

Imperial College
London

Centre for Bio-Inspired Technology

Annual Report 2012



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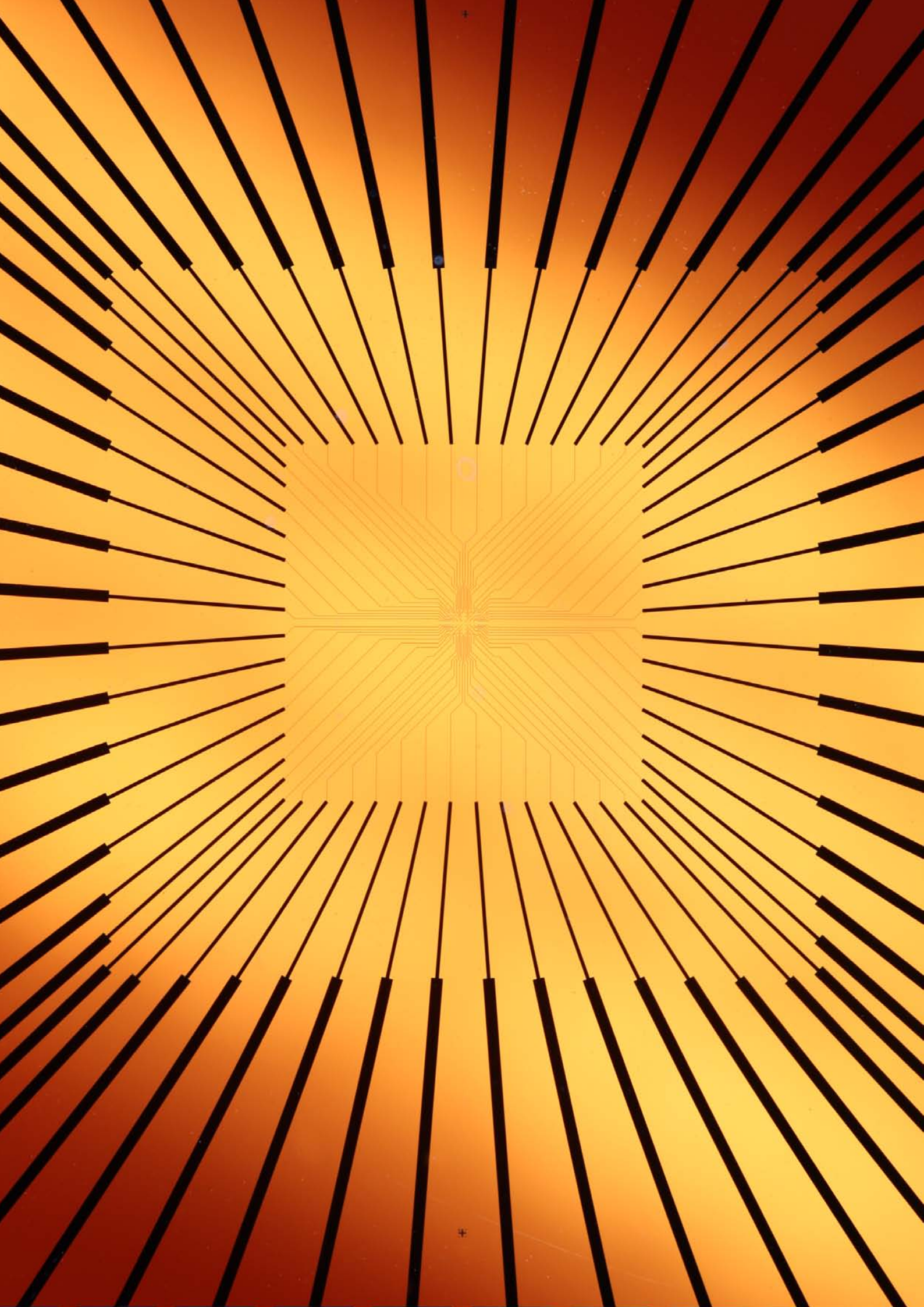
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Centre for Bio-Inspired Technology

Annual Report 2012

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Director's foreword

This Research Report for 2012 describes the research activities of The Centre for Bio-Inspired Technology as it completes its third year of research. 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. I hope you will enjoy reading about our activities over the past year and our achievements.



One of the consequences of longevity is that we are building a network of 'alumni' who have either completed their PhD with the Centre or research assistants and fellows who have worked on research projects. It is one of the roles of a leading research group to collaborate with colleagues not only within the UK but worldwide and, as a multi-disciplinary

research institute, our collaborators include engineers, scientists, medical researchers and clinicians. We include here some brief reports of these colleagues and how their current research has developed from their work in the Centre.

One of the prime aims of the Institute of Biomedical Engineering, from which the Centre developed, was to transfer technology from the laboratory into a commercial environment and ensure that the products of our research have a direct benefit to improve the healthcare and lifestyle of individuals. We continue to pursue this goal and in this Report we focus on some of the work underway towards this end. Within the Centre we have secured funding for facilities and technical support which is directly linked to the transfer of our technology and we highlight some of this in the Report. We also include the latest news from our 'spin out' companies, Toumaz Ltd and DNA Electronics Ltd, demonstrating our successes and challenges as we commercialise our research into marketable products.

We continue in our strategy of devices and processes for early diagnosis, and therapy for chronic disease, which continue to be major challenges for the medical professionals in treatments and funding. Recent Reports have highlighted the demands in healthcare, not least in the NHS, for accurate, low cost diagnostic devices and systems for enabling those with chronic disease to lead independent lifestyles and reduce the financial burden on hospitals and GPs.

I am pleased to report that we have continued to be successful in attracting funding for our research and it is particularly satisfying that we are continuing to receive funding from both the research councils and our private funders who recognise the contribution which bio-inspired technologies are making towards the challenges facing the health service. I hope you will enjoy reading about our research and the progress we are making in meeting our aims.

Professor Chris Toumazou FRS, FREng

Founding Sponsor's foreword

This Centre brings together my passions for medical device technology and semiconductors. I first decided to make a donation to Imperial College London to found this specialist Centre in 2010. I came to know Professor Toumazou from his work in developing silicon technology, especially in relation to personalised healthcare devices, and I knew, from our many discussions, that he held a strong belief that biological systems hold the key to innovative technologies. He told me of his vision to continue inventing and developing devices which mimicked living systems and I found that an equally fascinating proposition.

I am delighted to have enabled the Centre for Bio-Inspired Technology to become a reality. I am very pleased to continue my close association with the Centre and to see the progress being made towards new devices for the diagnosis and management of chronic disease. In this, as in previous Reports, the researchers describe the work they are undertaking, share their ideas and hypotheses and demonstrate the progress they have been able to make.

We have all become more demanding of healthcare at a time when ageing and so many 'lifestyle' diseases, such as type 2 diabetes and cardio vascular problems are challenging the care systems and services. We are



becoming less tolerant of reducing our independence and have no wish to spend time in hospitals if this can be avoided. It is heartening to see that so many of these challenges are being confronted and that the Centre's researchers are developing some real solutions which will be of widespread benefit. The progress in some areas towards clinical trials is of particular note.

I 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

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 Nir Grossman

Dr Olive Murphy

Dr Belinda Nedjai

Dr Herrero-Vinas Pau

Dr Themistoklis Prodromakis

Dr Monika Reddy (Clinical)

ASSOCIATES

Dr Dylan Banks

Dr Amir Eftekhari

Dr Ali Khiat

Dr Yan Liu

Dr Iulia Salaoru

Dr William Spinner

Dr Irina Spulber

Dr Jakub Trzebinski

Dr Thomas Weissensteiner

Research students

Mr Deren Barsakcioglu

Mr Onur Guven

Mr Yuanqi Hu

Mr Walid Juffali

Ms Melpomeni Kalofonou

Mr Kwok Wa Lui

Ms Christina Morris

Ms Sivylla Paraskevopoulou

Mr Ayodele Sanni

Mr Alexander Serb

Mr Mohammadreza Sohbati

Ms Tatiana Trantidou

Mr Ian Williams

Mr Stephen Woods

Assistants

Mr Mohamed El-Sharkawy

Mr Song Luan

Mr Matthew Lubelski Katz

Mr Keshava Murthy

Mr Peter Pesl



Administrative staff & consultants

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

Visiting academics

PROFESSORS

Professor Tor Sverre Lande

University of Oslo

Professor Bhusana Premanode

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

Professor Gareth Jenkins

Nanjing University of Posts and Telecommunications, China

Dr Jamil El-Imad (Honorary Senior Research Fellow)

W Investments, UK

Graduates in 2011–2012

Dr Abdul Al-Ahdal

Assistant Professor,
Umm Al-Qura University, Saudi Arabia

Dr Yan Liu

Research Associate,
Centre for Bio-Inspired Technology

Dr Surachoke Thanapitak

Lecturer, Mahidol University, Thailand

Dr Virginia Woods

Assistant Professor, New York University, USA

Researchers who have taken up appointments elsewhere

Mr Siavash Saremi-Yarahmadi

Research Assistant, Circuits and Systems Group,
Department of Electrical and Electronic Engineering,
Imperial College London

Ms Oghenevorhe Omeru

PhD Student, Circuits and Systems Group,
Department of Electrical and Electronic Engineering,
Imperial College London

Dr Nir Grossman

Postdoctoral Fellow, MIT, USA

Dr Zhaolei Lang

Molecular Biologist, DNA Electronics Ltd

Mr Bard Haaheim

IC Design Engineer, Hittite Microwave AS,
Arctic Design Center, Norway

Dr Gareth Jenkins

Professor of Advanced Bio-analytical Micro Devices,
Nanjing University of Posts and Telecommunications,
China

News

Honours and awards

APRIL 2012

Dr Konstantin Nikolic has been promoted to Senior Research Fellow in the Department of Electrical and Electronic Engineering. Konstantin joined the Institute of Biomedical Engineering in 2005 and will continue his research in the Centre for Bio-Inspired Technology.



Dr Nir Grossman has been awarded a Wellcome Trust-MIT Postdoctoral Fellowship for the project entitled 'Optical Transcranial Magnetic Stimulation'. He will spend three years at MIT in Harvard working with Professor Ed Boyden's group and will return to Imperial to undertake the final year in the Centre for Bio-Inspired Technology.

The Fellowship offers opportunities for postdoctoral scientists to undertake research at the interfaces between biology/medicine and mathematics, engineering, computer, physical or chemical sciences, firstly at MIT and then at a UK institution. Candidates for the Fellowship have to identify an important biomedical research question and to propose a personal interdisciplinary training programme to achieve their research aims. The Fellowship aims to support post doctoral scientists to train in a new research area that is complementary to, but distinct from, their current field of expertise, thereby enabling an interdisciplinary approach to their research.

Professor Chris Toumazou has been awarded an Honorary DSc from Mahanakorn University in Thailand.

Professor Chris Toumazou received the 2011 IET JJ Thomson Medal for Achievement in Electronics. The award cited his 'innovative applications of silicon technology and integrated circuit design and successful applications of semiconductor technology to biomedicine and the life-sciences, most recently to DNA analysis, leading to striking innovations in the fields of genetics and molecular biology'.



News

People and events

SEPTEMBER 2012

Centre's PhD students attend Royal Academy of Engineering Young Researchers Meeting

Three of the Centre's PhD students, Ian Williams, Deren Barsakcioglu and Sivylla Paraskevopoulou attended the Royal Academy of Engineering Young Researchers Futures Meeting, Panel on Biomedical Engineering. The Panel was held at the University of Warwick in the Institute of Digital Healthcare, and covered various areas and disciplines underpinning neural engineering, from neural interfacing, to neural modelling, computational intelligence, neurorehabilitation and neural networks/ cybernetics.

This was an excellent opportunity for the students to interact with their peers and to explore more widely the focus of their own research. Ian Williams said: 'The small scale and residential format of this conference made it easier for all the attendees to meet each other, ask questions and discuss their work, both formally in the presentations and informally over meals and drinks.'

AUGUST 2012

Centre's Director speaks at Global Business Summit

Professor Chris Toumazou was an invited speaker at the UKTI's Healthcare and Life Sciences Global Business Summit at Lancaster House, an event at the British Business Embassy, organised by the Prime Minister, which formed the centrepiece of the UK international Olympics business legacy strategy.

During the Olympic Games the Prime Minister, Deputy Prime Minister, Chancellor, Business Secretary, Foreign Secretary and 30 Government ministers welcomed over 3,000 business leaders and global figures to the Global Investment Conference and a series of Global Business Summits. The series was the largest and most ambitious set of trade and investment events ever held in this country allowing businesses and Governments to exchange views and ideas, discuss local and international economic challenges, develop strong global partnerships for future growth and showcase the best of British business to the world.

Professor Toumazou spoke at the summit, entitled 'Rising to the Healthcare Challenges of the Next Decade – the Global Business Summit on Healthcare and Life Science', which focussed on the challenges facing healthcare delivery around the world, in both developed and emerging economies. It debated ways in which transformational change in healthcare can be achieved through collaboration between industry, academia and healthcare providers. The event was hosted by Lord Green of Hurstpierpoint, Minister of State for Trade and Investment and Professor Lord Darzi of Denham, UK Business Ambassador for the Life Sciences and Chair of the Institute of Global Health Innovation at Imperial College London.

Professor Toumazou's presentation, 'Disposable Semiconductor Healthcare – from the bedside to point of care genetics' showed how a revolution in genetics and molecular biology is being driven by the confluence of advances in life science and semiconductor-based technologies. He described the key disruptive innovation of the first label-free DNA amplification and detection based upon ISFET (Ion-Sensitive, Field-Effect Transistor) technology, which is enabling the creation of on-the-spot DNA diagnostic tests. He examined the technology trends and business models for rapid, lab-free and pipette-free DNA diagnostic testing, and the transformative opportunities it presents in global healthcare provision.

JUNE 2012

A new perspective on memristors

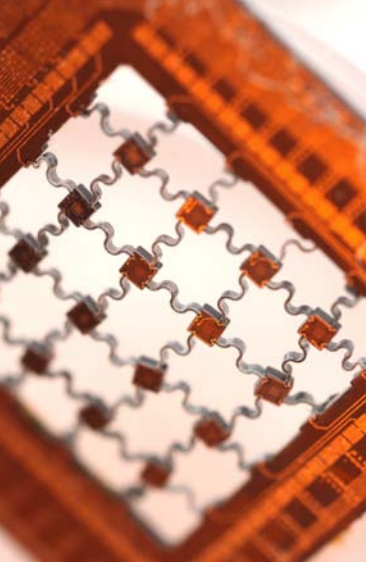
Dr Themis Prodromakis co-authored a paper with Professors Chris Toumazou and Leon Chua* published in *Nature Materials*. This benchmark article provides a new perspective for memristors (memory-resistors) that could stimulate fruitful discussions while at the same time provide inspiration for discovering novel experimental approaches. The paper demonstrates that memristance occurs naturally in both organic and inorganic systems that exhibit inertia.

T. Prodromakis, C. Toumazou and L.O. Chua, 'Two Centuries of Memristors', *Nature Materials*, vol. 11, no 6, pp. 478–481, June 2012.

*Professor Leon Chua is in the Electrical Engineering and Computer Sciences Department at the University of California, Berkeley and a regular visitor to Imperial College.



Members of the memristor's research team led by Dr Themis Prodromakis (3rd from right) with Professor Leon Chua (centre) who visited the Centre.



MAY 2012

DNA technology showcased at Imperial Festival

The inaugural Imperial Festival took place on 11 and 12 May 2012. The Festival celebrated the College through hands-on demonstrations, music, comedy, dancing and art. All activities were free, open to the public and for all ages. Friends, neighbours and the wider community were welcomed to explore the best on offer from Imperial staff and students.

In collaboration with DNA Electronics Ltd, a 'spin-out' company from the Centre, two of the Centre's PhD students, Ms Melpomeni Kalofonou and Mr Mohammadreza Sohbati (3rd and 4th from left of picture) represented DNA related research by demonstrating the latest updates on technologies applied on lab-free, real-time molecular diagnostics forming the next generation of biomedical devices for genetic testing.

One of the key advances of these technologies is the development of a novel platform (Genalysis®) for DNA detection using microchip technology. The platform was demonstrated in the form of a three-step lab-free system where theoretically DNA is collected from the patient (eg. saliva sample or swab) then purified and prepared for amplification and finally passed on the chip that is plugged into a USB interfacing with a pc, tablet or mobile phone, where real-time amplification and detection takes place.

Genalysis® is able to perform simultaneous DNA amplification and detection using the technology of a CMOS microchip within around 30 minutes, offering semiconductor solutions to multiple genetic questions.



NOVEMBER 2011 – MAY 2012

Centre's research presented on the world stage

A group of researchers from the Centre attended the IEEE Conferences of the Circuits and Systems Group and delivered papers.

At the May International Symposium on Circuits and Systems (ISCAS) held in Seoul, the Centre presented 10 papers. Tim Constandinou, Amir Eftekhar, Matthew Katz, Pantelis Georgiou, Song Luan, Yuanqi Hu, Sivylla Paraskevopoulou and Ian Williams attended.

Nine researchers attended the 2011 BioCAS Conference in San Diego: Tim Constandinou, Pantelis Georgiou, Melina Kalofonou, Song Luan, Sivylla Paraskevopoulou, Themis Prodromakis, Mohamed El-Sharkawy, Alex Serb and Ian Williams.

In March 2012, Professor Toumazou gave the Key Presentation at the Future of Genomic Medicine Conference held at the Scripps Translational Sciences Institute in La Jolla, California.

His lecture was entitled 'Hand held transistors and DNA sequencing'. The conference focussed on the extraordinary advances that are occurring in the field of genomic medicine which include whole genome and exome sequencing, pharmacogenomics, and advances in cancer treatment as an outgrowth of genomics. Some of the speakers were non-scientists and included journalists, regulatory experts, and lawyers. The aim of the conference was to spearhead efforts to change medicine using genomics.

OCTOBER – NOVEMBER 2011

Centre's Director at TEDMed and the Royal Society

Professor Chris Toumazou was invited to present two prestigious public lectures.

He gave a lecture in the Royal Society's Public Lecture Series entitled 'Bioinspired technology: from cochlear implants to an artificial pancreas'. The lecture was very well attended by members of the public and was well received with a lively question and answer session. The lecture is available as a webcast on the Royal Society website www.royalsociety.tv



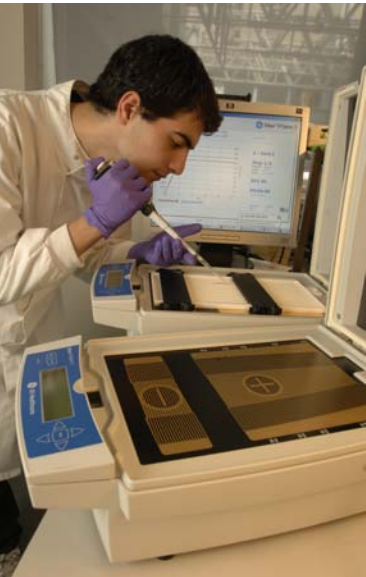
He was also invited to speak at the prestigious TEDMED conference in San Diego. TEDMED is renowned for speakers who are 'cutting edge thinkers and doers who will provide inspiration' and 'innovators' who give a window into the future of medicine.

His lecture, entitled 'When Will Wireless Medicine Change Healthcare', included a real time demonstration of the DNA Genalysis technology, a rapid sample-to-answer platform for nucleic acid detection. The Genalysis® three-step system is a pipette-free, lab-free system which redefines «point-of-care» nucleic acid testing and can be used by even unskilled users to perform accurate nucleic acid tests anytime, anywhere.

The lecture is available at:
www.youtube.com/watch?v=qY8dlhdhJDCM

News

from the Centre's 'spin-out' companies



JULY 2012

Centre's spin-out companies award scholarships at Imperial

DNA Electronics Ltd and Toumaz Ltd are pleased to announce they have awarded scholarships for study at Imperial College London. The first recipients, Daniel Khoo Eng Chin and Andrew Khoo Eng Kee, are from Malaysia and have chosen to study for the MEng degree in the Department of Bioengineering. The students will select their project options in collaboration with the Centre and their industrial sponsor.

Professor Toumazou said 'I am delighted that DNA Electronics and Toumaz are able to support students in this way enabling young people from overseas to take advantage of the excellent education and learning experience which Imperial College London provides. These scholarships are awarded to support young professionals to study in the field of medical devices and enable them to select the course most suited to their development needs.'

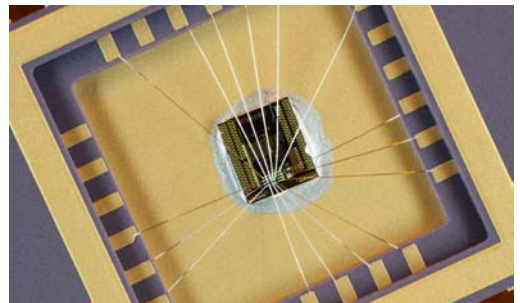
It is in the field of biomedical engineering that Professor Toumazou's companies have been so successful. Toumaz Limited is applying the technology of the silicon transistor and integrated circuit design to ultra-low power devices for medical diagnosis and therapy. Amongst these devices is the Sensium™ Ultra-Low Power Wireless Body Monitoring System which is being deployed in US hospitals for the treatment of chronic illness. DNA Electronics Ltd is creating a suite of electronic microchip-based solutions to enable faster, simpler and more cost-effective DNA analysis including targeted DNA sequencing for point of care diagnosis and therapy.

JULY 2012

What makes a centenarian?

DNA Electronics technology will be used in a race to unlock genetic clues behind living to 100. The race, which will start in September 2013, is for the \$10m Archon Genomics X Prize. Entrants will be given 30 days to work out the full DNA code of 100 centenarians at a cost of no more than \$1,000 per genome. The first entrant to declare their intention to compete is Dr Jonathan Rothberg of Ion Torrent which holds a license to use the DNA Electronics technology.

Being able to sequence the full human genome at a cost of \$1,000 or less is regarded as a milestone in science. It is seen as the threshold at which DNA sequencing technology becomes cheap enough to be used widely in medicine, helping in diagnosis and in matching drugs to a patient's genetic make-up.



Genetic entrepreneur Dr Jonathan Rothberg, Head of Ion Torrent, is entering the challenge to identify genes linked to a long, healthy life. Dr Rothberg's team from Life Technologies Corporation in California is the first to formally enter the race claiming his machine, the Ion Proton sequencer, can sequence DNA more quickly and cheaply than ever thought possible. Ion Torrent holds a worldwide, non-exclusive, licensing deals giving them access to parts of the DNA Electronics technology for use in semiconductor genetic sequencing and it is this technology which will be at the heart of the DNA analysis. One hundred people aged 100 have donated their DNA for the project.

Scientists believe people who reach a very old age may have certain rare changes in their genes which protect against common diseases of later life, such as heart disease and cancer. If these genes can be identified by analysing the DNA codes of centenarians, it will help scientists search for new medical treatments and perhaps ways to prolong life.

MARCH 2012

Presenting DNA Electronics technology to a wider audience

DNA Electronics Ltd, a fabless semiconductor provider of solutions for real-time DNA and RNA analysis unveiled its Genalysis® point of care technology at the Personalized Medicine World Conference 2012 in Silicon Valley. DNA Electronics' Yan Lin Lye showed the technology for sample-to-answer genotyping in under 30 minutes using the Sample Preparation Kit and USB-stick based analyser.

Genalysis is a real-time, nucleic acid testing platform that delivers point-of-need results in about 30 minutes, using a sample processing kit and interchangeable test cartridges plugged into a USB stick or other electronic reader. Using a saliva sample from a mouth swab, purified, amplification-ready DNA is delivered to a complementary metal oxide semiconductor-based test cartridge, which amplifies and detects genetic signatures in the DNA.

DNA Electronics has made its nucleic acid testing platform available to geneOnyx for cosmetic and skincare applications. The commercial license and supply agreement gives geneOnyx access to DNA Electronics' Genalysis platform, which geneOnyx will use to analyze a person's genetic makeup to determine how that person will react to certain cosmetic product ingredients. geneOnyx provides cloud-based genetic analytics services and technology for cosmetic applications. Pilot trials focused on the clinical diagnostics space for Genanalysis are set to begin later this year.

DNA Electronics said that the licensing arrangement takes it into the non-*in vitro* diagnostic space.

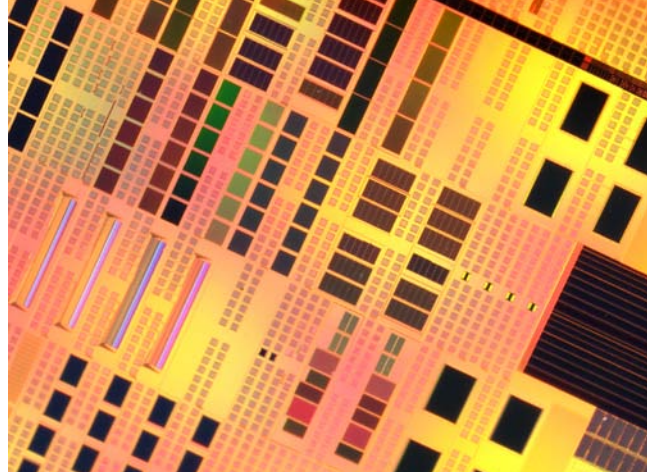
www.dnae.co.uk

JULY 2012

Toumaz Ltd acquires a leading supplier of semiconductor and software solutions

Toumaz Ltd a pioneer in and provider of ultra-low power, high-performance wireless communications technologies and solutions, has acquired Frontier Silicon (Holdings) Limited, a leading supplier of semiconductor, module and software solutions for digital radio and connected audio systems.

Frontier is a market leading supplier of digital audio chips and modules to global consumer electronic brands and this acquisition will bring an important electronic engineering resource to Toumaz, with R&D centres in the UK, Hong Kong and China. The strong technological alignment of Toumaz's healthcare, radio and wireless chip technologies and Frontier's expertise in semiconductor, module and software systems creates a genuine total solution provider and is an opportunity for Toumaz to exploit Frontier's established tier one customer base, including Bang &



Olufsen, Bose, JVC, Panasonic, Philips, Pure, LG, Roberts Radio and Sony.

Anthony Sethill, CEO of Toumaz, said: "This acquisition is consistent with our strategy for providing ultra-low power, high performance wireless communications across the healthcare, fitness and consumer electronics markets. Bringing these two innovative UK technology companies will enable the enlarged Group to exploit the strengths and opportunities of both businesses. Our wireless solutions have huge potential and combined with the software systems, commercial expertise and tier one customer access of Frontier, will create a significant total solution provider for the wireless communications market.

This acquisition will enable Toumaz Ltd to strengthen its commercial presence and accelerate its profitable expansion towards becoming the global leader in complete wireless platforms.

JUNE 2012

Toumaz chips in PURE products going global

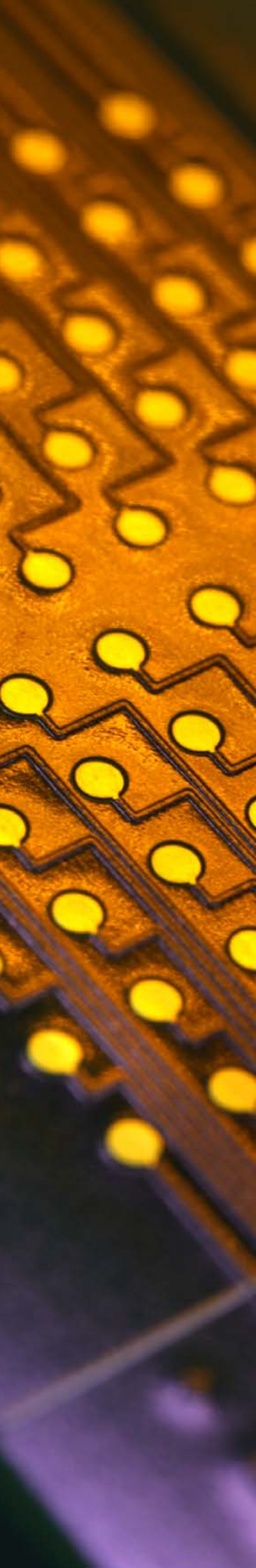
Toumaz Microsystems, which develops highly integrated, low power SoCs (systems on chip) and solutions for the growing wireless multimedia and embedded connectivity markets, has announced that a growing number of the latest new products from Pure, the world-leading maker of wireless music and radio systems, are now shipping world-wide.

The highly integrated Toumaz TZ1090 'Xenif' device enables Pure to deliver the most advanced connectivity and multimedia capabilities in the latest members of its innovative radio and wireless music product ranges, while hitting aggressive price points and power consumption targets. The Toumaz TZ1090 Xenif SoC delivers all of the functions from tuner to audio and display output on a single chip needed to create a wide range of advanced multi-media capable connected consumer products.

www.toumaz.com

Research funding

Project	Sponsor	Start Date	Duration
Volatile Memristors	EPSRC	May 2012	6 months
Automated Blood Pressure Monitoring	Wellcome Trust	March 2012	3 years
NEUral Memristive Architecture	EPSRC	September 2011	3 years
Automated Blood Pressure Monitoring	Wellcome Trust	August 2011	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
Advanced Shot Detection	Defence Science and Technology Laboratory	February 2012	3 months
Adaptive Hearing Protection	Defence Science and Technology Laboratory	January 2011	1 year
HIV patents in ICHT	Imperial College Healthcare NHS Trust – BRC Funding	October 2010	1.5 years
Next Generation Neural Interfaces	EPSRC	October 2010	4 years
Non-invasive Stent Blood Flow	Imperial College Healthcare NHS Trust – BRC Funding	September 2010	2 years
Glucose Monitor	Imperial College Healthcare NHS Trust – BRC Funding	August 2010	2 years
CMOS Electro-Optical Platform	EPSRC	October 2009	3 years
Power/Data Transfer Platform	EPSRC	October 2009	3 years
Supercapacitors	EPSRC	October 2009	2 years
Wellcome Medical Engineering Centre	Wellcome Trust / EPSRC	October 2009	5 years
Bio-Inspired Artificial Pancreas	Wellcome Trust	September 2009	4 years
Implantable SAW Transponder	Wellcome Trust	September 2009	3 yrs 8mths
3 Tier Sensor Platform	EPSRC	April 2008	3yrs 6mths
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, more decentralised approach centred on the patient – known as personalised healthcare. They also open up new ways of coping with the huge problems of ageing populations and surges in chronic ailments such as diabetes and heart disease.

We believe this shift in the model will result in a more portable, precise and personal way to deliver healthcare using user-friendly devices such as 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 by removing the need for onsite clinic visits for monitoring and shorter stays in hospital beds because patients can be diagnosed and monitored more quickly and in many cases remotely.

Researchers within the Centre for Bio-Inspired Technology work 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.

The bio-inspired control algorithm for our artificial pancreas has already undergone an *in silico* validation using a commercial simulator (UVa T1DM simulator), approved by the US Federal Drug Administration as a substitute for animal trials. The results confirm good control of 200 simulated diabetes patients with 93% time spent in target glycaemia and with no episodes of severe hypoglycaemia.

We are delighted to report that 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 over six-hours in 10 subjects with type 1 diabetes (75% male, mean (SD) age 44(12) years, duration of diabetes 22(8) years, HbA1c 58(9) mmol/mol, body mass index 25(5) kg/m²) report good control and no incidences of hypoglycaemia with a mean (SD) sensor glucose at 6.6(1.5) mmol/L.

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

Diagnostic lab-on-chips for early detection of disease – which includes devices which fully integrate chemical sensors and low power processing algorithms to provide cheap, disposable and intelligent chemical monitoring systems with long battery lifetimes. These are currently being used 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.

A detailed, high-magnification image of a microchip, showing a complex grid of circuitry in shades of blue, green, and yellow. The image is oriented vertically on the left side of the page.

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

DNA is a biological molecule in the form of chains with millions of base pairs which 'code' the genetic information which makes us an individual. By investigating this biological code, the gene, early detection of hereditary disease or an allergy can be realized for individual client. 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 sensor's output has been made.

The 'SNP-DR' (silicon system for the prediction of drug response) is a low cost microchip based device which can predict drug efficacy or toxicity at point-of-care. This technology can enable pharmacogenetic testing in personalised medicine, i.e. tailoring drug prescription and dose to the 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 for patients.

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 in either DNA or RNA. Disposable, low cost, 'lab-on-chip' cartridges housing biochemical reagents, advanced microfluidics and low-power silicon biosensors are key to this novel technology for the detection of genetic sequences or mutations.

The micro-volume gene 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 the is technology is being undertaken by DNA Electronics Limited, a company which was 'spun-out' from the Centre and 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.

HLA B*5701 genotypes can have a fatal reaction to Abacavir, one of the most widely used drugs in the long-term treatment of HIV. We are addressing an urgent need for rapid and accurate HLA B*5701 typing in the case of an emergency prescription which cannot be provided by current laboratory-based methods.

Osteoarthritis is a degenerative disease affecting the majority of the population over 60, with 1-2% developing clinical signs including severe pain and joint failure. We aim to develop assays for published nucleotide and nucleotide repeat markers that might help to identify individuals at risk, select preventive measures and guide clinical intervention.

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.



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 INTERFACING TECHNOLOGIES

Recording – Interfaces to monitor neural activity typically record electrical signals using electrodes in close proximity to neural tissue (eg. using MEA's, ECoG, EEG, etc). Emerging methods aim to provide further insight by additionally observing the chemical neural activity. Our research is both streamlining traditional interfaces for the central and peripheral nervous systems (CNS and PNS) and also investigating alternative methods.

Stimulation – In the same way that electrical activity can be recorded within the CNS and PNS, this can also be modulated through electrical neural stimulation (ENS). Our research involves developing ENS technology to improve the efficiency and effectiveness of such interfaces. This includes electronics for efficient stimulus generation, stimulation profiles to maximise charge delivery efficiency and electrode lifetime, and strategies for the selective modulation of neuronal pathways, i.e. increasing the spatial resolution.

Processing – Recording systems capture multiple resolutions of neurological function, extracting single to multiple neuronal clusters. To understand the neurological mechanisms and translate the signals to a diagnosis, early warning or feedback to closed-loop stimulation strategy we employ a variety of signal processing methods. These include computationally efficient algorithms that can deal with non-linear and non-stationary time series data, extracting features or signal dynamics of EEG data and for single neuron clusters, to detect and classify them from their neighbours. These algorithms, we design to be computationally and hardware efficient. For this we investigate different forms of data representation, signal compression and hardware implementation strategies.

Communication – Neural systems rely on wireless means for communication including both through-air (for wearable devices) and transcutaneous transmission (for implanted devices). Our research in this area is investigating methods for achieving: (1) high bandwidth transcutaneous communication (UWB and optical), and (2) high efficiency power transfer (inductive and ultrasonic).



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.

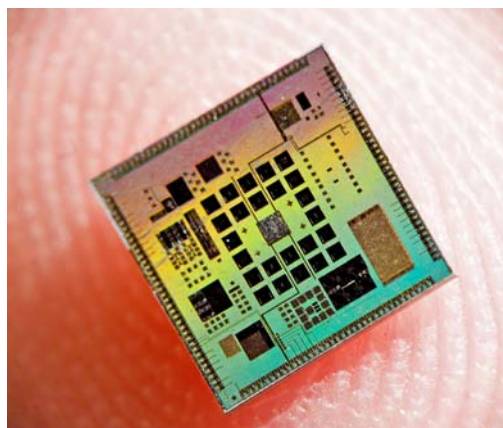
One of the strengths of the Centre, and a significant attraction for researchers, is the 'state-of-the-art' facility. Professor Toumazou ensured that the initial endowment to the Institute of Biomedical Engineering recognised the quality of the infrastructure, laboratories and equipment needed to make 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.



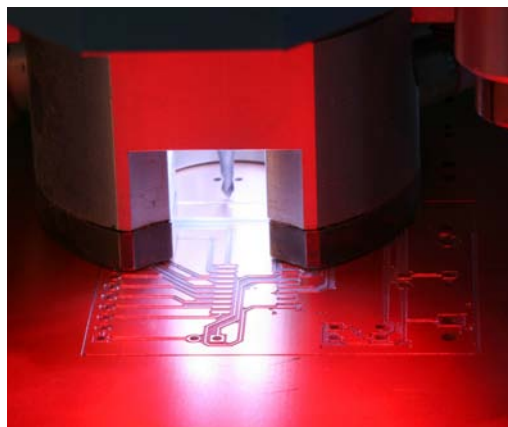
BIO-INTERFACING LABORATORY

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 processes 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.

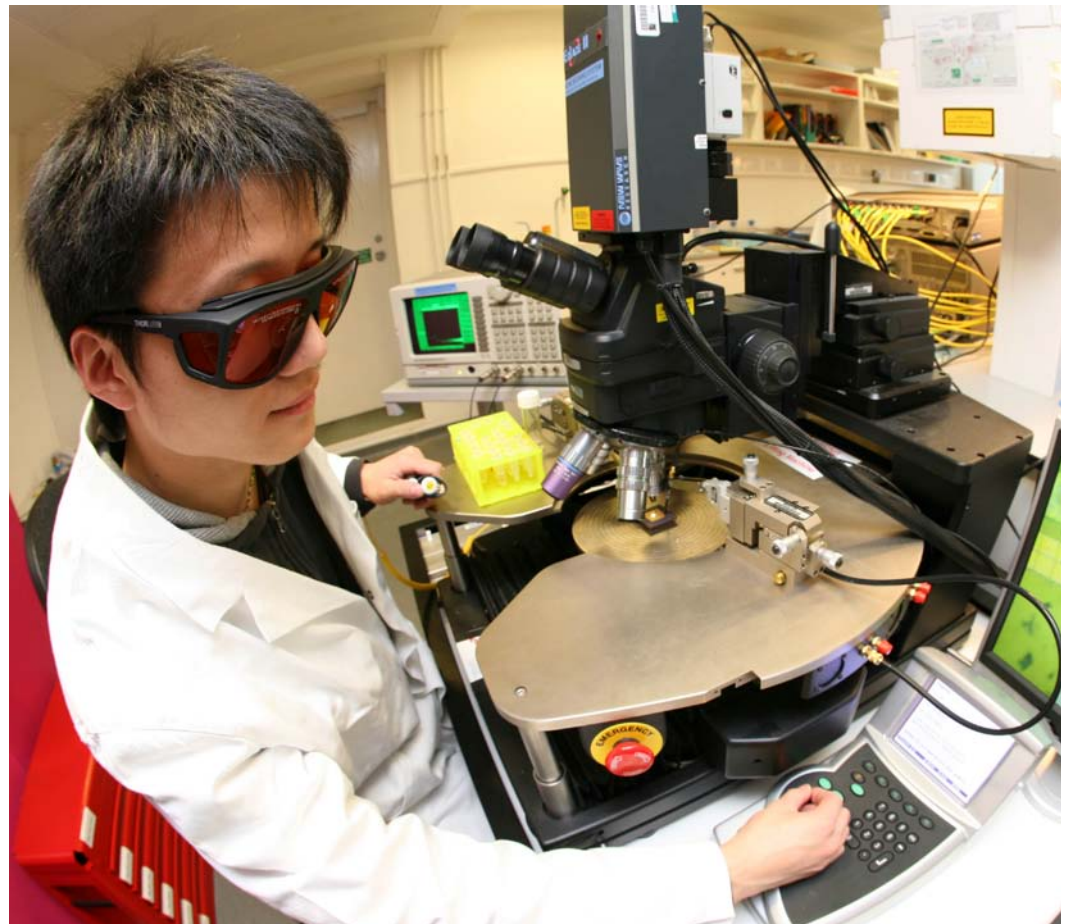


MICROELECTRONICS LABORATORY

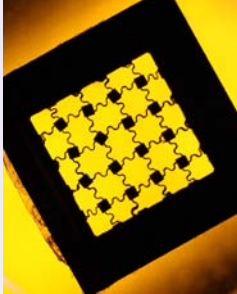
The Microelectronics Laboratory is comprehensively equipped for the development, testing and measurement of biomedical circuits and systems. It offers multi-channel low noise recording enabling accurate comparison between the performance of sensors.

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.



From the earliest doctors who walked amongst the Pharaohs, through Hippocrates and Galenos to today's medics who spend their lives in white coats, surrounded by intricate machinery, the medical profession has revolved predominantly around healing the sick. Typically people go about their business until they notice something amiss. They then investigate with the help of a medical professional and once the problem is determined, a treatment plan is put into action.



Medical science in the 21st century: a young engineer's view

Alexander Serb

Research Student

This is all nice and well but, already, we are seeing the seeds of change in this paradigm. In my view, we have already started expanding the scope of medicine beyond the traditional roles of healing the sick and preventing disease and seen it develop branches that deal with stopping the natural degeneration of the human body and extending life span. As such, we now have 3 distinct branches of medicine: palliative, preventative, and regenerative.

Palliative medicine can be subdivided further into two important branches, which are called 'acute' and 'chronic'. Acute medicine is meant to deal with diseases that can be cured through a relatively limited administration of medication, i.e. has a short treatment routine; chronic medicine deals with chronic conditions whereby people are dependent on medication for life. I see acute medicine as the 'real' medicine whereby we heal people for good and 'chronic' medicine as the last resort when we simply don't have the means to beat an illness.

Preventative medicine includes, of course, vaccination and hygiene, but in the future it has the potential of being much more. 'Pie in the sky' though it might be at the moment, I believe that in the future we will be able to create artificial cells that complement or outperform (or both) our own immunocytes (the cells of the immune system). These don't even need to be full-fledged cells, being instead nano-bots that have some simple capabilities like destroying very specific targets (such as cancer cells) and after a given period of time are expelled from the body. Such medication can be then administered periodically to population groups deemed most at risk and thereby prevent disease with great success. Research in this domain is very intensive. [1,2] shows one example of what science today is capable of – this particular example being a molecular carrier that detects the presence of cell markers that indicate cancer and opens up to release a deadly load to the cancerous target. Assuming we ever reach that stage, we will witness an era where people hardly ever succumb to invading bacteria, viruses and certain internal failures such as

runaway cell multiplication (cancer). Hospitals will then be able to service far larger numbers of people and will deal primarily with accidents and degenerative conditions. The latter is what regenerative medicine will seek to address. Also note how the 'weapons' bequeathed upon humanity by preventative medicine will also have great potential in being used to combat any disease retroactively, that is to say after it appears. It is my hope that I will live to see palliative medicine being almost completely displaced, or rather swallowed, by preventative medicine, an era when prevention and cure will effectively become one and the same.

Finally, we come to regenerative medicine: the rising star of medical science. The point here is to slow down the natural degeneration of the human body. In the future the aim will probably gradually shift towards stopping it completely and perhaps even augmenting our bodies so that they work better than nature ever intended them to. Here we will have to dabble with genetics and perhaps create artificial cells that have the capability of fixing our bodies as time attempts to take its toll. One way to think of it is adding a whole new 'system' to the human body. Just like the immune system attempts to combat disease and fend off invading micro-organisms, the gastrointestinal system is tasked with breaking down food into molecules that the body can distribute via the blood stream and use for metabolism and the neural system is tasked with all of the fast signalling within the body, we can create a new system, 'repair' system let's call it, that is tasked with repairing damage done by degeneration. This would involve rebuilding bones that time has worn thin (multiple sclerosis), reintroducing collagen in parts of the skin that have lost it, replacing degraded retinal cells in the eye to restore vision, etc.

Stem cells are the most promising inroad into regenerative medicine as far as I understand. For this reason my idea of a 'repair' system for the body would be to create a system whereby stem cells can be stored and distributed to any region of the body that has degenerated, followed by an operation to 'nudge' them

into developing into the correct cell type with the eventual aim of replacing the damaged parts. For bone it would work slightly differently since degeneration of bone has a lot to do with displacement of inorganic material, but the principle is there.

Alternatively, a set of purpose-built viruses could modify our DNA in specific categories of cells with the purpose of tweaking the rules by which these cells play, as has already been famously done to combat cystic fibrosis. Thus, by changing the rules of what are fundamentally cellular automata, perhaps we could manage to beat evolution and create a system that defies degeneration. Of course the difficulties involved in this endeavour are enormous beyond imagination, however with concerted effort from a huge scientific workforce, the world is becoming increasingly capable of taking the task upon itself.

IMPERIAL COLLEGE: ADDING BRICKS TO THE EDIFICE OF SCIENCE

For now, institutions, such as here in the Centre for Bio-Inspired Technology at Imperial, carry out exactly the type of research that promises to bring medicine into a new era. A few characteristic examples would be the efforts we are devoting towards improving genetic technology and the creation of an artificial pancreas.

Our research in the domain of genetic technology revolve around creating portable systems with the capability of analysing patient DNA in an effort to provide more of the healthcare at the point of care. This should help considerably with a 'hidden' 4th branch of medicine, the one which is tasked with lowering the cost of currently available technology and making it accessible to large numbers of people who cannot ordinarily afford the staggering cost of state-of-the-art modern healthcare. This effort should not be underestimated. Miniaturising a DNA analysis system from bench-top size to fingertip size, and consequently from a 5-figure £ device to a 3-figure £ or less device, is important in the day-to-day lives of millions.

A project dealing with exactly this issue is attempting to create a cheap, portable yet effective lab-on-chip system that can detect the methylation state of DNA samples (that is to say presence of methyl group-based biomarkers in DNA). The methylation state of DNA can be correlated to cancer rather well [3,4] and for that reason overcoming the challenges of creating a nimble, elegant, cheap and functional system for its measurement constitutes research of potentially very high impact. The ability to detect cancer earlier and

with greater accuracy will mean a lot both to patients and to the healthcare system as a whole.

The artificial pancreas project is a great example of science taking over from where nature has failed. It is difficult to categorise it with respect to the branches stated above, but in my mind it fits into a section of regenerative medicine not described above, namely the domain where instead of fixing parts of the body we replace them. Success has already been marked by developments of devices such as cochlear implants, but moving on to an organ with a complex biochemical function is taking technology to the next step. The concept of replacing malfunctioning parts of the body with good quality artificial ones is very important since it replaces the usual problems of degeneration and invasion by foreign micro-organisms with the admittedly much more tractable issues of maintenance and reparability of the said artificial substitutes.

These are merely a few examples out of a much larger domain of research activity currently ongoing at the Centre and really illustrates that medical and life sciences are being carefully tended to and hold a lot of promise for the future.

In conclusion, I believe that medical science has a very, very exciting road ahead and those of us lucky enough to survive long enough will see tremendous changes in the way medical science works. We might be able to witness the end of the antibiotic and the ushering of the era of nanobotic medication or 'live' medication in a paradigm shift that the world hasn't experienced since the days of Alexander Fleming. This will be followed by the greatest attempt to engineer life itself and augment our bodies so that we generate our own, supercharged immune system and operate our very own self-repair system and artificial parts. How the world adapts to such precipitous changes will be equally interesting to witness.

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Clinical assessment of the bio-inspired artificial pancreas in subjects with type 1 diabetes

Dr Monika Reddy

Clinical Research Fellow

It is estimated that 5% of today's UK population has diabetes and it is predicted that the incidence of diabetes will continue to rise. 10% of the whole diabetes population have type 1 diabetes mellitus (T1DM), which is caused by T-cell mediated autoimmune destruction of the pancreatic beta-cells. This results in an inability of the pancreas to produce insulin in response to a glucose stimulus. If left untreated, the condition is fatal. The majority of patients with T1DM are managed in specialist diabetes clinics and are either on daily multiple subcutaneous insulin injections or continuous subcutaneous infusion of insulin via a pump.

However, there are still multiple reasons why these patients do not achieve optimal glycaemic control, including insulin resistance, non-compliance with multiple insulin injections, needle-phobia and significant hypoglycaemic (low blood glucose) episodes needing correction with carbohydrates. Poor control of diabetes is associated with long-term microvascular complications including blindness, kidney failure and nerve damage as well as macrovascular complications such as heart disease and strokes. It is well established that intensive treatment of T1DM reduces the risk of developing complications. Achieving optimal glycaemic control can be very challenging for patients with T1DM due to the increased risk of hypoglycaemia with intensive treatment. The closed-loop insulin delivery system, also known as the artificial pancreas, has the potential to prevent hypoglycaemia and avoid large fluctuations in blood glucose levels by adjusting the insulin delivery dose frequently i.e. every 5 minutes according to the glucose concentration.

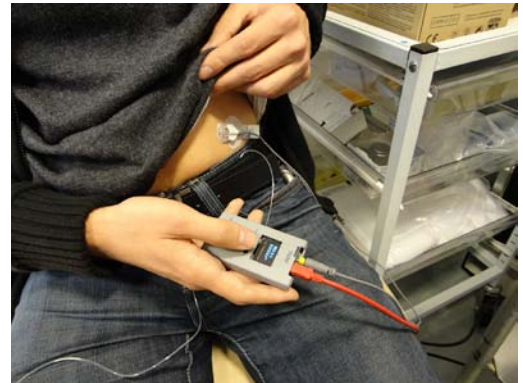


Figure 1 The artificial pancreas in use

The Imperial College artificial pancreas system consists of a subcutaneous glucose sensor (Enlite, Medtronic), a novel bio-inspired glucose controller and a subcutaneous insulin pump (Accu-Check Combo Spirit, Roche). The control algorithm is implemented on a microchip within a handheld device and allows communication between the three components of the system.

The development of the Wellcome Trust funded Imperial College novel bio-inspired artificial pancreas (B-iAP) started in 2009 and the device has been *in-silico* validated in an FDA-approved virtual T1DM population. 2012 has been an exciting year as clinical trials are now underway at the Imperial College-Wellcome Trust Sir John McMichael Centre. The aim of the clinical trials is to assess the safety and efficacy of the bio-inspired artificial pancreas in 20 subjects with T1DM, starting with a fasting trial over 6 hours. We will then progress to an overnight study with a meal challenge and finally a 24-hours ambulatory study with three meal challenges.

A brief outline of the study protocol for the 6-hours fasting study is as follows:

At 08.00: Subject arrives at the clinical research unit.

The technology for closed-loop insulin delivery system (the continuous glucose sensor connected to the B-iAP unit which holds the control algorithm, and the insulin pump) is applied to the subject. An intravenous cannula is inserted and blood samples taken every 15 minutes throughout the study for measurement of venous blood glucose using the YSI glucose analyser.

At 10.00: Start of closed-loop control

The insulin dose recommendation by the B-iAP is approved by the attending physician before it is delivered to the subject every 5 minutes.

At 16.00: End of study. Subject is allowed to eat and can go home if the blood glucose is stable.

Each closed-loop study is attended by the subject, a medical doctor, a research nurse and an engineer.

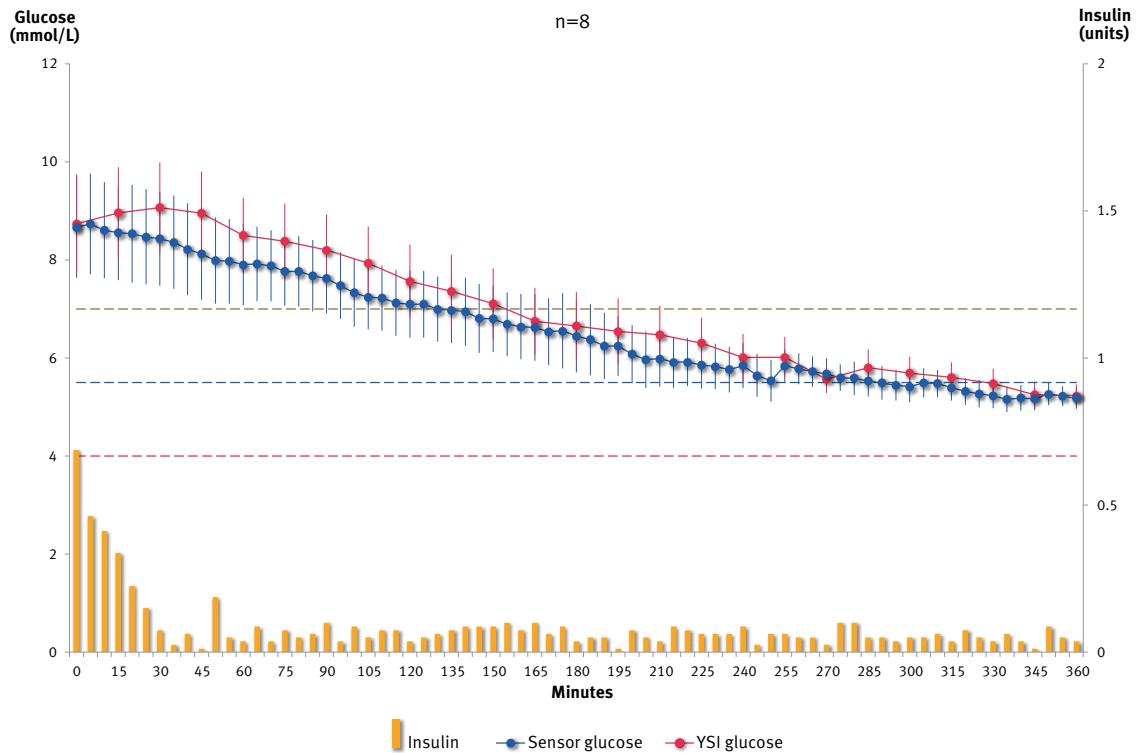


Figure 2 shows the mean sensor glucose (+/- standard error), mean YSI (plasma) glucose (+/-standard error) and mean insulin dose delivered for the first 8 subjects, over a six-hour fasting closed-loop study.

The Imperial College London Bio-inspired Artificial Pancreas team is made up of engineers and clinicians, working in collaboration to develop the device.

The results from the initial studies are encouraging and show that the bio-inspired closed loop artificial pancreas achieves normoglycaemia without hypoglycaemia in subjects with T1DM during fasting conditions. No adverse events occurred.

We aim to complete the fasting studies by the end of November 2012 and to start the overnight studies with a meal challenge by the end of the year.

The achievement of developing a safe and user-friendly artificial pancreas would be a major step towards eliminating the need for injections and hypoglycaemia in subjects with T1DM. The ultimate goal of an ideal artificial pancreas is to significantly reduce diabetes complications and improve patients' quality of life.



From left to right: Mr Mohamed El-Sharkawy, Professor Chris Toumazou, Mr Peter Pesl, Dr Nick Oliver, Dr Pantelis Georgiou, Dr Herrero-Vinas Pau, Dr Monika Reddy, Dr Shivani Misra. Not shown in the photograph Professor Desmond Johnston

Development of a genetic analysis platform to create innovative and interactive databases combining genotypic and phenotypic information for genetic detection devices

Dr Belinda Nedjai

Research Fellow in genetic and functional genomics

SUMMARY

Bridging the gap between gene discovery and our ability to use genetic information to benefit health requires population-based knowledge.

Semiconductor technology has enabled accurate, real time, non-invasive acquisition of an individual's genetic data. Where genetic polymorphisms affect the way individuals metabolise, or determine their hypersensitivity to, compounds such as drugs or ingredients in cosmetics, the availability of an individual's genetic information makes the 'personalisation' of such compounds a reality. The application of genetic information to enable the 'personalisation' of treatments is growing. This project relates to the understanding of human genomic variation and the impact of environmental factors and lifestyle to predict human phenotypic response.

Just 50 years after the structure of DNA was identified, the entire human genome had been sequenced and a new era of understanding and possibility arose as a consequence. However the difficulty of interpretation and the complexity of how the code is ultimately expressed in the daily activities of a cell are still challenges.

In stark contrast, CMOS based DNA detection and sequencing technologies developed within the Centre for Bio-Inspired Technology are making amazing progress. Leveraging on this unique environment we are developing an innovative genetic analysis platform combining genotypic and phenotypic information. This will provide the 'proof-of-principle' and validation to implement advanced lab-on-chip expertise SNP detection to feed back into healthcare and commercially available systems chips.

This innovative project is a collaborative project between a genetic team and an IT team which are implementing software tools and frameworks to tackle new computational and analytical challenges arising from next generation sequencing, as well as performing imputation and genetic analyses in existing datasets.

The Project's aims are:

- to identify, compile and analyse data in human genome epidemiology (HuGE) to create a comprehensive database of SNP related to a specific query (disease, trait)
- to evaluate and validate identified SNP targets in clinical trials to test various polymorphisms within populations.

The project outcomes will open up the high-growth, emerging market in personalisation, where genetic detection will be used in many aspects of our lives. The applications could range from disease prevention and medical diagnosis to cosmetics. The ultimate goal is to create an analysis platform to implement databases for genetic detection devices.

THE HELEN TRIAL

This project is investigating the role of human genetic variation in skin ageing and aims to establish a correlation between genetic variation and the effectiveness of the active ingredients used in over-the-counter (OTC) cosmetic products to slow down ageing.

The skin care industry spends a large amount of money in Research and Development to find products which are more effective. The ability of an individual to metabolise the ingredients in a cosmetic is based upon their genetic makeup. We have been able to identify the metabolic pathways of many ingredients in cosmetics and have created a list of those that either became inactive due to the presence of a 'SNP' or become highly beneficial to an individual because the 'SNP' creates a lack corrected by this ingredient. In the Helen Trial we are checking these hypotheses in real time.

A major feature of aged skin is the fragmentation of the dermal collagen matrix. Fragmentation results from actions of specific enzymes (matrix metallo-proteinases) and impairs the structural integrity of the dermis. In aged skin, collapsed fibroblasts produce low levels of collagen and high levels of collagen-degrading enzymes. This imbalance advances the ageing process in a self-perpetuating, never-ending, deleterious cycle. Collagen fragmentation is responsible for the loss of structural integrity and impairment of fibroblast function in aged human skin. Treatments that stimulate production of new, non-fragmented collagen should provide substantial improvement to the appearance and health of aged skin. Matrix metallo-proteinases are responsible for physiologic degradation of various extracellular matrix proteins. Of the 4 collagenases expressed in humans, only interstitial collagenase (MMP-1) is involved in the normal turnover of skin collagen.

In an attempt to identify what contributes to skin ageing and the photoageing phenotype in the general population, we evaluated the incidence of MMP-1 SNP (Rs1799750), a key gene involved in the collagen degradation pathway. Our hypothesis is that MMP-1

polymorphisms might provide some insight into differential rates of skin ageing.

We screened 37 subjects for MMP-1 SNP (Rs1799750) and evaluated their response to one specific anti ageing cream. MMP1 SNP has a direct effect on collagen, as it increase MMP-1 expression and therefore collagen degradation. The topical anti ageing cream we selected, will stimulate collagen synthesis using several key ingredients such as tocopherol (vitamin E), palmitoyl oligopeptide, palmitoyl tetrapeptide-7, and Retinyl palmitate. We will first estimate the basal level of skin ageing phenotype and also we will observe the response of each subject to the proposed cream. Both these parameters will be correlated with the subject genotype.

This study protocol, see Figure 1, focused on cosmetic improvement at 7 weeks of topical treatment as proposed by Watson REB, *et al.* We will address the following questions:

1. are there identifiable differences in skin ageing symptoms at the basal level for tone, fine lines, and hyperpigmentation in the group of subjects with or without MMP-1 SNP?
2. are there noticeable effects on treatment, and therefore prevention, using retinol and other ingredients?
3. are the same results obtained using the on-the-spot chip detection system and TaqMan® Real-Time PCR method?

METHOD

37 subjects between the ages of 27 and 55 with Fitzpatrick skin types I-III were invited to the study. Those subjects with inflammatory acne, rosacea or facial eczema, previous allergic contact dermatitis to cosmetics, severe facial scarring, concomitant treatment with oral isotretinoin (roaccutane), active facial psoriasis, solar urticaria, perioral facial dermatitis or angio-oedema, were excluded. Those subjects currently using any over the counter anti-ageing cream containing a retinoid were also excluded from the study.

Saliva samples were obtained at baseline for SNP testing of MMP-1 using both a chip detection method, using the technology designed by DNA Electronics Limited, and the second being the current RT-PCR gold standard method. Specifically designed primers were designed and a DNA polymerase with strand displacement activity used for the amplification reaction.

Each subject also completed a self-assessment questionnaire containing 10 questions evaluating nine efficacy attributes – fine lines and wrinkles around the eyes, evenness of skin tone, red blotchiness, evenness of skin texture, age spots, skin radiance, skin hydration, skin firmness and overall appearance – using a 10-point continuous scale at weeks 0, 2, 4, 6.

Imperial College Research Ethics Committee (ICREC-12-1-112) granted full ethical permission for the study. All data was anonymised and kept securely at Imperial College London during the study period.

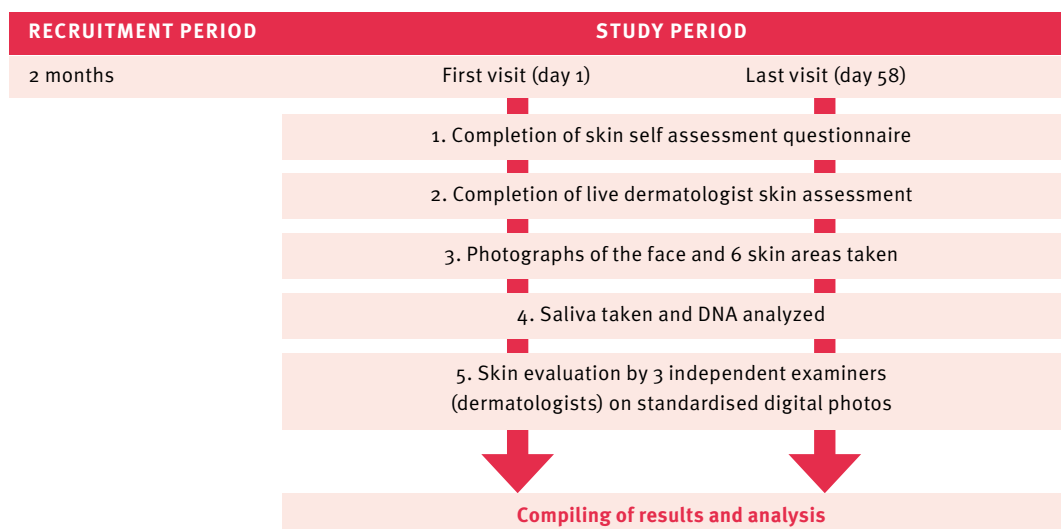


Figure 1. Helen Trial – Study design including the protocol and the scheduled procedures

RESULTS TO DATE

The analysis of the results of the trial is still underway and will be published very shortly. We are gathering extensive knowledge about the ingredients used in the cosmetic industry and have established methods to improve data meaning and create an Interconnected system between genetic and phenotypic information applied to cosmetics, see Figure 2. We have also created a database establishing a relationship between 'SNPs' and the ingredients used in cosmetics.

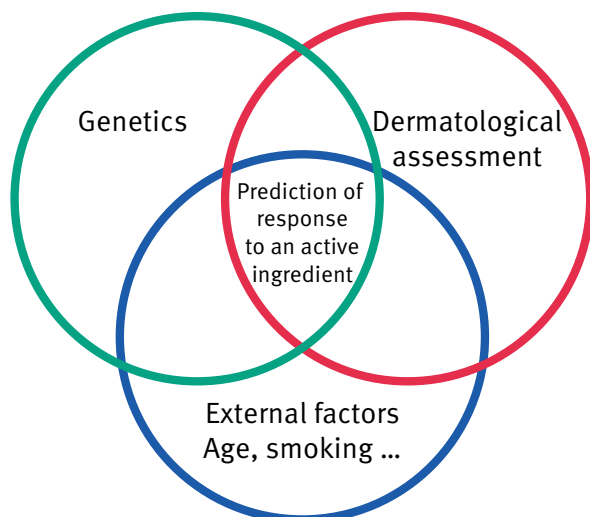


Figure 2. The interconnection between genetic and phenotypic information

NEXT STEPS

A paper is already in preparation presenting the results for the Helen Trial 'Use of semiconductor technology to detect on the spot single nucleotide polymorphism (SNP) variations in NQO-1 and MMP-1 and their impact on visible signs of ageing before and after use of a cosmetic 'anti-ageing' product: a pilot study'.

We are also designing new populations studies using more target (SNP) and a larger cohort to create the genetic-phenotypic database. We would also like to use microarray technology for the analysis of gene expression profiles at the mRNA level for the related SNP and improve the informatics tools to organize and analyse such data. Our aim is to develop chip-based analysis of samples.

The emergence of models of gene networks hold much promise for the future of the 'Genomic Era'. We hope that the outcome of this research is to find ways to substantially improve the cosmetics available for personalized skin care.

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2. Juffali W, *et al.*, 'ISFET based urea: creatinine translinear sensor' *Electronics Letters* 46 746–748.
3. Juffali W, *et al.*, 'The WiNAM Project: Neural Data Analysis with Applications to Epilepsy', *IEEE BioCAS Conference*, 2010.

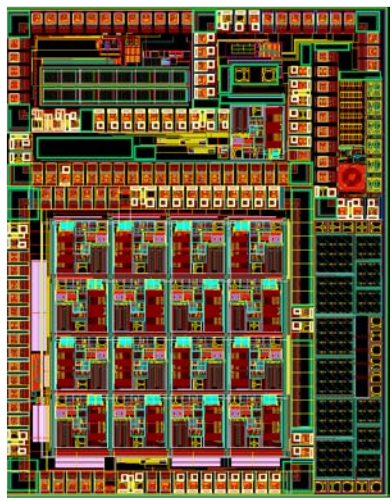
PUBLICATIONS

1. Turner MD, A Chaudhry and B Nedjai, 'Tumour necrosis factor receptor trafficking dysfunction opens the TRAPS door to pro-inflammatory cytokine secretion' *Biosci Rep.* Apr 1;32(2): 105–12, 2012. Review PMID: 22115362 [PubMed – indexed for MEDLINE]
2. Nedjai B, H Li, IL Stroke, EL Wise, ML Webb, JR Merritt, I Henderson, AE Klon, AG Cole, R Horuk, N Vaidehi and JE Pease, 'Small molecule chemokine mimetics suggest a molecular basis for the observation that CXCL10 and CXCL11 are allosteric ligands of CXCR3', *Br J Pharmacol* Jun;166(3): 912–23, 2012. doi: 10.1111/j.1476–5381.2011.01660.x.
3. Nedjai B, GA Hitman, LD Church, K Minden, ML Whiteford, S McKee, S Stjernberg, T Pettersson, A Ranki, PN Hawkins, PD Arkwright, MF McDermott and MD Turner, 'Differential cytokine secretion results from p65 and c-Rel NF-κB subunit signaling in peripheral blood mononuclear cells of TNF receptor-associated periodic syndrome patients', *Cell Immunol* 268(2):55–9, 2011. Epub 2011 Mar 1.
4. Nedjai B, N Quillinan, RJ Coughlan, L Church, MF McDermott, GA Hitman and MD Turner, 'Lessons from anti-TNF biologics: infliximab failure in a TRAPS family with the T50M mutation in TNFRSF1A', *Adv Exp Med Biol* 691:409–19, 2011.
5. Nedjai B, GA Hitman, N Quillinan, RJ Coughlan, L Church, MF McDermott and MD Turner, 'Proinflammatory action of the antiinflammatory drug infliximab in tumor necrosis factor receptor-associated periodic syndrome', *Arthritis Rheum* Feb;60(2):619–25, 2009.

Chip gallery

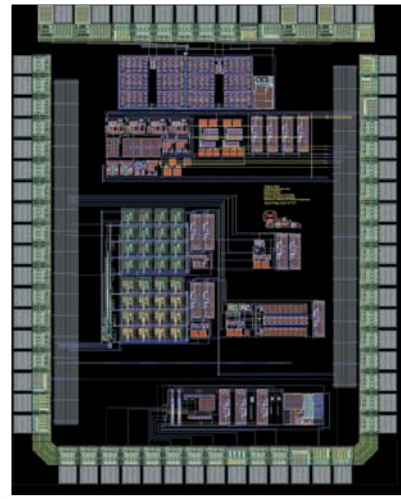
The Centre's focus is primarily the application of modern semiconductor technology to develop new bio-inspired systems and medical devices. This has in part been made possible through the EU-subsidised multi-project wafer (MPW) brokerage service provided by Europractice which provides our design tools via STFC (UK) and technology access via IMEC (Belgium) and Franhofer (Germany). Over the past seven years, we have fabricated a total of 26 integrated circuit designs in a variety of CMOS technologies.

The 'Chip Gallery' is also available online at: www3.imperial.ac.uk/bioinspiredtechnology/research/chips



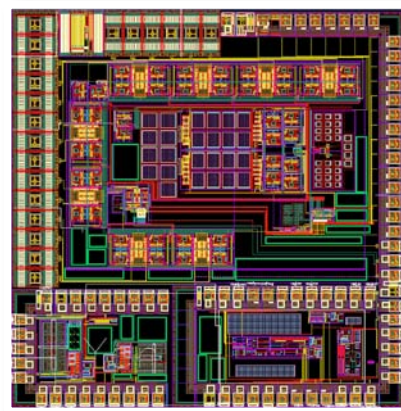
IBE12H01 (NGNI) – August 2012

- Technology:** Austriamicrosystems
0.18 μ m 1P4M HV CMOS
- Purpose:** Neural interface circuits and electro-optical modulator test structures
- Designers:** Yan Liu, Song Luan, Alexander Serb, Lieuwe Leene, Timothy Constandinou



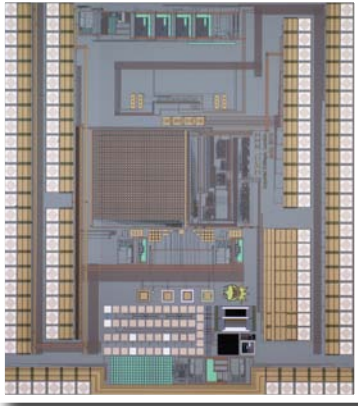
IBE12J01 (KIMI) – October 2012

- Technology:** Austriamicrosystems
0.35 μ m 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



IBE12D01 (Ian) – April 2012

- Technology:** Austriamicrosystems
0.18 μ m 1P4M HV CMOS
- Purpose:** Neural interface circuits
- Designers:** Ian Williams, Sivylla Paraskevopoulou, Yan Liu, Timothy Constandinou

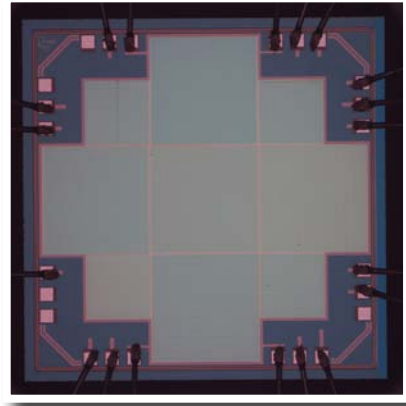


IBE12C01 (Kermit) – March 2012

Technology: Austriamicrosystems
0.35 μ m 2P4M CMOS

Purpose: Chemical sensor interface, LOC, neural front end

Designers: Mohammedreza Sohbaty, Melpomeni Kalofonou, Yan Liu, Mohamed Fayez El Sharkawy, Pantelis Georgiou, Timothy Constandinou, Themis Prodromakis, Chris Toumazou

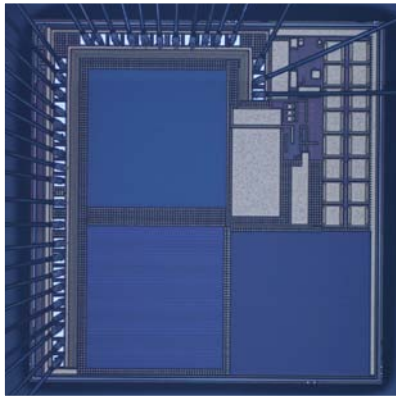


IBE11H01 (Teddy) – August 2011

Technology: UMC
0.13 μ m 1P8M CMOS

Purpose: Electro-optical modulator

Designers: Alexander Serb, Timothy Constandinou

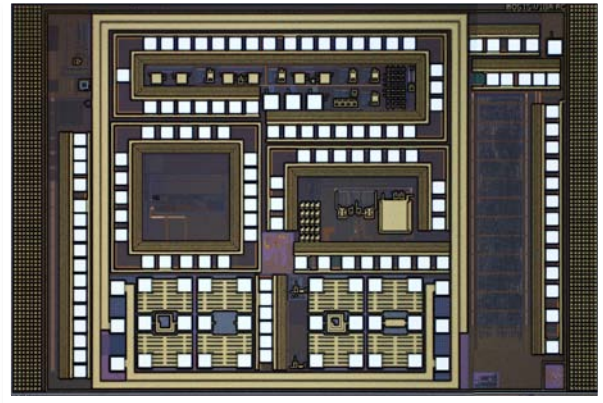


IBE11G02 (Bean) – July 2011

Technology: Austriamicrosystems
0.18 μ m 1P4M CMOS

Purpose: Electro-optical nodulator, power management (nodulator or modulator)

Designers: Alexander Serb, Timothy Constandinou

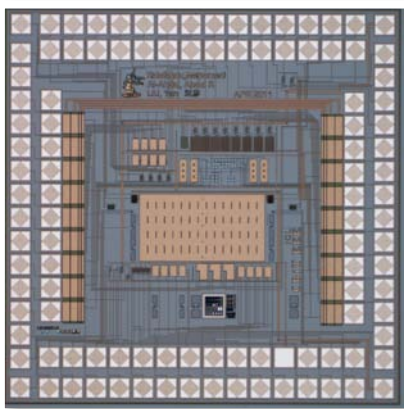


IBE11G01 (Neural) – July 2011

Technology: Austriamicrosystems
0.18 μ m 1P4M HV CMOS

Purpose: Neural interface circuits

Designers: Sivylla Paraskevopoulou, Song Luan, Bard Haaheim, Timothy Constandinou, Yan Liu, Yuanqi Hu, Pantelis Georgiou, Themis Prodromakis

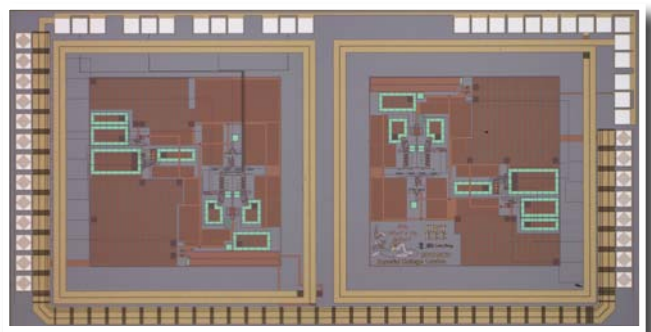


IBE11D01 (Asterix) – April 2011

Technology: Austriamicrosystems
0.35 μ m 2P4M CMOS

Purpose: Chemical sensor interface

Designers: Abdul Al-ahdal, Melpomeni Kalofonou, Yan Liu, Themis Prodromakis, Pantelis Georgiou, Chris Toumazou

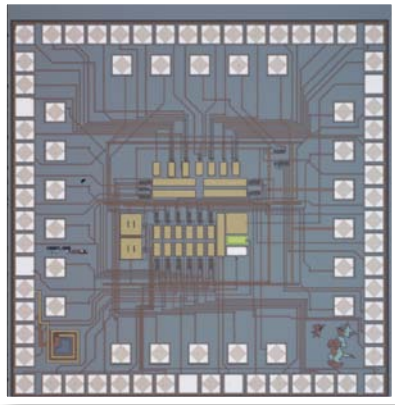


IBE10K01 (Bugs Bunny) – November 2010

Technology: Austriamicrosystems
0.35 μ m 2P4M CMOS

Purpose: Bondpad-less Chip

Designers: Song Luan, Amir Eftekhar, Olive Murphy, Timothy Constandinou

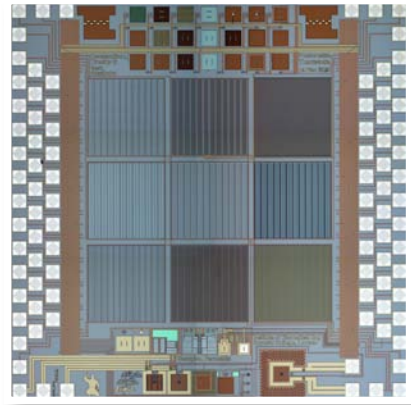


IBE10G01 (Tom and Jerry) – July 2010

Technology: Austriamicrosystems
0.35 μ m 2P4M CMOS

Purpose: Chemical sensors and microfluidics

Designers: Abdul Al-ahdal, Yan Liu, Themis Prodromakis, Chris Toumazou

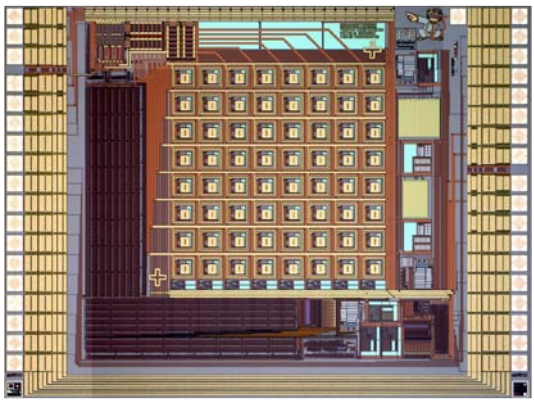


IBE10B01 (Ninja) – February 2010

Technology: Austriamicrosystems
0.35 μ m 2P4M CMOS

Purpose: Electro-Optical Modulator and chemical Sensors

Designers: Alexander Serb, Timothy Constandinou, Yan Liu, Pantelis Georgiou, Themis Prodromakis

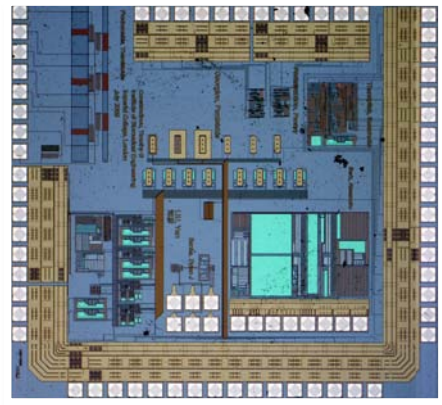


IBE09G01 (Crazy Monkey) – July 2009

Technology: Austriamicrosystems
0.35 μ m 2P4M CMOS

Purpose: Lab-on-chip Platform

Designers: Pantelis Georgiou, Timothy Constandinou, Themis Prodromakis, Chris Toumazou

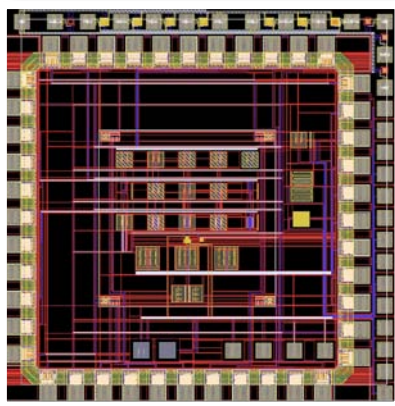


IBE09G02 (Kidschip) – July 2009

Technology: Austriamicrosystems
0.35 μ m 2P4M CMOS

Purpose: Chemical sensors and interface circuits

Designers: Yan Liu, Pantelis Georgiou, Themis Prodromakis, Alexander Serb, Surachoke Thanapitak, Panavy Pookaiyaudom, Dylan Banks, Chris Toumazou

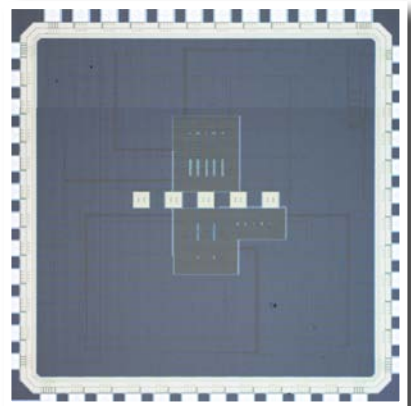


IBE09D02 (Hypothesis) – April 2009

Technology: Austriamicrosystems
0.35 μ m 2P3M CMOS

Purpose: Chemical sensors

Designers: Pantelis Georgiou, Themis Prodromakis, Yan Liu, Chris Toumazou

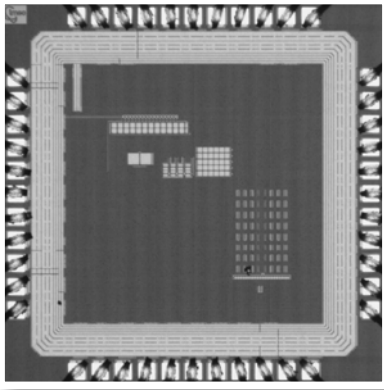


IBE09D01 (Geometry) – April 2009

Technology: Austriamicrosystems
0.35 μ m 2P3M CMOS

Purpose: Chemical sensors

Designers: Pantelis Georgiou, Yan Liu, Chris Toumazou

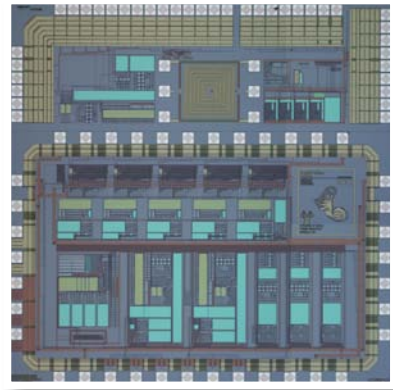


IBE08J01 (Wai) – October 2008

Technology: UMC
0.18 μ m 1P6M CMOS

Purpose: Chemical sensor and front-end

Designers: Wai Pan Chan, Chris Toumazou

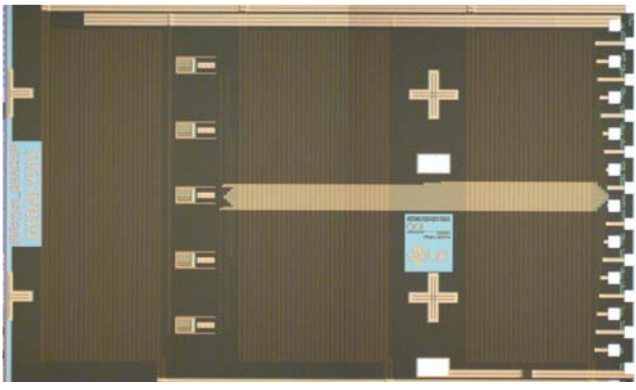


IBE08G01 (Vestibular) – July 2008

Technology: Austriamicrosystems
0.35 μ m 2P4M CMOS

Purpose: Vestibular prosthesis

Designers: Timothy Constandinou, Yan Liu, Siavash Saremi-Yarahmadi, Dylan Banks, Julius Georgiou, Chris Toumazou

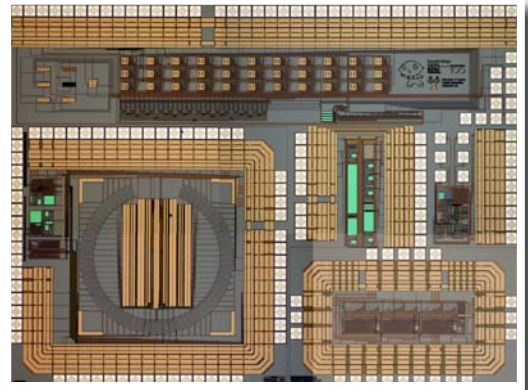


IBE08A01 (DNASensors) – January 2008

Technology: UMC
0.18 μ m 1P6M CMOS

Purpose: DNA sensors

Designers: Pantelis Georgiou, Timothy Constandinou, Chris Toumazou

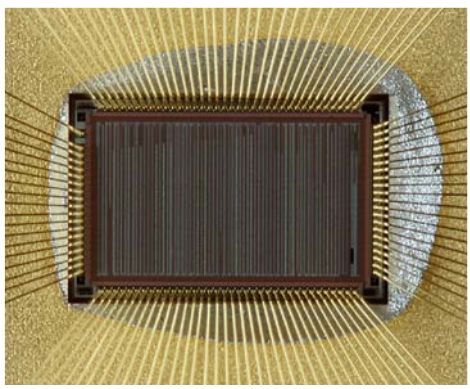


IBE07G01 (Stewie) – July 2007

Technology: Austriamicrosystems
0.35 μ m 2P4M CMOS

Purpose: Tilt sensor, neural stimulator, chemical imager, vestibular processor

Designers: Timothy Constandinou, Savvas Koudounas, Pantelis Georgiou, Julius Georgiou, Chris Toumazou

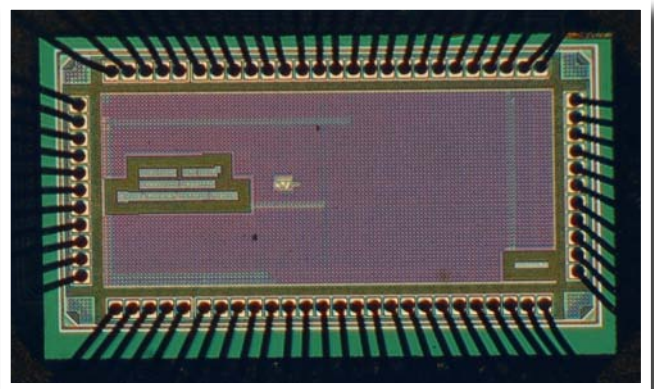


IBE06L01 (Correlator) – December 2006

Technology: ST
130nm 1P8M CMOS

Purpose: Bitstream cross-correlator

Designers: Timothy Constandinou, Amir Eftekhar, Tor Sverre Lande, Chris Toumazou

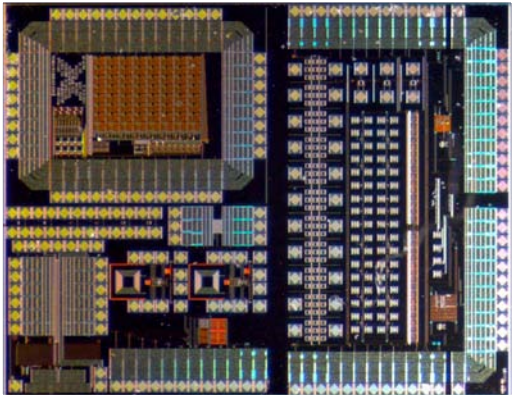


IBE06E01 (Chiccio) – May 2006

Technology: ST
90 nm 1P9M CMOS

Purpose: FDSM Converter, current-mode subthreshold logic

Designers: Francesco Cannillo, Chris Toumazou

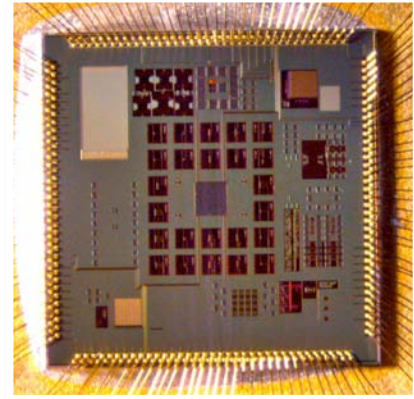


IBE06G01 (Cyborg) – July 2006

Technology: Austriamicrosystems
0.35 μ m 2P4M CMOS

Purpose: Neural bridge (sense and stimulate)

Designers: Cindy Li, Amir Eftekhar, Timothy Constandinou, Pantelis Georgiou, Iasonas Triantis, Leila Shepherd, Francesco Cannillo, Chris Toumazou, Savvas Koudounas, Julius Georgiou

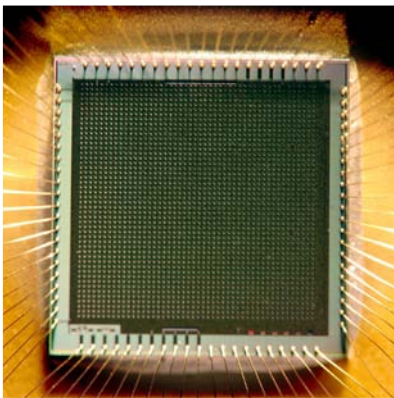


IBE05J01 (Darth Vader) – October 2005

Technology: UMC
0.25 μ m 1P5M CMOS

Purpose: Chemical sensors, imagers, bionic pancreas, sensor interface

Designers: Pantelis Georgiou, Timothy Constandinou, Leila Shepherd, Francesco Cannillo, Dylan Banks, Kostis Michelakis, Sofia Vatti, Kritsapon Leelavatananon, Themis Prodromakis, Chris Toumazou

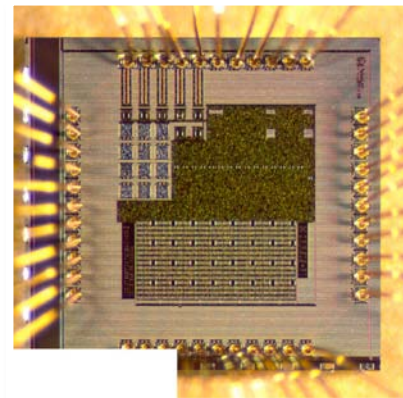


IBE04H01 (Orasis-P2) – August 2004

Technology: UMC
0.18 μ m 1P6M CMOS

Purpose: Vision chip (Orasis)

Designers: Timothy Constandinou, Chris Toumazou



IBE04B01 (Orasis-P1) – February 2004

Technology: UMC
0.18 μ m 1P6M CMOS

Purpose: Vision chip (test structures)

Designers: Timothy Constandinou, Chris Toumazou





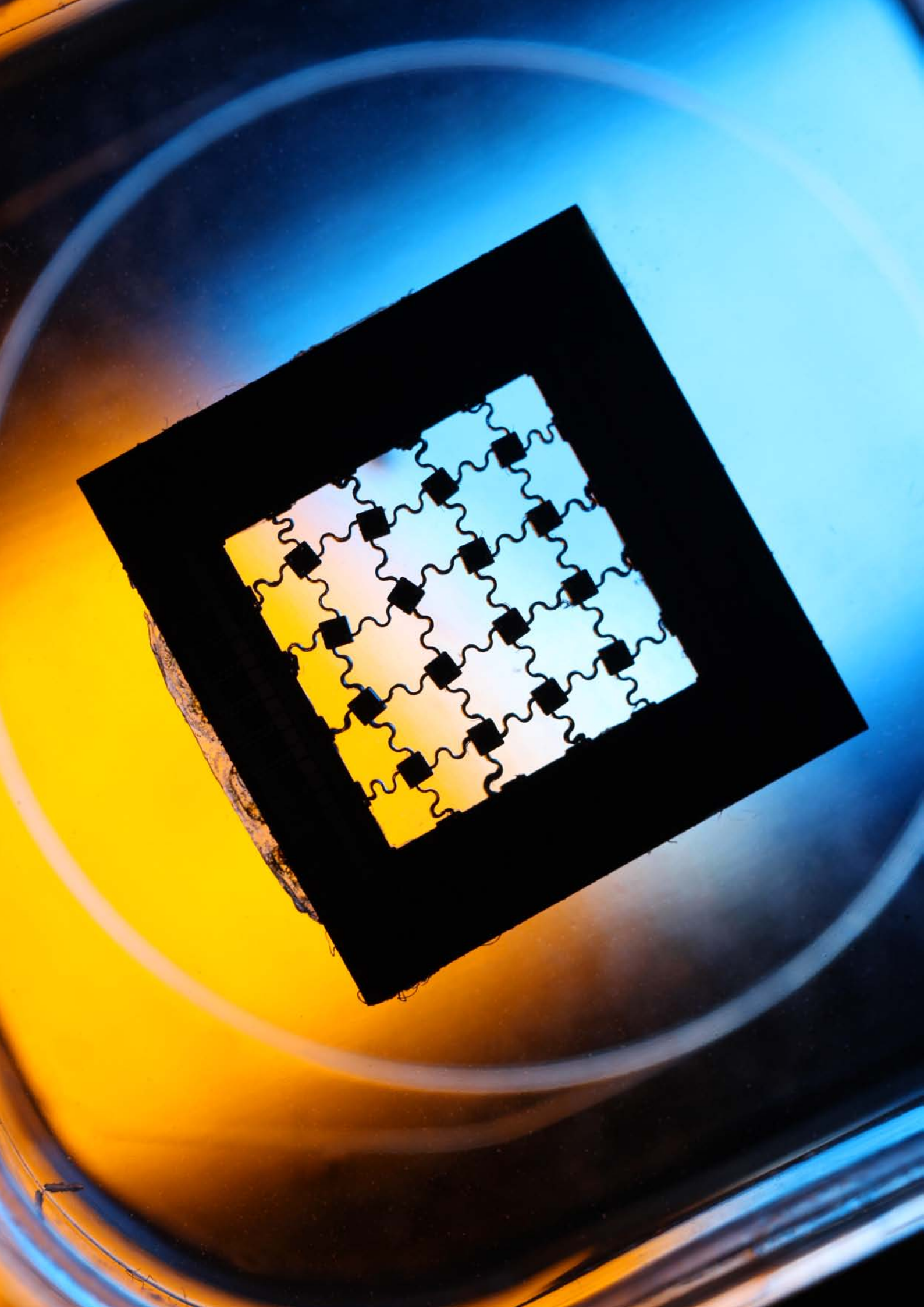
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Professor Chris Toumazou

FRS, FREng, CEng, FIET, FIEEE

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 2008 he was awarded a Fellowship of both the Royal Society and the Royal Academy of Engineering and 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 prestigious TEDMED Conference in San Diego (see News). 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 received both his BEng and PhD degrees in Electrical and Electronic Engineering from Imperial College London, in 2001 and 2005 respectively. He then joined the Institute of Biomedical Engineering as Research Officer until 2009, when he was appointed Deputy Director of the newly formed Centre for Bio-Inspired Technology. In 2010, continuing as Deputy Director, he joined the Department of Electrical and Electronic Engineering, where he currently holds an academic faculty position within the Circuits and Systems 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 current research is focused on electronic devices for interfacing with neural pathways in human populations, for example, in restoring lost function in sensory and motor impaired patients. Specific projects include:

- **Next generation neural interfaces for motor control** – Development is underway of an implantable brain machine interface for the real-time monitoring of hundreds (to thousands) of individual neurons within the cortex. Such platform technology is expected to empower the next generation of neural interfaces, at first instance, to be deployed as a research tool for neuroscience.
- **Wireless intraspinal microstimulation for spinal cord injury** – Intraspinal microstimulation is an emerging technique to directly stimulate motor neurons in the spinal cord, holding the promise of recruiting better co-ordinated and less fatigue-prone muscle movements with lower stimulation energy than the traditional muscle stimulation. To enable this potential, this research is developing an interface for achieving highly selective intraspinal micro-stimulation via a wireless platform for the transmission of power and data.
- **Proprioceptive feedback platform 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. This research is investigating the provision of artificial proprioceptive feedback in individuals with prosthetic limbs (or suffering from certain types of neural damage) by direct electrical stimulation of nerves using a neural implant.

- **Electro-optical platform for bondpad-less CMOS chips** – A key challenge in integrating micro-{electronics and fluidics} in lab-on-chip platforms is to achieve reliable and mass-manufacturable packaging. Specific challenges are: (1) to engineer a robust seal, and (2) to isolate delicate bond wires. This work aims to avoid bondwires altogether, by developing a fully-optical (power and data) link based on modulating free-carrier absorption in standard CMOS technology.
- **Wireless capsule endoscopy for targeted drug delivery** – Wireless capsule endoscopes (or pill cameras) are currently used for diagnostic purposes only. This work is engineering a novel microrobotic platform for therapeutic intervention within such devices. This can then be used for both the detection and treatment of pathologies of the GI tract such as Crohn's disease, small intestinal tumours such as lymphoma and small intestinal cancer.
- **Continuous-time digital bio-signal processing** – Recent advances in data converters have proposed clock-less, event-driven topologies for continuous-time digital processing. This work aims to apply such techniques and exploit inherent properties of bio-signals to develop new methods for resource-efficient (i.e. low power and/or low silicon area) processing using standard microelectronic technology.

Dr. Constandinou is a Senior Member of the IEEE (Institution of Electrical and Electronic Engineering), a Fellow of the IET (The Institution of Engineering and Technology), a Chartered Engineer and Member of the IoP (Institute of Physics) and SPIE (The International Society for Optical Engineering). He serves on the BioCAS (Biomedical Circuits and Systems) and Sensory Systems technical committees of the IEEE CAS Society, 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 and also serves on the IET Awards and Prizes committee.



Dr Pantelis Georgiou

MEng (Hons), DIC, PhD, 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.

His current research includes low-power microelectronics, bio-inspired design, integrated sensing systems and development of novel medical devices. He 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. Specifically we aim to create glucose-sensing arrays inspired by biological function to improve accuracy and functionality in ambulatory applications for diabetes.
- **Decision support systems for diabetes** – Diabetes, Type 1 & 2 results in extremely high blood sugar. To minimise the adverse effects good control through intensive insulin infusion is required for insulin 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) and IET (The Institution of Engineering and Technology) and has been elected a member of the Sensory Systems and BioCAS Technical Committees of the IEEE Circuits and Systems 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

Dipl Eng, DIC, PhD, 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 Department of Physics and Astronomy, University College London.

He joined the Institute of Biomedical Engineering, Imperial College London in 2005 and in 2006 he became Corrigan Research Fellow. Konstantin was appointed Senior Research Fellow in 2012.

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:

- **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.
- **Optogenetics:** Photo-cycle models of channelrhodopsin2 (ChR2), halorhodopsin and archaerhodopsin, modelling of neurons expressing ChR2 mutants/other ion pumps. Modulation of neural activity using light (visible, NIR, MIR). Manipulation of neural circuits.

- **Mathematical models of 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 Wiener kernels and maximally informative dimensions
- **Retinal implants** (image processing, stimulator driver algorithms and electronics, etc). Event-based representation of sensory input and its processing.

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. To date, his papers have more than 900 citations, two papers have more than 100 citations each.

He has extensive experience in organising and running collaborative projects, currently he is the Principal Investigator of an EU project ('SeeBetter – Seeing Better with Hybrid Backside Illuminated Spatio-Temporal Silicon Retina', which aims to design and fabricate a novel type of the retinomorph vision sensor), and a Co-Investigator of a Wellcome Trust Institutional Strategic Support Fund grant: 'Network of Excellence for Optogenetic Manipulation of Neural Circuitry'.

ADMINISTRATIVE STAFF PROFILES



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 Chairman and Chief Executive of DNA Electronics Ltd, organises PR and events associated with his commercial activities and is Secretary to the Board of DNA Electronics Ltd.



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 August 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 a central 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 Reza 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 otherwise performed very intermittently by expensive and somewhat risky catheterisations.

Surface acoustic wave (SAW) resonators have been used for wireless pressure measurement in the automotive industry and may be adapted to make implantable sensors for cardiovascular, intra-ocular and intra-cranial blood pressure measurements. Using micro-fabrication techniques, SAW resonators can be made into pressure sensitive sensors. These sensors possess inherent characteristics of SAW devices, namely small size, high stability and very long life. When connected to an antenna, such sensors would form a transponder that can be interrogated for pressure information wirelessly.

Using SAW devices for pressure measurement in the body poses a number of challenges compared to their typical use in tyre pressure monitoring. These include device biocompatibility, delivery system, reliable RF signal transmission and reception, while complying with telecommunication regulations, and signal acquisition and processing.

In order to investigate different aspects of RF interrogation and obtain optimal operating parameters, a portable and flexible system suitable for *in vitro* / *in vivo* animal testing, was required.

We have prototyped a complete system for wireless measurement of the blood pressure inside the circulatory system. Based on the results of animal trials, we received further funding from the Wellcome Trust for three years. The main objective of our current research is to improve and optimize the existing elements of the developed system and make them suitable for clinical trials. This task involves compliance with a number of standards to make sure 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 within the project is in the following areas:

RF interrogating systems: improving the previously designed system through interaction with our external contractor to produce the compliant units. There are a few challenges here: 1. Overall size and weight reduction to make the interrogator portable enough to be worn by patient for continuous monitoring. 2. Optimization of the electronic circuits to reduce power consumption while increasing the sensitivity. 3. Designing to meet safety as well as RF emission regulations.

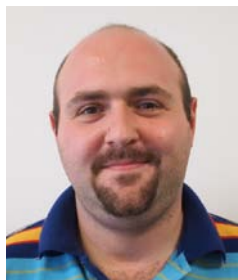
Sensor microfabrication: Working with our external contractor in the US to achieve a reliable fabrication process for sensor production. Since the sensor is to be implanted permanently, it must have a very low drift over its life time (target: ~10 years). Such low drift essentially means that high hermeticity levels in the sensor cavity must be achieved. This requirement together with biocompatibility issues impose limitation on the material that may be used and makes the sensor microfabrication challenging.

Implantable antenna design: Possible improvements on previous design are being studied. To meet safety standards, biocompatible insulating material must be used in the antenna structure. This together with slight changes in antenna dimensions mean that antenna design may need fine tuning.

Signal processing: Improving the developed algorithm in order to achieve the same accuracy with a lower signal to noise ratio. The quality of the signal transmitted from the implant will eventually depend on implantation depth that varies from patient to patient. Making the signal processing algorithm noise robust ensures that accuracy of the overall system will not be compromised.

PUBLICATIONS

The results have been prepared for publication as three journal articles and are awaiting clearance from the Wellcome Trust.



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). It is associated with high health expenditure: in UK the 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 material for the support structure, both for its biocompatibility and super-elastic properties. A number of configurations for the support structure have been designed and – in accordance with ISO standards – mechanical response has been characterized by means of both tensile testing and finite element modelling.

A specific delivery system has been designed in collaboration with a subcontracting company and tested in a mock anatomical model. Preliminary tests *in vivo* (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.

Future work will involve finite element modelling of endovascular delivery and assessment of wall stress levels caused by the support structure, *in vivo* delivery of prototypes for assessing *in vivo* host reaction and migration, and finalization of the prototype design as well as scale-up for the production process in view of future safety trials on patients. Along with the development of the prototype, the group will look at the regulatory process for having CE mark granted for the final device. Mechanical tests according to ISO and ASTM standards will be performed both in-house and in certified laboratories and the technical file for the submission to the notified body will be produced.

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Dr Olive Murphy

Research focus

Totally automated blood pressure monitoring at home to improve the care of patients with heart failure or pulmonary hypertension

Funding

Wellcome Trust and Department of Health – Health Innovation Challenge Fund

This project is a continuation of the project based around the use of an implantable surface acoustic wave (SAW) device as an alternative to a wearable blood pressure monitor. 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.

The project is now in the manufacturing and approval phase – with considerable attention to outsourcing to approved providers and will have to meet the necessary standards contained within the R&TTE, Medical Devices and Active Implantable Medical Devices Directives in order to commence human trials 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.

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 extensive knowledge of the radio standards and spectral regulations with a view to optimizing the system and guiding external collaborators.

The facilities available in the IBE are unique in providing a platform for pre-compliance as contained within the Electromagnetic test facility is a large certified anechoic chamber, valid up to 34GHz and 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. The remaining facilities within the electromagnetic chamber complement projects which are focused on technology transfer, with a particular emphasis on meeting pre-compliance for regulatory approval.

PUBLICATION

Murphy OH, CN McLeod, M Navaratnarajah, M Yacoub and C Toumazou, 'A Pseudo-Normal-Mode Helical Antenna for Use With Deeply Implanted Wireless Sensors', *Antennas and Propagation, IEEE Transactions on*, vol.60, no.2, pp.1135–1139, 2012.



Dr Belinda Nedjai

Research focus
Genetics and functional genomics

Personalized health care is rapidly moving beyond theoretical application into real-world medicine. Advances in understanding how genetic differences influence treatment and prevention of disease have leapt forward based on the understanding of the human genome. However, despite these advances in understanding the genetic basis of disease, the post-genome era will need to focus on understanding how gene and protein networks interact with environmental stimuli to create complex human diseases.

The aim of my research is to create a database in order to customise the 'normal value' to one person. Human illness is not solely the result of simple genetic inheritance. Interaction with environment and behaviour using sensor data is needed. Integrating results from various data modalities and knowledge retrieval engines is still challenging for clinically meaningful use. This database will take into account the attributes specific to each patient (genetic test, disease markers, ethnicity and lifestyle), which are combined to provide for each patient a unique value applicable for diagnosis or simply health monitoring and management.

The resulting changes in metabolite levels, and their physiological consequences, create a network that can be monitored by high-throughput methods and analyzed by multimodal approaches. We suggest that the fine regulation of this network is specific to each human individual and depends, in part, on the constellation of regulatory single nucleotide polymorphisms (SNPs) in his or her genome. In addition lifestyle exposure will have different accumulative consequences on the expression of the respective target genes. These differences will influence the individual's susceptibility to ageing-related diseases, such as type 2 diabetes, atherosclerosis, cancer, and osteoporosis and will be taken into account and highlighted by the database. Furthermore, it is anticipated that the database will also help to identify the most critical genes, or abnormal metabolite levels, in each person that will serve as biomarkers for the early detection of these diseases. Our mission is to deliver solutions that improve medication-related decisions to enhance clinical care, patient safety and healthcare outcomes worldwide.

We propose to consider the uniqueness of each patient and use the full range of the expertise and knowledge to provide them with a personalised 'normal value'. This knowledge will provide the patient with an

appropriate and unique solution to manage his own health. The health management will consist of data consultation among peers and the giving of advice based on expertise, rather than a norm model as used nowadays. Decision support would consist of access to a wide variety of knowledge resources in the database, as well as to tools for creative problem solving and research.

Database efforts have kept pace with the furious rate at which this sequence data is being generated, providing investigators access to all public data in a practically instantaneous fashion. While most biologists are familiar with the databases comprising the International Nucleotide Sequence Database Collaboration (DDBJ, EMBL NCBI. and GenBank), numerous other specialized databases have emerged. These specialized databases often arise out of a particular need, whether it is to address a particular biological question of interest or to better serve a particular segment of the biological community. So far no database is able to give an easy readout to the patient. Although companies such as '23 and me' give an idea about gene susceptibility to disease our database will go much further providing specific and customized information directly to the patients or medical professionals.

There is a need for a comprehensive understanding and integration of personalized health care among physicians as well as patients beyond the scientific research community. The implicit goal of my research is to advance the discussion and understanding of personalized health care beyond research to focus on real-world implications. Three main applications will emerge for this database; 1) Diagnosis purpose; 2) Clinical trial drug discovery and 3) Personal health care monitor (Mobile phone or Neural chip).

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2. Juffali W, *et al.*, 'The WiNAM Project: Neural Data Analysis with Applications to Epilepsy', *IEEE BioCAS Conference*, 2010.

PUBLICATIONS

See page 28.



Dr Herrero-Vinas Pau

Research focus
Bio-inspired artificial pancreas

Funding
Wellcome Trust

My main research interest lies in the field of diabetes technology and in particular in developing algorithms for the realization of a bio-inspired artificial pancreas (BIAP) for ambulatory use. The final aim of this research is to transfer this technology to a commercially available system.

Algorithms which I have developed as part of this research include: a novel bio-inspired glucose controller based on the β -cell physiology, which is currently being validated 'in-clinic' over 20 type 1 diabetic subjects during fasting, over-night and 24-hour conditions; a simple technique for estimating the rate of glucose appearance from mixed meal which is being used to build a meal model library to be incorporated into diabetic subject simulators in order to account for more realistic and varied meals; a robust model-based fault detection system to detect possible adverse events in insulin delivery systems, such as disconnections of the infusion kit, which are currently undetectable by existing commercial insulin pumps; a reliable technique for parameter estimation of models of the glucose-insulin regulatory system based on interval analysis; and a type 1 diabetes subject simulator for in-silico testing of bihormonal, i.e. glucagon and insulin, blood glucose controllers.

I am also involved in the development of an advanced bolus calculator for diabetes management (ABC₄D) based on Case Based Reasoning (CBR), an artificial intelligence technique that solves newly encountered problems by applying the solutions learned from solving previous problems. Such a system is aimed at providing superior glycaemic control with respect to existing insulin bolus calculators embedded in current insulin pumps. ABC₄D is currently in the process of being clinically tested over 12 type 1 diabetic subjects.

Finally, I am involved in a research project that aims to optimise antibiotic prescribing in the intensive care unit by improving the point-of-care information available to clinicians on local resistance and sensitivity data. The application provides prescribing decision support through CBR technology, which will help clinicians across the healthcare community to make the right choices for antibiotic therapy from the beginning of the treatment.

PUBLICATIONS

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Dr Themistoklis Prodromakis

Research focus

Reliably unreliable nanotechnologies

Funding

Winston Wong Centre for Bio-Inspired Technology, EPSRC, The Royal Society, eFutures XD

CMOS technology is fast approaching the nanoscale floor, with devices attaining comparable dimensions to their constituting atoms, confronting us with challenges associated with the performance, reliability and manufacturability of conventional analogue and digital circuits. We have nowadays reached the point where it is imperative to substantiate ‘beyond CMOS technologies’, based upon inherently unreliable information processing and memory elements; fulfilling Feynman’s vision on fabricating and operating emerging devices by ‘manipulating a few atoms’.

The realization of a nanoscale memory-resistor (memristor) by Hewlett Packard in 2008 came almost 40 years after its theoretical inception and manifests a prominent paradigm for extending CMOS beyond its current physical limits, due to their infinitesimal dimensions, their capacity to store multiple bits of information per element and the miniscule energy required to write distinct states. Yet, most of their impact is anticipated through the realisation of bio-inspired/mimetic systems.

My research exploits the strong emergence of ultra-thin functional oxides, nanoscale resistive switching elements and large-scale systems of the same. Such systems exhibit rich dynamics, offering opportunities in novel design paradigms and emerging ICT applications for substantiating unconventional computation formalisms.

PUBLICATIONS

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Dr Amir Eftekhar

Research focus

Neural interfacing, acquisition and analysis

Funding

Winston Wong Centre for Bio-Inspired Technology

SUMMARY

My work primarily involves the development and commercialisation of technology for interfacing the central and peripheral nervous systems. Any neural interface system composes the front-end electronics, analogue signal processing, acquisition and digital signal processing. The latter utilising algorithms and/or feature extraction and classification to facilitate clinical inference or closed-loop intervention strategies. My work deals with this signal chain and the technology needed to realise it.

I am working on several projects that will create integrated solutions for several neural interface applications:

- With Kings College London we are working on advanced single pulse electrical stimulation (SPES) systems for identifying the focal region of epileptic seizures. This pioneering technique identifies brain abnormal responses to stimulation of the brain's cortex.
- In collaboration with Kings College London, we are developing systems for real-time, wireless ambulatory EEG monitoring in the clinic and to some degree the home. This system is designed to be quickly setup by the patient, and designed for ease of use and reduced invasiveness into the patients' lifestyle.

These two projects initially target epilepsy. 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 better epilepsy diagnosis and treatment.

My work is peripheral interfaces for monitoring electrical and chemical signatures associated with action potential propagation. 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 for

application such as vagus nerve stimulation (VNS). Using a combination of electrode types we have shown *in-vitro* results which once further studied will move to *in-vivo*.

VNS therapy has emerged over the last 20 years as an effective non-drug treatment. An estimated 50% reduction of epileptic seizures can be achieved that increases over time. Although estimated to greatly improve quality of life, it has a number of unwanted side effects. These are due to high amplitude and non-selective stimulation that is activated frequently regardless of whether any epileptic activity manifests. The platform we are developing aims to add recording input to the stimulation parameters providing more effective and intelligent therapy. Recently, we have formed collaboration with Professor Steve Bloom at Imperial College London to study vagus activity in relation to obesity and the pancreatic (for diabetics) mechanisms the vagus nerve is responsible for.

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. Other projects include a multi-neuron recording system with on-chip spike sorting (with Leicester University and Newcastle Institute of Neuroscience) and novel methods for ECG processing (with Texas Instruments) and removal of baseline drift in low-power electronics. All of these aim to create novel solutions that utilise our groups unique bio-inspired principles for medical diagnostic and treatment.

PUBLICATIONS

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2. A Guilvard, A. Eftekhar, S. Luan, C. Toumazou, T. G. Constandinou, 'A fully-programmable neural interface for multi-polar, multi-channel stimulation strategies', *ISCAS*, pp: 2235–2238, 2012
3. I Spulber, P Georgiou, A Eftekhar, C Toumazou, L Duffell, J Bergmann, A McGregor, T Mehta, M Hernandez, A Burdett, 'Frequency analysis of wireless accelerometer and EMG sensors data: Towards discrimination of normal and asymmetric walking pattern', *ISCAS*, pp: 2645–2648, 2012.
4. K B Mirza, S Luan, A Eftekhar, T G Constandinou, 'Towards a fully-integrated solution for capacitor-based neural stimulation', *ISCAS*, pp: 2243–2246, 2012.



Dr Ali Khat

Research focus
Fabrication of nanoscale ReRAM cells

Funding
EPSRC

SUMMARY

Synapses are important biological units that are conjectured to support both memory and computation. Engineers are thus interested in emulating their dynamics with VLSI circuits for leveraging nature's advanced functionalities. My research is aimed at 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.

Based on my research background on micro and nanotechnologies, micro-actuators, micro-sensors, carbon nanotubes and cleanroom expertise, my work focuses on exploiting state-of-the-art micro/nano fabrication techniques for establishing memristive devices and complex architectures.

METHOD

The memristor we fabricated is based on a two terminal architecture, metal/insulator/metal (MIM) structure, whose simplicity makes it rather attractive. My work during this year was focused on developing and optimizing process steps to ensure reliable fabrication of memristive devices with surface areas down to the limit of optical lithography. Cross-bar and array configurations were considered.

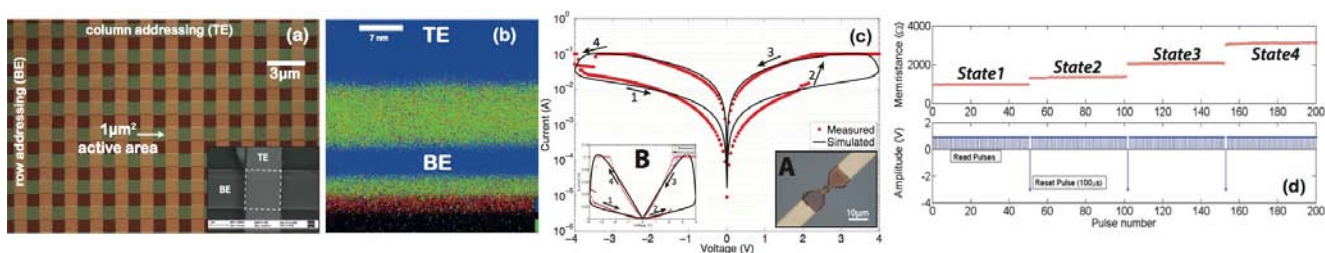
Memristive behaviour is contingent on the processing method used to fabricate the device, thus a large number of specimens were fabricated for characterisation. I have fabricated TiO_2 , Ta_2O_5 and ITO based memristive devices and various deposition and geometric parameters were investigated.

NEXT STEPS

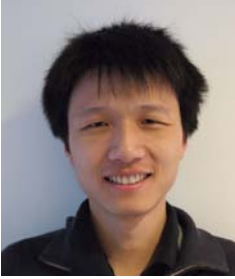
To enhance memristive characteristics further, miniaturisation is required. Therefore, we have considered Nano-Imprint Lithography (NIL) technology. I have designed the first masks which are currently being fabricated by E-beam. I will develop the new fabrication steps and optimise the process to realise memristors with features down to 50 nm. This technology will enable obtaining more dense but at the same time more reliable devices.

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Solid-state TiO_2 -based memristors fabricated in house. (a) Microphotograph of a memristor cross-bar array, (b) CHEMI-STEM map of a memristor cross-section, (c) Simulated and measured pinched hysteresis I-V and (d) multi-state programming of a TiO_2 -based memristor.



Dr Yan Liu

Research focus

Towards next generation neural recording interface

Funding

EPSRC

My PhD on chemical sensing systems, was completed in 2011. The research, 'Engineering Robust CMOS ISFET Smart Sensor Systems' developed an understanding of the characteristics of CMOS-based ISFETs, in particular, non-ideal behaviour, and proposed several methods to minimize these. These included interface circuit techniques and design of an intelligent instrumentation system with low power consumption, hardware complexity and ability of correcting intrinsic non-ideal behaviour. This research fundamentally aimed to simplify the sensor and processing overhead, and ultimately lead to the implementation of large scale sensor arrays for lab-on-chip.

On completing my PhD I was appointed a postdoctoral research associate in neural interfaces working on EPSRC funded research with Dr Timothy Constandinou.

This 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.

My role in this project is to leverage these limits, and design the system platform for large-scale neural recording. The aims include: 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.

PUBLICATION

Liu Y, Al-Ahdal A, Georgiou P, and C Toumazou, 'Minimal readout scheme for ISFET sensing arrays based on pulse width modulation', *Electronics letters*, Vol:48, Pages:548-U282012.



Dr Iulia Salaoru

Research focus
Plasticity in NEUral memristive architectures

Funding
EPSRC

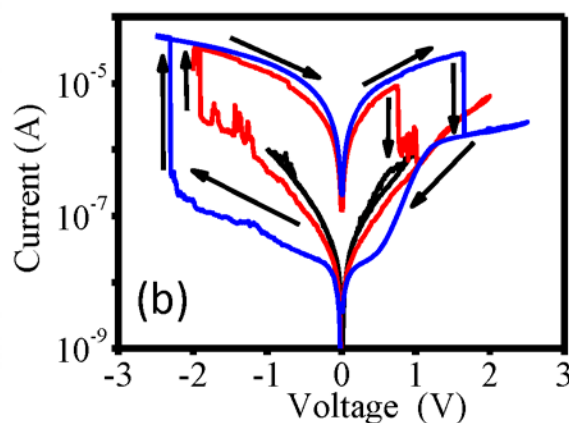
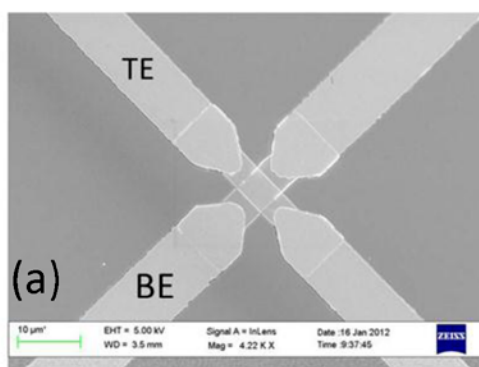
The current trend in modern electronics is to produce devices that are faster, smaller, reliable but also possess unconventional dynamics that enable emerging bio-inspired applications. From the scaling perspective, Moore's law is the driving force that pushed the conventional electronics to reach the fundamental limits of atomic scale. As such, memory technologies have been at the forefront of research exploiting new materials, device architectures and other properties that can facilitate cells with advanced characteristics, ie. multistate capacity per unit cells, good endurance and writing/reading fast speeds. The main application of memories are in computing, nonetheless these elements are also currently exploited to facilitate the neuromorphic doctrine.

Memory can be supported over a large variety of materials, from organic to inorganic and for different device configurations. Over the past years, I have worked on polymer based memory cells [1-4]. My previous expertise is currently exploited within the Centre for Bio-Inspired Technology to study metal-oxide based resistive memory. Such cells are also known as memristor.

In my research I will be characterising solid-state devices, fabricated in-house. Apart from the electrical characterisation of these cells (endurance, multistate programming, retention, etc) I will utilize a number of advanced metrology techniques such as SEM, FIB and TEM towards deciphering the origins of the switching mechanisms.

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(a) SEM image of cross point array of Pt/TiO₂/Pt device; (b) Current-Voltage characteristics by applying three progressively increasing bipolar voltage sweeps of a Pt/TiO₂/Pt ReRAM cell



Dr Irina Spulber

Research focus

Wireless body sensors system for management of osteoarthritis

Funding

Wellcome Trust, EPSRC

SUMMARY

Osteoarthritis (OA) is a chronic disorder resulting in degenerative changes to the joints that cause pain and loss in mobility. In the UK alone, this condition affects 8.5 million people and is a leading cause of disability and the most common cause of chronic pain, with huge social and economic costs. To date, there is no cure for osteoarthritis, the condition is mainly managed through lifestyle modifications complemented by pain-killing treatments. Correct regular exercise has been shown to significantly improve function, alleviate pain, and delay the need for surgical intervention. Despite the proven benefits, it is often the case that physiotherapy fails to fulfil its full potential mainly due to poor attendance to sessions, poor compliance to the prescribed regimen or even incorrect execution of exercises due to lack of feedback.

This collaborative research brings together expertise from Imperial College's Musculoskeletal Surgery Department at Charing Cross Hospital, Institute of Biomedical Engineering – Centre for Bio-Inspired Technology and Toumaz – a low cost, ultra-low power wireless technology company.

METHOD

The project aims to exploit Toumaz Limited's recent technological advances to develop a medical wireless sensor system capable to assist 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.

The project builds on the Toumaz Sensium™ platform which requires refinement and tailoring for this specific application. Preliminary parallel tests have been conducted on Sensium 'pebbles' and standard gait laboratory equipment in order to evaluate the performance of the 3-axes accelerometers and validate them against the standard optical system. Further sensor integration (gyroscopes), algorithms implementation and data interpretation studies are required before proceeding to clinical trials.

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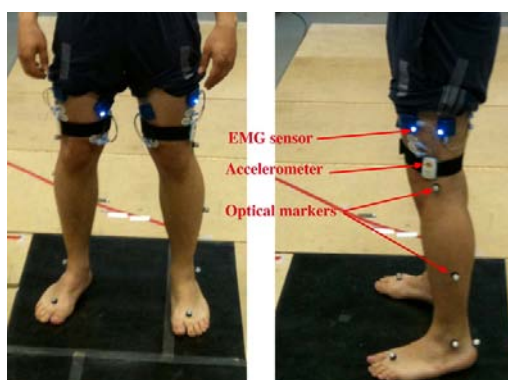


Figure 1 Sensor placement around the knee

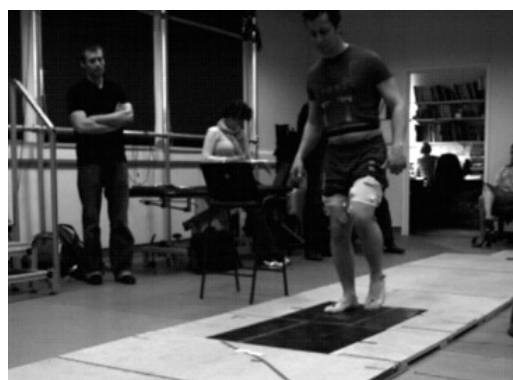


Figure 2 Sensor evaluation in the Human Performance Laboratory, Charing Cross Hospital



Dr Jakub Trzebinski

Research focus

Point-of-care diagnostics, neural interfacing

Funding

Centre for Bio-Inspired Technology

Following my PhD at Imperial College and Brunel University on the development of biosensors for monitoring glucose and lactate I am continuing my research on the development of minimally invasive sensors and drug delivery devices. I am also developing a novel chip for intraneural chemical recording using ISFET technology.

I am working on three projects: minimally invasive sensors for monitoring glucose concentration in interstitial fluid (ISF); a controlled drug delivery device; chemical intraneural biosensors.

The aim of the minimally invasive sensor project is to develop a biosensor able to bridge the top skin layer, the epidermis, and access the ISF in minimally invasive fashion, where glucose can be measured. This is achieved by using microfabrication and lithographic techniques to develop microneedles, which are then functionalized with enzymes to act as biosensors.

I am also designing a wearable device able to deliver drugs 'on demand' minimising patient compliance. Such a device, in combination with biosensing technologies, will act as a feedback mechanism to the sensor signal by allowing electronically controlled drug(s) release to the patient.

The main focus of my research on chemical intraneural biosensors is to develop a biosensing platform able to record intrafascicular chemical changes inside the nerve. This is achieved by fabricating arrays of chemically sensitive microspikes, whose tips are able to penetrate to the inside of the nerve and directly measure chemical changes during stimulation. It will allow the monitoring of the chemical neural dynamics in therapies such as vagus nerve stimulation (VNS).

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4. Radomska-Botelho Moniz A, J Trzebinski, DG Johnston, AEG Cass *et al.* 'Continuous glucose monitoring using minimally invasive microprobes' *Journal of Diabetes Science and Technology*, Vol:6, Pages:479–480, 2012.



Dr Thomas Weissensteiner

Research focus

Point of care diagnostics for osteoarthritis based on DNA enzymology and CMOS sensors

Funding

Wellcome Trust, EPSRC

SUMMARY

Osteoarthritis is a degenerative disease affecting the majority of the population over 60, with 12% developing clinical signs including severe pain and joint failure. Although the disease is poorly understood at present, future molecular diagnostics might help to identify individuals at risk, select preventive measures and guide clinical intervention. My project is the development of assays for point-of-care genetic testing, using CMOS sensors. In particular, I have been working on improving the chemical signal that is detected by the sensor.

METHOD

Single nucleotide polymorphisms are discriminated by enzymatic extension of allele-specific primers, such as in a polymerase chain reaction. A byproduct of the reaction, under appropriate conditions, is a change in free proton concentration which is sensed in our device by an ion-sensitive field effect transistor.

RESULTS

I selected candidate SNPs from the Osteoarthritis literature and designed primer sets for typing. A major challenge has been to adapt the PCR reaction to reliably produce pH changes of a suitable magnitude, while retaining allele specificity. A number of factors proved beneficial but their combined effect has so far not led to satisfactory performance. I investigated the contribution of different reaction components and found a new way to improve the proton signal.

NEXT STEPS

I am intending to generalize these findings to a number of polymerase reactions that can be used with the ISFET device.

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Dr Gareth Jenkins

Research focus

Novel biosensors for POCT applications and lab-on-chip technology

Funding

BIS UK-China Fellowship for Excellence; National Science Foundation of China – NSFC (21075104); National Basic Research Program of China (2010CB732402); Nanjing Technology and Entrepreneurship award; Jiangsu “Shuang Chuang” Innovation and Entrepreneurship award.

Professor of Advanced Bio-analytical Micro Devices, Nanjing University of Posts & Telecommunications, China

In March 2011 I was awarded a UK-China Fellowship for Excellence by the UK Department for Business Innovation and Skills and moved from Imperial College London to work with Professor Chaoyong James Yang, in the State Key Laboratory of Physical Chemistry of Solid Surfaces, Xiamen. The group is pioneering new methods in a number of areas.

I became involved with an elegant project aimed at using agarose droplet microfluidics for performing massively parallel reverse transcription PCR assays for single molecule RNA studies and single cell gene expression studies. Using a microfluidic approach, we were able to exercise exceptional control over the individual RT-PCR reaction condition in millions of highly monodisperse agarose droplets. Such techniques could have excellent potential in applications such as high-throughput DNA sequencing, viral diagnostics and gene expression studies. In this work, we designed and fabricated a simple microfluidic droplet generator for generating highly mono-disperse water-in-oil emulsions.

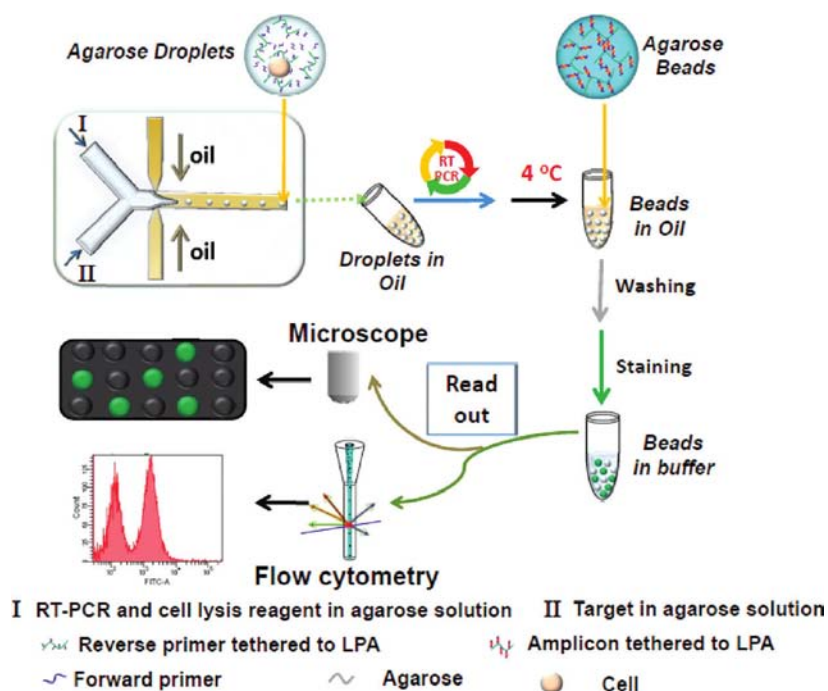
EXPERIMENTAL SCHEME

In this way, single molecule detection of RNA was achieved and also the simple determination of genetic mutations in cell populations could be performed. We demonstrated this by testing two different cell lines each expressing a different level of the Epithelial cell adhesion molecule (EpCAM). EpCAM is overexpressed in most solid cancers and it has recently been identified as a cancer stem cell marker. Two different cells (Kato III and MDA-MB-231) which have different EpCAM expression levels were used as the targets for single cell RT-PCR in agarose droplets. Flow cytometry results were able to rapidly determine a strong difference in gene expression between the Kato III and MDA-MB-231 cell lines.

I have moved to Nanjing researching the application of advanced carbon based nanomaterials for biosensing with a particular focus on their application to low cost, point of care diagnostics and personalised medicine. The integration of microfluidics with such biosensors is a particularly important aspect of my work in order to deliver not just results on the laboratory bench, but also devices which can be manufactured in a cost effective way. As part of this effort we are seeking commercialisation opportunities and Jiangsu province is supporting us with two awards related to innovation and entrepreneurship. International collaborations are actively encouraged and I am seeking to strengthen ties between Imperial and Nanjing.

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- Zhang H, *et al*, ‘Massively Parallel Single-Molecule and Single-Cell Emulsion Reverse Transcription Polymerase Chain Reaction Using Agarose Droplet Microfluidics’, *Analytical Chemistry*, In Press
- Zhu Z, *et al*, ‘Single-Molecule Emulsion PCR in Microfluidic Droplets’, *Analytical and Bioanalytical Chemistry*, 2012.





Mr Deren Barsakcioglu

Thesis topic
Resource Efficient Fully Integrated Spike Sorting

Supervisor
Dr Timothy Constandinou

Funding
EPSRC DTA

SUMMARY

Neuroprosthetics aim to restore lost sensory and motor function of millions of people by interfacing directly with their nervous system. Brain-based neuroprosthetic interfaces achieve this using microelectrode arrays that record multiple neuronal spiking activities close to each electrode.

To identify which of these neurons have fired, a signal processing step called spike sorting is used. With trends in electrode technology, thousands of channels can now be recorded. It is beyond current bandwidth capabilities to transmit raw data of this magnitude for totally implantable systems.

In order to overcome the power-bandwidth bottleneck due to the ever increasing number of channels recorded, on-chip spike sorting is essential.

My work is part of an inter-university multidisciplinary project to develop a fully integrated implantable neural interface. The aim of my project is to develop a fully integrated real-time spike sorter with minimal power and area consumption, while maintaining the high performance achieved by offline equivalents. Moreover, considering the dynamic recording environment, autonomy and self-calibration is another important aspect of the system being developed.

METHOD

Within this context, the first step in the project is to identify and establish the accuracy and complexity trade-off of key parameters on spike sorting.

This includes testing several signal processing techniques to improve the accuracy, while estimating the required hardware resources such as memory used, number of operations, and power consumption. In the following stages, novel algorithms will be developed to ensure automatic and adaptive operation (classification and calibration). Once all trade-offs are established and algorithms are selected, the ways in which these algorithms can be most efficiently implemented in hardware will be investigated.

RESULTS

As the first step in my research, the work to date has investigated the parameters associated with template matching and the analogue front-end preceding the spike sorter. Having identified these parameters, they were quantified in terms of spike sorting accuracy as well as complexity (power and area). After establishing the key hardware trade-offs, the next stage in the project is to explore and develop new algorithms and implement them in CMOS.

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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

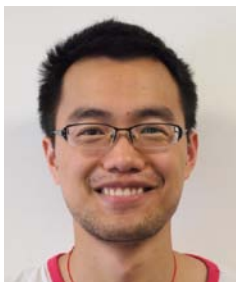
Investigate the method by which the beta cells (insulin producing cells) synchronize their bursting behaviour using gap junction coupling [2]. Design an array of coupled beta cells on a CMOS chip with a low power potentiostat as the sensing front end. Attempt to show that output signal has a higher SNR and better precision than averaging. Design a sub-1V CMOS potentiostat with sufficient gain, bandwidth, low noise and tunable current sensing range for the given application. In addition investigate and optimize fault detection systems for implementation in hardware. There are two fault detection schemes available, one is model based and the other is based on signal processing.

RESULTS

Matlab simulations of coupled beta cells have shown the noise shaping potential of synchronized networks. It is clear from the initial simulation results that synchronization has the same noise shaping capability as averaging. The next step is to investigate if we could outperform averaging and increase the SNR further. In addition a CMOS potentiostat has been designed and fabricated that senses current in the nA range and produces a pulse signal whose frequency is proportional to the current. This can be used as the front end for the beta cell array as described before. 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 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.

My PhD research involves the design of a novel ISFET array for DNA sequencing and an FPGA platform for the sequence assembly. The new detection array should be capable of dealing with some lingering problems in ISFET such as trapped charge, drift and capacitor division. I aim to make improvements with differential structure, long-time measurements and amplification unitization being the most characteristic. Via the cooperation with auxiliary system, the new detection system would dramatically decrease the bandwidth requirements to off-chip environment. In order for this to be possible, significant research must be conducted to overcome the technological constraints which exist when scaling such devices to deep sub-micron technologies.

On the other hand, the FPGA assembly platform requires a novel comparison algorithm which can be easily parallel implemented. The new algorithms should have the capability to process the real-time signal so that we can utilize the detection time to do the processing work. Additionally, cluster FPGA system could be realized as long as the parallel architecture is well designed.

My final goal is to lay down a significant scientific foundation for the design of such a combination of systems. 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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Ms Melpomeni Kalofonou

Thesis topic

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

Supervisor

Professor Chris Toumazou

SUMMARY

The analysis of DNA methylation-based biomarkers is a rapidly advancing area of research, being actively studied in multiple cancers, with the possibility of the methylation profile to distinguish tumour types and perhaps the response to chemotherapeutic agents. Already, DNA methylation patterns in cancer related genes have been identified in blood of cancer patients and characterised as very promising biomarkers for tumour detection, validation of tumour types or stages of progression and even prediction of the risk of tumour development.

Currently DNA methylation detection methods are limited by the use of optical methods that entail high levels of complexity, post-processing steps for implementation and are not easily scalable or low in cost. Hence, there is an urgent need for the development of detection assays, using well-established CMOS technologies that meet the current demands of healthcare such as simplicity, portability, sensitivity, low cost, scalability and intelligence, leading to a well-targeted closed loop strategy for detection and therapy and better prognosis of cancer.

METHOD AND RESULTS

My research focuses on the application of semiconductor technology for detection of DNA methylation based biomarkers in early screening of cancer using ISFETs, with the aim of developing the biochemical and electrical front-ends for a system that will be applied in detecting the presence of DNA methylation of specific gene markers associated with tumour growth. This will be used as an early detection tool for identifying warning signs of cancer. The system developed utilises intelligent sensor design due to the integrative capability of ISFETs with standard well-known circuit techniques with the capability to provide real-time continuous detection and processing.

The sensor front-end is based on the pH sensitive, CMOS based ISFET technology, whereby the acquired signal, the pH change, obtained from the targeted DNA samples is measured by the ISFETs, providing information dependent on the instrumentation chosen for the DNA analysis. This development is part of the bigger picture of a lab-on-chip system that will be able to detect the DNA methylation signature of specific genetic markers that undergo significant irregularities in the case of cancer development.

During the course of this research, a principal, multistage method was developed, able to determine and validate the methylation status of a DNA template,

structuring a principal biochemically processed DNA methylation based system platform. In parallel, the electrical front-end of the system was developed, forming the alpha prototype of the 'Methylation Cell'. The instrumentation of such principal prototype consisted of an ISFET based ratiometric circuit, formulating the process of using the ratio of DNA methylation to determine the level of aberrancies between an early developed tumour-affected gene and a normally methylated 'version' of the same gene. In parallel, an ISFET based readout circuit was proposed based on the 'Gilbert Gain Cell', for differential amplification of current signals originated from PCR oriented biochemical reactions, allowing stable drift reduction, tuneable gain and a low power consumption.

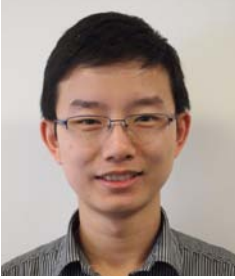
A full integration of both biochemical and electrical front-ends has been achieved proving that DNA methylation can be detected in CMOS forming the very first fully integrated semiconductor based system platform for DNA methylation detection, paving the way for the next generation of real-time DNA methylation specific assays for early screening and further monitoring of cancer.

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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 used in neural prosthesis nowadays to restore the damaged or lost sensory, cognitive and motor modality of an individual. The nerve being stimulated can be part of central nervous system (CNS), such as cortex, or peripheral nervous system (PNS), such as sciatic nerve. To perform such stimulation, Implantable Neural Stimulator (INS) is often used. Together with 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 a stimulus through several electrodes simultaneously, better selectivity can be achieved due to the interferences among the stimulus, 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

At the current stage, a novel counter-based charge-metering method for voltage-mode neural stimulation is proposed to improve charge control, charge recycling and the power efficiency. A successful verification has been made on a chip fabricated [1]. The next step is to verify the field-shaping possibility of multi-polar stimulation. A neural stimulator chip is being designed for this purpose. There is also possibility of integrating a communication system with the stimulator, which is a future step [2][3].

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Mr Matthew Lubelski Katz

Thesis topic
Bio-inspired modelling of the retina

Supervisor
Dr Konstantin Nikolic

Funding
EU (FEP-Proactive 7 – ICT) ‘SeeBetter’

Conventional cameras are fundamentally limited in comparison to biological retinas, because they produce redundant sequences of images at a limited frame rate. By contrast, neuromorphic ‘silicon retina’ sensors attempt to mimic the biological retina’s event-based architecture to provide superior information processing capabilities.

At present, the range of application of these retinas remains restricted because of technical challenges in their design. It is the goal of the SeeBetter project to address these technical challenges and to explore the possible neuromorphic architectures that could be realised in their design. The project is a collaboration between Imperial and experts at imec, University of Zurich, and Friedrich Miescher Institute for Biomedical Research.

At Imperial, our work is focused on the mathematical and computational simulation of retinal architectures. We have used a PlayStation 3 Eye (PS-Eye) to produce a behavioural emulation of event-based vision sensors. To build the emulation we characterised the optical, functional, and noise characteristics of the camera in detail. Using a custom driver, the camera was integrated into the jAER framework and models implemented of the Dynamic Vision Sensor (DVS), Colour-DVS, and a proposed Hybrid Vision Sensor. This emulation allows us, and others, to analyse the behavioural properties of the proposed vision sensor and study its application in real-world scenarios while also including the effects of non-idealities such as fixed pattern and temporal noise.

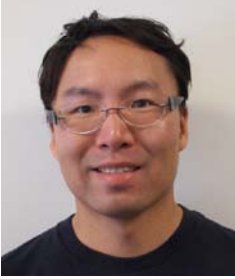
Currently, we are using a Mutual Information (MI) based system analysis technique in order to analyse the response of unidentified retinal ganglion cells to natural stimuli. By extracting the most informative features from the high dimensional stimulus space, we hope to deduce the functional roles of the cells and provide inspiration for novel architectures that can be incorporated into the silicon retina design.

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Mr Kwok Wa Lui

Thesis topic

A Wirelessly-powered Sensor Platform using a Novel Textile Antenna – Antenna design and microwave engineering

Supervisors

Dr Olive Murphy and Professor Chris Toumazou

This project is developing a wirelessly powered RF energy harvesting platform to provide power-over-distance for low power applications (low microwatts to low milliwatts). Body-worn devices (eg. temperature sensors) that typically operate on batteries for months or years can benefit from this RF energy harvesting technology. This leads to more efficient monitoring of patients vital signs or remote monitoring in hazardous or toxic environments as the battery lifetime is no longer an issue.

A new type of wearable wideband circularly polarized textile antenna has been developed for such an application on the human body. The textile is flexible, robust and light weight and can be easily integrated into clothes. The antenna geometry is simple and doesn't require a ground plane. Therefore it is very low cost to make with high manufacturing tolerance. The textile antenna can be left-handed or right-handed circularly polarized by simply flipping to the opposite side. It is shown that the textile antenna has 3dB axial ratio bandwidth 430 MHz (18%) and -10 dB impedance bandwidth 970 MHz (39%) on a human body with the maximum gain of 4.9 dBi.

The current results show that it is possible to power up a complete wirelessly-powered temperature sensor on a human arm independent of the orientation within 1.7 metres by using 0.05 W RF energy from the base station. This power level is about 20000 less than that from a cellular phone. It was also shown that temperature data can also be received at regular intervals from the sensor to the base station.

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Ms Sivylla-Eleni Paraskevopoulou

Thesis topic

Ultra low-power implantable platform for next generation neural interfaces

Supervisor

Dr Timothy Constandinou and Professor Chris Toumazou

Funding

EPSRC

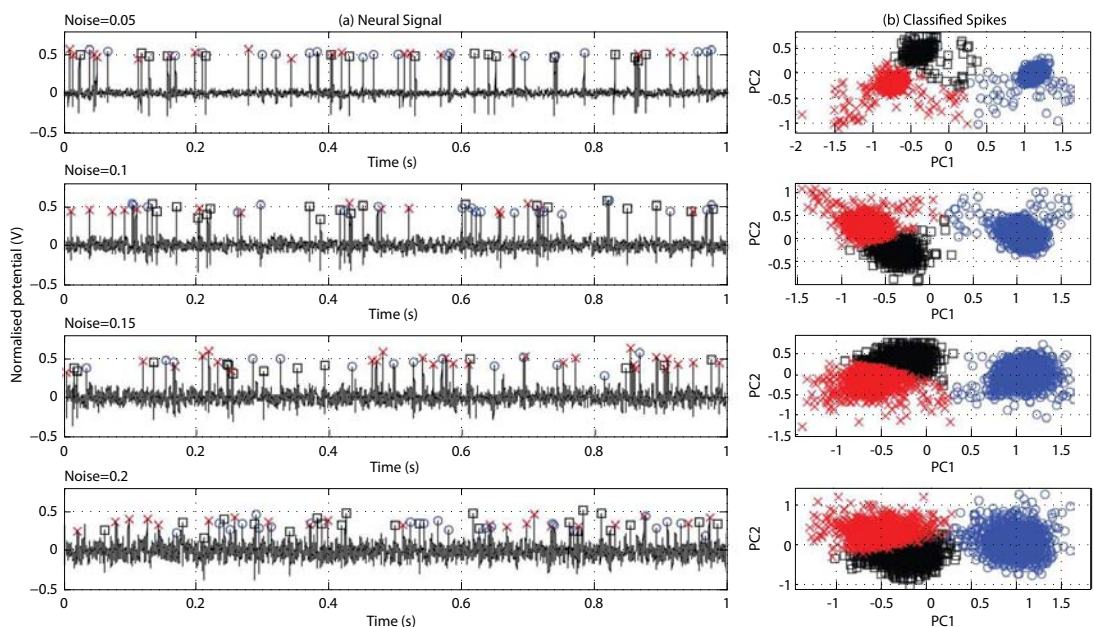
Next-generation implantable neural interfaces will provide a strong investigative tool for neuroscience research, aimed at understanding how information is represented in the nervous system. More importantly, a targeted neural interface can be used for therapeutic purposes, for example to aid individuals with severe motor disabilities regain their independence by enabling them to effectively control facilitative appliances, such as computers, speech synthesizers, or neural prostheses, by feeding back electrical signals into the nervous system.

Implanted recording arrays are used to tap into the single neuron activity of the brain, manifesting as electrical impulses or spikes. To extract useful information from the recorded spikes, signal conditioning and processing is required. The level of processing integrated on chips differs between different implementations, and is mainly dictated by two constraints: stringent power budget and limited communication bandwidth. The power constraint is imposed by the challenge of wirelessly power-supplying the implanted device and the potential damage caused to the surrounding biological tissue by an increase of the chip temperature beyond the limit of 1°C , major issue when dealing with valuable brain tissue.

My research is focusing on the design of signal amplification and conditioning 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. Moreover, I am interested in investigating neural signal dynamics with the aim of developing new signal processing algorithms suitable for low-power hardware implementation.

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1 second segment neural signal at noise levels of 0.05 to 0.2 (from top to bottom) and a two dimensional representation of the clustering space when using three principle components.



Mr Peter Pesl

Thesis topic
Intelligent decision support for type 1 diabetes

Supervisor
Dr Pantelis Georgiou

Funding
Biomedical Research Council (BRC)

SUMMARY

Type 1 diabetes is a chronic disease resulting in elevated blood glucose concentrations, which, if not managed, increases the risk of cardiovascular problems and can lead to blindness, kidney failure, and nerve damage. The standard treatment involves multiple daily injections of insulin to lower blood sugar levels accordingly. In order to calculate the right amount of insulin, simple bolus calculators exist, but often do not consider enough parameters to be effective and are not personalised. My research focuses on intelligent systems that help people with diabetes managing 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 recommendations 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 US 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 is individualised for each patient.



Insulin advisory system running on a smart phone

RESULTS

An intelligent insulin bolus advisory system has been developed in a simulated environment using a type 1 Diabetes Patient Simulator, showing improvement by increasing the time of blood glucose levels within target range. The algorithm of the DSS is now being integrated in a smartphone application, which will enable diabetics to use their phones for personalised insulin recommendations. In order to test the whole decision support software, we will start clinical trials including ten diabetic patients by the beginning of next year.

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Mr Siavash Saremi-Yarahmadi

Thesis topic

RF electrically resonating structures

Supervisors

Dr Kristel Fobelets and Professor Chris Toumazou

The main aim of my research is to look at the physical properties of electrolyte solutions using electrically resonating structures. This work can be used in the monitoring of blood flow through a stent or in chemical sensors. Due to inherent properties of such sensors, they can also be used in the implementation of remote interrogating systems.

The work I have done on RF electrical sensors allows for the implementation of a multi purpose sensor that can be used for medical and industrial applications. These sensors have the potential to be used in communication with implanted devices inside the human body. They can also be used in monitoring various physiological properties *in vivo* and *in vitro*. Other applications of this work are in the creation of localized communication systems in environments in which ordinary communication systems cannot operate.

Another area of research I have been involved in is stent and blood flow monitoring using passive systems. This work entailed setting up an apparatus to mimic blood flow inside an artery and monitor the electrical properties of a coil placed in the vicinity of this tube.

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Mr Alexander Serb

Thesis topic

Developing optically coupled, standard CMOS wireless integrated circuits

Supervisor

Dr Timothy Constandinou

Funding

EPSRC

SUMMARY

The aim of this project is to develop all individual, integrated components required to set-up a truly wireless IC; that is to say, a chip that requires no wire-bonds whatsoever in order to communicate data back and forth and receive the necessary power. As such, the project is split into 3 sub-sections: a) create the data read-out structures; b) design the data read-in structures; c) develop a power scavenging system able to operate the data transfer structures and provide extra power for some signal processing.

METHOD

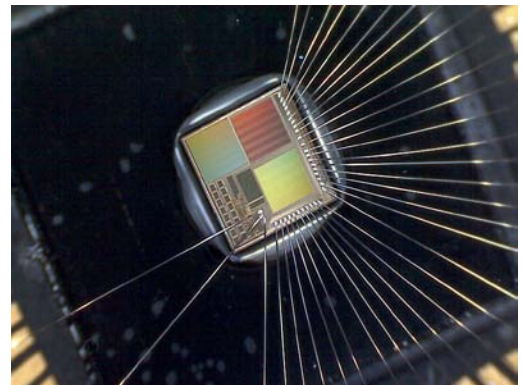
Photo-receptive elements are well-known and widely used for data read-in. Challenges in this domain are expected to concern noise and generally very low levels of incoming signal. The data read-out structures are very challenging to realise, mostly because of the indirect-bandgap nature of Silicon. Due to this impediment, Silicon is a very low grade optical emitter. As such, building an optical modulator appears to be a far more attractive solution. The fundamental idea is

thus to generate IR light off-chip, send it into the modulator and then capture it at an off-chip detector. Thus, only the modulator needs to be integrated and the effort involved in coaxing silicon to emit light can be safely circumvented. Once again, extremely low levels of signal (modulation) constitute the main challenge. This section of the project is by far the most innovative one.

The power unit will consist of standard solar cells and a management unit whose task is to upconvert the low incoming photovoltaic cell voltage and stabilise it at a level that is amenable for use by signal processing circuitry and the data read-in/out structures. Many such power management architectures have been created over the years, however real applications always turn out to hide much more detail and many more traps than academic papers usually tend to reveal. As such, the main challenge in this sector concerns gaining in-depth understanding of the function of power management units and using that to create a system that will ultimately be able to work over a wide range of possible parameters (illumination, loading etc.) and work in even the most simplistic and primitive of CMOS technologies.

RESULTS

A couple of devices have been fabricated and are currently undergoing testing. The aim is to obtain comparative results that indicate how die manufactured on different technological nodes perform with respect to each other in both the domain of power recovery and the domain of modulation. A die carrying a power management system is currently being subjected to preliminary testing too.



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Mr Mohammadreza Sohbaty

Thesis topic

ISFET Arrays for Genotyping and Sequencing

Supervisor

Professor Chris Toumazou

Funding

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

DNA sequencing and genotyping conventionally use optical methods requiring labelling of the sensed molecules and the use of bulky scanners which is expensive, time consuming and limited to laboratories. Having a fast, low-cost alternative has been of interest, driving research towards a fully label-free, electronic and integrated method.

The advent of Ion-sensitive Field-effect Transistor (ISFET) into detection of single nucleotide polymorphisms (SNP) with Professor Toumazou's invention inspired the application of these semiconductor based sensors to large-scale DNA sequencing, which aims to sequence the whole human genome in an affordable manner (under \$1000) by leveraging all the benefits of the silicon technology. An example of such a technology is the Genalysis™ platform by DNA Electronics Ltd, a spin-out company from the Centre, which provides user friendly portable set-ups for SNP detection.

However, the ISFET transistor has many non-idealities suffering mainly from drift, dc offset and cross talk that influence the accuracy of the test arrays. In this research such unwanted characteristics are studied along with the effects of large scale integration of sensors on silicon wafers. We aim to optimise the performance of ISFET arrays for genotyping and sequencing by introducing new pixel configurations, designs and processing methods.

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PUBLICATION

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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 tissues with applications in drug development, organ-assist devices, surgical tissue transplantation and, eventually, engineered patient-specific organs.

There are two main challenges in fabricating cell culture platforms. The first 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, Figure 1. On the other hand, chemical monitoring has been accomplished in many ways: optically through confocal microscopy and the use of fluorescent dyes, and electrically through ISFETs, single electrodes and nanowire nanosensors.

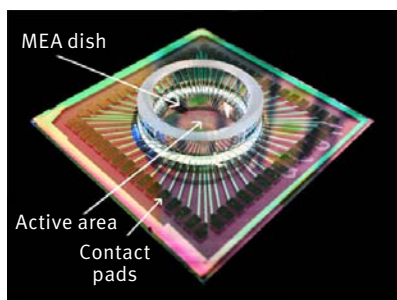


Figure 1 State-of-the-art Multi-Electrode Arrays for electrical monitoring of 2-D cell cultures.

My 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. In preliminary results with cardiomyocytes, patterning has been achieved through the use of flexible substrates, such as polymers, 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 the cardiomyocytes, Figure 2, enabling a cell

morphology similar to native myocardium. This technology has recently been transferred to commercial MEAs for comprehensive interrogation of the cells electrophysiology. In addition, chemical sensing modalities are currently being incorporated into these bioengineered substrates to allow a thorough study of the cellular metabolism.

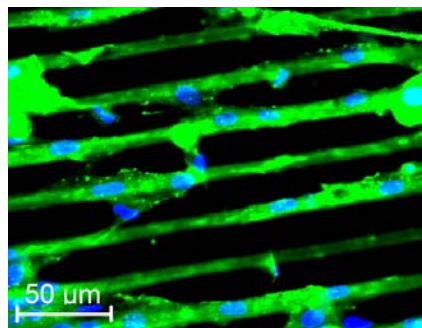


Figure 2 Micro-engineered flexible substrates facilitating the self-alignment of cardiomyocyte cells.

The 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 delivering a powerful, universal tool with high scientific and commercial impact in the understanding of tissue physiology, disease modelling, and drug toxicity.

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PUBLICATION

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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 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.

This research will investigate the provision of artificial proprioceptive feedback from a prosthetic limb by direct electrical stimulation of nerves using a neural implant and will focus on providing a user with intuitively understood information. As such the research will look at creating neural signals that mimic those naturally found in the body.

METHOD

The movements and joint torques of a robotic arm are translated into the equivalent muscle activation patterns and muscle strains in a model of a human arm (using the open source software package OpenSim). This muscle activation and strain information is then translated into neural firing patterns for muscle spindles and Golgi Tendon Organs using published mathematical models in MATLAB. Finally a low power neural implant has been developed that is designed to safely stimulate the appropriate peripheral nerves.

RESULTS

Initial testing of the neural stimulator has successfully been completed. The next step is to implement the translation of mechanical sensor data from a robotic arm to neural firing patterns in a real time system.

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Mr Stephen Woods

Thesis topic

Swallowable microbiotic platform for microscale diagnosis and targeted therapy

Supervisor

Dr Timothy Constandinou

SUMMARY

Endoscopes and colonoscopies are used to diagnose and treat pathologies such as Crohn's disease in the gastrointestinal (GI) 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 (WCE). These pill-sized cameras take pictures of the intestinal wall which are then used to diagnose pathologies. The problem with this method is that it does not offer the ability to administer therapy to an affected area.

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.

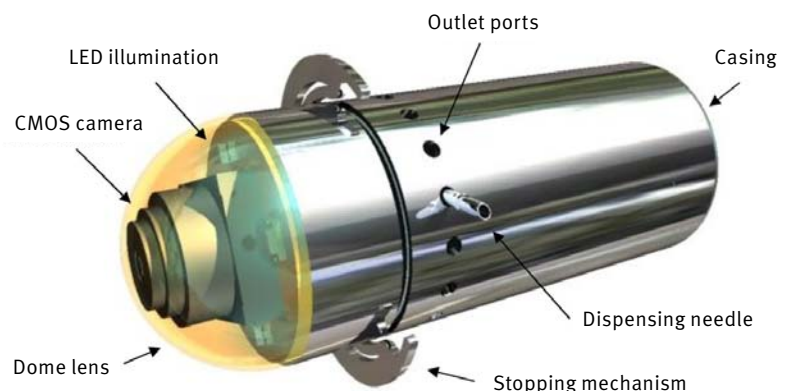
METHOD

My research will focus on developing a swallowable micro-robotic platform which has novel functionality that will enable a WCE to deliver targeted therapy. The platform will consist of two highly novel sub-systems: one is a micro-positioning mechanism which can deliver 1 ml of targeted medication and the other is a holding mechanism which gives the functionality of resisting natural movement from peristalsis.

RESULTS

The work I have carried out so far has been the detailed design and analysis of the micro-positioning mechanism and holding mechanism. The figure shows a 3D conceptual model of the proposed design. The design is based on conventional wireless pill-sized camera geometry.

Micro-robot concept design capable of overcoming peristalsis and delivering 1 ml of targeted medication to the gastrointestinal tract



A number of proofs of concept prototypes have been produced for the micro-positioning mechanism using a high resolution stereolithography manufacturing process. The prototypes have enabled evaluation of the system with initial results showing great potential for the mechanism. However limitations with the resolution of the manufacturing process prevent complete system verification.

NEXT STEP

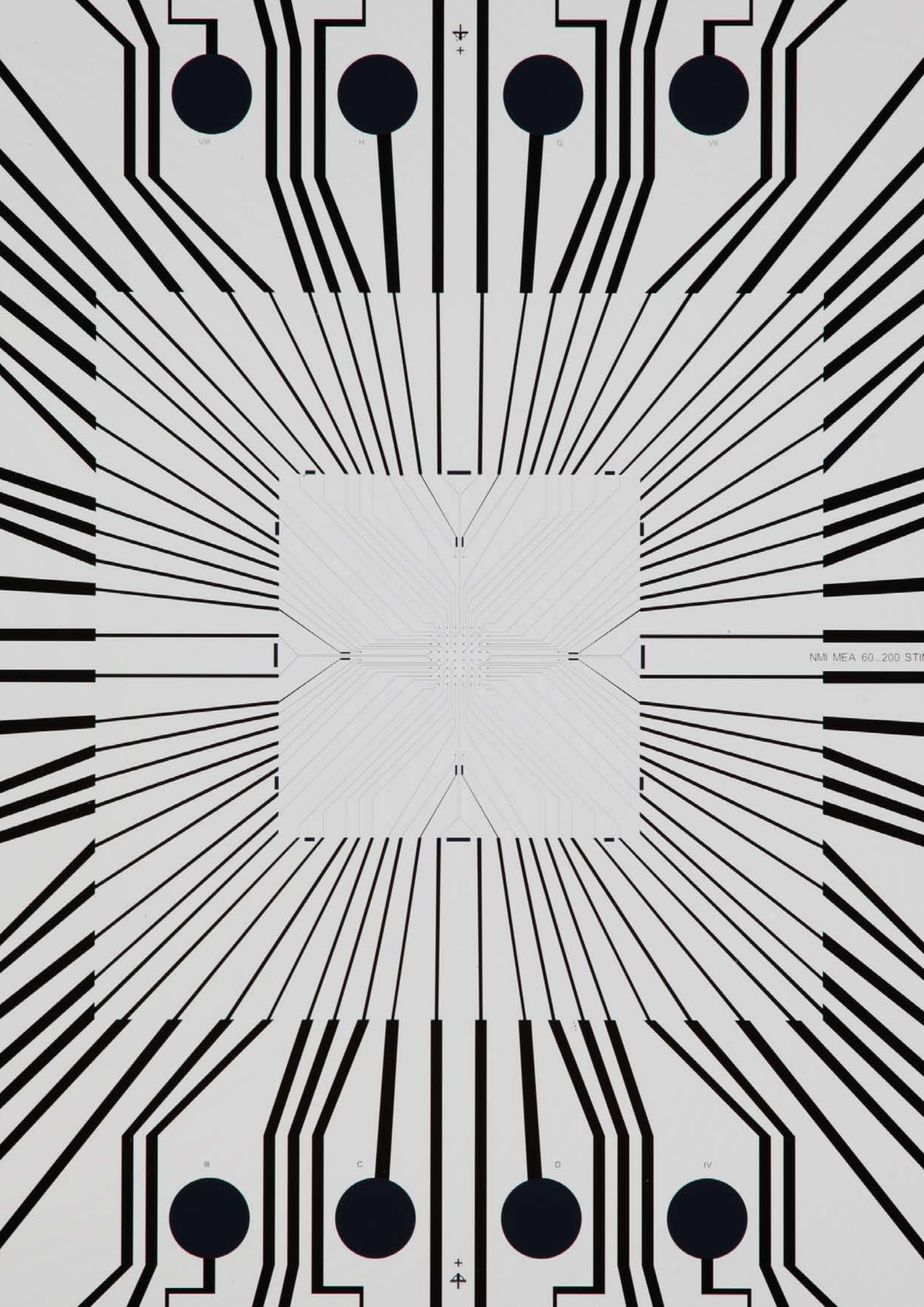
I aim to develop a working prototype of the micro-positioning mechanism which has a user interface for controlling the deployment of the dispensing needle. Also proof of concept prototypes will be produced for validation of the holding mechanism.

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