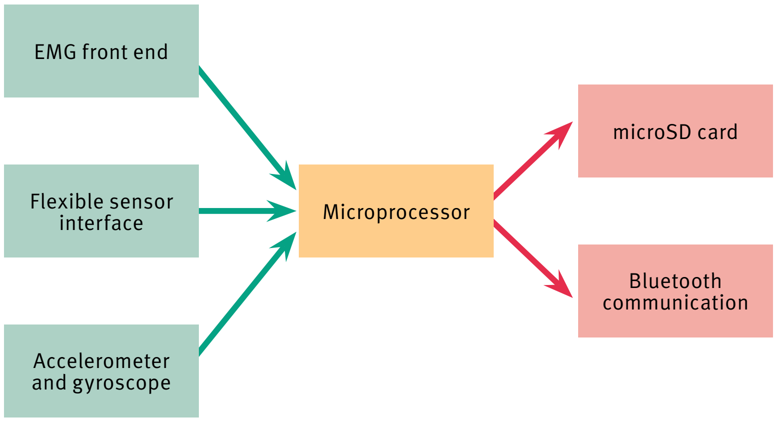
Figure 1. Subject wearing optical markers, Sensium pebble and wireless EMG sensors

The frequency shifts were quantified by the median frequency, a frequency domain parameter that seems to incorporate discriminative power. The EMG sensors complemented the accelerometer and it is expected that a multi-parameter approach will enhance the discrimination capability of the system. The ultimate aim is to factor in key signal features (spatio-temporal and frequency domain parameters) for both acceleration and EMG data into a single index that can be used for intelligent assessment of pathological gaits. This will assist physiotherapists in devising customized rehabilitation strategies to improve therapy outcomes.

SMART GARMENT – A MULTI-SENSOR WIRELESS PLATFORM INTEGRATION FOR FUNCTIONAL REHABILITATION

Non-invasive sensors have huge potential for disease prevention, diagnosis and rehabilitation. When integrated into smart clothing they can enhance healthcare both in the hospital and home environment. The aim of this research is to develop a clinically driven, patient-centered, integrated smart garment for osteoarthritis management. The garment should be able to accurately measure knee joint kinematics and to assess patient's functional activities in their daily environment, providing clinicians with markers of performance and change and ultimately enable biofeedback based rehabilitation. The smart garment can thus support independence and reduce functional decline by guiding the patient in exercises appropriately designed to rebuild joint function.

Figure 2. Block diagram of the multi-sensor wireless node



The project revolves around two key components: the development of a multi-functional, multi-sensor wireless node tailored for addressing specific needs of an OA patient; and flexible conductive polymer sensors integrated into a smart garment for monitoring rehabilitation process.

A multi-functional, multi-sensor OA platform was developed in the form of a novel wireless node. The aim was to develop a small, unobstructive sensor node that can be discretely attached to the garment or placed in a pocket, run from a 3V battery with the ability to collect kinematic data and monitor the knee joint activity for the purpose of rehabilitation. Alongside the embedded triaxial accelerometer and gyroscope, the platform also incorporates an EMG front end and the analogue interface circuitry for the flexible polymer sensor. The node offers the option of on-board data storage on a micro-SD card or can stream data wirelessly to a PC via Bluetooth. A diagram depicting the multi-functionality of the developed sensing node is shown in Figure 2.

Flexible sensors can be defined as sensors that can deform without breaking. Conductive polymer sensors alter their resistance when stretched and were considered for integration onto the smart garment. A carbon composite material consisting of 20% conductive graphitized carbon black nanopowder (CN) and 80% non-conductive polyether resin was developed in thin film sheets that were subsequently sliced in 10 mm wide strips. Each sensor strip had connectors attached at each end and are mounted on the garment to cover the knee joint. When attached to the joint, movement stretches the sensor changing its resistance from which measures of range of motion can be determined, thus showing potential to be a simple but valuable objective clinical marker of knee function.

A first prototype of the sensor node was successfully designed, fabricated and tested and is currently being used in preliminary trials at Charing Cross Hospital's Human Performance Laboratory. A second generation of the node with added functionalities is currently being fabricated and assembled with a focus on size and the power consumption minimization.

The smart garment is designed and developed for OA management but it can be easily tailored for sports and fitness applications, and it is envisaged that the technology is readily transferable over a broad spectrum, ranging from the high end, high specification applications in improving sports performance to a low end, accessible, affordable tool for home rehabilitation with widespread social impact.

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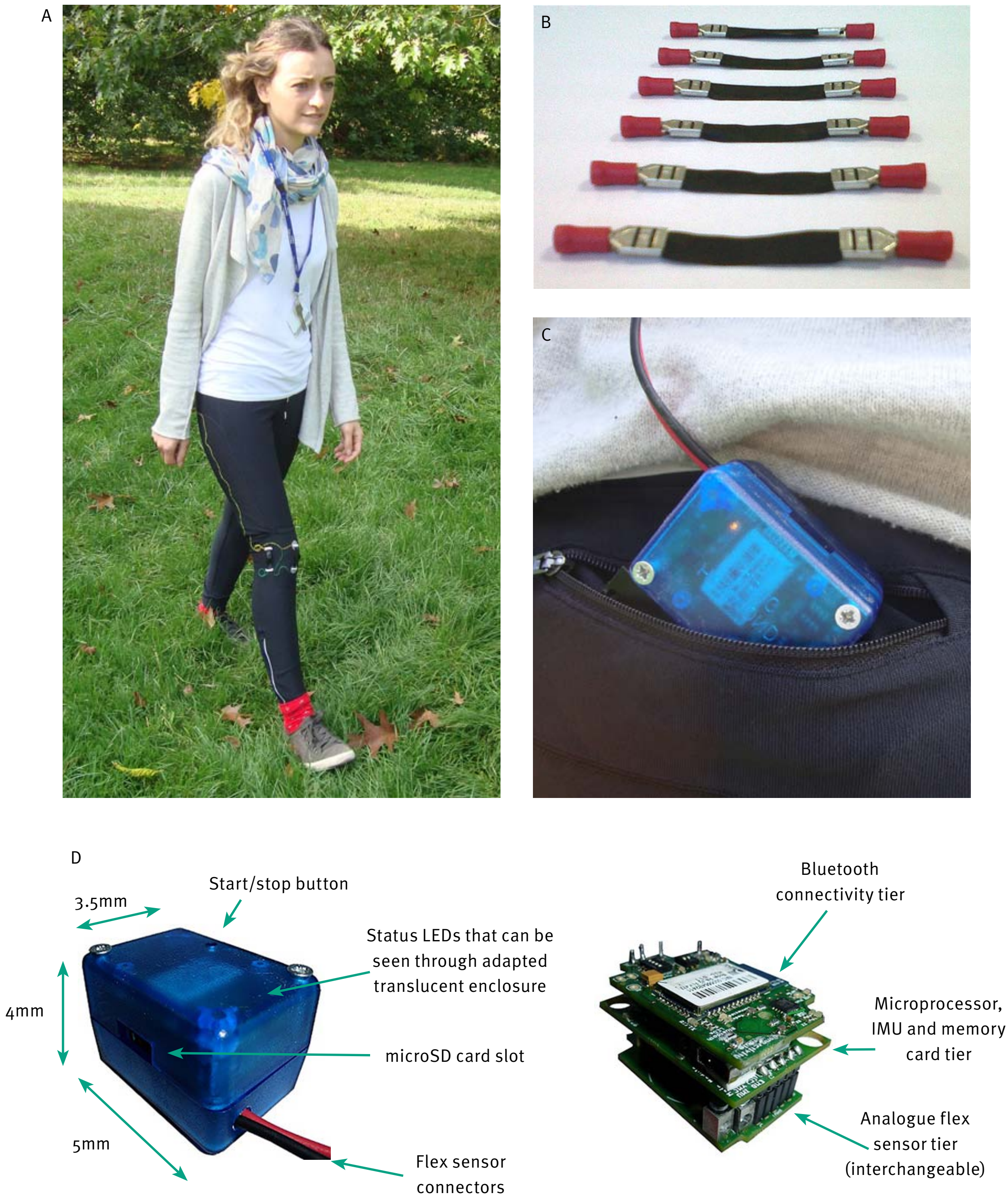

Figure 3. Smart garment prototype (A), flexible sensors (B), wireless sensor node positioned into the back pocket of the smart garment (C) and sensor node tiers and its overall dimensions (D)

The i2move Project: Intelligent implantable modulator of vagus nerve function for the treatment of obesity

Dr Andrea Alenda Gonzalez

Research Fellow in Neuroscience and Scientific Writer

Obesity is a major healthcare challenge in the developed world and, increasingly in the developing world. Innovative treatments are needed to find new ways of meeting this challenge.

In this project, researchers are developing an implant to interface with the vagus nerve to treat obesity. A new generation of neural interface will provide an innovative treatment for people who suffer from overweight and obesity. There is currently no satisfactory treatment available, existing surgical treatments do not always provide a solution and the risks are not always acceptable.

SUMMARY

The World Health Organization (WHO) defines obesity as an excessive fat accumulation that may impair health. The consequences of obesity include cancer, diabetes, heart disease and musculoeskeletal disorders. In 2010, the WHO estimated that in Europe 1 in 5 adults were obese. Currently in England, 60% of the adult population is overweight or obese and these numbers are predicted to rise steadily in the future.

Obesity and overweight affects all age groups. In 2011 the WHO estimated that 40 million children under five were obese, in England three out of ten children are obese or overweight. Being obese and overweight shortens life span. The current life expectancy of children in the United States is already lower than that of their parents due to obesity; the first time since the beginning of the twentieth century that a younger generation has a shorter life expectancy than that of its parents.

Obesity and overweight is the result of a chronic energy imbalance where both diet and exercise have an impact. However, what may seem to be an individual lifestyle problem, where people lack the will to stick to a healthy diet and fail to exercise sufficiently, is not really capturing the whole picture. Our socio-economic environment promotes obesity. Modern life demands less physical effort but the cheap supply of high-calorie foods means we are more likely to end up gaining weight rather than losing it. A diet substituting fruit for cake is healthier but quantity is also a factor – too many apples is still too many apples. Any excess in calories, regardless of their source, is stored in the body as fat.

BACKGROUND

Today the most effective treatment for obesity is bariatric surgery, a procedure which results in a dramatic reduction in excess weight of between 50–70%. In the last few years, the number of bariatric operations performed by the NHS has increased dramatically to around 8000 each year. Gastric band surgery has seen a two-fold increase from 2006 to 2008 and it has continued at this level whilst gastric bypass surgery has increased up to 6 times between 2006 and 2012. In England, more than 60% of adults are obese or overweight, which makes it economically unfeasible to perform bariatric surgery in all cases.

Bariatric surgery is not an ideal treatment and is only used as a last resort for patients with morbid obesity as it involves risks of perioperative mortality, long-term complications and does not guarantee long term weight loss. Bariatric surgery is not recommended for all obese patients, and especially for children. A safer alternative treatment is urgently needed.

The vagus nerve, which mediates the information between the gut, the brainstem and the brain, is starting to draw some attention as an alternative way to tackle obesity. Patients who have had a complete (vagotomy) or a partial removal of the vagus nerve were observed to lose weight. However, this procedure is irreversible and is associated with uncomfortable side effects. A safer option is to implant a device which will stimulate or block the activity of the vagus nerve causing an impact on the satiety messages the nerve sends to the brain and thereby control appetite.

The aim of this Project is to develop an implant for vagus nerve stimulation that would provide a better alternative to bariatric surgery for treating obesity.

THE RESEARCH TEAM

Professor Sir Stephen Bloom, a leading researcher in the fields of obesity and diabetes based at St Mary's Hospital (Imperial College Healthcare NHS Trust) and Professor Chris Toumazou, Director of the Centre for Bio-Inspired Technology and a specialist engineer in the development of biomedical devices, are leading a multidisciplinary team of electrical engineers, physiologists and clinicians.

Professor Bloom's laboratory studies the mechanisms by which bariatric surgery is effective in producing weight loss. They have demonstrated that gut hormones regulate appetite, energy expenditure and glucose levels in the blood.

Initially it was thought that following bariatric surgery patients lose weight because of their restricted capacity to eat. It has since been shown that after surgery patients show a modification in gut hormones and gut microbial flora that affect their satiety levels, and their desire for high-caloric food is decreased which consequently has an impact on weight loss.

Professor Toumazou has extensive experience in developing bio-inspired technology with a direct application in medicine. His group of engineers is interested in using obesity as a paradigm for the development of a new generation of neural interfaces.

"If we can develop technology which can venture into parts of the biological system that have never been ventured into before, we will discover new biological mechanisms. We will then use these to inspire technology which we can use to replicate those biological systems.

In this particular case, we have the wonderful idea of using the vagal nerve – the wondering nerve – as a way of understanding hormone behaviour from the gut. We will then use technology that has never been used before in that domain to copy and replicate the signature of those hormones to send the messages we need to the brain which the brain will then understand and use to control biological systems, in this particular case, obesity."

Professor Chris Toumazou

Body mass index

The body mass index (BMI) is a measurement of weight relative to height.

The BMI is reached by dividing a person's weight by their height squared, (kg/m2). A result of 25 or more is classified as overweight; 30 or more is classified as obese; more than 35 is classified as morbidly obese.

The BMI can fail to capture the true state of a person's health. It is an overall measure that takes into account the total weight of a person, it does not indicate what percentage of that weight is body fat and what is muscle (lean tissue). What is critical in the impact of overweight and obesity is the amount of body fat.

An elite athlete might have a BMI over 25, which is classified as overweight. However, this additional weight might be due to muscle tissue rather than body fat. Contrary to what the BMI is indicating, the athlete would not have an unhealthy weight.

With advancing age there is a gradual change in metabolism and, often, a decrease in physical activity. This can lead to a higher proportion of fat tissue compared to lean tissue. The BMI result might indicate a healthy weight but it does not show the proportion of body weight which is fat.

The Research Team: from left to right – Dr Amir Eftekhar, Professor Chris Toumazou, Prof Sir Steve Bloom, Dr James Gardiner and Mr Ioannis Christakis.

The multidisciplinary team includes surgeons, physicians, engineers, chemists and neuroscientists. This creates a stimulating environment which challenges previous conceptions and aids a wider understanding across fields. One of the main challenges is communication between professionals with different levels of expertise.

"It is a cross-disciplinary environment, everyone has to come to the same level […]. When everyone can start speaking the same language and understand each person's capabilities and limitations, you really start finding solutions […]. The challenge is making sure that communication is clear, concise and works."

Dr Amir Eftekhar

OUR APPROACH

The implants currently in use for vagal nerve stimulation are able to block the activity of the vagus nerve by applying electrical pulses. Although they have had some rate of success, the stimulation strategy is general and unrefined. The coarse stimulation can also reach adjacent areas producing unwanted side effects.

The first engineering challenge is to create a device capable of providing a sophisticated range of stimulation that can be delivered with precision. We have designed a bio-compatible device that combines two cutting edge, stimulation strategies: multi-contact cuff-electrodes wrapped around the nerve to deliver a local, yet broad, stimulation combined with specialized nerve penetrating electrodes aimed at fine nerve fibres to provide fine stimulation. This innovative solution will give the implant a fine control of vagus nerve activity.

"Talking with surgeons about the difficulty of implanting electrodes in the vagus nerve is enough to get our brains ticking to finding solutions. The more feedback we get, the better the design we will be able to come up with."

Dr Amir Eftekhar

Current knowledge on how the vagus nerve works relies on data extracted from anesthetized animals or from dissected nerves, thus there is a limited understanding as to how the vagus nerve responds to dynamic changes in the gut. There are no devices capable of measuring the activity of the vagus nerve in an awake, moving animal. A neural interface that reads the electrochemical signals of the vagus nerve would result in a major technical breakthrough that would enable the understanding of the role of the vagus nerve in the control of appetite and metabolism.

The second engineering challenge is to design an implant that is able to monitor the electrochemical signals of the vagus nerve. For this purpose, we have designed a device with a potentiometric chemical sensor embedded on the penetrating electrodes. The principle behind this is a Field Effective Transistor (FET) that has its metal gate replaced by an electrode immersed in electrolyte solution that contacts the transistor's gate oxide serving as an ion sensitive membrane. So the modified FET would work as an Ion Sensitive Transistor (ISFET).

This innovative technical solution opens the possibility of identifying the electrochemical patterns of the vagus nerve for both normal and pathological conditions and to understanding the dynamic response of the vagus nerve to gut hormones released in food ingestion.

The novelty of this approach is to deliver a stimulation that would resemble the natural behaviour of the vagus nerve, providing a baseline of the safest, most efficient way of stimulation tailored to each patient's physiology. This state-of-the-art neural interface will be able to modulate its activity according to the dynamic changes of the vagus nerve.

The third engineering challenge is to design an intelligent chip with the capacity to mimic the neural signals for appetite control. The implant would act like a sophisticated pacemaker, modulating its activity according to the input from the gut, regulating food consumption by sending the brain satiety signals.

This allows unprecedented electrochemical monitoring combined with a sophisticated range of stimulation with an intelligent chip that would mimic the individual's physiological signals of satiety. A new wireless neural interface with this state-of-the-art technology will provide an innovative solution to a major public health crisis.

The study and treatment of obesity is only one example of a specific application of this neural interface. This technology holds the potential of serving as a solution to any setting where there is a need to understand the dynamics of the nervous system, such as neuropathy, epilepsy, drug monitoring and prosthetics.

This new device will serve as the basis of a new generation of neural interfaces.

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Socioeconomic factors affecting obesity

Obesity has reached epidemic levels affecting high-income and emerging countries. It affects people regardless of gender, culture and age. The factor that seems to have the highest incidence in obesity is the socio-economic background.

"Obesity is a disease of the poor. Poor people cannot afford healthy food, so they will only eat junk food, while wealthy people can afford having a healthy diet" explains Mr Ioannis Christakis, Bariatric Surgeon and a member of the Project Team.

Exposure to fast food at a young age increases the chances of becoming obese: children are more likely to become overweight as adults if they are overweight as teenagers. In 2011, WHO reported that more than 40 million children worldwide under the age of five were overweight or obese. Of these, 30 million were in developing countries and 10 million in the highest income countries.

Mexico leads the ranks of the highest rate of obesity among its population. Nearly 4 out of 5 adults are overweight or obese. Elsa Cornejo – a community health worker in Mexico – explains that when trying to promote healthy diet in the rural areas of Mexico, mothers reply that they base their food choices on economic value, feeding their children with ramen and soft drinks. Elsa Cornejo quotes "I will buy what is cheapest in the supermarket, whatever I can afford".

The development of an easily deployable intraocular wireless pressure sensing implant for patients with rapidly progressing and blinding glaucoma

Dr Mohammadreza Bahmanyar

Research Fellow in Cardio Vascular Technology

Glaucoma is the commonest cause of irreversible blindness in the world. Diagnosis is by measurement of the intraocular pressure but this monitoring and assessment can only be done infrequently. Using the principles established in developing a continuous blood pressure monitor, we aim to improve the diagnosis and monitoring of glaucoma.

BACKGROUND

The aim of this project is to develop a pressure sensing structure of suitable dimensions that can be coupled with an implantable antenna to form an RF interrogable implant that will hopefully be used in glaucoma patients in future.

Glaucoma is the commonest cause of irreversible blindness in the world. It affects about 4% of the population over 40 years of age, and because it is asymptomatic and is often diagnosed late, unless adequately treated, it leads to blindness. A key feature in diagnosing and monitoring glaucoma is measuring the intraocular pressure (IOP). However, like blood pressure, the IOP varies normally with respect to time and physiological changes. Currently all therapies in glaucoma aim at lowering the intraocular pressure, but the monitoring and assessment of patients' IOP is performed by infrequent measurements usually in a hospital clinic.

Glaucoma patients are typically assessed with single, day time one-off measurements, and it is increasingly recognized that these snap-shot readings cannot adequately reflect an individual's IOP over several days or week, not to mention a single day. Although IOP measurements are sometimes performed more frequently for diurnal curves they are rarely monitored for a full 24- hour period. As in-patient procedures, their use is limited routinely due to their expense, impracticality, nonphysiological and unproven benefit. Despite progress in this field, an implantable device suitable for clinical use in all patients has not yet been developed.

OUR APPROACH

The proposed pressure sensing implant can be described as a wireless passive device, which resonates at a frequency that is proportional to the environmental pressure the device is implanted in. This implanted pressure sensitive resonating structure is pinged by an RF pulse that causes it to oscillate at the pulse frequency. The pulse frequency is chosen close to resonator's natural frequency in order to maximize the energy transfer to the resonator. Once the radio frequency pulse is turned off, the pressure sensitive resonator will resonate at its natural frequency, which is proportional to the eye pressure. This resonance will be detected in the form of a short electromagnetic wave that is radiated back from the implant. This signal can be acquired for signal processing to extract the pressure information.

The implant will be made in a cylindrical shape with the flexibility to conform to the eye surface curvature and will consist of three main parts: an implantable antenna; an acoustic wave resonator integrated with a pressure sensing element and a biocompatible insulating encapsulation.

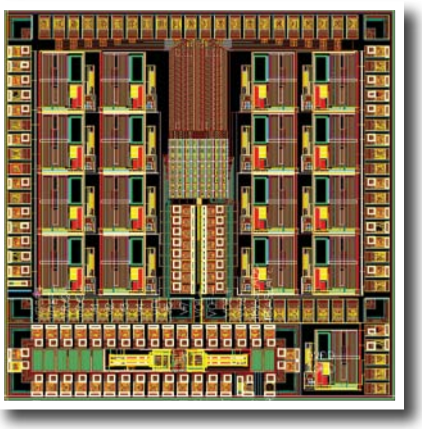
The implant will have a diameter of 500µm and a length of 6mm so that it can be placed, under local anaesthetic, in a simple in-clinic procedure. It will be patient-safe, so that in use and in any failure mode the patient is not at risk. It will also have unlimited readability and lifetime.

This research is being conducted by the Cardio Vascular Group at the Centre, led by Professor Chris McLeod, in collaboration with Professor Maria F Cordeiro of the Imperial College Department of Surgery and Cancer at St Mary's Hospital (Imperial College Healthcare NHS Trust).

Chip gallery

The Centre's researchers have produced five new chips this year making a total production so far of 32 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: **www3.imperial.ac.uk/bioinspiredtechnology/research/chips**

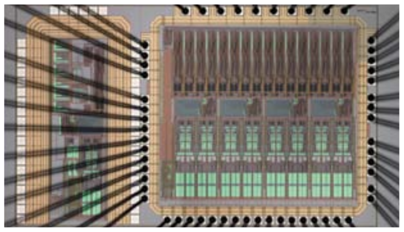


IBE13G03 (Astroboy) – July 2013

Technology: Austriamicrosystems 0.18μm 1P6M CMOS

Purpose: Thermal Microstimulation Lab-on-Chip Array

Designers: Kiichi Niichu, Yan Liu, Ferran Reverter, Konstantin Nikolic, Themis Prodromakis, Pantelis Georgiou, Timothy Constandinou

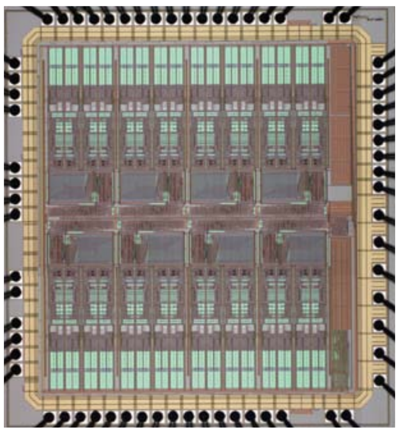


IBE13G01 (NGNI_Smart) – July 2013

Technology: Austriamicrosystems 0.35μm 2P4M CMOS

Purpose: 16-ch Neural Interface

Designers: Yan Liu, Lieuwe Leene, Song Luan, Timothy Constandinou

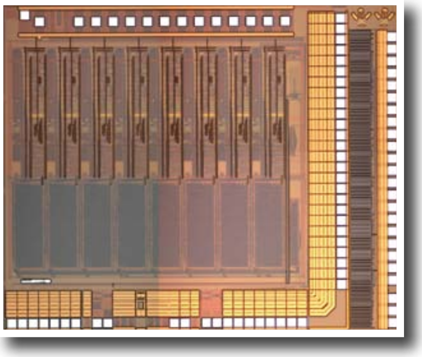


IBE13G02 (NGNI_Dummy) – July 2013

Technology: Austriamicrosystems 0.35μm 2P4M CMOS

Purpose: 32-ch Neural Interface

Designers: Yan Liu, Lieuwe Leene, Song Luan, Timothy Constandinou

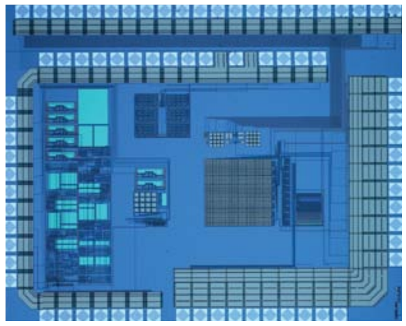


IBE13D01 (Homer) – April 2013

Technology: Austriamicrosystems 0.35µm HV 2P4M CMOS (3.2x3.8mm)

Purpose: 8-ch HV Neural Stimulator

Designers: Song Luan, Yan Liu, Lieuwe Leene, Timothy Constandinou

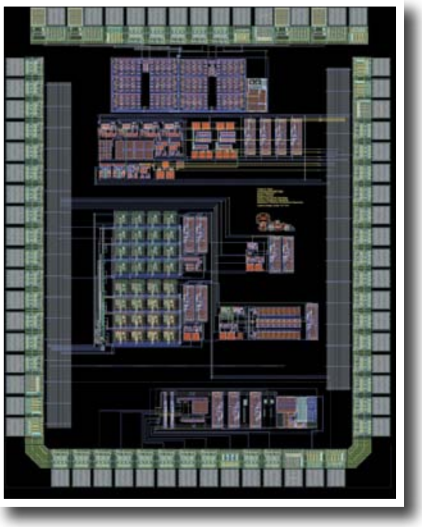


IBE13C01 (Gonzo) – March 2013

Technology: Austriamicrosystems 0.35µm 2P4M CMOS (tbc)

Purpose: tbc

Designers: Yuanqi Hu, Mohammedreza Sohbati, Chris Toumazou, Pantelis Georgiou

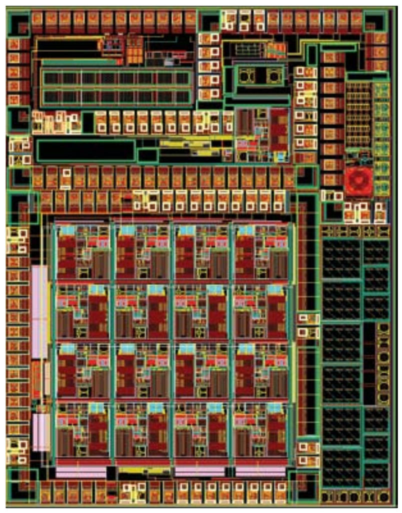


IBE12J01 (KIMI) – October 2012

Technology: Austriamicrosystems 0.35µm 2P4M CMOS

Purpose: ISFET sensing array, multi-channel glucose sensor instrumentation and oscillator

Designers: Yuanqi Hu, Siraporn Sakphrom, Mohamed El-Sharkawy, Yan Liu, Pantelis Georgiou

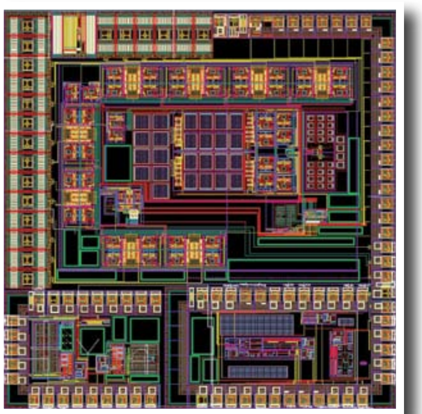


IBE12H01 (NGNI) – August 2012

Technology: Austriamicrosystems 0.18µm 1P4M HV CMOS

Purpose: Neural interface circuits and electro-optical modulator test structures

Designers: Yan Liu, Song Luan, Alexander Serb, Lieuwe Leene, Timothy Constandinou



IBE12D01 (Ian) – April 2012

Technology: Austriamicrosystems 0.18µm 1P4M HV CMOS

Purpose: Neural interface circuits

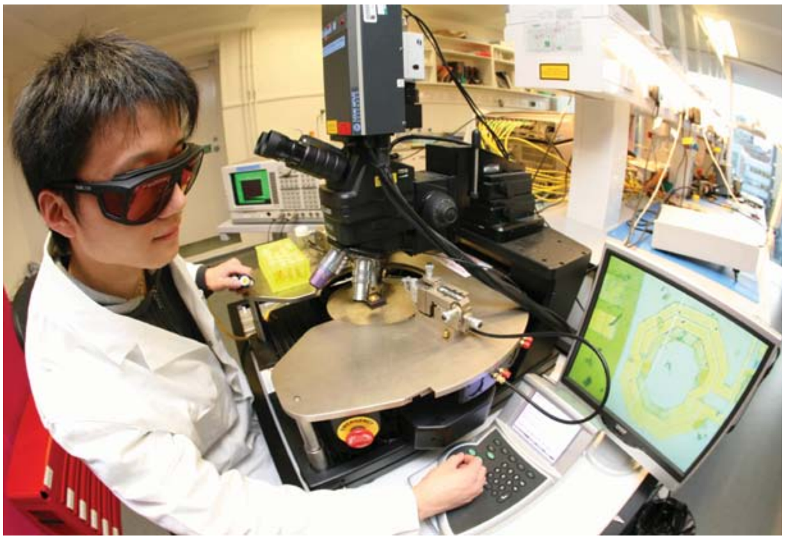
Designers: Ian Williams, Sivylla Paraskevopoulou, Yan Liu, Timothy Constandinou

One of the strengths of the Centre, and a significant attraction for researchers, is the 'state-of-the-art' facility. Professor Toumazou ensured that the initial endowment to the Institute of Biomedical Engineering recognised the quality of the infrastructure, laboratories and equipment needed to make it a centre of excellence not only in research but in the technology transfer essential to fulfilling the Institute's aims.

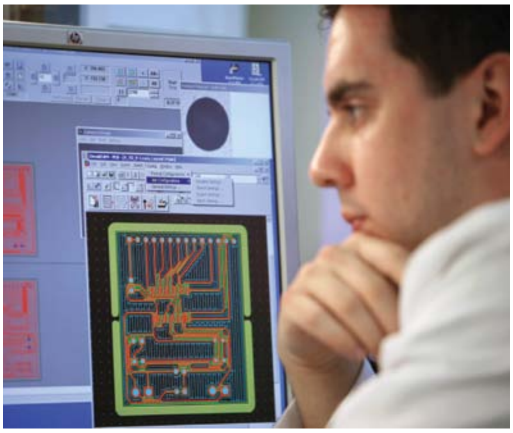
Research facilities

The laboratory areas have been designed to meet the needs of the four main application areas within the Centre's research strategy. The laboratory space is enhanced by specialist facilities which support a range of projects and technology transfer activities including the cleanrooms and anechoic chambers.

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 circuit architectures but to develop novel processing techniques utilising well-established technologies in an innovative way for developing architectures that imitate the functions of biological systems.

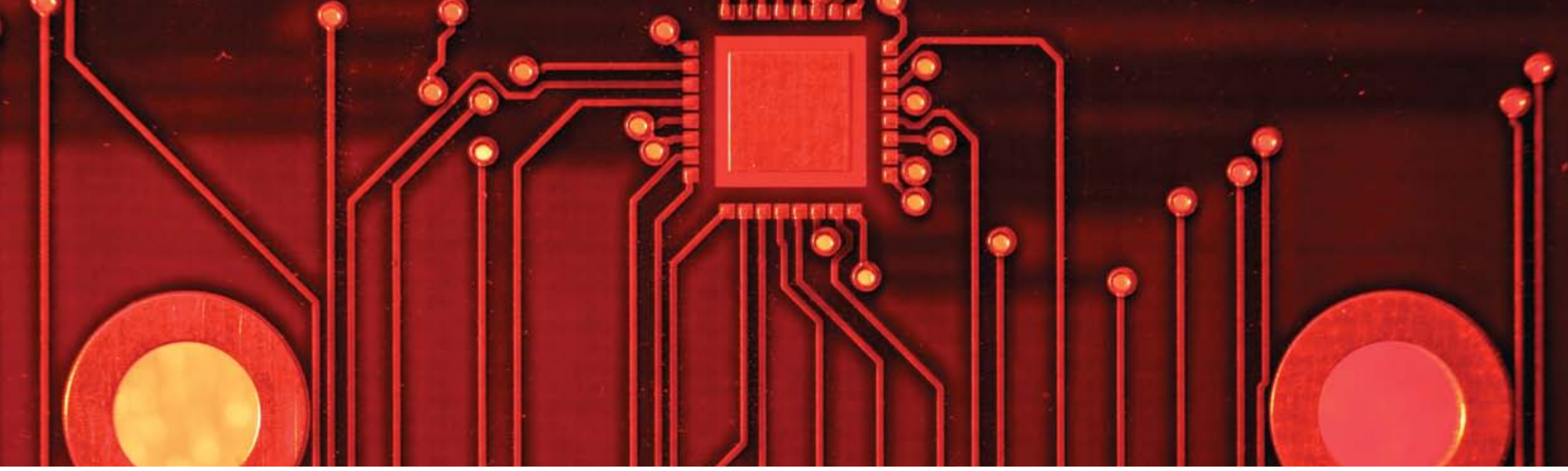


All members of the Centre have access to the full range of facilities and equipment and some researchers have developed a high level of expertise in specific areas to ensure that these are exploited to the full.



BIO-INTERFACING LABORATORY

The primary objective of the research at the Bio-Interfacing Technology (BIT) lab is to develop knowledge and tools to monitor and modulate biological phenomena. This is done by exploring the basic biophysical principles of selective animal and cellular models and testing interfacing technologies developed at the Centre. The purpose of the laboratory is to provide a stimulating and safe environment to conduct experiments that are both engineering and biologically challenging.



CAD LABORATORY

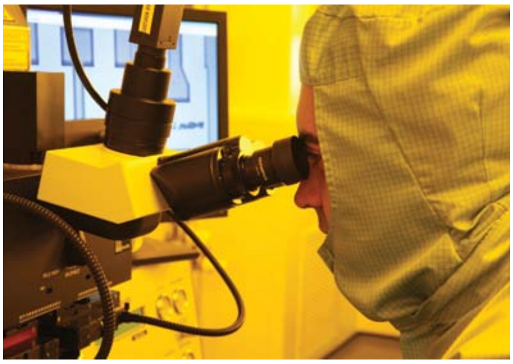
CAD design is an indispensable procedure in modern integrated circuit design and workflow and the laboratory is equipped with high performance workstations and servers. Here researchers develop application-specific integrated circuits (ASICs) which for fabrication at CMOS foundries. All the servers can 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.

PCB WORKSHOP

The workshop includes software for the design, simulation and layout of printed circuit designs. The design is imported to a CNC milling machine for the engraving of PCB tracks and drilling of copper laminate. The fabricated PCB can be enhanced using a solder-mask printing tool kit. Surface mount components can then be attached to the circuit board using our pick-and-place system and the populated circuit board processed in the reflow oven to achieve uniform, reliable soldering.

CLEANROOM SUITE

There are two ISO class 6 cleanrooms (equivalent to US standards class 1000) accessible through the same gowning hall. The largest room, the

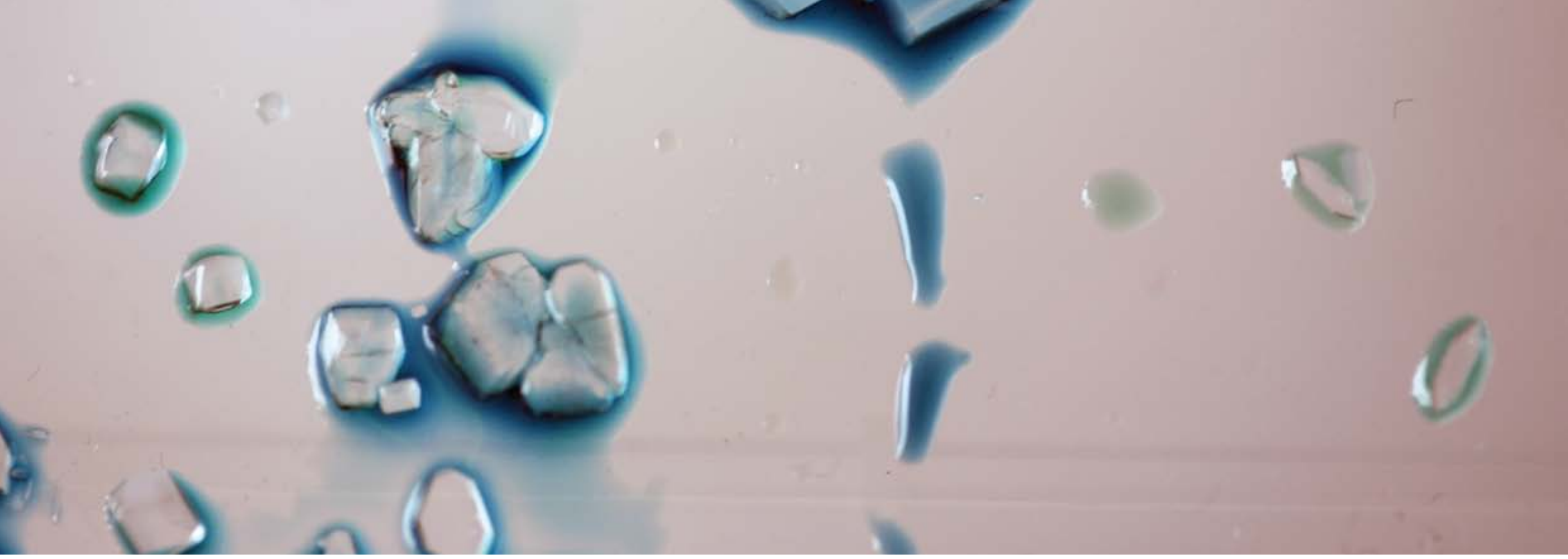


'yellow' room, houses most of the fabrication tools/processes and all relevant inspection and measurement facilities. It is fitted with yellow lights for photolithography, one of the key processes sited within the lab. The second cleanroom is also dedicated to processess requiring an extremely clean environment and houses the wire bonding tool and a PDMS casting bay for creating microfluidic devices. (PDMS is the most widely used silicon based polymer).

ELECTROMAGNETICS LABORATORY

Contained within the electromagnetic test 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.

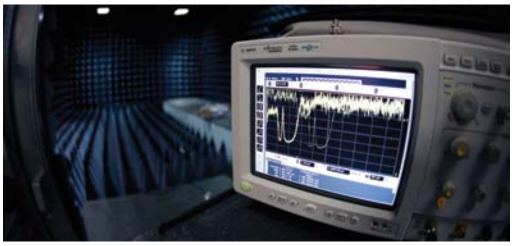


ACOUSTIC ANECHOIC CHAMBERS

The facility includes a large (5m x 5m x 2m) anechoic (acoustic) shielded chamber providing an extremely low-noise environment suitable for all low frequency acoustic, optical and mechanical device/sensor characterisation.

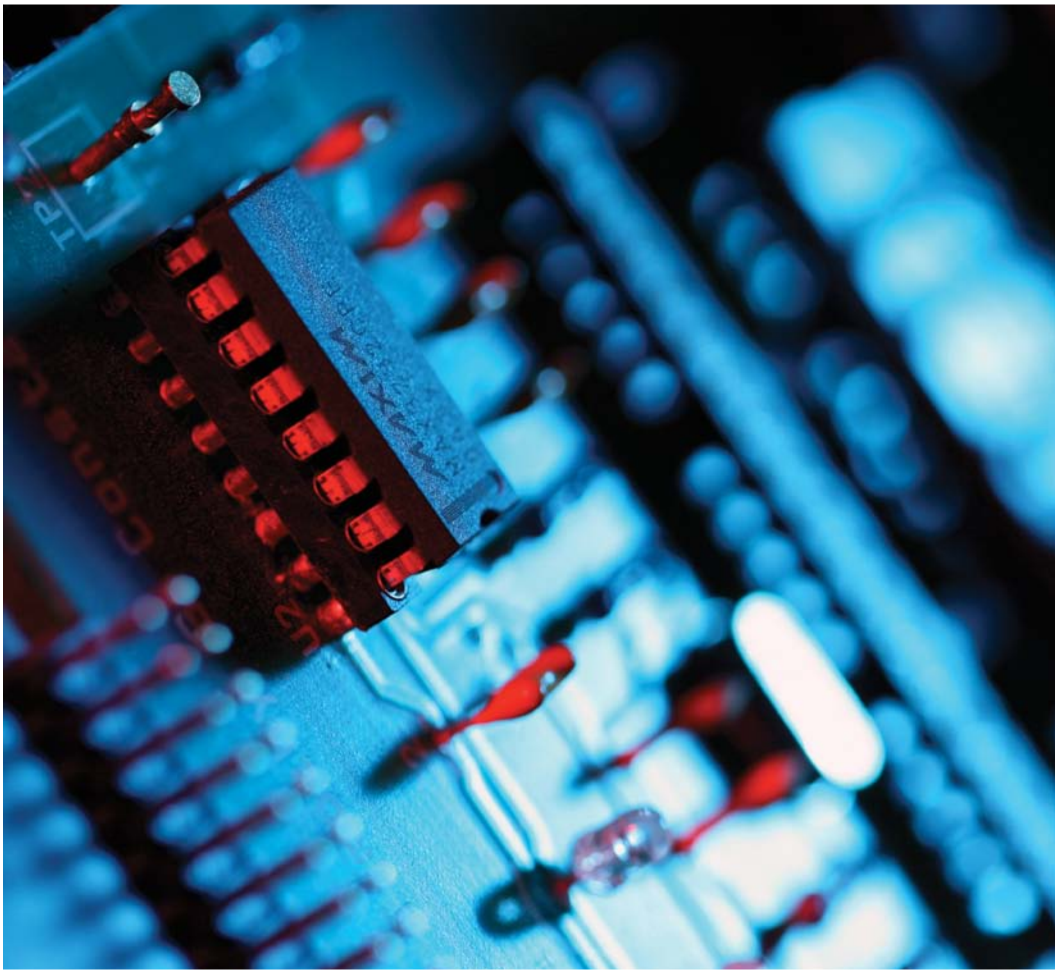
MICROELECTRONICS LABORATORY

The Microelectronics Laboratory is comprehensively equipped for the development, testing and measurement of biomedical circuits and systems. It offers multi-channel low noise recording enabling accurate comparison between the performance of sensors.



OPTOELECTRONICS LABORATORY

The experimental setup has been tailored for photodiode characterisation in the optical to infra-red wavelength including a full suite of automated instrumentation to extract typical photodiode characteristics.



Who we are

Professor Chris Toumazou

FRS, FREng, FMedSci, CEng, FIET, FIEEE

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

Chris Toumazou has made outstanding contributions to the fields of low power analogue circuit design and current mode circuits, and systems for radio frequency and biomedical applications. Through his extensive record of research he has invented innovative electronic devices ranging from dual mode cellular phones to ultra-low power devices for both medical diagnosis and therapy. He has developed a range of innovative electronic devices, utilising analogue mobile phone technology, for use in patient care. This includes the Sensium™ Ultra-Low Power Wireless Body Monitoring System which gives physicians constant access to vital signs including ECG, body temperature, respiration and physical activity of patients, with chronic illnesses, based at home.

Whilst working on his PhD, he made major advances in the field which led to a radical transformation of analogue signal processing. An insight, which in retrospect may look simple, was to give current rather than voltage the main role in signal processing. Using transistors in the weak inversion regime, the current mode methodology led to markedly superior performance, most dramatically in reduced power consumption. These advances opened up a range of applications, in telecommunications and also in the design of prosthetic implants. In recognition of his outstanding research he was made a Professor at Imperial College London at 33, one of the youngest ever to achieve this distinction.

His pioneering research showed how the natural analogue physics of silicon technology could be used to mimic and replace biological functions. Amongst his many achievements are: the development of one of the world's first implantable cochlear chips, which gave hearing back to the born deaf; the development of an artificial retina using local intelligence to achieve micropower consumption; the development of the silicon pancreas, which mimics the function of the pancreatic beta cell to regulate insulin flow for people with type 1 diabetes and, in collaboration with Professor Sir Magdi Yacoub, the development of a miniature sensor to monitor the hearts of people who have undergone heart operations or who have conditions that could lead to heart failure. In 2001 he invented a silicon chip technology to detect DNA sequences, a fundamental breakthrough in the field of genetics with enormous potential to transform medicine. Moreover, the technology has profound implications for agricultural and food industries, forensics and biosecurity.

In order to realize the enormous potential of these technologies, Professor Toumazou led a campaign to raise £26 million to create a new, postgraduate research institute at Imperial College London and in 2004 established the Institute of Biomedical Engineering, a state-of-the-art facility drawing scientists, medical researchers, clinicians and engineers together to advance medical innovation by applying engineering platform technology to medicine. His own specialism is in the field of personalised healthcare, providing worn or implantable devices for early diagnosis and detection of disease.

He is the founder of four technology based companies with applications spanning intelligent wireless technology for chronic disease management (Toumaz Technology Ltd, UK), biomedical devices (Applied Bionics PTE, Singapore), Digital Audio Broadcasting (Future-Waves Pte Taiwan) and DNA Sequencing (DNA Electronics Ltd, UK). These companies employ over 50 RF and low power engineers worldwide many of whom are his former graduate students.

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 2008 he was awarded a Fellowship of both the Royal Society and the Royal Academy of Engineering and in 2013 he became a Fellow of the Academy of Medical Sciences. He 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 an 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 and in October 2011 was invited to give a lecture at the presitigous TEDMED Conference in San Diego. His publications include over 400 research papers in the field of RF and low power electronics and he holds 23 patents in the field many of which are now fully granted.

Dr Timothy Constandinou

BEng (Hons), DIC, PhD, CEng, FIET, SMIEEE

Lecturer Department of Electrical and Electronic Engineering
Deputy Director Centre for Bio-Inspired Technology

Timothy Constandinou is a Lecturer within the Department of Electrical & Electronic Engineering at Imperial College London and is also the Deputy Director of the Centre for Bio-Inspired Technology. He received both his BEng and PhD degrees in Electrical and Electronic Engineering from Imperial College London, in 2001 and 2005 respectively. During his PhD, he proposed a biologically inspired paradigm for implementing pixel-level, current-mode processing applying local feedback to compensate for poorly matched elements. This prompted him to apply bio-inspired concepts to the design of advanced medical devices (implantable, body-worn and point-of-care). 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 develop ultra low power implantable devices, brain-machine interfaces, lab-on-chip/wireless capsule endoscope platforms and medical devices in general. His main focus is to develop microelectronics 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 current research is developing ultra low power platforms for neural interfacing (both electrical recording and stimulation).

Ongoing collaborative projects include:

- **Ultra Low Power Implantable Platform for Next Generation Neural Interfaces** (supported by the EPSRC): a wireless, multi-channel neural recording interface with on-node spike sorting for real-time motor prosthetic control.
- **iPROBE – *in vivo* Platform for the Real-time Observation of Brain Extracellular activity** (supported by the EPSRC): a digital 1k+ channel neural recording interface for neuroscience research.
- **Wireless Intraspinal Microstimulation Platform**: a wireless, programmable neural stimulator for highly targeted spinal cord interfacing.
- **Proprioceptive Feedback Platform for Upper-Limb Prosthetics** (supported by the EPSRC): a platform facilitating artificial proprioceptive feedback from a prosthetic limb by direct electrical neural stimulation.
- **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.
- **Thermal Microstimulation of Excitable Cells** (supported by the Wellcome Trust): a lab-on-chip platform for the microscale thermal stimulation of excitable cells *in vitro*.

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), and Frontiers in Neuromorphic Engineering, is vice chair of the IEEE Sensory Systems Technical Committee (SSTC) and also serves on the IEEE Biomedical Circuits & Systems Technical Committee (BioCAS-TC). In 2009, he has been named the recipient the IET Mike Sergeant Achievement Award in recognition of research/academic career achievements. He was Technical Program Co-Chair of the 2010 and 2011 IEEE BioCAS Conferences, Publications Chair of the 2010 IEEE BioCAS Conference, Technical Program Track Co-Chair (Bioengineering) of the 2012 IEEE ICECS Conference, Technical Program Track Chair (ASICs) of the 2012 BSN Conference. He is currently the chair of the IET Awards and Prizes committee.

ACADEMIC STAFF PROFILE

Dr Pantelis Georgiou

MEng (Hons), DIC, PhD, CEng, MIET, MIEEE

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

Pantelis Georgiou received the MEng degree in Electrical and Electronic Engineering with 1st class honours in 2004 and a PhD degree in 2008 both from Imperial College London. He moved to the Institute of Biomedical Engineering where he was appointed as a research fellow and conducted pioneering work on the silicon beta cell leading towards the development of the first bio-inspired artificial pancreas for type I diabetes. In 2011, he joined the academic faculty where he became a lecturer within the Department of Electrical and Electronic Engineering. 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.

His current research includes low-power microelectronics, bio-inspired design, integrated sensing systems and development of novel medical devices. One of his key focuses is on technologies for treatment of Diabetes. He currently heads the Bio-inspired Metabolic Technology lab and has been involved in the development of several commercial technologies such as a point-of-care portable platform technology for genetic detection (DNA Electronics Ltd).

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. Specific- ally 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 dependant diabetes and controlled exercise and diet for no-insulin dependant 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 DNA sequencing** – Semiconductor based DNA sequencing is now becoming an attractive alternative to conventional genome sequencing which uses optical techniques. Due to scaling of Moores law, ISFET based sensors can now be integrated in the millions to create large scale sensing arrays able to decode the human genome cheaply and reliably. This project aims to implement a next generation ISFET based DNA sequencing system capable of real-time genome detection and assembly in CMOS increasing reliability of detection and time to result.
- **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 also sits on the IET Awards and Prizes committee.

Professor Chris McLeod

MA, MSc, DPhil, MIPEM

Principal Research Fellow, Centre for Bio-Inspired Technology

Chris graduated from Cambridge University in 1971 with a degree in Engineering and from the University of Strathclyde in 1975 with an MSc in Bioengineering. After working in medical research posts in Oxford for the intervening years, he graduated from the University of Oxford in 1986 with a DPhil in Bioengineering.

He moved to a lecturing post at Oxford Brookes University in 1984, maintaining his research links to clinical departments (Neurophysiology, Anaesthetics and Paediatrics), was appointed Professor in 2002 and became an Honorary Research Fellow in Anaesthetics in 1989. In 2005 he was appointed Visiting Professor in the new Institute of Biomedical Engineering at Imperial College London, later joining the Institute in 2008 as a Principal Research Fellow.

From 1975–84 he was a Research Associate at Oxford University developing wireless telemetry of physiological data in studies in Cot Death Syndrome (SIDS); novel, minimally invasive monitoring devices for neonatal intensive care and methods and systems for measuring the nutritional intake of breast-fed babies for studies on weaning in regions with low-calorie weaning foods. Between 1984 and 2008 he furthered his research into the non-invasive neonatal monitoring systems which has resulted in the first of a range of new devices coming to the market this year, and instigated a programme to study the mechanisms underlying the depression of breathing by anaesthetic agents. He attracted research funding and published in all of these application areas, particularly on non-invasive, continuous thoracic imaging using electrical impedance tomography and on tissue characterisation using electrical impedance spectroscopy.

Chris instigated and led the development of implantable pressure sensors for the cardiovascular system since 2004, initially at Oxford Brookes, then at Imperial College London with funding from the Wellcome Trust Technology Translation Fund and then from the Wellcome Trust – Department of Health Healthcare Innovation Challenge Fund. He has published 36 papers on this work.

His current research is to take the implantable pressure sensors through manufacture for regulatory approval and through a Phase 1 ‘first-in-man’ safety trial by 2015 and leading to a Phase 2 efficacy trial. 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. The implants and system will be applied to other indications following a successful Phase 1 trial.

Dr Konstantin Nikolic

PhD, DIC, MIEEE, MInstP

Senior Research Fellow, Centre for Bio-Inspired Technology

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, and a Senior Research Fellow at the Dep. of Physics & Astronomy, University College London. 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 current research interests include bio-inspired technologies, systems and computational biology. His work is focused on computational neuroscience, sensory systems neuroscience, enabling technologies for optogenetics and on developing new sensing and information processing paradigms based on molecular biology and neuroscience, and applied to retinal prostheses. Specifically:

- **Optogenetics** – Photo-cycle models of channelrhodopsin2 (ChR2), halorhodopsin and archaerhodopsin, modelling of neurons expressing ChR2 mutants/other ion pumps; manipulation of neural circuits.
- **Mathematical models** – the functional relationship between stimuli and neural response, in particular: characterisation of several recently discovered retinal ganglion cells using the tools developed for nonlinear dynamic systems, such as information theory
- **Retinal implants** (image processing, stimulator driver algorithms and electronics, etc) event-based representation of sensory input and its processing.
- **Modulation of neural activity by changing the temperature** (e.g. by using Infrared light or thermal MEAs).
- **Bio-inspired circuits and systems** – based on the retina circuitry and cellular signalling and metabolic pathways; Stochastic models of phototransduction and G-protein coupled cascade.

He is a co-author of two very successful physics textbooks for university students, a book about the 3D nanoelectronic computer architecture, 7 book chapters (in the areas of physics, nanoelectronics, and the eye photoreception), and a number of publications in journals and conference proceedings. His papers have more than 1000 citations so far. He has an extensive experience in organising and running collaborative projects, currently he is the PI of an EU project, '*SeeBetter* – Seeing Better with Hybrid Backside Illuminated Spatio-Temporal Silicon Retina', which is about designing and fabricating a novel type of the retinomorphic vision sensor, and a Co-I of a Wellcome Trust Institutional Strategic Support Fund grant: 'Network of Excellence for Optogenetic Manipulation of Neural Circuitry'.

Patricia Chapman

BA (Hons)

Business Administrator to Professor Chris Toumazou

Patricia joined the newly formed Institute of Biomedical Engineering in 2004 as the first Manager and oversaw the project which created the state-of-the-art laboratory facilities, offices and meeting areas. As a graduate in Biology, she was excited about 'returning' to science after a career in management and customer service.

As Manager of the Institute, she was responsible for appointing the first staff, research assistants and technicians and implementing the scholarship programmes which enabled the Institute to attract well qualified postgraduates to its PhD programmes.

Following its endowment, she assisted Professor Toumazou in establishing the Centre for Bio-Inspired Technology which became a specialist research focus within the Institute. She now provides support to the Centre's Research Groups and compiles the Annual Report.

She also supports Professor Toumazou in his role as Director of the Centre and Chairman and Chief Executive of his 'spin out' companies organising PR and events associated with his commercial activities.

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 and additionally has the role of PA to the Head of Department. She joined the Department of Electrical and Electronic Engineering in 1990 and has kept a key role in supporting the CAS group ever since.

Her role within the Centre for Bio-Inspired Technology is to support our postgraduate research students from PhD registration and bursaries to thesis submission and examination.

ADMINISTRATIVE STAFF PROFILES

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 and CEO to Toumaz Ltd and 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.

Dr Mohammadreza Bahmanyar

Research focus
Implantable SAW transponder for acute and chronic blood pressure monitoring

Funding
Wellcome Trust and Department of Health – Health Innovation Fund

Many cardiovascular and respiratory diseases cause blood pressure changes in the chambers of the heart and the vessels linking the heart and lungs. Measuring such localised pressures has had to rely either on inaccurate external measurements or measurements performed very intermittently by expensive and somewhat risky catheterisations.

Surface acoustic wave (SAW) resonators can be used to fabricate miniature and highly stable pressure sensors. When connected to an antenna, such sensors would form a transponder that can be interrogated for pressure information wirelessly.

Implantation in body poses a number of challenges. These include device biocompatibility, low level signal detection and processing, while complying with telecommunication regulations.

A complete system for wireless measurement of the blood pressure inside circulatory system was previously developed and tried in a porcine model. Different elements of the system are currently being optimised for phase 1 clinical trial. This task involves compliance with a number of standards to demonstrate that the (class III) implant is safe to use and that the interrogating system is not interfering with other equipment during the clinical trial.

My research is focussed on the following:

RF interrogating system design and verification: Digital receiver design, high frequency data acquisition. The first outsourced prototype was delivered and recently tested at our EM laboratory. A number of modifications are requested and are currently being performed by the contractor.

Sensor microfabrication: mask design, process development suitable for single crystal quartz wafers, sensor characterization. Working with our external contractor in the US to achieve a reliable fabrication process for sensor production.

Implantable antenna design: antenna simulation and model verification, fabrication and bio-phantom measurements. A suitable antenna was simulated and laser cut from fine Nitinol tubing. A biocompatible insulation process is currently being developed to meet long term implantation requirements.

Signal processing: algorithm development and optimization for embedded systems. The quality of the signal transmitted from the implant will eventually depend on implantation depth that varies from patient to patient. Improving the developed algorithm in order to achieve the desired accuracy with a lower signal to noise ratio and implementing it on an embedded platform is ongoing.

PUBLICATION

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, DOI 10.1007/s10544–013–9759–7, 2013.

Fellow

Dr Alessandro Borghi

Research focus
Implantable SAW transponder for acute and chronic blood pressure monitoring

Funding
Wellcome Trust and Department of Health – Health Innovation Fund

Heart failure is a common, disabling and deadly disease, which affects 1 to 2% of the population in developed countries, with a higher incidence in the elderly population (6-10% of the population over 65 years of age). It is associated with high health expenditure: in the UK the estimated costs have been estimated to be up to 2% of the NHS budget. Heart failure is linked to increased left atrial pressure and, when associated with chronic obstructive pulmonary disease, it can cause pulmonary hypertension (increased pulmonary artery pressure). Hence, the on-going assessment of localized pressures becomes crucial for the monitoring of cardiac failure patients. So far, it has had to rely on inaccurate external measurement or intermittent and invasive and, therefore, partial and risky internal measurements. This project focuses on the design of a novel pressure sensor based on the surface acoustic wave (SAW) technology, previously employed in telecommunication as well as automotive sectors.

My role in the project is to design a way to position the pressure sensor inside the body and ensure its mechanical stability and biocompatibility, which is the key to maximize the cohort of patients who could benefit from this technology. Nitinol has been chosen as the material for the support structure, both for its biocompatibility and super-elastic properties. A delivery system is being finalized and dimensions have been minimized in order to make delivery suitable in both animal and human models.

Forces in a mock artery have shown that trauma on the vessel wall during delivery will be minimal. Preliminary animal tests *in vivo* in swine, have shown feasibility in tracking a large delivery system up to the target location (main PA – PA branches). The test has permitted the creation of a specific experimental protocol which will be used in future animal tests. Finite element modelling has shown that the device is safe for long-term fatigue and that radial forces exerted on the vessel wall are in the same range as similar devices. The design has been finalized and the manufacturing method has been defined.

Future work will involve a full safety trial on a group of 6 animals for 6 months; the trial will provide information about biocompatibility (according to ISO 10993) and device and delivery safety. CE mark application will be finalized and the technical file for the submission to the notified body will be produced. In the meantime, an in-human safety trial will be organized for the first in-man experiment.

PUBLICATIONS

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2. Borghi A, Ma J, Murphy OH, Bahmanyar R, McLeod C, 'Self expanding structures for cardiovascular sensor attachment', Proceedings of the *International Conference on Shape Memory and Super Elastic Technologies*, Prague, Czech Republic, 20–24 May 2013.

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2. Lam CS *et al.*, 'Age-associated increases in pulmonary artery systolic pressure in the general population', *Circulation* May 26;119(20):2663–70, 2009. Epub May 11 2009.
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Dr Amir Eftekhar

Research Focus
Neural interfacing, acquisition and analysis

Funding
European Union ERC Synergy

My work primarily involves the development and commercialisation of technology for interfacing the peripheral nervous systems. Any such interface is made up of front-end electronics, analogue signal processing, acquisition and digital signal processing. The signal processing chain utilises algorithms and/or feature extraction and classification to facilitate clinical inference or closed-loop intervention strategies.

The majority of focus on neural interfaces has centred on the brain, and little to the periphery. The peripheral nervous system is the main pathway of communication between all major organs, muscles and sensory information to the brain. The ability to tap into it and regulate it opens the doors to many unresolved disorders.

We were recently rewarded an ERC Synergy grant to exploit our peripheral nerve technology and novel sensing modes. Specifically we monitor electrical and chemical signatures associated with action potential propagation (the nerve signal). This type of information allows us to obtain recordings with less interference from electrical sources and give more detailed information about the underlying neural dynamics.

Using a combination of electrode types we have shown *in vitro* results and our now moving to *in vivo*. The project itself is targeting the Vagus' nerve role in appetite regulation. In collaboration with Professor Sir Stephen Bloom's group at Hammersmith Hospital we aim to:

- first investigate the mechanisms by which the Vagus nerve regulates appetite, including brain, stomach and gut hormone release.
- based on these novel findings regulate (through electrical stimulation) the Vagus nerve to regulate these appetite signals.

I am managing the technology development of this work. My work in general deals with projects that will create integrated solutions for neural interface applications.

I continue to work on seizure prediction and detection algorithms for epileptic patients, wireless EEG (brain scalp monitoring) for various applications, brain stimulation techniques (single pulse electrical stimulation (SPES) at Kings College London), and the signal processing chain of an implantable brain interface (in collaboration with Leicester and Newcastle Universities) and novel methods of ECG acquisition and processing (with Texas Instruments).

Seizure detection and prediction in epilepsy was the focus of my PhD, and one of our recent studies. Epilepsy affects around 450,000 people in the UK and an estimated 0.85% of the world's population. It is characterised by hypersynchronous neural firing in the brain (seizures) that can manifest as brief absences to complete loss of consciousness and motor control. Only 70% of patients can be seizure free with medication, although there are many associated cognitive side effects.

According to a recent Joint Epilepsy Council briefing, only 52% of patients receive optimal treatment. In addition 1000 people per year die of epilepsy related causes. Only a small percentage are eligible for surgery which has an estimated efficacy of seizure frequency reduction of 20% and a surgery backlog that is predicted will never be cleared. Overall it is estimated £150 million per year needs to be invested to improve and facilitate epilepsy diagnosis and treatment.

During my PhD, I used the Hilbert-Huang Transform (a time-frequency method), translating it into real-time processing, and applying it to seizure data. More recently we utilised and adapted a pattern recognition algorithm (n-gram). N-grams are typically used in text analysis, such as to count the number of words or phrases and their occurrences in a text. We applied this method to EEG data that was translated into symbols (representing characters in a text), using quantisation. We achieved higher accuracy compared to the current state of the art and are looking to expand this work. Both studies have been submitted for publication.

This is a snapshot of the type of work I am involved in of which all have both clinical and commercial impact that we are realising through IP development. All of these aim to create novel but realisable solutions that utilise our groups unique bio-inspired principles for medical diagnostic and treatment.

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2. SE Paraskevopoulou, DY Barsakcioglu, MR Saberi, A Eftekhar, TG Constandinou, 'Feature extraction using first and second derivative extrema (FSDE) for real-time and hardware-efficient spike sorting', *Journal of Neuroscience Methods*, Vol 215, Issue 1, 29–37, 2013.
3. DY Barsakcioglu, A Eftekhar, TG Constandinou, 'Design Optimisation of Front-End Neural Interfaces for Spike Sorting Systems', *IEEE International Symposium on Circuits and Systems* (ISCAS), 2013.

Fellow

STAFF RESEARCH REPORT

Dr Andrea Alenda González

Research Focus
Bio-inspired implant to treat obesity

Funding
European Union ERC Synergy

BACKGROUND

The rise of an obesity epidemic has been spreading in the last four decades. It initially affected high-income countries in the 1970s and by the 1990s had reached the middle and developing countries. Regardless of public health policies, no country has been able to reverse its obesity rates. It is now a global pandemic.

The global prevalence of obesity is not explained solely by an individual choice of poor healthy lifestyle. What seems to be contributing decisively to the pandemic are the changes in the global food system – where cheap high caloric food is easily available – combined with less physical effort due to mechanization of labour and transport. This environment promotes excess of food consumption and sedentary lifestyle. Obesity is the response of an individual living in this environment.

Being obese and overweight increases the risk of suffering from cancer, diabetes, musculoskeletal and heart disease. It reduces life expectancy. Obesity is one of the largest preventable causes of death today.

Despite the increasing number of people suffering from obesity, there are few treatments that result in sustained weight reduction. Bariatric surgery is the most effective treatment for obesity today, but this operation is only recommended for specific cases as it entails risks for the patient. It is crucial to find a new treatment for weight loss.

THE PROJECT

The i2Move Project aims to develop a new generation of neural interface to treat obesity. The aim is to stimulate the vagus nerve – which mediates information between the brain and the gut – and hence mimic a natural satiety response, providing the patient with appetite control.

The multidisciplinary team, led by Professors Christofer Toumazou and Sir Stephen Bloom, includes surgeons, physiologists, engineers, chemists and neuroscientists. For this project I work both as a science writer and as a neuroscience consultant.

As a writer my aim is to make science accessible to audiences with different levels of expertise. I have worked as a freelance science writer and science blogger. I also write my own science blog at **www.thecuriousneuron.com**

In the i2Move Project, the area of interest is the vagus nerve. The information available on the vagus nerve is limited as it relies on research of dissected preparations of the nerve in anaesthetized animals. Little is known about the dynamics of the vagus nerve response during digestion. As a neuroscientist my role is to understand the physiology and morphology of the peripheral nervous system and to liaise with the engineering team to find the optimal nerve-implant interface solutions.

The technological innovation used for the implant in the vagus nerve will provide a treatment for obesity and it will open a window to the elusive brain-gut communication.

I have worked as a neuroscientist for over a decade on somatosensory perception and spatial cognition, in other words, on how the brain perceives touch and also how it constructs a map of its environment. After 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.

Dr Pau Herrero Vinas

Research focus
Diabetes technology

Funding
Wellcome Trust

My main research focus lies in the field of diabetes technology and in particular in development and clinical validation of a Bio-inspired Artificial Pancreas (BiAP). BiAP has already been validated *in-clinic* over 20 subjects with type 1 diabetes during fasting and over-night conditions and is currently being tested in a 24-hour trial.

Further clinical trials to test this technology during exercise, mixed meals and ambulatory conditions are planned for the next 2 years.

Among the algorithms I have developed in the context of BiAP there are: a novel bio-inspired glucose controller based on the β-cell physiology; a type 1 diabetes subject simulator for *in-silico* testing of bi-hormonal, i.e., glucagon and insulin, blood glucose controllers; a mixed meal model library to be incorporated into diabetic subject simulators in order to account for more realistic and varied meals; an Extended Kalman Filter (EKF)-based algorithm for smoothing noisy data coming from continuous glucose sensors; a calibration algorithm for continuous glucose monitors based on EKF; an EKF-based fault detection system to detect possible adverse events in insulin delivery systems and continuous glucose sensors; a hypoglycemia prediction algorithm based on EKF; and a technique to evaluate glycemic variability metrics based on discriminant ratios.

Another diabetes technology project I am involved in consists of developing an advanced insulin bolus calculator for diabetes management (ABC4D) based on Case Based Reasoning (CBR) and continuous glucose monitoring data. Such a system, which is implemented on a smartphone platform, is aimed at providing superior glycaemic control with respect to existing insulin bolus calculators embedded in current insulin pumps. ABC4D is currently being clinically tested over 12 subjects with type 1 diabetes.

Finally, I am also working on a research project that aims to optimise antimicrobial therapy in the intensive care unit. The application provides prescribing decision support through CBR technology, which will help clinicians across healthcare to make the right choices for antibiotic therapy from the beginning of the treatment. Such technology is currently being tested at the Imperial College Healthcare NHS Trust.

PUBLICATIONS

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2. Pagkalos I, P Herrero and P Georgiou, 'An analogue implementation of the beta cell insulin release model', *IEEE International Symposium on Circuits and Systems,* (ISCAS), 2489–2492, 2013.
3. González C, P Herrero, JM Cubero, *et al*, 'PREDIRCAM eHealth Platform for Individualized Telemedical Assistance for Lifestyle Modification in the Treatment of Obesity, Diabetes, and Cardiometabolic Risk Prevention: A Pilot Study', (PREDIRCAM 1). *J Diabetes Sci Technol*, Vol:7, 888–897, 2013

Fellow

STAFF RESEARCH REPORT

Dr Olive Murphy

Research focus

Totally automated blood pressure monitoring at home to improve the care of patients with heart failure or pulmonary hypertension. Development of a remote sensing intercranial pressure monitoring system

Funding

Wellcome Trust, Department of Health Health Innovation Challenge Fund and Imperial College Research Collaboration Kick-start Scheme

My role within the wider project is the development of an RF implantable and wearable antenna design, SAW sensor characterization and regulatory approval

SUMMARY OF RESEARCH BEING UNDERTAKEN

The original work on the use of an implantable surface acoustic wave (SAW) device as an alternative to a wearable blood pressure monitor has now been extended to cover use within the brain as an intracranial pressure monitor. The experience garnered during the initial research is now used to expedite this work. Again, the inherent properties of the piezoelectric device with its small size and high stability are therefore exploited and are used to track pressure variations. In addition the passive sensor is powered from outside the body, producing a reliable and safe method of continuous monitoring.

Regarding the cardiovascular pressure monitor, the project is in the manufacturing and approval phase. The project will have to meet all of the necessary standards contained within the R&TTE, Medical Devices and Active Implantable Medical Devices Directives in order to commence human trails and gain CE marking.

Therefore, the research focus is now on adapting the current designs to meet these standards without compromising the precision of the sensor and its communication system. The aim is then to extensively test the entire system prior to human trials.

My particular areas of research within this project involve sensor characterization and assembly along with the design, optimization and *in vitro/in vivo* testing of deeply implanted and body worn antennas. The position and orientation of the implanted and body worn antennas are crucial to the efficiency and performance of the whole implanted system.

I have also developed an extensive knowledge of the radio standards and spectral regulations with a view to optimizing the system and guiding external collaborators.

PUBLICATIONS

1. Murphy OH, Mohammad Reza Bahmanyar, Alessandro Borghi, Christopher N. McLeod, Manoraj Navaratnarajah, Magdi H Yacoub, and Christofer Toumazou, 'Continuous *in vivo* blood pressure measurements using a fully implantable wireless SAW sensor' *Biomedical Microdevices*: Vol 15, Issue 5, 737–749, 2013
2. Lui KW, OH Murphy and C Toumazou, 'A Wearable Wideband Circularly Polarized Textile Antenna for Effective Power Transmission on a Wirelessly-Powered Sensor Platform', *Antennas and Propagation*, IEEE Transactions on, vol.61, no.7, 3873–3876, July 2013
3. Lui KW, OH Murphy, and C Toumazou, '32- μW Wirelessly-Powered Sensor Platform With a 2-m Range', *Sensors Journal*, IEEE , vol.12, no.6, 1919–1924, June 2012

Fellow

STAFF RESEARCH REPORT

Dr Monika Reddy

MbChB MRCP

Research Focus
An update on the clinical evaluation of the bio-inspired artificial pancreas in adults with type 1 Diabetes

Funding
Wellcome Trust

Type 1 Diabetes Mellitus (T1DM) is an autoimmune condition, which leads to destruction of the insulin-producing beta cells of the pancreas by the body's own immune system. This results in an inability of the pancreas to maintain glucose homeostasis, and if left untreated can be fatal. The majority of patients are managed in specialist diabetes clinics and are either on daily multiple subcutaneous insulin injections or continuous subcutaneous infusion of insulin via a pump. Intensive treatment reduces the risk of developing complications. However, achieving optimal glycaemic control can be very challenging for patients due to the increased risk of hypoglycaemia (low blood glucose) with intensive treatment. Severe or prolonged hypoglycaemia is a major concern and can result in seizures, cardiac arrhythmias and the 'dead-in-bed' syndrome.

A closed-loop insulin delivery system, also known as the artificial pancreas, consists of a subcutaneous glucose sensor, a control algorithm and a subcutaneous insulin pump. It has the potential to improve glycaemic control, reduce the incidence of hypoglycaemia and improve quality of life. The control algorithm used in the Bio-inspired Artificial Pancreas (BiAP) is based on a mathematical model of the beta-cell physiology. It has been implemented on a microchip within a handheld device. The miniaturisation of the system is of great importance for device usability and acceptability.

Clinical trials assessing the safety and efficacy of the artificial pancreas commenced in May 2012 at the NIHR/Wellcome Trust Imperial Clinical Research Facility. The first stage of the study assessed 20 subjects in a 6-hour fasting study. We showed that the artificial pancreas was safe and achieved good glycaemic control during fasting conditions. Following the initial stage, the system has been evaluated in 17 subjects overnight and after a breakfast meal challenge (13-hours in total).

The clinical results from the overnight and post-breakfast study are encouraging and show that the Bio-inspired Artificial Pancreas achieves normoglycaemia (3.9–10.0 mmol/l) without hypoglycaemia overnight. The post-meal glucose levels were good, but there is scope to improve the post-meal glucose peak in the next stage of the study by tuning the control algorithm more aggressively.

FUTURE WORK

The next stage of the project is a randomised controlled crossover study over 25-hours with three standard meals, and this is currently underway. The aim is to compare the BiAP system with the subject's standard pump therapy. We aim to complete this stage of the study by April 2014. Future work will include evaluating the system during and after exercise in a controlled clinical environment, before testing it in the home environment.

An artificial pancreas may eliminate the need for injections and hypoglycaemia in people with T1DM. The ultimate goal of a user-friendly artificial pancreas is to reduce diabetes complications and improve patients' quality of life.

An overview of the study protocol for the overnight and post-breakfast closed-loop study

Every 15–30 minutes a venous blood sample was taken and analysed immediately for blood glucose using the YSI 2300 analyser. The subject, a medical doctor, a research nurse and an engineer attend each closed-loop study

Overnight and meal challenge closed-study (13 hours)

AT 18:00
- Attend clinical research facility
- Meal of own choice with normal meal bolus
- Insert two Enlite sensors

AT 20:00
- Connect bio-inspired closed-loop system to subject
- Run basal insulin at normal rate

AT 22:00
- Closed-loop start

AT 06:00
- Standard 40g breakfast with 70% pre-meal bolus

AT 11:00
- End of closed-loop study

Fellow

STAFF RESEARCH REPORT

Dr Sanjiv Sharma

Royal Society of Chemistry Chevening Technology Fellow

Research focus
Micro- & nanostructured devices for healthcare applications

Funding
EPSRC, Centre for Bio-Inspired Technology

The advances in microfabrication in the 1990s followed by those in nanofabrication a decade later, have led to the transformation of micro and nanostructured platforms to low cost tools for high throughput fabrication. For health care applications, in addition to the cost, minimally invasive and low pain characteristics and the use of device without the intervention of a specialist ensures a better patient compliance in home conditions.

I am a Research Fellow in the Department of Chemistry, with Professor Tony Cass, and collaborate with researchers in the Institute of Biomedical Engineering in the area of Biosensors and Bionanotechnology. In the Centre for Bio-Inspired Technology I am working with Professor Chris Toumazou and as the Clean Room Facilities Director.

My expertise lies in the areas of desktop nanofabrication (dip pen nanolithography), micro fabrication, microfluidics and biosensors. My current research focuses on minimally invasive glucose biosensors devices for continuous monitoring in the interstitial fluid present in the skin compartment.

We have already successfully completed the preclinical evaluation of our devices through testing the mechanical stability, *in vitro* and *ex vivo* studies. Having obtained the necessary approvals we are now preparing for clinical trials in healthy volunteers and Type 1 diabetics to assess the accuracy and precision of our devices.

PUBLICATIONS

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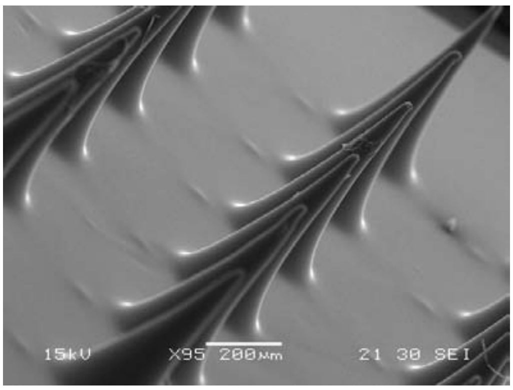

Microprobe device fabricated in the Clean Room using photolithography

Associate

Dr Yan Liu

Research focus
Towards a next generation neural recording interface

Funding
EPSRC

The Project is aimed at developing a highly innovative front-end neural monitoring system towards a next generation brain machine interface. In recent years, neural recording and stimulation systems have been integrated on chip to enable scalability and real time operation. State of the art systems typically interface with 100+ electrodes using front-end circuits that occupy a silicon area of under 20mm2. However, this trend is limited by the power constraints and data bandwidth if conventional recording topology is used in the future.

In the Project my aim is to leverage these limits, and design the system platform for large-scale neural recording. This includes: delivering a front-end system to record the neural signal, implementing pre-data processing methods on chip for raw neural data, and investigating circuits for next generation neural interface.

I am currently focussing on integrating amplification and conditioning circuits onto an integrated circuits system based on CMOS technology. By doing so, large throughput of neural signal recording with critical signal to noise ratio can be realized in a platform with high data bandwidth, small physical feature size and low power consumption. These are crucial for both *in vivo* and *in vitro* measurements.

Over the past year, I have recorded neural signals from non-human primates with an amplifier designed and assembled within the Group. It shows consistent noise and power performance with simulation and specification, which meets the requirement for large-scale system integration. Furthermore, the version 1 recording chip has been tested for individual channels, and the drawbacks and problems which were identified, have led to the redesigned version 1.1.

We have developed a recording system with high integration, which includes front end, memory, and DSP within each channel. This reduces the power consumption and data bandwidth required. This system is designed and now under production.

We are aiming to test and assemble our fully functional recording systems for both versions, and carry out corresponding *in vitro*/*in vivo* tests.

Apart from recording, the neural spike sorting algorithm has been implemented into micro-controller and FPGA platforms. Further work is in process to integrate these two systems, which will eventually work alongside the recording chips for smart neural signal recordings.

PUBLICATION

Liu Y, A Al-Ahdal, P Georgiou and C Toumazou, 'Minimal readout scheme for ISFET sensing arrays based on pulse width modulation', *Electronics Letters*, Issue 10, Vol 48, 548–549, 2012.

Dr William Spinner

Research focus
Genetics and functional genomics

Funding
Geneonyx Limited

Our DNA is what makes us unique. We are all unique because of small variations in each of our DNA blueprints. Much of this variation comes as a result of single nucleotide polymorphisms (SNPs) found in our genes. These SNPs can be responsible for functional variations in gene products that can cause differences in our metabolic pathways that can result in differences in our ability to metabolise and respond to chemicals, drugs and products.

The completion of the human genome in 2003 (1) paved the way for a wealth of genomic data to form the foundations of future biomedical research. However, with all this knowledge about the human genome, there are very limited opportunities for most people to obtain or discover their own personal genome information.

With the application of semi-conductor technology it has now become possible to quantify these variations in an accurate, rapid, non-invasive procedure that until now has not been feasible (2). After a more streamlined sample preparation, we are now able to analyse a DNA sample on the semi-conductor microchip and a result obtained within 15–30 minutes.

How this DNA result is then best translated into a treatment for the patient is the key aim for my research. This aim is to develop a dataset of functional gene single nucleotide polymorphisms that can be used as markers to analyse an individual's genetic predisposition to metabolise a variety of chemical compounds (i.e. drugs/ingredients). Using this information, in conjunction with the rapid DNA sample analysis, we can personalise these optimum chemical compounds according to each individual's genetic make-up to maximise the efficacy of the treatment.

Working closely with DNA Electronics Ltd, an Imperial College London 'spin-out company', we are taking the recent advances in semi-conductor technology to transfer this innovative technology from the laboratory in a variety of ways including healthcare and more general applications.

KEY REFERENCES:

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A prototype DNA test kit, incorporating a semi-conductor minilab, that allows 'live' DNA testing.

The semi-conductor microchip being inserted into the DNA analyser.

Associate

Dr Irina Spulber

Research focus
Smart clothing system for functional rehabilitation monitoring

Funding
Wellcome Trust, EPSRC

Osteoarthritis (OA) is a long term condition that develops when articular cartilage starts to break down, usually as a result of trauma or ageing. Symptoms include pain, stiffness, weakness, joint instability, tenderness in the joints and surrounding muscles and ligaments and a reduced range of motion. Treatment ranges from conservative rehabilitation interventions to surgical joint replacement. In its early and mid stages OA requires active management through correct exercise and physiotherapeutic interventions.

Emerging technologies such as wearable body sensors have the potential of helping patients to self-manage their condition.The focus of our work is to exploit the recent technological advances and develop a medical wireless sensor system capable of assisting OA patients by facilitating correct rehabilitation and monitoring the effectiveness of exercise in the home, as well as ensuring compliance.

An unobtrusive, smart garment system was developed to monitor knee functional activities. The system comprises of an array of conductive polymer sensors attached to the knee joint and a low-power wireless sensing unit integrated into the clothing. The polymer sensors are flexible and when stretched, their resistance is altered thus allowing the detection of movement. Alongside the analogue interface circuitry for flexible polymer sensors, the wireless sensing unit also incorporates an embedded triaxial accelerometer, a triaxial gyroscope and an EMG front end. The node offers the option of on-board data storage onto a micro-SD card or can stream data wirelessly to a PC via a Bluetooth module.

The multi-sensor prototype node was designed, fabricated and tested, and a graphical user interface was developed to support data collection. The aim was to develop small, low power electronics that can be discretely placed in a pocket or attached to the body and run off a 3V battery.

The smart garment will allow the on-going monitoring of joint motion, muscle activation (EMG) and body movement patterns and is intended to be used by OA patients as an assisting tool in their rehabilitation process.

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Figure 1. Smart legging prototype

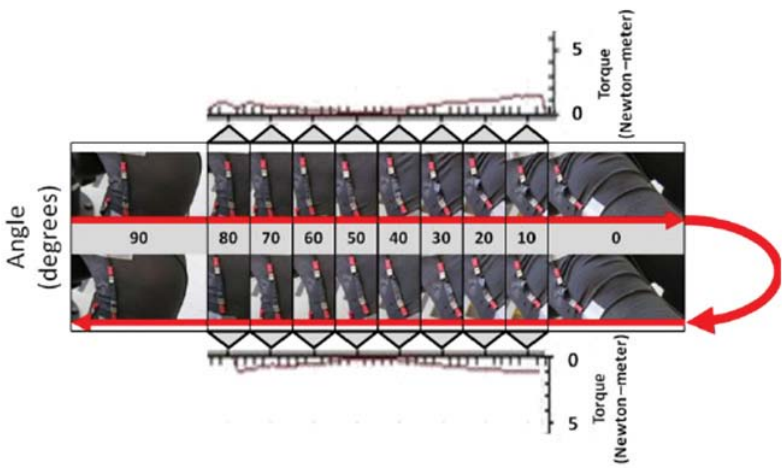


Figure 2. Flexible sensor deformation during knee extension and flexion

Visiting Research Fellow

RESEARCH REPORT

Dr Kiichi Niitsu

Research Focus
VLSI design for lab-on-chip technology

Funding
Nagoya University Venture Business Laboratory

Lecture, Graduate School of Engineering, Nagoya University, Japan

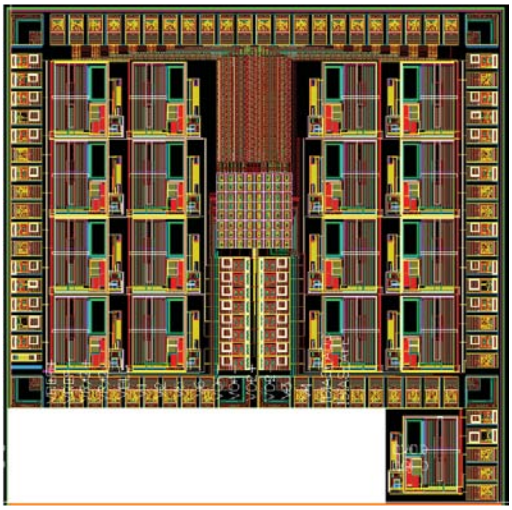
Between April and September 2013, I have worked in the Centre for Bio-Inspired Technology as a visiting researcher. This was made possible with support from the Nagoya University Venture Business Laboratory in Japan.

My research topic during this period has included VLSI design for cell manipulation and neural recording. In the neural recording research, one of my targets is to stimulate thermally and analyse its response in action potential using micro electrode array (MEA).

In order to evaluate the feasibility of the thermal MEA lab on chip technology (thermal MEA LOC), I have designed the VLSI chip in AMS 180 nm CMOS technology. I have also designed and implemented heaters, temperature sensors, and amplifiers for action potential.

NEXT STEPS

After the fabrication of the VLSI chip, the chip will be measured in the future. Through this visiting research fellowship, my aim has been to strengthen ties between Imperial College London and Nagoya University.



Chip layout for evaluating thermal MEA LOC

PUBLICATIONS

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Mr Deren Barsakcioglu

Thesis topic
Resource Efficient Fully Integrated Spike Sorting

Supervisor
Dr Timothy Constandinou

Funding
EPSRC DTA

SUMMARY

The ability to interface neurons using electronics is presenting new opportunities for neural rehabilitation with prosthetic devices. Commonly referred to 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.

Demands from neural analysis and prosthetics have pushed the recording technology to increase the number of recording sites and resulted in an ever increasing number of neurons recorded.

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 compression prior to transmission can be achieved by on-chip spike sorting, which is the identification and grouping of spikes recorded. Hence my research focuses on developing a fully integrated real-time spike sorter with minimal power and area consumption, while maintaining the high sorting performance.

METHOD

In order to achieve an optimum on-chip spike sorting implementation, one must identify and analyse all parameters that affect the spike sorting process. Therefore, one of the main objectives of this research is to identify both the hardware specific and sorting related parameters, and establish their trade-off regarding sorting performance and hardware resources (power and area) utilised. Once all trade-offs are established, the second phase of the research involves designing and testing the on-chip system by considering various circuit design and optimisation techniques.

RESULTS

The work to date has dealt with optimisation of the system parameters. More specifically, trade-offs of the parameters associated with front-end electronics have established via both parametric design optimisation and behavioural front-end modelling studies.

In addition, parameters related to back-end digital processing have also been investigated. These include (but not limited to) some critical aspects of spike sorting such as alignment, template creation, and window size.

KEY REFERENCES

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Mr Radu Berdan

Thesis topic
Application of memristors in conventional analogue circuits

Supervisors
Dr Christos Papavassiliou and Dr Themis Prodromakis

Funding
EPSRC Doctoral Training Award

Chua predicted the existence of a novel passive circuit element that he named 'memristor' (memory-resistor, with Ohms as its state variable), along the established resistor, capacitor and inductor. The new two terminal device exhibited theoretical electrical characteristics, with the most important one being non-volatility, or the ability of the memristor to 'remember' how much charge has passed through it; ie the memristor has a resistance that depends on the previous biasing parameters.

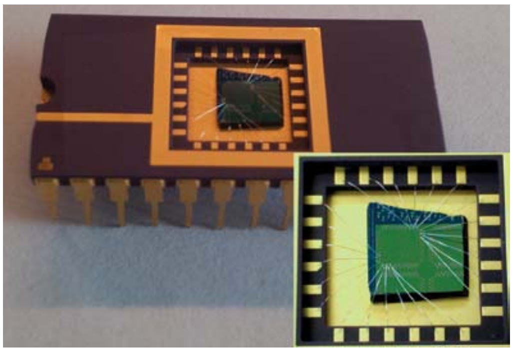

Figure 1. TiO2 memristor crossbar array (inset) bonded on a standard DIP24 package.

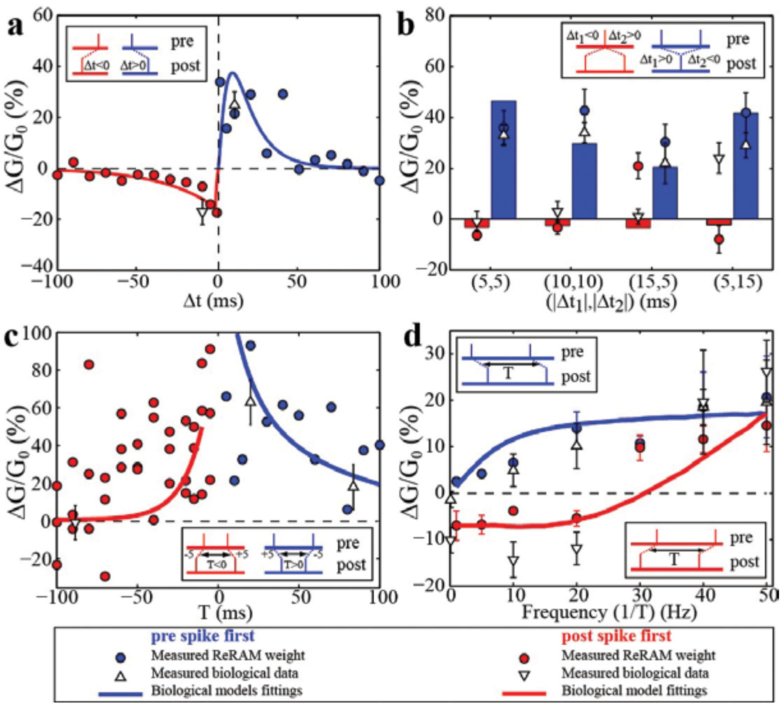

Figure 2. The memristive synapse demonstrates long-term plasticity in excellent agreement with biological data. Shown are: a) pair-based STDP, b) triplets protocol, c) quadruplet protocol and d) frequency dependence of pair-based STDP. Circular markers indicate measured data of our ReRAM memristors, while triangular markers indicate scaled data from biological synapses taken from literature, respectively for a), b), c) and d). Solid-lines and bars show the Voltage-Triplet rule fitted on the memristor measurements. Insets show the employed protocols for each case.

My research is concerned with the inclusion of solid state TiO2 memristors in conventional analogue circuits. This is enforced in two different ways: exploit the capability of the memristor of acting like an electrically tuneable variable resistor and setting a parameter of a system (gain, RC constant, etc.); or exploit its transient dynamics in novel neuromorphic circuits. I have utilised a solid state memristor as a parameter setting element in a programmable gain amplifier achieving eight distinct gain levels encoded in the variable resistance of one circuit component. Comparing with conventional implementations of variable resistors in IC design, my approach can benefit from reduced parasitics and lower chip real-estate requirement.

I am developing novel neuromorphic circuits which make use of volatile resistance switching observed in over-stressed solid state TiO2 memristors. Under weak biasing the devices undergo a temporary reduction in their resistance which then settles at its initial state in a matter of seconds once the stimulus has been interrupted. From a qualitative point of view, the volatile switching under a weak stimulus combined with non-volatile switching under a strong stimulus resembles the temporal dynamics of biological synapses, where the volatile switching is similar to Short Term Plasticity while non-volatile switching is similar to Long-Term Plasticity. Such, solid state TiO2 memristors can exhibit short term facilitation and saturation dynamics which have been utilised to perform sequence detection in a simple artificial neural network (ANN). Standard biological learning rules have also been demonstrated and fitted with standard mathematical models showing a strong and intriguing degree of resemblance with real biological data. The memristor thus holds great promise of replacing conventional CMOS artificial synapses in ANNs where the intrinsic material of the solid state device yields biorealistic responses.

PUBLICATIONS

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Mr Mohamed El-Sharkawy

Thesis topic
A CMOS based system for glucose sensing

Supervisor
Dr Pantelis Georgiou

Funding
Wellcome Trust

SUMMARY

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. These include retinopathy, which can lead to blindness, neuropathy, kidney failure and heart disease including strokes. Therefore it can be seen that this is a serious disease which cannot be left unchecked. Many health organizations have even described it as a growing epidemic. In addition there are severe economic consequences for example WHO predicts that from 2006 to 2015 China alone will lose 558 billion dollars in national income to cope with the disease.

However, most of these consequences can be avoided if good blood glucose control is maintained (1). Consequently there is a need for low power continuous glucose monitors CGMs which are wearable, accurate and have a long lifetime. Currently there are a number of initiatives aimed at fabricating micro-needles which are glucose sensitive and can be worn on the body in the form of a patch. My goal is to design the sensor front end instrumentation for such devices and perform signal processing in a way that mimics the method used by the beta cells in the pancreas.

METHOD

Investigate the method by which the beta cells (insulin producing cells) synchronize their bursting behaviour using gap junction coupling (2). Design an array of coupled beta cells on a CMOS chip with a low power potentiostat as the sensing front end. Attempt to show that output signal has a higher SNR and better precision than averaging. In addition study the effect of coupling on circuit mismatch using Monte Carlo analysis. Design a sub-1V CMOS potentiostat with sufficient gain, bandwidth, low noise and tunable current sensing range for the given application.

RESULTS

Matlab simulations of coupled beta cells have shown the noise shaping potential of synchronized networks. Currently, this matlab model is being implemented in silicon. It can be seen that a CMOS based system integrating low power glucose sensing and novel signal processing inspired by biology will help diabetics manage their blood glucose levels more effectively and thus help them avoid the short and long term consequences of the disease which arise due to hypo and hyper glycaemia.

KEY REFERENCES

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Mr Onur Guven

Thesis Topic
Ultra low power microelectronics for robust ECG signal conditioning

Supervisor
Dr Timothy Constandinou

Funder
Centre for Bio-Inspired Technology and Texas Instruments

SUMMARY

This research investigates methods for ultra low power data acquisition of bio-potential signals. One such signal is the electrocardiogram (ECG), which will be the target application for this research. It should be noted however, that any fundamental methodologies developed herein are directly applicable to other bio-signals by adjusting relevant parameters.

The ECG signal band is generally defined to be between 50mHz and 150Hz, and is therefore susceptible to interference from other bio-signals, in addition to environmental noise (within this signal band). In particular, the elimination of interfering bio-potential signals such as electromyograms and respiration signals is a major concern in preserving the ECG signal integrity. Since both these signals' spectral range overlaps with the ECG spectrum, care must be taken in filtering and processing. Various approaches have been reported in the literature to achieve this. However, these often neglect distortion to key features within the ECG signal, for example, the ST segment which crucial in diagnosis of certain conditions like myocardial ischemia. Therefore, it is essential to preserve the signal integrity when applying any filtering to eliminate sources of interference.

A closed loop system approach for maintaining this ECG signal integrity has been investigated throughout this work. Unlike the conventional high resolution ADCs digitizing both the ECG signal and the noise interferences and processing them in the digital domain, a closed loop system investigates noise interference removal of electrode DC offset, baseline wander and motion artefacts in the analogue domain through a feedback mechanism. This relaxes high resolution ADC design requirements and maintains home care solutions without requiring bulky computerised systems. In addition to that, the 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.

Proposed closed loop system utilises single/dual feedback loop with a high resolution DAC to meet the noise requirements defined by the IEC and AHA standards. Therefore, system level architectures and block specifications have been identified before implementing the circuit. The proposed system architecture utilises a low gain instrumentation amplifier as the first stage to suppress the high common mode noise and relax the noise performance requirements of the high resolution DAC. The next stage, amplifies the ECG signal further to cover the full dynamic range once the estimated baseline is subtracted from the ECG signal and a low resolution ADC digitizes this signal to be processed by the DSP. The estimated baseline wander and electrode DC offset is then converted back to analogue and subtracted from the signal of interest via the high resolution DAC at the second amplifier stage to maintain a clean ECG signal. This proposed architecture will be applied to address key challenges in ECG processing and be implemented in a commercial CMOS technology to demonstrate the benefits of this approach compared to the current state of the art techniques.

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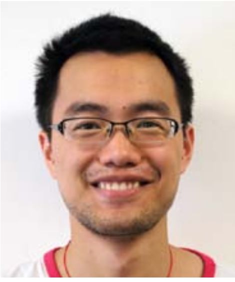

Mr Yuanqi Hu

Thesis topic
A CMOS based DNA sequencing engine

Supervisor
Dr Pantelis Georgiou

Funding
Department of Electrical and Electronic Engineering

The integration of DNA sequencing with semiconductor technology is gaining significant popularity due to the capability of CMOS technology to detect DNA base pair matches with high density and low cost. This is slowly becoming an established platform for DNA sequencing, which provides the capability of integrating other CMOS based functionality. These kinds of integrated systems could benefit from size, power, memory size, and most significantly speed and cost, compared with conventional detecting & sequencing methods.

This research involves the design of a novel ISFET array for DNA sequencing and a FPGA platform for the concurrent DNA sequence assembly. The new detection array developed is capable of dealing with some challenging problems that exist in ISFET sensors such as trapped charge, drift and signal attenuation. A novel readout front-end has been developed which is robust to these and well suited for short-term and medium-term chemical reaction monitoring applications. Furthermore, our system can compensate for process variation through a novel automatic calibration system.

In addition to this the system will be capable of DNA sequence assembly. The assembly platform designed for an FPGA implementation requires a novel comparison algorithm, which can easily utilise parallel computation. The new algorithm developed should have the capability to process the detected signal in real-time to utilise the detection time for processing of the data. Hence we have developed a hybrid algorithm that achieves this which can search for the overlap matches during the detection time by the exact comparison of bases, which is achieved through dynamic programming. This algorithm can be easily segmented into discrete phases, allowing it to deal with the incomplete data as it is being sensed. Furthermore, it has very good scalability that allows it to be implemented on a cluster of FPGAs to facilitate comparison of larger arrays.

The final goal of the PhD is to lay down significant scientific foundation for design of such a combined system DNA detection and processing system. The ultimate aim will be the introduction of the world's first CMOS based DNA microarray capable of sequencing the genome on chip.

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Dr Melpomeni Kalofonou

Thesis topic
ISFET technology for detection of DNA methylation based biomarkers for early screening of cancer

Supervisor
Professor Chris Toumazou

Graduated 2013

SUMMARY

The role of DNA methylation based biomarkers in several stages of cancer development is a rapidly advancing area of research. The aberrancies on the methylation profile of gene promoters play a critical role in gene silencing, thus contributing in different phases of tumour initiation, progression and recurrence, also associated with predicting the response to chemotherapeutic agents, therefore leading to a better assessment of the clinical effectiveness of cancer therapies and so of better prognosis. The need for detection of DNA methylation has become one of the most important assays in early cancer screening.

METHOD AND RESULTS

My research focuses on the application of semiconductor technology for detection of DNA methylation based biomarkers, laying down the foundation of a Point-of-Care (PoC) system for the early screening of cancer. A proof-of-concept approach was developed using a CMOS based ion sensor, the ISFET, enabling the detection of DNA methylation using the methods of pH-PCR and pH-LAMP, with the latter to be applied on a commercially available fully integrated System-on-Chip platform. Furthermore, the concept of real-time ratiometric detection of DNA methylation was developed and demonstrated using novel low power interfaces, integrating both electrical and chemical front-ends under a Lab-on-Chip (LoC) set-up. A hardware efficient system, referred to as the "Methylation Cell", able to compute the ratio of DNA methylation was designed, allowing real-time sensing of pH signals originated

from DNA reactions. In addition to this, a novel differential monitoring system capable for differential reaction monitoring of pH signals combined with gain tunability and drift reduction, termed the ISFET based Chemical Gilbert Cell, was developed, achieving ultra low power operation.

We believe that genetic testing using DNA methylation as the biomarker for early screening of cancer will yield a more accurate result for early detection over current methods which require imaging and possible invasive intervention for diagnosis. The future vision for the work in this thesis is depicted in the figure, whereby the screening methods of cancer would gradually converge from bulky, slow and expensive which are located in a hospital to portable, miniaturised, cheap and with local intelligence which can be made available for the GP clinic, expanding its use to a wider population.

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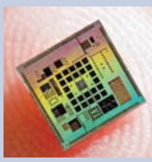
Future vision of early cancer screening

CURRENT SCENE
- In a hospital
- Large
- High-risk
- Bedside technology
- Costly
- Uncomfortable

CMOS
- Miniature
- Low cost
- Fast
- Scalable
- Low power
- Analogue
- Local intelligence



FUTURE SCENE
- At the GP clinic
- Small
- Cheap
- Portable
- Rapid time to result
- Accurate

Mr Ermis Koutsos

Thesis topic
A low-power real-time sEMG fatigue monitoring ASIC for rehabilitation of osteoarthritis.

Supervisor
Dr Pantelis Georgiou

Funding
EPSRC DTA

SUMMARY

The aim of this project is to create a real time method for tracking muscle fatigue for applications in rehabilitation. Through specific continuous time techniques, a compact, energy efficient, wearable device will be developed in CMOS that extracts muscle fatigue through monitoring of EMG. Processing of the EMG will take place locally, in real time, resulting to an information driven system rather than a conventionally data driven system, reducing requirements on data transmission and thus saving power.

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, Vastus Lateralis (VL) and Vastus Medialis (VM). VM is prone to atrophy, thus rehabilitation times are longer than VL. As a result, VM will exert less force on the patella, causing a patellar tracking dysfunction. Careful tracking of muscle fatigue of these two muscles can provide essential adjustments to the rehabilitation procedure and eventually help to avoid the above mentioned phenomenon.

METHOD

The Power Spectral Density function of the EMG signal undergoes a progressive compression towards lower frequencies and change of shape during fatigue. It has been shown that the instantaneous median frequency of the surface EMG signal correlates with muscle fatigue very well. Current research focuses on designing a low power CMOS analogue implementation capable of tracking the abovementioned spectral compression.

Future work will involve the addition of a front end amplification module, chip fabrication and testing of the low power ASIC.

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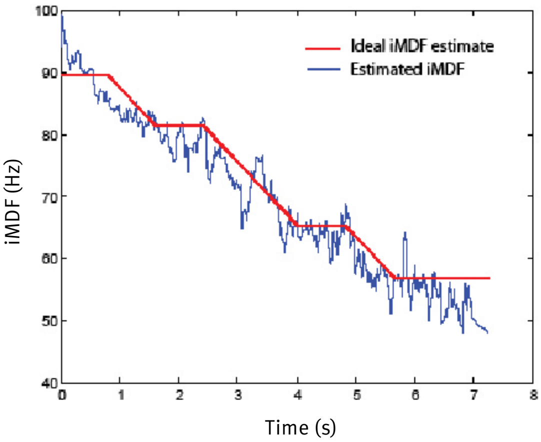

Figure 1. IMDF tracking during a fatiguing static contraction.

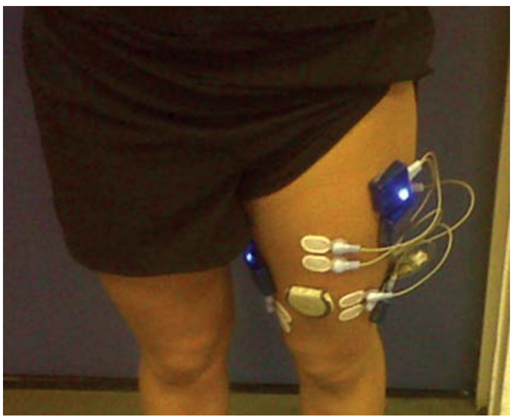

Figure 2. Wireless EMG sensors.
Electrodes attached to leg muscles VL and VM.

Mr Lieuwe Leene

Thesis topic
High density recording arrays for next generation neural interfaces

Supervisor
Dr Timothy Constandinou

Funding
EPSRC

SUMMARY

The recent trend in on-chip instrumentation for neural electrophysiological recording, has largely been motivated by the growing interest in observing large scale neuronal activity using small chronic implants. Such tools are crucial in the quest to better understand the brain, but also in revealing fundamental mechanisms behind neurological and psychiatric diseases for developing new diagnostics and therapeutic devices. Microelectronic bio-instrumentation systems are currently capable of recording the fine detail of neuronal activity with unparalleled special resolution. These advantages are the main motivation towards CMOS based recording that will enable state-of-the-art performance.

METHOD

The endeavour of this project is developing and exploring novel system architectures that will enable very compact recording arrays to record from thousands of integrated channels on a single chip. This will require a different system of blocks being integrated together with aggressive area reduction techniques and a dense mixed signal backend to processes information. There remain multiple areas in mixed signal recording that are still unexplored, particularly those that involve signal driven processing and exploiting the parallelism in recording arrays.

RESULTS

Our initial findings have demonstrated the possibility of recording arrays at a 100 recording sites per mm^2. This result is closely tied to a new system topology that aggressively seeks a mixed signal implementation to mitigate large analogue devices.

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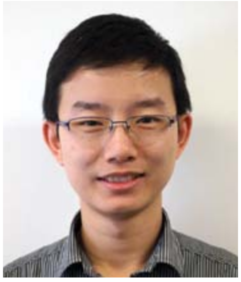


Mr Song Luan

Thesis topic
Implantable microelectronics for advanced neural stimulation

Supervisor
Dr Timothy Constandinou

Funding
ESPRC

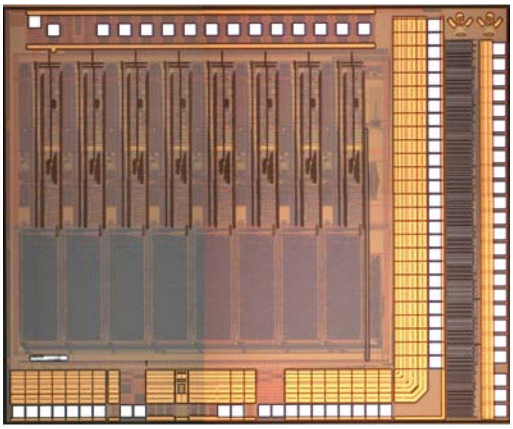
SUMMARY

Neural stimulation is a method currently used in neural prosthesis to restore the damaged or lost sensory, cognitive and motor modality of an individual. The nerve being stimulated can be part of the central nervous system (CNS), such as the cortex, or the peripheral nervous system (PNS), such as the sciatic nerve. To perform such stimulation, Implantable Neural Stimulator (INS) is often used. Together with the neural recording project on-going within the Centre, a bi-directional neural interface can be envisioned.

METHOD

Several targets in the design of an advanced INS surpass the existing systems. Firstly, a precise control scheme is required on the charge delivered to innervate target neurons. Excessive charge delivered consumes more power thus less efficient. Secondly, all the charge injected must be recycled because the accumulated DC voltage causes tissue damage. These two targets can be met provided the charge can be monitored.

Thirdly, a multi-channel INS can increase the bandwidth between the individual and the prosthetic device. It is also beneficial that by sending the stimulus through several electrodes simultaneously, better selectivity can be achieved due to the interferences among the stimuli, thus limiting the side effect of stimulation. Fourthly, power and data telemetry can provide battery-less and wireless operation without restricting the freedom of the individual.



PROGRESS

The novel charge mode stimulation was verified *in vitro* with a toad's sciatic nerve. A system level chip with 8 individually programmable channels has been fabricated and is currently under test. The aim of this chip is to further investigate and verify the ability of field shaping for better stimulation focalisation.

KEY REFERENCES

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PUBLICATION

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Mr Keshava Murthy

Thesis topic
A mobile application to facilitate the recommendation of antibiotics in the intensive care unit.

Supervisors Dr Pantelis Georgiou and Dr Pau Herrero Vinas

Funding
Imperial College Faculty of Engineering/Imperial College Faculty of Medicine Research Collaboration Kick-start Scheme

SUMMARY

Antibiotic prescribing is a high impact intervention in the intensive care unit (ICU). The potential for the emergence and spread of antibiotic resistance and treatment failure is as significant as the potential for positive patient outcomes. The overuse of antibiotics in ICU drives the emergence of local resistance rates.

To address this, specialist Microbiology and Infectious Diseases teams conduct daily reviews of patients in ICU and actively advise on the treatment of infections in this population. However, one of the problems they face is that it is currently not possible to access laboratory data on local resistance patterns and patient records at the point of care. Evidence also suggests the use of clinical decision support systems at the point of care can improve patient outcomes.

We, therefore, have begun, and are reaching the final stages of, creating a smartphone application that assists with the treatment of patients in ICU by

- recommending antibiotic prescription based on a case-based reasoning algorithm accessing a patient case memory (database) of successful and unsuccessful antibiotic recommendations and
- collating and displaying all pertinent patient data, such as local unit level antibiotic sensitivity data.

The aims of this project are:

- to pilot the utility and the adoption of this application by the Microbiology and Infectious Diseases teams
- measure the additional value of this technology to service delivery and patient outcomes *and*
- to roll out this application in full in multiple hospitals.

METHODS

The main engineering principle for this project is to choose a method for determining how similar patients are. We want to display entries in the patient case memory that are similar to the current patient. The selection of this algorithm is a strong indicator of whether or not this project will be a success. We have settled on using a form of k-Nearest-Neighbours, where the weights are chosen by Class-Augmented-PCA.

Pertinent patient data is split into three categories: demographics, sensitivity and pathology. The demographic data collection method has already been written and tested, while the methods for sensitivity and pathology data are soon to be tested.

RESULTS AND FUTURE WORK

An informal trial in an intensive care unit has already been conducted, with results looking promising. We hope to have the whole application ready for clinical trials by mid-November 2013.

Dr Sivylla-Eleni Paraskevopoulou

Thesis topic
Resource-efficient algorithms and circuits for highly-scalable BMI channel architectures

Supervisors
Dr Tim Constandinou and Professor Chris Toumazou

Funding
EPSRC

Graduated 2013

The study of the human brain has long fascinated mankind. This organ that controls all cognitive processes and physical actions remains, to this day, among the least understood biological system. Several billions of neurons form intricate interconnected networks communicating information through complex electrochemical activities. Electrode arrays, such as EEG, ECoG, and MEAs (microelectrode arrays), have enabled the observation of neural activity through recording of these electrical signals for both investigative and clinical applications. Although MEAs are widely considered the most invasive such method for recording, they do however provide highest resolution (both spatially and temporally).

Due to close proximity, each microelectrode can pick up spiking activity from multiple neurons. My research focuses on the design and implementation of novel circuits and systems suitable for high channel count implantable neural interfaces. Implantability poses stringent requirements on the design, such as ultra-low power, small silicon footprint, reduced communication bandwidth and high efficiency to avoid information loss. The information extraction chain typically involves signal amplification and conditioning, spike detection, and spike sorting to determine the spatial and time firing pattern of each neuron.

My research aims to design signal conditioning and processing nano-power circuits; implementing topologies such as a low-noise neural amplifier, a tunable cut-off frequency gm-C filter, and a variable gain amplifier, that will enable the uncalibrated monitoring of a large number of channels. During the past academic year, I have focused on hardware-efficient algorithms for spike sorting. This research has produced a new feature extraction method based on first and second derivative (FSDE) features, using only three features (thus achieving significant dimensionality reduction). The main advantage of this method is a unique balance between high accuracy and low computational complexity. But most importantly, during this year I have completed and successfully defended my PhD work.

PUBLICATIONS

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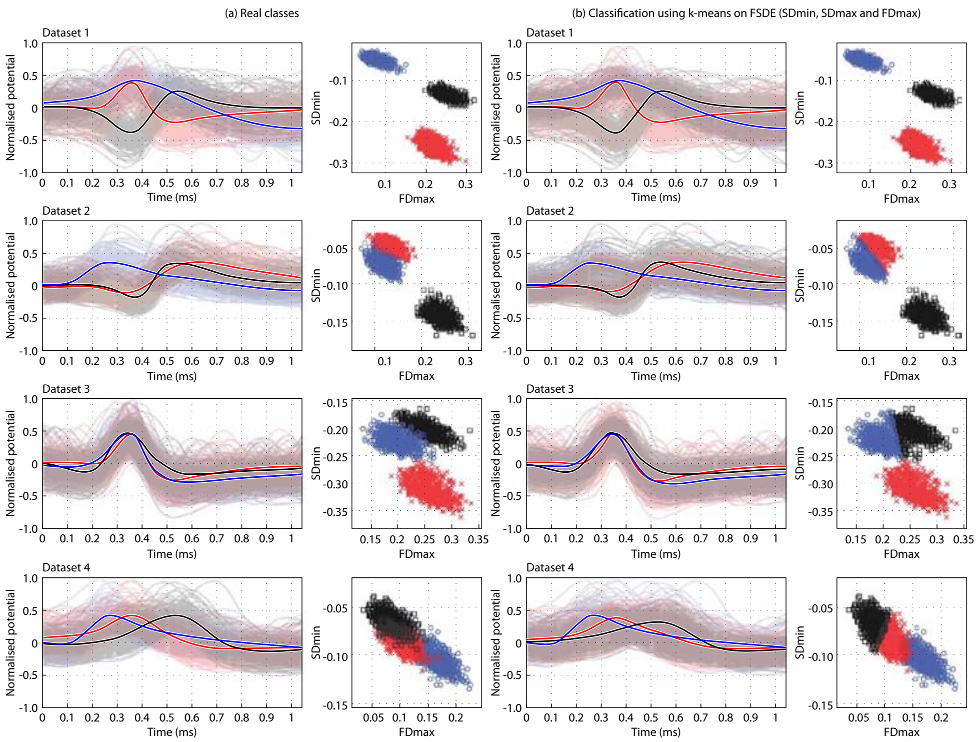
Spike classification using FSDE features



Mr Peter Pesl

Thesis topic
Intelligent decision support for type 1 diabetes

Supervisor
Dr Pantelis Georgiou

Funding
Biomedical Research Council

SUMMARY

Diabetes represents a major health burden for both individual patients and more globally for the health care system. Current treatment of diabetes involves intensive self-management which aims to keep the blood glucose concentration at a constant level. However, the task of maintaining healthy blood glucose levels as a diabetic is challenging, yet failure to do so can lead to serious complications which include blindness, cardio-vascular diseases, kidney failure, foot or leg amputations, nerve damage and complications during pregnancy. The amount of insulin needed to administer in order to achieve target control is determined according to the current blood glucose concentration, the quantity of carbohydrates consumed and other factors including time of day, exercise and illness. As many diabetic patients struggle to include all this important information into their insulin therapy, it is of interest to provide decision support with personalised consultation based on available glucose related data.

My research focuses on intelligent systems that help people with diabetes manage their blood glucose levels, thus reducing aforementioned long term complications and improving the quality of life of patients.

METHOD

One important part of my work is to analyse how various human and environmental factors such as exercise, stress and alcohol consumption, influence blood glucose levels and how these parameters can be incorporated in intelligent decision support systems (DSS). One application of DSS in diabetes management is to provide recommendation for the amount of bolus insulin that is being administered when eating a meal. In order to test the performance of the decision support algorithm, I use a Type 1 Diabetes Patient Simulator that is approved by the U.S. health regulatory body FDA (Food and Drug Administration) as a substitute for animal trials.

The current DSS is built on Case-Based Reasoning [1,2], an artificial intelligence technique that learns over time based on past experiences and therefore will provide individualised recommendations for each patient.

RESULTS

An innovative decision support algorithm for meal insulin dosing has been developed which provides enhanced adaptability and flexibility to current bolus calculators. In simulations the algorithm demonstrates improvement by increasing the time of blood glucose levels within target range. The algorithm has being integrated in a smartphone application, which will enable diabetics to use their phones for personalised insulin recommendations. At the moment, the whole system is being used by people with type 1 diabetes in clinical trials in order to evaluate usability and efficacy.

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Mr Mohammadreza Sohbati

Thesis topic
Circuits and systems for pH-based DNA detection

Supervisor
Professor Chris Toumazou

Funding
Winston Wong Centre for Bio-Inspired Technology and DNA Electronics Ltd

SUMMARY

With significant advancements in the field of molecular biology and studies in the molecular roots of inherited traits, the development of instruments that will facilitate applying this to everyday life is quite demanding. Conventional methods of analysis relied on optical methods and were limited to laboratories but now the need for such tests is required at the point of care. Consequently, fully electronic methods compatible with semiconductor technology that can provide cost-efficient, fast and robust analyses will be preferred.

Professor Toumazou's invention of an Ion-sensitive Field-Effect Transistor (ISFET) into the detection of single nucleotide polymorphisms (SNP) inspired the $1000 genome project to utilise this CMOS compatible transistor in such assays, leveraging all the benefits of the silicon technology. A sample product is Genalysis by DNAe Ltd, that provides user friendly portable set-ups for SNP detection. The other application is for implementation of sequencing arrays that lets tens to hundreds of millions of this transistor on a silicon wafer sequence the whole genome within a couple of hours at a much lower price; a dramatic improvement to the conventional technologies.

In this work ISFETs as one of the most successful and promising platforms for the aforementioned lab-on-chip instrumentation is studied. Besides its tangible potentials, there are also non-ideal characteristics like drift and offset that require proper calibration strategies before they are used. There are other challenges: it is shown that by scaling the technology to smaller feature sizes in order to achieve higher levels of integration, low frequency noise becomes an issue, especially the frequency range of the nucleotide incorporation. Diffusion of ions is another issue for very large scale integrated arrays. Therefore, proper signal conditioning circuits that can improve the signal to noise ratio as well as high speed converters in highly integrated arrays become substantial.

This research has focused on providing proper algorithms and methodologies to suppress the aforementioned unwanted characteristics. In studying ISFETs and providing a more complete formula and model to explain the characteristic of this micro-sensor, a design methodology is introduced that can suppress the effect of drift. New signal conditioning and readouts for ISFETs have also been designed.

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Ms Tatiana Trantidou

Thesis topic
Microengineered platforms for growing, controlling and monitoring cells *in vitro*

Supervisors
Professor Chris Toumazou and Dr Themistoklis Prodromakis

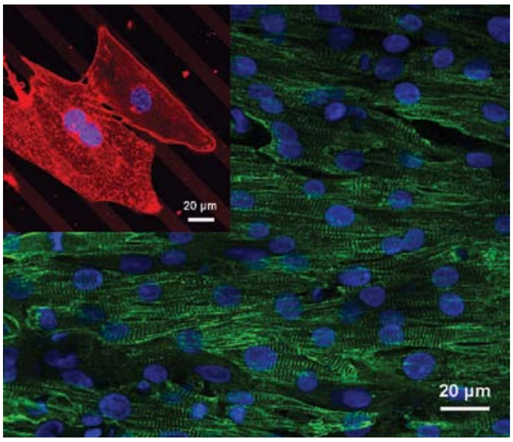
Funding
The AG Leventis Foundation, Scholarship in Bio-Inspired Devices

Latest technology driven by emerging micro/nano-fabrication techniques has provided the appropriate knowledge to fabricate *in vitro* platforms for growing, controlling and monitoring cells and tissue with applications in drug development, organ-assist devices, surgical tissue transplantation, and eventually, engineered patient-specific organs.

The main challenges in fabricating cell culture platforms are two; the first one is the development of bio-realistic cultures, i.e. culture systems that preserve important structural and functional properties of the tissue *in vivo*, and are therefore more representative models for disease and pharmacological studies. The second major challenge is monitoring at all stages the electrochemical activity of cultured cells, which is tightly connected with their development process and function. Electrical monitoring of 2-D cell cultures is well established with state-of-the-art being planar Multielectrode Arrays. On the other hand, chemical monitoring has been accomplished in many ways; optically through fluorescent microscopy and the use of dyes, and electrically through ISFETs, single electrodes and nanowire nanosensors.

This PhD project is targeted on developing culture constructs that control cells maturation and function by regulating culture conditions, particularly physical constraints to cell growth and application of static stretch. Patterning of rat ventricular myocytes has been achieved through the use of flexible polymer substrates in order to preserve the contractile properties of the cells *in vitro*. Selective hydrophilic modification of the polymer surface properties through standard lithography and oxygen plasma treatment facilitated the self-alignment of cardiac cells (figure), enabling a more *in vivo*-like cell morphology and Ca2+ function, which was found to be dependent on the inherent properties of the substrate (thickness, flexibility). This technology is currently being transferred to commercial MEAs for comprehensive interrogation of the cells electrophysiology. In addition, chemical sensing modalities based on inexpensive technologies have been developed to be incorporated into these bioengineered substrates to perform extra- pH monitoring, facilitating a thorough study of the cellular metabolism.

Our long-term goal is to investigate scientific and technological aspects of tissue engineering that involve cell and tissue growth in micro-fabricated scaffolds, intercellular communication and mechanotransduction mechanisms in cells and tissues. Towards this direction we anticipate to deliver a powerful, universal tool with high scientific and commercial impact in tissue physiology understanding, disease modelling, and drug toxicity studying.



Cardiac cells aligned on micro-engineered polymer substrates. Inset: Single cells view.

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Mr Ian Williams

Thesis topic
A neural-electronic interface providing proprioceptive feedback for prosthesis control

Supervisor
Dr Timothy Constandinou

Funding
EPSRC DTA

SUMMARY

Sensory feedback from the body is key to enabling fine motor control, natural (low cognitive load) movement and non-visual awareness of the position of your body. Individuals with prosthetic limbs lack this proprioceptive feedback and as such struggle to learn to control their artificial limbs and are unlikely to achieve high levels of coordination.

This research will investigate neural stimulation as a method of providing artificial proprioceptive feedback from a prosthetic limb. Our approach makes use of a peripheral neural implant for stimulation and will focus on providing the user with intuitively understood information. As such the research will look at creating neural signals that mimic those naturally found in the body.

METHOD

Sensors fitted to a robotic arm measure the joint angles and torques during its motion. Biomechanical modelling is used to translate these angles and torques into estimates of equivalent muscle lengths and muscle activations in a 17 muscle, 7 degree of freedom model of the human arm. This muscle activation and strain information is then fed into models of 2 key proprioceptive receptors (muscle spindles and Golgi Tendon Organs) producing estimates of the neural signals from these receptors. Finally these neural signals are induced in the user using a low power neural implant that has been developed to safely stimulate the appropriate peripheral nerves.

RESULTS TO DATE

The neural stimulator has successfully been tested on a frog peripheral nerve and demonstrates good charge balancing and a significant reduction in power consumption. A combined biomechanical and proprioceptive model in C has been developed and tested – results indicate a good match with existing models combined with an orders of magnitude improvement in computational efficiency, as such the model is expected to be suitable for real time operation on a microprocessor.

NEXT STEPS

Our research will now look at validating the modelling and investigating stimulation strategies using proprioceptive illusions induced by muscle vibration.

KEY REFERENCES

1. Dhillon GS and KW Horch, 'Direct neural sensory feedback and control of a prosthetic arm', *IEEE Transactions on neural systems and rehabilitation engineering*, 13(4), 2005.
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3. Song D, N Lan, GE Loeb, J Gordon, 'Model-Based Sensorimotor Integration for Multi-Joint Control: Development of a Virtual Arm Model', *Annals of Biomedical Engineering*, vol 36, Issue 6, 1033–1048, June 2008.

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1. Williams I and TG Constandinou, 'An Energy-Efficient, Dynamic Voltage Scaling Neural Stimulator for a Proprioceptive Prosthesis', *International Symposium on Circuits and Systems* (ISCAS), 2012.
2. Williams I and TG Constandinou, 'An Energy-Efficient, Dynamic Voltage Scaling Neural Stimulator for a Proprioceptive Prosthesis', *Transactions of Biomedical Circuits and Systems* (TBioCAS), 2013.

Mr Stephen Woods

Thesis topic
Wireless capsule endoscope for targeted drug delivery

Supervisor
Dr Timothy Constandinou

SUMMARY

Endoscopes and colonoscopies are used to diagnose and treat pathologies such as Crohn's disease in the gastrointestinal tract. However the small intestines pose a problem for these conventional methods as the small intestines are very difficult to access. One method employed to overcome this problem is the use of wireless capsule endoscopes. 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.

The aim of my research is to design a swallowable micro-robot which is capable of diagnosis and also has the functionality to deliver targeted therapy.

METHOD

My research will focus on developing a swallowable micro-robotic platform which has novel functionality that will enable a wireless capsule endoscope to deliver targeted therapy. The platform will consist of three highly novel sub-systems: one is a micro-positioning mechanism which can deliver 1 ml of targeted medication, the second is a holding mechanism which gives the functionality of resisting natural movement from peristalsis and also offers the ability to slow the transit of the micro-robot and the third is a system to control the release of the onboard medication.

RESULTS

Detailed designs of the micro-positioning mechanism and holding mechanism have been completed and loading and stress analysis have been carried out on the holding mechanism. A concept design for the power management has been developed which overcomes the problem of delivering power through the micro-robot.

Prototypes of the holding mechanism and micro-positioning mechanism are in development. A conceptual design based on conventional wireless pill-sized camera geometry is presented in the figure and represents the components being prototyped.

NEXT STEPS

I will develop more detailed proof of concept prototypes of the micro-positioning mechanism and of the holding mechanism. I will also develop a user interface which will control the position and release of the holding mechanism.

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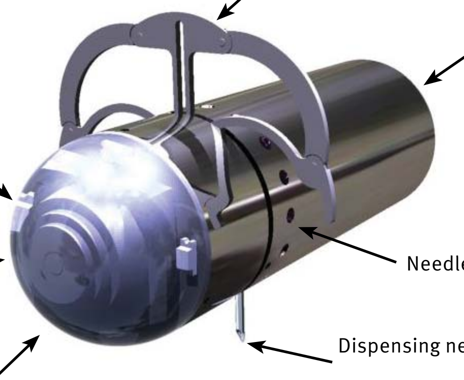
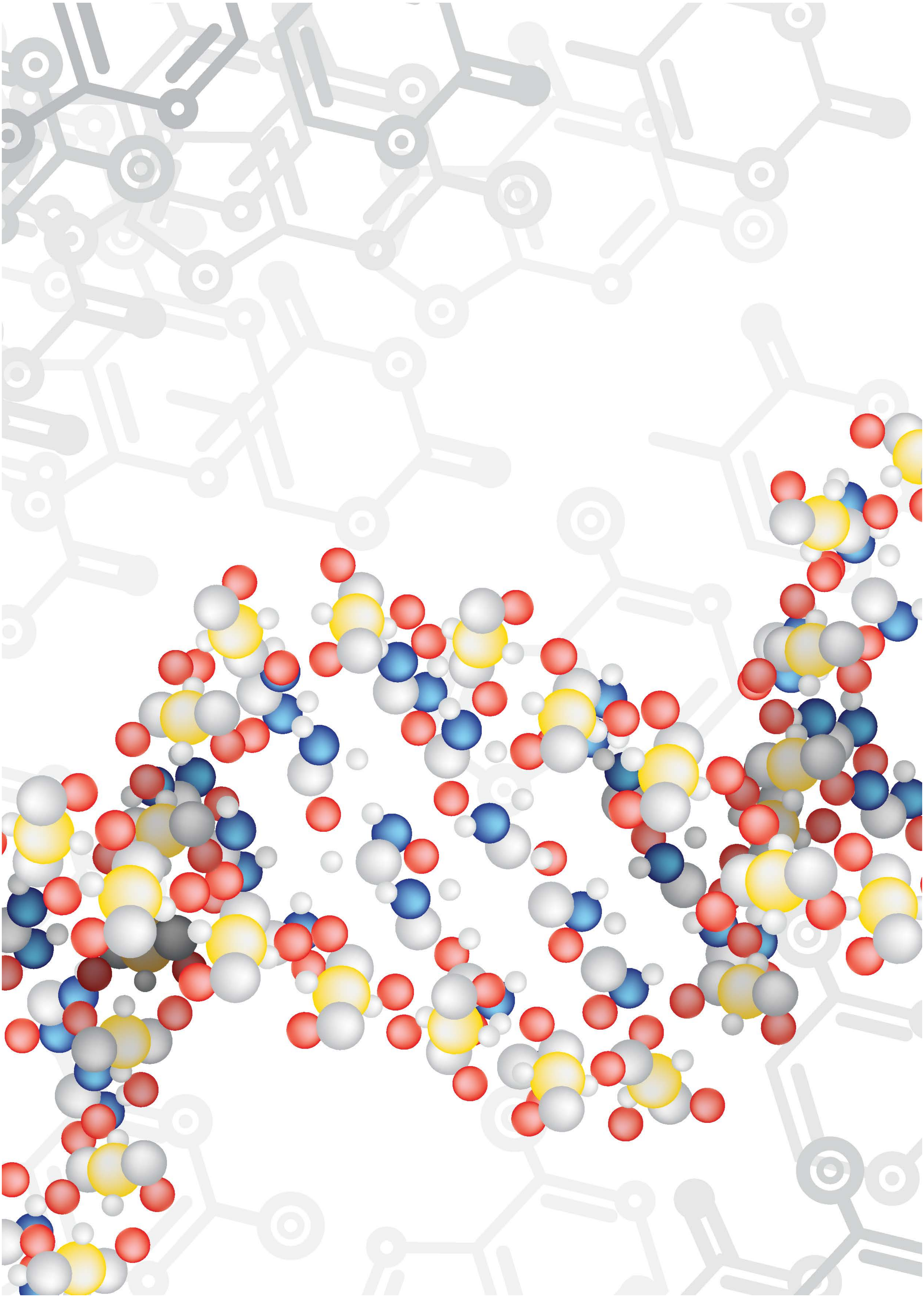
A concept design showing the holding mechanism fully deployed and the dispensing needle deployed diametrically opposite the holding mechanism





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