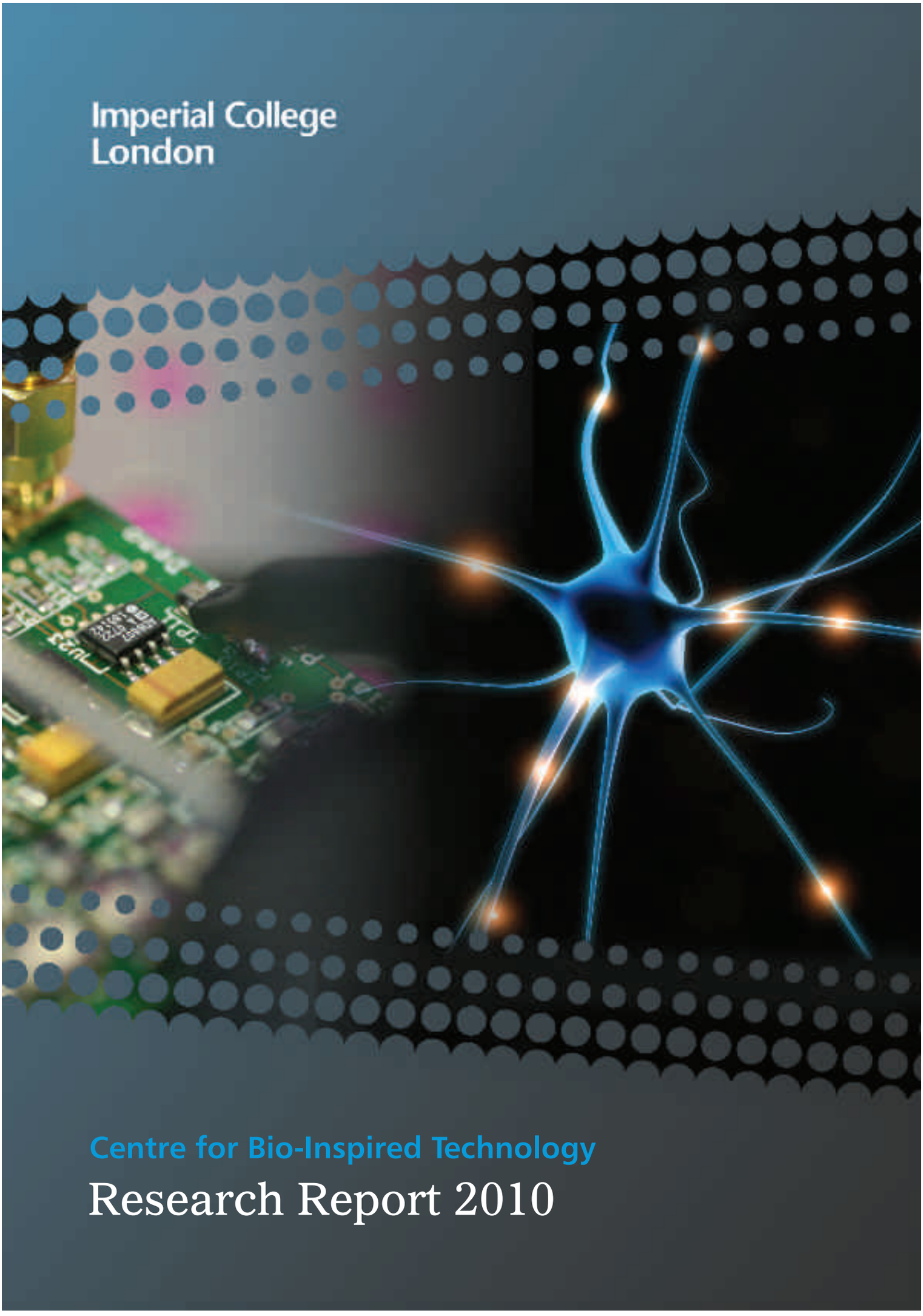
Imperial College London



Centre for Bio-Inspired Technology

Research Report 2010

9024 IMP AnnRep.indd 1 02/06/2010 16:00

Contents

9024 IMP AnnRep.indd 2 02/06/2010 16:00

9024 IMP AnnRep.indd 3 02/06/2010 16:00

Director's Foreword

Centre for Bioinspired Technology

Over the next two decades, the personalisation of therapy and healthcare will lead to lower mortality rates for diseases such as cancer and stroke and to an increased quality of life for an ageing population. During this time, significant improvements in health outcomes will come about through the application of engineering principles and technology in areas such as biosensors, implants, tissue engineering and information-driven control of therapy for personalised therapy and healthcare.

The Institute of Biomedical Engineering at Imperial College was established to enable research teams to apply engineering principles and technologies to improve medical therapies and healthcare. With access to Imperial College's Faculty of Medicine and Healthcare NHS Trust with its associated hospitals, it is uniquely placed to deliver major advances in the areas of medical technology which will provide personalised healthcare within the next decade.

The concept of a Centre for Bio-Inspired Technology within the Institute grew from the belief that biological systems hold the key to innovative technologies, which will meet the challenges of our life-style aspirations. The generous donation from Dr Winston Wong, after whom the Centre is named, is inventing, developing and demonstrating devices by mimicking living systems to create innovative and advanced technologies. These will enable us to improve diagnosis and offer individual solutions for managing chronic disease, including personalised healthcare devices, which give patients more control over their treatment and enable them to continue with an independent lifestyle. The Centre's aim is for these devices to provide low cost, and thus disposable solutions, for diagnosis and monitoring which can be applied at the point of care, often outside the clinic or hospital.

As Director of the Winston Wong Centre for Bio-Inspired Technology it is a pleasure to introduce the first of our research reports describing the work we are undertaking and our plans for continued development of technologies and platforms.

Professor Christofer Toumazou FRS, FREng
Director and Chief Scientist

9024 IMP AnnRep.indd 4 02/06/2010 16:00

"The generous donation from Dr Winston Wong, after whom the Centre is named, is inventing, developing and demonstrating devices by mimicking living systems to create innovative and advanced technologies."

9024 IMP AnnRep.indd 5 02/06/2010 16:00

Mission Statement

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

Research Strategy

Our strategy is to apply engineering technologies in innovative ways to provide personalised healthcare devices for chronic disease management. We are working in 3 main domains: early detection, diagnosis and therapy. Research Teams are designing novel methods for the continuous, real-time sensing/monitoring of bio-chemicals/biosignals to personalise healthcare in areas such as genetics, metabolic, neurological and cardiovascular disease.

Our research 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 electronics work with biological processes, while still remaining small and consuming tiny amounts of electricity. By applying radio-frequency semiconductor technology, we are looking at ways to reduce the power consumption required to operate healthcare devices.

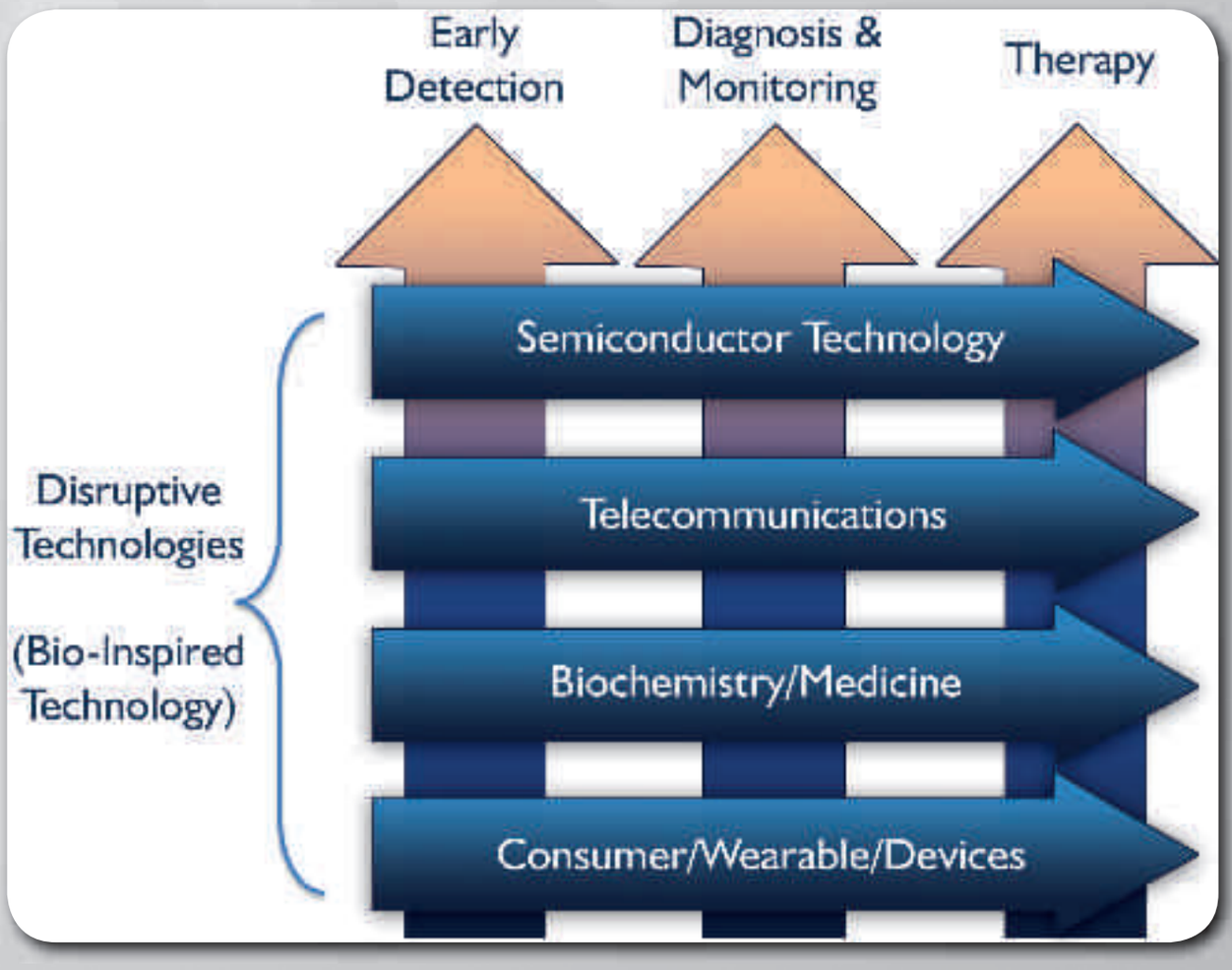
Advances in genomics and information/communication technologies are enabling research in areas of healthcare in which progress had previously been slow, to advance more rapidly. These include nanotechnology, robotics, molecular diagnostics and micro-fluidics. These advances mean that there can be a shift in care away from a centralised model that puts the physician at its core to a smarter, more decentralised approach centred on the patient. 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 health care using user-friendly devices such as personal digital assistants and mobile phones. These are very useful for 'hiding medical monitoring' whilst displaying data in ways that enable patients to act on that information.

The diagram illustrates how the intersections between the enabling technologies and application domains have defined research projects. We plan to widen the applications of the technology to encompass other disease areas as the technology platforms become developed.

In the project to create an artificial pancreas bio-inspired metabolic technology is under trial in a therapeutic domain, diabetes treatment, where analogue semiconductor chips have been configured to mimic the function of pancreatic beta cells that usually regulate insulin. A glucose sensor is measuring blood sugar whilst the semiconductors are gathering data, which determines the insulin dispensed by an insulin pump. The whole system continuously monitors blood sugar and secretes the amount of insulin required at any time to keep them in balance.

In the Prediction of Drug Response (SNP-Dr) Project, semiconductors are being used to detect single-nucleotide polymorphisms (SNPs), the small mutations in the genome that distinguish one person from another, for early detection of disease. Some of these SNPs are also medically significant in determining whether someone can metabolise a particular drug.

9024 IMP AnnRep.indd 6 02/06/2010 16:00



9024 IMP AnnRep.indd 7 02/06/2010 16:00

Centre Staff & Researchers

Director and Chief Scientist
Prof Christofer Toumazou FRS, FREng

Research Officer
Dr Tim Constandinou

Principal Research Fellow
Professor Christopher McLeod

Clinical Research Fellow
Dr Nick Oliver

Research Fellows
Dr Mohamed Reza Bahmanyar, Dr Alessandro Borghi, Dr Belinda Garner,
Dr Pantelis Georgiou, Dr Kostantinos Michelakis, Dr Olive Murphy, Dr Konstantin Nikolic,
Dr Dimitrios Sideris, Dr Antonio Vilches

Research Associates
Dr Dylan Banks, Dr Amir Eftekhar, Dr Pau Herrero-Vinas, Dr Gareth Jenkins, Dr Themistoklis Prodromakis,
Dr Manassi Ramanna, Dr Marian Rehak, Dr Iasonas Triantis

Research Assistants
Dr Onur Guven, Dr Mohamed El-Sharkawy

Research Students
Mr Abdulrahman Al-Ahdal, Mr Santos Bunga, Mr Wai Pan Chan, Mr Walid Juffali, Miss Melpomeni Kalofonou,
Mr Jatgrarath Leenutaphong, Mr Yan Liu, Mr Kwok Wa Lui, Miss Christina Morris, Miss Sivvlla Paraskevopoulou,
Mr Panavy Pookaiyaudom, Mr Ayodele Sanni, Mr Siavash Saremi-Yarahmadi, Mr Alexandru Serb,
Mr Surachoke Thanapitak, Mr Winston Wong Jr, Mr Stephen Woods, Miss Virginia Woods

Visiting Professors
Professor Tor Sverre Lande, Professor Winston Wong, Professor John Lidgey, Professor Sir Magdi Yacoub

Visiting Senior Research Fellow
Dr Alison Burdett

Honorary Senior Research Fellow
Dr Jamil El-Imad

Visiting Researchers
Mr Mohamed Juffali, Mr Peter Pesl

Administrative Staff & Consultants
Business Administrator to Prof Toumazou - Patricia Chapman
PA to Professor Toumazou - Ms Wanda Pilipkiewicz
Postgraduate Administrator - Mrs Wiesia Hsissen
Consultant – Rapid Prototyping - Mr Ray Thompson

9024 IMP AnnRep.indd 8 02/06/2010 16:00

Honours & Awards

March 2010
Professor Christofer Toumazou was awarded the Doctorate in Engineering (DEng) from Oxford Brooks University and the Fellowship of the City and Guilds Institution (FCGI).

July 2009
The World Technology Award for Health and Medicine was awarded to Professor Christofer Toumazou. The prestigious World Technology Awards are given in recognition of those individuals and companies doing innovative work of "the greatest likely long-term significance" in their respective fields. Nominees are proposed by Fellows and Founding Members of the World Technology Network (WTN) – a global community of the key players working in technology, from technologists, financiers and entrepreneurs to government officials, policy analysts and futurists.

October 2009
The Times Higher Education (THE) Award for innovation was awarded to The Institute of Biomedical Engineering. The Institute was named overall winner in the category of "Outstanding Contribution to Innovation and Technology".

November 2009
The IET Mike Sargeant Young Professionals' Career Achievement Award was awarded to Dr Timothy Constandinou. The Award celebrates individual excellence and innovation and is presented to the young professional judged to have made the most significant progress in their career over a number of years.

December 2009
The Elektra09 European Electronics Industry Awards for R&D was awarded to DNA Electronics Ltd, a 'spinout' company from the Institute of Biomedical Engineering. The award was given for DNA's "SNP-Dr" real-time gene testing innovation.

9024 IMP AnnRep.indd 9 02/06/2010 16:01

Research Funding

Professor Winston Wong, an alumnus of Imperial College, London, made a generous donation of £2m in 2010 to found the Winston Wong Centre for Bio-Inspired Technology. Professor Wong graduated from Imperial in 1971 with a degree in Physics and later, in 1976 with a PhD. In 2007 he was awarded the degree of DSc at Imperial College, an honour bestowed by HM The Queen.

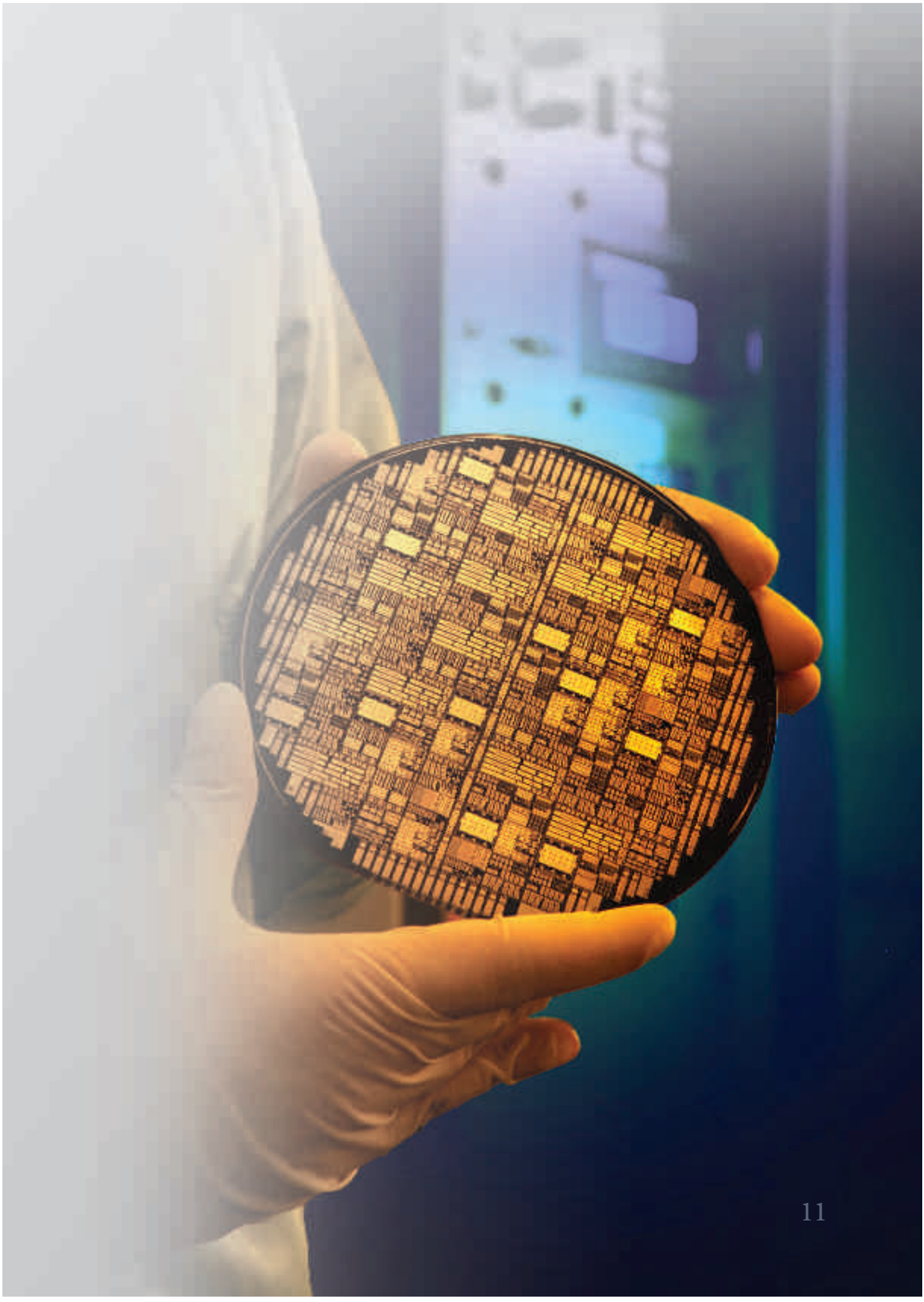
Professor Wong was inspired by Professor Toumazou's research and chose to endow the Centre in recognition of his innovative approach to developing silicon based technology for personalised healthcare. As the Founding Director of China's Grace Semi-conductor Manufacturing Corporation in Taiwan and principal founder of the Grace HW Group, China, he takes a keen interest in Prof Toumazou's research which leverages on semi-conductor technology.

The Centre forms part of the College's Institute of Biomedical Engineering of which Dr Wong is a Visiting Professor.

We also acknowledge the following sponsors for supporting the centre and funding ongoing research:

- Esmee Fairbairn Foundation
- Engineering and Physical Sciences Research Council (EPSRC)
- The Wellcome Trust
- Technology Strategy Board (TSB)
- Wilfred Corrigan for the Corrigan Fellowship/Scholarship Programme
- The Government of Thailand for the Royal Thai Scholarships
- London Development Agency (LDA)
- European Union Seventh Framework Programme (FP7)

9024 IMP AnnRep.indd 10 02/06/2010 16:01



9024 IMP AnnRep.indd 11 02/06/2010 16:01

Research Projects

Activities in the Winston Wong Centre for Bio-Inspired Technology all have a fundamental link to a research project which is addressing a particular medical need in one of the 3 domains: early detection, diagnosis or therapy. In this Section, we feature the larger projects in which teams of engineers and medics are collaborating to ensure that the research is guided by clinical need and focused on patient benefits.

Advanced Interfacing Technology for Neural Rehabilitation

Research Team: Dr Timothy Constandinou, Dr Amir Eftekhar, Dr Jamil El-Imad, Dr Belinda Garner, Dr Pantelis Georgiou, Mr Walid Juffali, Dr Konstantinos Michelakis, Dr Themistoklis Prodromakis, Prof Christofer Toumazou, Dr Iasonas Triantis, Ms Virginia Woods

Collaborator: Dr Benjamin CT Field

Research in systems that interface with the central and the peripheral nervous system (CNS and PNS respectively) can be categorized in three main areas: neural recording, biosignal processing and neurostimulation.

A milestone in neurostimulation technology was achieved in 1959 with the development of the heart pacemaker. The first functional electrical stimulation (FES) systems were reported in the early sixties and have since developed in various degrees for treatment of conditions including foot drop, hand grasp, spinal cord injury, cochlear and retinal diseases, pain relief and epilepsy.

Today, there is a massive surge in neural interfacing research, mainly due to recent advances in microelectronic and electrode technology. Various platforms have been developed both for recording and stimulation, ranging from external surface-electrode systems to fully implantable devices. As biotechnology progresses, its potential in reshaping healthcare is driving companies and academic institutions to seek formulas for combining expertise from different disciplines, including microelectronics, biology, medicine and chemistry.

In addition, there is a surge in available analysis techniques and tools to extract features from the multiple sensing modalities this technology provides. These range from simple statistical tools to real-time, nonlinear analysis algorithms and visualisation tools. The Group has an overall interest in the sensing front-end, analysis techniques and treatment, or diagnostic back-end, as depicted in the figure.

Benefits and Impact

Neural disorders, such as epilepsy, spinal cord injury, paralysis, sensory/sensation loss, affect the quality of life for millions of patients worldwide. By developing an implantable, neuro-chemical monitoring and stimulation platform for chronic disease management, we are seeking improvements in medical care and quality of life for patients. At present, neural monitoring technology offers solutions for low amplitude electrical signal recordings, but has yet to address the ionic aspect of the neural signal, thus missing out on vital neurological information. Our research on integrating state of the art nerve cuff electrodes with solid-state chemical sensors for an advanced monitoring platform will provide better insights into neurogenic conditions. Complimenting this novel neural recording scheme is a stimulation strategy, which exploits natural physiological properties of neural tissue. The goal of employing recorded neural activity as an intelligent trigger to an implantable neurostimulator will significantly impact neurophysiology and neuropathology studies, in medical diagnostics, drug monitoring and rehabilitation neuroprosthetics.

In addition, the Group also analyses brain electrical activity through the electroencephalogram (EEG) and the like for conditions, such as epilepsy in adult patients and for seizures in neonatals. Not only do these studies pose significant academic impact into the understanding of brain functionality but they also impact a significant clinical and patient need. Clinical analysis tools in brain analysis for real-time monitoring and

9024 IMP AnnRep.indd 12 02/06/2010 16:01

diagnosis are limited and do little to take advantage of the scientific and academic development in these areas. For example, the incidence of neonatal encephalopathy (NE) can cause long term effects, such as cerebral palsy (10-15%) and other significant severe disabilities (40%) including blindness, deafness, autism, global developmental delay, or problems with cognition, memory, fine motor skills and behavior. In many cases NE can be fatal (10-15%) and is the cause of immense litigation costs in the NHS (£3 billion since 1996). Tools used in these environments are mainly visually diagnosed and have been shown to result in up to 50% of seizures being missed (seizures can be related to incidences of NE).

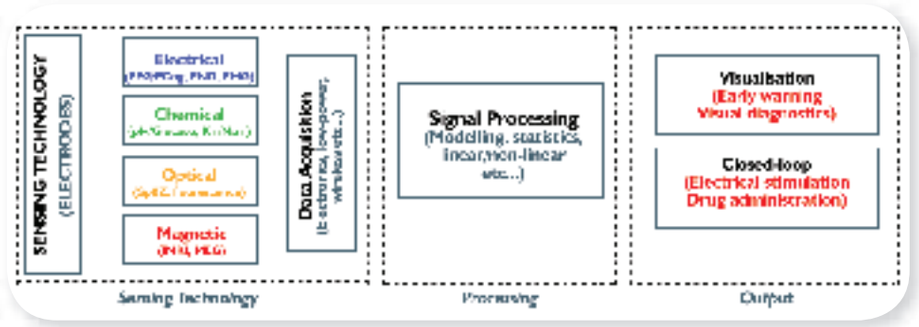
Current Progress

Advanced Interfacing Technologies for Neural Rehabilitation use a combination of both electrical and chemical sensing/stimulation for targeted response to develop intelligent platforms for interfacing to neurobiology. The Team has established neural recording and stimulation techniques and is now moving towards novel methods for neuro-chemical monitoring and selective stimulation. Initial application is targeted towards Vagal (Cranial nerve X) interfacing specifically for epilepsy, depression and appetite control. The interfacing technology is being developed for a neuro-chemical hybrid electrode. The technology is near completion for use in clinical studies in the above-mentioned applications and a new project based on tumour growth studies is starting.

The signal processing has produced significant results in seizure detection in general with studies in prediction currently underway. New techniques and a general analysis framework are being developed for software and hardware development. Work is also being carried out for analysis and isolation of nerve fascicle recordings for selective interfacing.

References

1. W. Horch and Gurpreet Dhillon, "Neuroprosthetics: Theory and Practice", World Scientific Publishing, ISBN: 9812380221, 2002.
2. IF Triantis, C Toumazou, "Advanced Mixed-mode Nerve Cuff Interface", CT/GB2007/002552, 2006.
3. IF Triantis, V Woods, A Eftekhar, P Georgiou, TG Constandinou, EM Drakakis, C Toumazou, "Advances in Neural Interfacing", IEEE Circuits & Systems Society Newsletter, "Short Tandem Repeat", Vol. 1, No. 1, 2007.



The general flow that the interfacing group tackles; combing multiple sensing modalities for processing and treatment/diagnostics.

9024 IMP AnnRep.indd 13 02/06/2010 16:01

Bio-Implantable Sensor Monitoring Platform

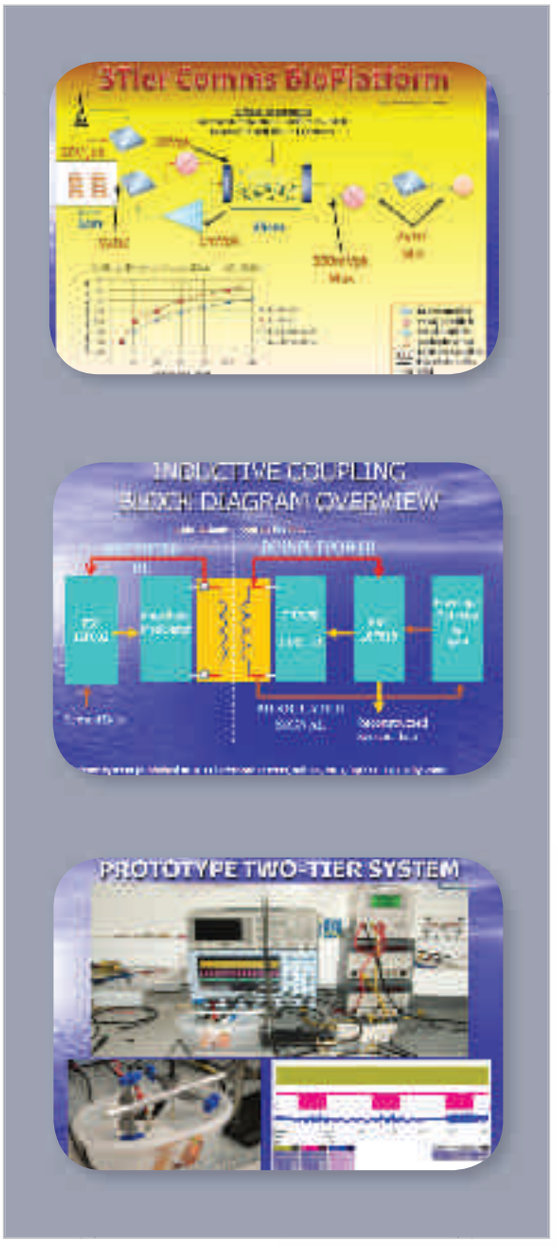
Research Team: Mr Santos Bunga, Dr Kostis Michelakis, Mr Ayodele Sanni, Prof Christofer Toumazou, Dr Antonio Vilches

Funding: Engineering and Physical Sciences Research Council (EPSRC)

The possibility of creating cheap miniature bio-implants has led the research community to attempt to use these in the continuous monitoring of patients. A variety of sensors have been reported for the purpose, including devices aimed at monitoring blood pressure, sugar levels, temperature, etc.

One of the current hurdles to the effective use of these technologies is the problem of remotely (externally) gathering data from deeply bio-implanted sensors whilst causing minimum impact to the lives of the patients (e.g. without the need for cables replacing implanted batteries). This Project is pursuing a novel solution to the problem: a Three-Tier Network comprising sensor and ultrasonic transducer implants, a subcutaneously implanted transponder that communicates with the implants at ultrasonic frequencies and an external transponder that communicates with the subcutaneously implanted transponder via inductive coupling and externally at microwave frequencies.

Such a network will enable future designers of bio-implantable devices to focus solely on the operation of a sensor, without having to worry about the problematic task of communicating remotely with it. Interfacing any sensor to the system proposed will be a relatively simple matter. The work carried out in this project will be of benefit to researchers in the medical and bioengineering research community as it will help accelerate the current effort to remotely monitor the health of patients.



References

1. A Vilches, A Sanni, C Toumazou, “Single coil pair transcutaneous energy and data transceiver for low power bio-implant use”, IET Electronics Letters, Vol.45, No. 2, pp. 27-728, 2009.

9024 IMP AnnRep.indd 14 02/06/2010 16:01

9024 IMP AnnRep.indd 15 02/06/2010 16:01

Bio-Inspired Artificial Pancreas for Control of Type-1 Diabetes

Research Team: Mr Mohamed El Sharkawy, Dr Pantelis Georgiou, Dr Pau Herrero Vinas, Prof Desmond Johnston, Ms Christina Morris, Dr Nick Oliver, Mr Peter Pesl, Prof Christofer Toumazou

Funding: The Wellcome Trust

The project combines the expertise of physiologists, biomedical engineers and clinical investigators to develop a novel closed-loop insulin delivery system for Type 1 diabetes. Centred around the physiology of the pancreas, it incorporates a clinically approved glucose biosensor, a bio-inspired control algorithm mimicking the function of the alpha and beta cells found inside the pancreas and a dual infusion pump for secreting insulin and glucagon, hormones vital for glucose homeostasis.

Type 1 diabetes is caused by antibodies attacking insulin-producing beta cells in the pancreas. The usual treatment for this form of diabetes is regular insulin injections, informed by glucose measurements from finger prick blood samples. However, these do not mimic the normal behaviour of the beta cell and this leads to suboptimal blood glucose control and complications including kidney failure, blindness, nerve damage and heart disease. Aggressive treatment can help but may lead to potentially-dangerous low blood glucose levels (hypoglycaemia).

The Diabetes Control and Complications Trial (DCCT), a major clinical study conducted from 1983 to 1993 and funded by the National Institute of Diabetes and Digestive and Kidney Diseases, showed that keeping blood glucose levels as close to normal as possible slows the onset and progression of the eye, kidney, and nerve damage caused by diabetes. It demonstrated that intensive management of Type 1 diabetes reduced complications by 50-76% compared with conventional therapy. It also showed that any sustained lowering of blood glucose, (blood sugar) helps, even if the person has previously had a history of poor control.

The creation of an artificial pancreas for the treatment of insulin-dependent diabetes has been desired since artificial insulin was discovered. Such a system could bring significant improvements in the disease and quality of life of sufferers. Principally an artificial pancreas based on beta cell function, is a closed-loop system requiring a glucose sensor to determine the blood sugar levels, a control algorithm to calculate the required insulin dose and an infusion pump to deliver insulin to the blood. This closed loop system provides autonomous control of blood glucose, potentially improving HbA1c while avoiding hypoglycaemia. Ideally it should perform the same function as the biological pancreas.

The project will develop the worlds first artificial pancreas based on the physiology of the 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 hyperglyceamic events and glucagon to prevent hypoglyceamia. In non-diabetic subjects, the pancreatic beta-cell membrane depolarises in response to

9024 IMP AnnRep.indd 16 02/06/2010 16:01

elevated glucose. At glucose levels <7mM, the cell is electrically silent, but bursting activity occurs as glucose rises >7mM. We have replicated the activity of the pancreatic cells using a novel silicon chip simulation of the beta cell's bursting behaviour and this is now being refined to include the silicon alpha cell which exhibits similar behaviour for glucose concentrations below 5mM. The silicon beta and alpha cell will then form the core of the bio-inspired artificial pancreas controlling an insulin and glucagon pump.

Healthcare Benefit

Type 1 diabetes affects 250,000 people in the United Kingdom and its incidence is increasing rapidly. Since the mid 1940's the number of people with type 1 diabetes in the UK has doubled every 20 years. Diabetes 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. Hyperglycaemia is also associated with a large increase in cardiovascular risk, leading to heart disease and stroke. Diabetes remains the leading cause of blindness and kidney failure (requiring dialysis or transplant) in the developed world.

In the United States in 2007, diabetes was estimated to have cost $116bn in medical care and $58bn in disability, loss of work and mortality. The global market for diabetes therapeutics and diagnostics increased from $208.5 billion in 2007 to an estimated $213.8 billion by the end of 2008. It should reach $241.9 billion by 2013, a compound annual growth rate (CAGR) of 2.5%.

The development of this artificial pancreas will enormously improve the quality of life for people with Type 1 diabetes and will reduce the incidence of diabetes complications, improving quality of life and reducing the health cost of diabetes worldwide.

References

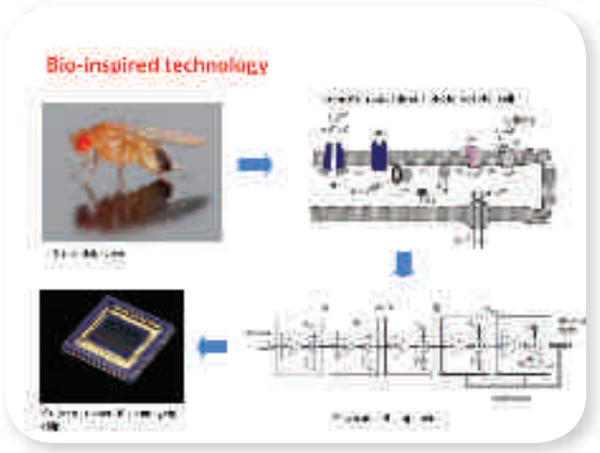
1. R Hovorka, "Continuous glucose monitoring and closed-loop systems", Diabetic Medicine, Vol. 23, No. 1, pp. 1 – 12, 2005.
2. NS Oliver, P Georgiou, D Johnston, C Toumazou, "A Benchtop Closed-loop System Controlled by a Bio-Inspired Silicon Implementation of the Pancreatic beta Cell", J. Diabetes Sci. Technol, Vol. 3, pp. 1419 – 1424, 2009.
3. P Georgiou, C Toumazou, "A Silicon Pancreatic Beta Cell for Diabetes", IEEE Transactions on Biomedical Circuits and Systems, Vol. 1, No. 1, pp. 39 – 49, 2007.

9024 IMP AnnRep.indd 17 02/06/2010 16:01

Bio-Inspired Technologies

Research Team: Prof Tony Cass, Dr Dylan Banks, Mr Amir Eftekhar, Dr Konstantin Nikolic, Dr Themistoklis Prodromakis, Prof Christofer Toumazou, Dr Iasonas Triantis

Funding: Engineering and Physical Sciences Research Council (EPSRC)



In this one year Project, we are undertaking feasibility studies which are based on applying state of the art engineering technologies to provide solutions for intricate physiological and medical problems, such as selective neural stimulators or implants. We are also deriving new technologies based on complex biological systems and biochemical processes, such as cell signalling mechanisms. Our aim is that these investigations lead to research which will provide proof of principle for several exciting new ideas and, if successful, they will be developed commercially. We foresee these new applications of technology having a significant impact on healthcare as well as non-biological, and widespread, devices such as mobile phone cameras, or sensitive chemical detector arrays.

Research is focussed on providing intelligent, physiological semiconductor chips based on models of the behaviour of biological systems such as the retina, cochlea, neurons, and beta-cells. We are designing electronic systems that interact with human organs and systems, as well as electronic circuits and devices designed following the basic principles of biological systems.

The project supports a suite of five research themes: the first explores the feasibility of converting the phototransduction process in an invertebrate's photoreceptor - a cascade of biological amplifiers - into electronic equivalents; the second ventures into a completely new research field of memristors - passive memory devices. The other three themes will assess new strategic paths in neural stimulation and neural prosthesis design; combined optical and electrical stimulation for achieving selectivity; then use of a photosynthetic reaction centre for imparting light sensitivity of neurons and muscles, and eventually the use of noise to enhance sensory perception in human auditory pathways.

References

1. http://gow.epsrc.ac.uk/ViewGrant.aspx?GrantRef=EP/H024581/1
2. http://www3.imperial.ac.uk/biomedeng/research/bioinspired/projects/bioinspired

9024 IMP AnnRep.indd 18 02/06/2010 16:01

Implantable SAW Transponder for Chronic Blood Pressure Monitoring

Research Team: Prof. Chris McLeod, Dr Olive Murphy, Dr Alessandro Borghi, Dr Mohammedreza Bahmanyar, Dr Manonava Narvaratnarajah, Prof. Sir Magdi Yacoub, Prof. Chris Toumazou

Funding: Wellcome Trust Technology Transfer Translation Award

Summary: The use of an implantable surface acoustic wave (SAW) device as an alternative to a wearable blood pressure monitor is being developed. SAW devices have been used for many years as resonators and filters in various transmitter/receiver architectures, providing extremely stable responses. 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.

Benefits/Impact: The on-going assessment of localised pressures has had to rely on inaccurate external measurement or intermittent and invasive and, therefore, partial and risky internal measurements. The difficulties associated with internal direct measurements are device size, power requirements, accuracy, performance degradation, and the risk of infection. Using the SAW pressure sensor cardiovascular, intra-ocular and intra-cranial pressures can be precisely measured. The traditional difficulties are reduced and in some cases eliminated as the SAW transponder is a minute, biocompatible, highly accurate passive device which is now being used to provide continuous pressure monitoring.

Research Progress: Currently partaking in advanced *in-vivo* trials for the use of the SAW transponder in the cardiovascular system. This involves analysing the biocompatibility of the devices, designing the delivery system and fine-tuning the external real-time reader system.

Next Steps: Preparation for regulatory approval of the devices and delivery systems in advance of clinical trials. Further develop current prototypes to reduce size whilst increasing sensitivity.

Project Leader's Commentary: Prof. Chris McLeod "Very challenging developments across several disciplines are required in this project but the potential impact of success on healthcare is sufficient incentive."

9024 IMP AnnRep.indd 19 02/06/2010 16:01

Silicon Nanosystem for the Prediction of Drug Response (SNP-Dr)

Research Team: Dr Timothy Constandinou, Dr Pantelis Georgiou, Dr Gareth Jenkins, Mr Yan Liu, Dr Marian Rehak, Dr Themistoklis Prodromakis, Mr Winston Wong Jr., Prof Christofer Toumazou

Collaborators: DNA Electronics Ltd, Pfizer Ltd.

Funding: Technology Strategy Board (TSB)

This project is developing a disposable, point of care, genetic chip, test chip for predicting patient drug response in clinical applications. The application of point-of-care, genetic testing to predict an individual's response to pharmaceutical products, aligns well with the shift to patient centric medicine, contributing to improved quality of life and patient safety.

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 will enable pharmacogenetic testing in personalised medicine, ie 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.

The SNP-Dr platform is capable of delivering fast, accurate on-the-spot tests for any target nucleic acid sequence (DNA/RNA). Disposable '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.

Avoiding adverse side effects will improve patient safety and reduce the number of hospitalizations due to adverse drug reactions, which are estimated to contribute to 6-7% of all hospitalizations and to increase the length of hospital stays by two days (New England Journal of Medicine 2008; 358;6). Currently, pharmacogenetic testing is not routinely carried out because of the interruption to clinician workflow arising from the need to send samples to a laboratory for genetic analysis. The SNP-Dr aims to give laboratory-quality genetic diagnosis at the point-of-prescription.

A handheld prototype capable of detecting genetic mutations called single nucleotide polymorphisms (SNPs) from saliva has been developed. The project is leveraging the

9024 IMP AnnRep.indd 20 02/06/2010 16:01

advanced 'lab-on-chip' expertise developed at the Institute of Biomedical Engineering to deliver increases in DNA chip functionality and scalability on a par with Moore's Law. Validation studies to gather clinical performance data will be undertaken as part of a Government funded, collaborative, R&D project led by the 'spinout' company DNA Electronics Ltd in collaboration with Pfizer, the world's largest research-based pharmaceutical company.

References

1. DM Garner, H Bai, P Georgiou, TG Constandinou, S Reed, LM Shepherd, W Wong Jr, KT Lim, C Toumazou, "A Multichannel DNA SoC for Rapid Point-of-Care Gene Detection", Proceedings IEEE International Solid-State Circuits Conference (ISSCC), Pages: 492–494, 2010.
2. C Toumazou, S Purushothaman, "Sensing Apparatus and Method", US Patent US2008032295, 2008.
3. S Purushothaman, C Toumazou, CP Ou, "Protons and single nucleotide polymorphism detection: A simple use for the ion sensitive field effect transistor", SENSOR ACTUAT B-CHEM, Vol. 114, pp. 964-968, 2006.

9024 IMP AnnRep.indd 21 02/06/2010 16:01

Research Staff Reports

BAHMANYAR, Dr Mohammadreza

Research Focus: RF Signal Acquisition and Processing (SAW BPM Project)

Funding: The Wellcome Trust

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, very intermittently, by expensive and somewhat risky catheterisations.

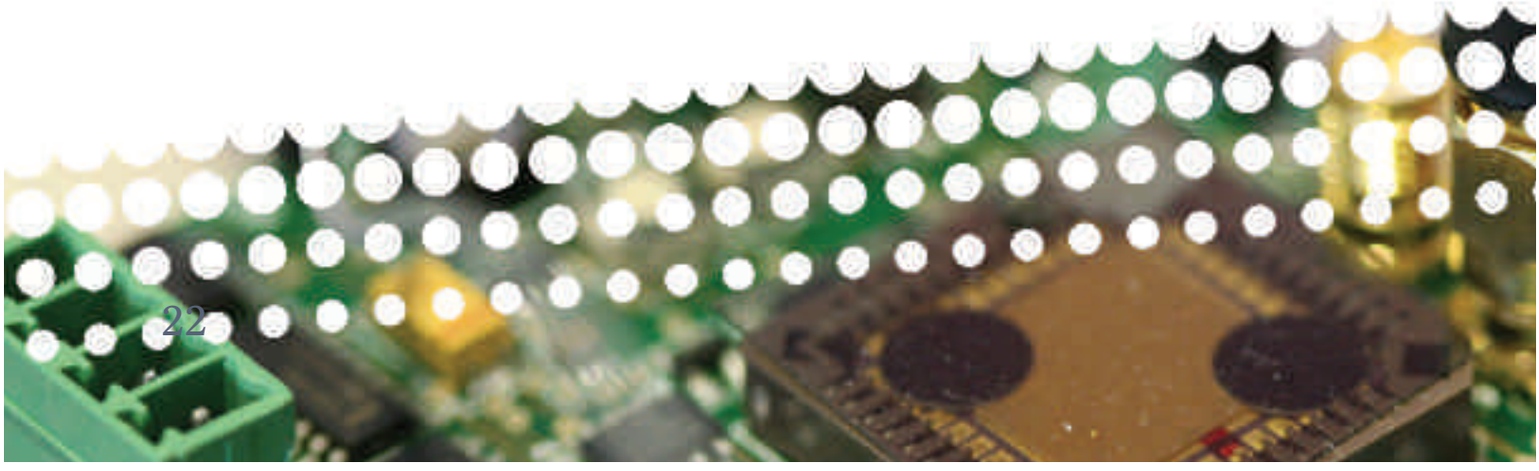
Surface acoustic wave (SAW) resonators have been used for wireless pressure measurement in the automotive industry and may be adapted to make implantable sensors for cardiovascular, intra-ocular and intra-cranial blood pressure measurements. Using micro-fabrication techniques, SAW resonators can be made 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 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, is required.

This part of the larger research project is mainly concentrated on the design and prototyping of the RF interrogating system as well as signal acquisition and processing. Based on the technical requirements of the project, an RF system is designed and tested and is currently being optimised. The test results show that this system may be reliably used for pressure measurement in animal tests that are planned for the next few months.

Key References

1. M Hamsch, R Hoffmann, W Buff, M Binhack, S Klett, “An Interrogation Unit for Passive Wireless SAW Sensors Based on Fourier Transform”, IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control, Vol. 51, No. 11, pp. 1388-1392, 2004.
2. SN Simrock, M Hoffmann, F Ludwig, MK Grecki, T Jezynski, “Considerations for the choice of the intermediate frequency and sampling rate for digital RF control”, Proceedings of European Particle Accelerator Conference (EPAC), 2006.



9024 IMP AnnRep.indd 22 02/06/2010 16:01

BANKS, Dr Dylan J

Research Focus: Artificial Retina

Funding: Corrigan Fellowship

Biomorphic, Neuromorphic and Retinomorphic imaging systems all mimic, to the extent their technology and designs will allow, functional aspects of animal vision systems. Often, they aim to detect edges with highly parallel signal processing arrays, compress data outputs through the convergence of inputs, and utilise asynchronous data transfer.

However, to date a number of issues remain common to these devices. They do not see in colour, they do not detect edges with a range of filters, and they do not filter images over a range of scales. These limitations have restricted the commercial viability of what are otherwise significant image-processing advancements.

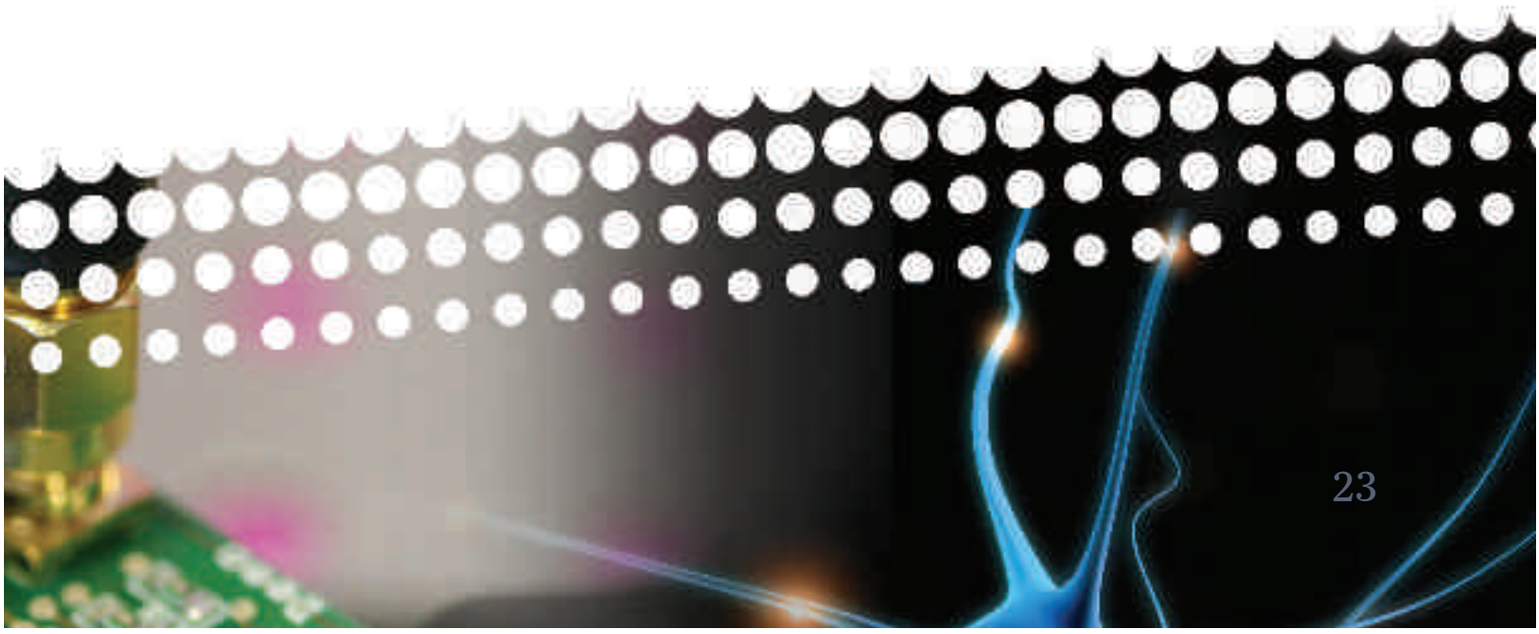
I have addressed these issues by re-examining, and reverse engineering, the functional signal processing of the human Macula Lutea, in the light of the environmental differences between the biological and silicon environments.

My approach has been to develop an understanding of commutability between the biological and complementary metal oxide semiconductor (CMOS) technologies. So that my designs may better represent the functional characteristics of the cones, horizontal cells, bipolar cells, ganglion cells, and their respective receptive fields within a standard (CMOS) process.

Loss of vision through Retinitis Pigmentosa or Maculae degenerative diseases is a severely debilitating and is in many circumstances unpreventable with drugs and other therapies. A number of research groups around the world are investigating prosthetic retinal replacement techniques with involve silicon photodiode arrays interacting with the optic nerve. The systems described within this thesis are designed to be a strategic component within such a vision system: offering improved salient feature extraction and mimicry of retinal processing over many other artificial image-processing techniques.

Key References

- S-C Liu, “Analog VLSI: Circuits and Principles”, MIT Press, ISBN: 0262122553, 2002.



9024 IMP AnnRep.indd 23 02/06/2010 16:01

BORGHI, Dr Alessandro

Research Focus: Endovascular Delivery of a Pressure Sensor (SAW BPM Project)

Funding: The Wellcome Trust

Heart failure is a common, disabling and deadly disease, which affects 1 to 2% of the population in developed countries, with higher incidence in the elderly population (6-10% of the population over 65years). It is associated with high health expenditure: in the 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 localised 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.

The technology has been developed and communication system design is underway. In order to provide a valid alternative to invasive techniques, an endovascular approach has to be designed and validated to minimise the risk of implantation of the sensor and maximise the population of suitable patients. Various types of dummy device configurations have been tested in several positions in animal models. The body response has been qualitatively analysed at 3, 6 and 12 weeks. A stent structure has been designed and geometrical prototypes have been produced for endovascular and transapical implantation. The next step will be to integrate the actual sensor into this geometry and perform endovascular delivery followed by in-vivo measurements of blood pressure.

Key References

- CS Lam, et al., "Age-associated increases in pulmonary artery systolic pressure in the general population", Circulation, Vol. 119, No. 20, pp. 2663 – 70, 2009.

9024 IMP AnnRep.indd 24 02/06/2010 16:01

CONSTANDINOU, Dr Timothy G

Research Focus: Bio-Inspired Medical Device Technology

With recent advances in the semiconductor industry, never before have there been so many opportunities to exploit commercially available technology in the wider application space. Driven by the economies of scale, modern microelectronics is capable of realizing low cost, portable systems for sensing, processing and communicating. By taking inspiration from biology (i.e. in organization, representation and process) and coupling this with modern semiconductor technology is leading to major innovation, particularly in healthcare.

Bio-Inspired medical device technology incorporates three aspects:

1. Bio-Inspired Design: Taking inspiration from biology, this design methodology exploits features in: architecture, organisation, process and representation, to engineer enhanced artificial systems. For instance, biological systems based on distributed architectures of simple primitives are known to perform particularly well in perceptive tasks, are inherently adaptive and offer a high degree of robustness and redundancy against component failure.

2. Integrated Microtechnology: The development and customisation of existing technologies to provide the relevant micro- and nano-scale features and have the ability to sense and interface to required media/quantities. For example, sensing of electrical, optical, chemical and/or mechanical properties of liquids, solids and/or gases.

3. Biomedical Application: The exploitation of (1) and (2) to develop biomedical systems (implantable, body-worn, point-of-care) to benefit human health and improve the quality of life.

My past research has exploited bio-inspired paradigms to implement ultra low power distributed architectures for smart vision systems and sensory implants (cochlear and vestibular prostheses). Continuing on this theme, my current research is focusing on developing medical devices (wearable/implantable/injectable/lab-on-chip) by exploiting bio-inspired microtechnology. Ongoing projects I am leading within this theme are:

- CMOS photonics for lab-on-chip interfacing
- Implantable platform for neuroprosthetics/brain machine interfaces
- Swallowable capsule technology for microscale diagnosis and targeted therapy

Key References

1. C Mead, “Analog VLSI and neutral systems”, Addison-Wesley, ISBN: 0201059924, 1989.
2. R Sarpeskhar, “Ultra Low Power Bioelectronics: Fundamentals, Biomedical Applications, and Bio-inspired Systems”, Cambridge University Press, ISBN: 0521857279, 2010.

Recent Publications

1. TG Constandinou, K Nikolic, C Toumazou, “Method and Apparatus for Optically Outputting Information from a Semiconductor Device”, UK IPO, 2010.
2. TG Constandinou, “Biologically Inspired Electronics for Micropower Vision Processing”, VDM Verlag, ISBN: 3639133919, 2009.

9024 IMP AnnRep.indd 25 02/06/2010 16:01

EFTEKHAR, Dr Amir

Research Focus: Neural interfacing, acquisition and analysis.

Funding: Esmee Fairbairn Foundation and Winston Wong Centre for Bio-Inspired Technology

The primary focus of my work involves the analysis of biological signals with the aim of extracting detective and predictive features. The ability to define the necessary methods or algorithms for extracting such features as well as translating them into realistic real-time software and hardware implementations aids in bridging the gap between the sensing front-end and treatment or visual back-end of any biomedical or personalised healthcare system.

There are many algorithms that achieve this bridge and the aim is to have a method that has clinical and biological relevance. My first project, which was the focus of my PhD, involved the use of time-frequency methods to extract features from the electroencephalogram (EEG) for seizure detection. Given the rhythmic nature of the brain neuronal activity, such a technique fitted clinical interpretation and biological mechanisms. Further work is being carried out to translate this research to a realisable system for neonates and epileptic patients.

Current available systems have been useful for observational purposes but give little aid to the immense periods of continuous care and observation needed by clinicians. Consequently, litigation due to birth problems in the neonatal period is immense - the NHS cost is approximately £3 billion since 1996. There are many elements of the brain dynamical changes that still are unknown and these analysis tools will impact this clinical and academic progression immensely. In addition, adult and neonate EEG seizure prediction is an unsolved problem with little done to aid those not able to control their epilepsy with medication or surgery.

We are also collaborating with Dr. Jamil El-Imad using unique analyses schemes with the aim of characterizing EEG behavior in a general framework. Electroneurogram (ENG) analysis is also being researched through a Cancer project in the group, using Vagus nerve interfacing to understand and treat tumour growth. The analysis requires isolation of fascicle information and directionality from cuff electrode recordings.

To improve personal well-being and provide academic insight into the mechanisms surrounding neural behaviour, new and advanced analysis methods are not only necessary but vital to the treatment and diagnosis of these conditions.

Key References

1. F Mormann, RG Andrzejak, CE Elger, K Lehnertz, “Seizure prediction: the long and winding road,” Brain Advance Access, 2006.
2. NE Huang and et al., “The empirical mode decomposition and the hilbert spectrum for nonlinear and non-stationary time series analysis,” Proceeding of the Royal Society, Vol. 454, pp. 903 – 995, 1998.

Recent Publications

1. A Eftekhar, D Abbruzzese, TG Constandinou, IF Triantis, V Woods, EM Drakakis, C Toumazou, “A programmable neural interface for delivering arbitrary stimulation strategies,” IFESS, 2009.
2. A Eftekhar, F Vohra, C Toumazou, EM Drakakis, K Parker, “Hilbert-Huang Transform: Preliminary studies in Epilepsy and Cardiac Arrhythmias,” IEEE BIOCAS 2008.

9024 IMP AnnRep.indd 26 02/06/2010 16:02

GARNER, Dr Belinda

Research Focus: The Role of the Vagus Nerve in Cancer

Funding: Winston Wong Centre for Bio-Inspired Technology

The microenvironment surrounding malignant cells plays an important role in tumour development and progression. Inflammatory cells and cytokines are present in the microenvironment of most, if not all, tumours. Accumulating evidence has shown inflammatory mediators have potent tumour-promoting effects, favouring transformation of pre-malignant cells, tumour growth, angiogenesis and migration, invasion and metastasis of malignant cells.

The vagus nerve provides the major neural pathway for transmitting immune-related information in the viscera to the brain. Recently, it was discovered that the vagus nerve exerts potent tonic control of the inflammatory response. It has been postulated that the vagus nerve might therefore play an important role in informing the brain about the presence of tumours and modulating their growth.

Vagus nerve stimulation (VNS), administered by a commercially available implantable electrode cuff, is clinically used for the treatment of refractory epilepsy and depression. However one of the significant shortcomings of existing VNS technology is that it does not allow selective stimulation of nerve fibre groups and it cannot be used for neural recording. Using novel, advanced neural-interfacing technologies, this new area of research aims to investigate whether the vagus nerve has a role in modulating tumour growth and progression and further, whether vagus nerve stimulation can inhibit the development and/or progression of cancer via its anti-inflammatory effects.

These studies will provide a greater understanding of how the vagus nerve might be involved in regulating tumour growth in the body. This research has the potential to discover new mechanisms underlying cancer and its progression, which could lead to the development of novel preventative and therapeutic strategies.

Key References

1. L Borovikova, et al., “Vagus nerve stimulation attenuates the systemic inflammatory response to endotoxin”, Nature, Vol. 405, No. 6785, pp. 458 – 62, 2000.
2. Y Gidron, H Perry, M Glennie, “Does the vagus nerve inform the brain about preclinical tumours and modulate them”, Lancet Oncology, Vol. 6, No. 4: p. 245 – 8, 2005.
3. N Erin, et al., “Vagotomy enhances experimental metastases of 4THMpc breast cancer cells and alters substance P level”, Regulatory peptides, Vol. 151, No. 1-3, pp. 35 – 42, 2008.

9024 IMP AnnRep.indd 27 02/06/2010 16:02

GEORGIOU, Dr Pantelis

Research Focus: Metabolic Technology and ISFET based lab-on-chip design

Funding: The Wellcome Trust (Metabolic Tech) and DNA Electronics Ltd (ISFETs/LoC).

Research is focused on developing chemical bionic technologies for early detection, diagnosis and therapy of medical conditions. We believe that our bodies are the most optimised machines after billions of years of evolution and are mimicking the functionality of the human body to design systems of equivalent efficiency and behaviour.

A big chapter of this research is the development of a bio-inspired artificial pancreas for the control of Type 1 diabetes. This involves mimicking the functionality of the metabolic cells in the pancreas, the beta cells, responsible for sensing blood glucose and releasing insulin using low-power silicon integrated circuits. As a result we create silicon beta cells that are used to control an insulin pump in a more physiological way. This offers a form control of the blood glucose diabetics that is closer to the natural control of a healthy pancreas. This work is currently funded by the Wellcome Trust, the goal of which is to transfer the technology to initial trials and ultimately commercialisation.

In addition to this, research is underway to create CMOS based chemical sensors for application in healthcare, to provide cheap, disposable, low power and intelligent systems to provide diagnosis and treatment of medical conditions. Ion sensitive field effect transistors (ISFET) are a class of these chemical sensors which are currently being used to create novel lab-on-chips for application in DNA Single-Nucleotide-Polymorphism detection, viral RNA detection, chemical imager arrays, ionic monitoring of neural behaviour and monitoring of metabolic analytes related to diabetes and renal function. This work is currently being commercialised by DNA Electronics Ltd to create a novel prototype for rapid, point-of-care detection of SNPs to determine various genetic predispositions.

Key References

1. R Hovorka, "Continuous glucose monitoring and closed-loop systems", Diabetic Medicine, Vol. 23, No. 1, pp. 1 – 12, 2005.
2. P Georgiou, C Toumazou, "A Silicon Pancreatic Beta Cell for Diabetes", IEEE Transactions on Biomedical Circuits and Systems, Vol.1, No.1, pp. 39 – 49, 2007.

Recent Publications

1. N Oliver, P Georgiou, P, D Johnston, et al, "A Benchtop Closed-loop System Controlled by a Bio-Inspired Silicon Implementation of the Pancreatic beta Cell", J. Diabetes Science and Technology, Vol. 3, pp. 1419 – 1424, 2009.
2. P Georgiou, C Toumazou, "ISFET characteristics in CMOS and their application to weak inversion operation" Sensors and Actuators B-Chemical, Vol.143, pp. 211 – 217, 2009.
3. P Georgiou, C Toumazou, "Chemical Bionics - A novel design approach using Ion Sensitive Field Effect Transistors", Proceedings of the IEEE Biomedical Circuits and Systems Conference, pp. 229 – 232, 2008.
4. T.Constandinou, P.Georgiou, T.Prodromakis and C.Toumazou, "A CMOS-based lab-on-chip array for the combined magnetic stimulation and opto-chemical sensing of neural tissue", Proceedings of the IEEE CNNA Conference, 2010.

9024 IMP AnnRep.indd 28 02/06/2010 16:02

HERRERO-VINAS, Dr Pau

Research Focus: Bio-Inspired Metabolic Technology

Funding: The Wellcome Trust

The main focus of my research is on developing control algorithms for the bio-inspired artificial pancreas project used for the control of Type 1 diabetes mellitus.

Until today, control algorithms used in the context of an artificial pancreas have been mainly based on classical closed-loop control techniques like, Proportional Integral Derivative (PID) control and Model Predictive Control (MPC). Nevertheless, these techniques still need to demonstrate better performance before being implemented in a commercial artificial pancreas. Recent developments of mathematical models of the beta cell physiology, which are able to describe the glucose-induced insulin release at a molecular level, have provided a new class of promising bio-inspired control algorithms, which can be potentially used in an artificial pancreas framework.

We are strongly convinced that trying to mimic the pancreatic beta cells functioning is the best way to achieve normoglyceamia in subjects with T1DM. In addition to this, I have ongoing research to create a fault detection system in order to supervise possible adverse events, such as glucose sensor failures and insulin infusion problems, occurring in the functioning of an artificial pancreas. This work is another indispensable piece of the puzzle towards a realistic realization of an artificial pancreas.

Further ongoing research that is under the focus of my interest is the development of a Decision Support System (DSS) for T1DM management based on Case Based Reasoning (CBR). CBR is a consolidated artificial intelligence technique, already successfully applied in medicine, which tries to solve newly encountered problems by applying the solutions learned from solving problems encountered in the past. This is similar to the way a human might solve a newly encountered problem. This DSS is intended to provide advices to the common situations a diabetic subject has to face, such as, meal related insulin doses, hyperglycemia and hypoglycemia, and is expected to be integrated in a telemedicine system already being developed within the Group.

Key References

- R Hovorka, "Continuous glucose monitoring and closed-loop systems", Diabetic Medicine, Vol. 23, No. 1, pp. 1 – 12, 2005.

Recent Publications

1. P Herrero, E Dassau, CC Palerm, H Zisser, L Jovanovic, Man C Dalla, C Cobelli, J Vehí, FJ Doyle III, "Glucose Absorption Model Library for Mixed Meals", Proceedings of 2nd European Diabetes Technology and Transplantation meeting, Igls/Austria, 2008.
2. E Dassau, P Herrero, H Zisser, BA Buckingham, L Jovanovic, CD Man, C Cobelli, J Vehí and FJ Doyle III, "Implications of a Meal Library & Meal Detection to Glycemic Control of Type 1 Diabetes Mellitus through MPC Control", IFAC World Congress, 2008.
3. P Herrero, J Vehí, R Corcoy, A Chico, B Pons, and A de Leiva, "Model Based Fault Detection in the Artificial Beta-Cell Framework", 8th Annual Meeting, Diabetes Technology Society, 2008.
4. J Armengol, J Vehí, MA Sainz, P Herrero, ES Celso, "SQualTrack: A Tool for Robust Fault Detection", IEEE Transactions on Systems, Man and Cybernetics- Part B, Vol. 39, No. 2, pp. 475 – 88, 2008.

9024 IMP AnnRep.indd 29 02/06/2010 16:02

JENKINS, Dr Gareth

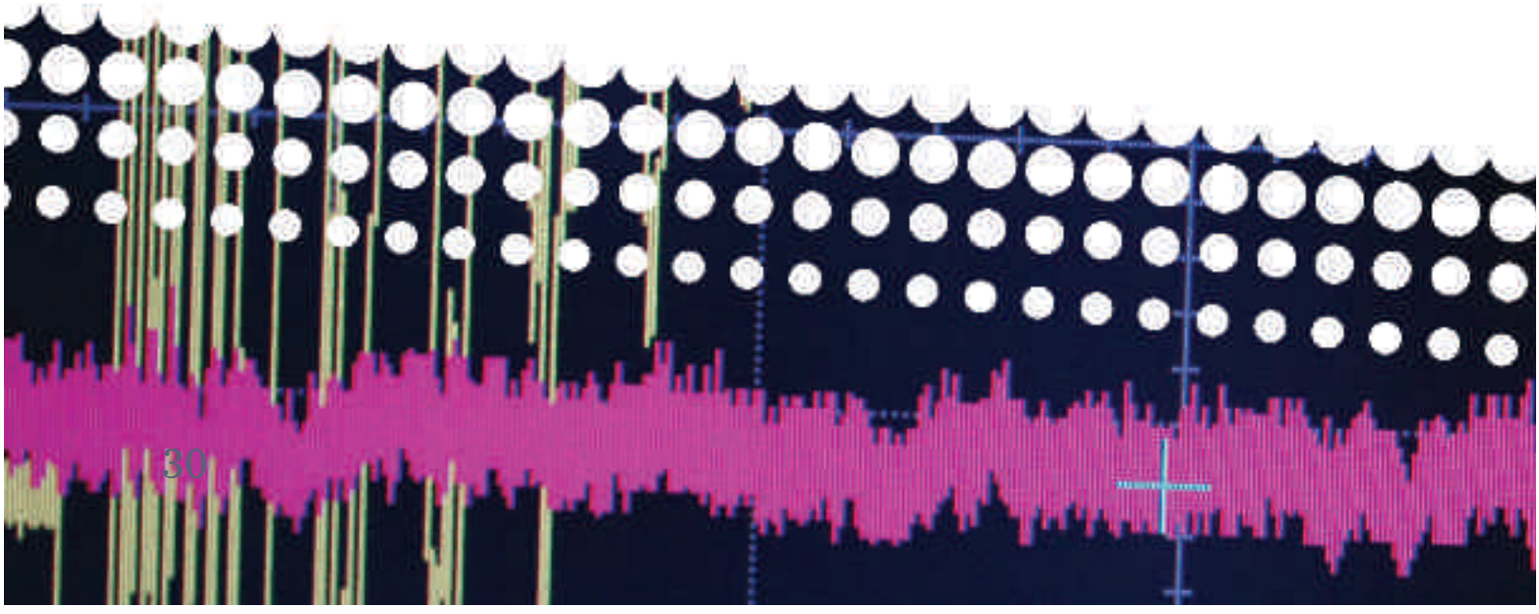
Research Focus: Silicon Nanosystem for the Prediction of Drug Response (SNP-DR)

Funding: Technology Strategy Board

The project is aimed at developing silicon-based biosensors to detect genetic mutations known as single nucleotide polymorphisms (SNPs) for the prediction of adverse drug response. Adverse reactions to prescribed medications are estimated to cost the NHS approximately £2bn per year and cause a significant number of otherwise avoidable deaths. Providing a simple to use, point-of-care device to test a patient's genetic predisposition to adverse drug reactions would help reduce this burden by giving the clinician a clear and immediate indication prior to administering a particular medication.

The project is seeking to develop a low cost, portable test for SNPs utilising lab-on-a-chip technology integrated with silicon biosensors to perform all necessary functions such as biological sample preparation and detection in a rapid and highly automated way. The test will take the form of a handheld analyser combined with a disposable cartridge to allow simple and rapid testing of a patient's genetic makeup in a safe and non-invasive way.

The work is building on prototype systems developed by DNA Electronics Ltd and will seek to validate SNP testing for particular targets in conjunction with Pfizer prior to further commercialisation. The project will also seek to further develop the required lab-on-a-chip elements including advanced fabrication and integration techniques to allow manufacturable, disposable devices, which are commercially viable.



9024 IMP AnnRep.indd 30 02/06/2010 16:02

MCLEOD, Professor Christopher

Research Focus: Implantable SAW Transponder for acute and chronic blood pressure monitoring

Funding: The Wellcome Trust

To provide safe and accurate continuous or intermittent blood pressure measurements from within the cardiovascular system. The measurement site is selected for the clinical problem being addressed, and the case for implanting a sensor is made on the risk-benefit analysis in each instance. The sensors are based on surface acoustic wave resonators and can be both excited and read from an external reader. There is no internal power source, so the sensors have indefinite life. The reader can be linked directly to any Telecare system, enabling monitoring in the community as easily as in hospital. Three examples are given:

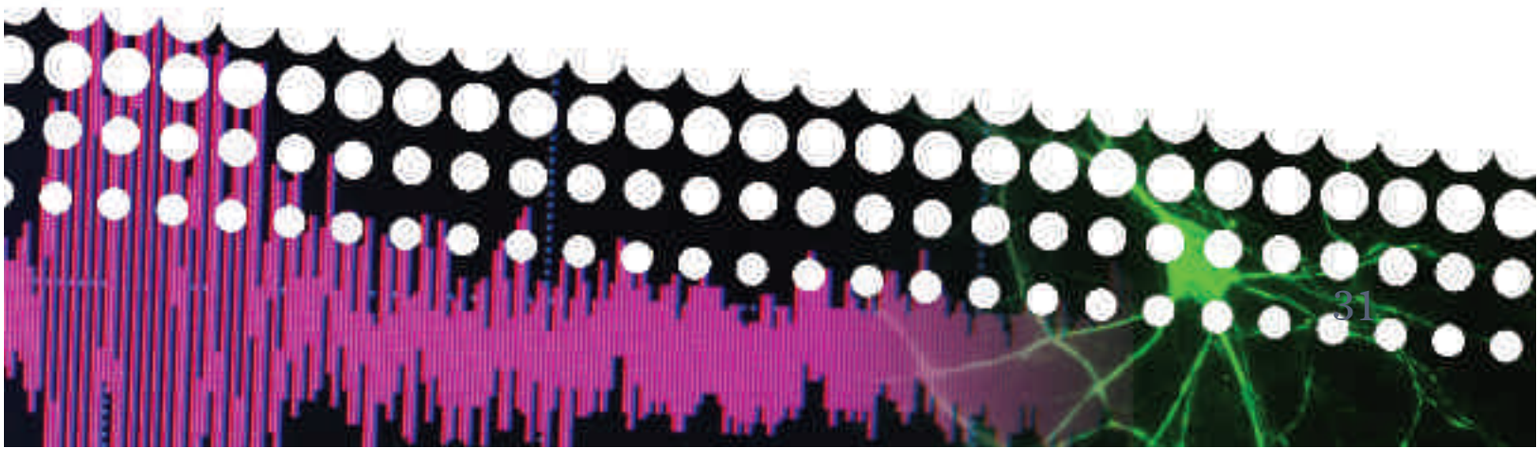
- Pulmonary hypertension: measurement in the Pulmonary Artery (PA) to monitor the effect of the therapy being given. These measurements are currently only available through an expensive and somewhat risky catheterisation of the PA. Repeated measurements are seldom performed. An implanted device will provide measurements to monitor the condition, generate an alarm if necessary and guide therapy.
- Left Atrial pressure: measurement in the left atrium will provide the single most useful monitor of chronic heart disease and chronic obstructive pulmonary disease, the two principal chronic conditions which affect large numbers of the population and involve very high personal and NHS resource costs.
- Hypertension: measurement in the systemic circulation. The argument for an implant is made on the grounds that continuous direct measurement provides the only accurate data. Non-invasive measurements are notoriously inaccurate and intermittent, missing many critical episodes. Haemorrhagic strokes arise from peaks in the blood pressure, and would commonly be missed by conventional measurements

The technology being developed for these applications will be suitable for pressure measurements almost anywhere else in the body.

The technology is patented and is intended to lead to the provision of medical devices and systems in the near future.

Key References

1. ICCH brochure from www.icch.org.uk
2. Heart Disease and Stroke Statistics—2007 Update
3. http://circ.ahajournals.org/cgi/content/full/115/5/e69



9024 IMP AnnRep.indd 31 02/06/2010 16:02

MICHELAKIS, Dr Konstantinos

Research Focus: Bionanotechnology

Funding: Winston Wong Centre for Bio-Inspired Technology

My role in the Institute is twofold: to address the process engineering needs of research projects that require the use of the Microfabrication Facility (Cleanroom) and to pursue my own research on electron devices and micro/nano-fabrication applications at the interface between biochemistry and microelectronics. For this reason, my research contribution extends to various research efforts and projects currently running in the Institute, some of which are:

- Microelectrodes and Microneedles (with Prof Tony Cass): This research exploits the benefits of using microfabricated electrodes and needles for the construction of novel biosensors and minimally invasive therapeutic and diagnostic tools. I am involved in the design, fabrication and integration of these devices [1]. The Institute has been recently awarded a three-year MRC grant to develop a sensor platform based on microneedles and there is also commercial interest.
- Memristors: The memristor, the recently physically realised "missing fundamental circuit element", has been heralded as a revolution in electronics, with electrical response that mimics the brain function. IBE is the first institution in the UK to have fabricated memristors and I am involved in the development of these devices in-house. Our work has led to a number of publications [2] [3], the latest of which has been chosen to feature in the online April 2010 issue of IET Micro & Nano Letters.
- ISFETs/ChemFETs: As an electronic engineer with extensive experience on electron-device physics, design and fabrication, I am involved in various research projects that make use of ISFETs/ChemFETs as sensing elements for protons and other ions [4] [5].
- Polymer films for myocardial tissue engineering: In collaboration with a multi-disciplinary research team under Prof Sir Magdi Yacoub, National Heart and Lung Institute, Harefield Hospital, I am involved in engineering suitable polymer films that allow spatially ordered growth of myocardial tissue for biomedical applications. I am also co-supervising a student who is pursuing an MRes in Biomedical Research (Faculty of Medicine), with the project title: "Polymer films and signalling molecules for myocardial tissue engineering".

Recent Publications

1. A Radomska, K Michelakis, S Sharma, N Oliver, A Cass, "Development of novel minimally invasive microprobes for continuous glucose monitoring", Biosensors and Bioelectronics, 2010.
2. T Prodromakis, K Michelakis, C Toumazou, "Switching mechanisms in microscale memristors", IET Electron Lett, Vol. 46, pp. 63 – 64, 2010.
3. K Michelakis, T Prodromakis, C Toumazou, "Cost-effective fabrication of nanoscale electrode memristors with reproducible electrical response", Micro & Nano Letters, Vol. 5, pp. 91 – 94, 2010.
4. S Sharma, A Radomska, I Triantis, K Michelakis, et al, "ISFET-based microfluidic devices for monitoring physiological changes", Biosensors and Bioelectronics, 2010
5. T Zoumpoulidis, T Prodromakis, H van Zeijl, K Michelakis, M Bartek, C Toumazou, R Dekker, "Stretchable Array of ISFET Devices for Applications in Biomedical Imagers", IEEE Sensors Conference, pp. 7 – 12, 2009.

9024 IMP AnnRep.indd 32 02/06/2010 16:02

MURPHY, Dr Olive

Research Focus: RF Antenna Design and Sensor Characterisation (SAW BPM Project)

Funding: The Wellcome Trust

The project is based around the development 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 on-going assessment of localised pressures has had to rely on inaccurate external measurement or intermittent and invasive and, therefore, partial and risky internal measurements. The difficulties associated with internal direct measurements are device size, power requirements, accuracy, performance degradation, and the risk of infection. Using the SAW pressure sensor cardiovascular, intra-ocular and intra-cranial pressures can be precisely measured. The traditional difficulties are reduced and in some cases eliminated as the SAW transponder is a minute, biocompatible, highly accurate passive device which is now being used to provide continuous pressure monitoring.

This contribution to the overall research project involve sensor characterization and assembly along with the design, optimization and in-vitro/in-vivo testing of deeply implanted antennas. The sensors are now becoming smaller and more sensitive, although their assembly is non-trivial. This allows the sensor to be placed in smaller vessels within the body and widen the number of applications. The antennas must be miniature but highly efficient for effective energy transfer and signal clarity. Recent in-vivo experiments have shown excellent results for antennas implanted within beating porcine hearts. The extent of the expertise and data acquired through this research is unique to the IBE and is easily applied to other deeply implanted sensors.

Key References

1. P-J Chen, DC Rodger, S Saati, MS Humanyun, and Y-C Tai, “Microfabricated implantable parylene-based wireless passive intraocular pressure sensors,” J. Microelectromech. Syst., Vol. 17, No. 6, pp. 1342 – 1351, 2008.
2. E Chow, Y Ouyang, B Beier, W Chappell, P Irazoqui, “Evaluation of cardiovascular stents as antennas for implantable wireless applications,” IEEE Trans. Microwave Theory Tech., Vol. 57, No. 10, pp. 2523 – 2532, 2009.

9024 IMP AnnRep.indd 33 02/06/2010 16:02

NIKOLIC, Dr Konstantin

Research Focus: Bio-inspired Technologies – Modelling and Computer Simulations

Funding: Engineering and Physical Sciences Research Council (EPSRC)

One of the current research topics at the IBE Bionics group is in the area of bio-inspired technologies, which is a cross-disciplinary field at the interface between biology/biochemistry, physics/engineering and medicine. The idea is to design electronic systems that interact with human organs and systems, as well as electronic circuits and devices designed following the basic principles of biological systems. My research focuses on several areas within this field: Biophysical Models, Computational Neuroscience, Optical Neural stimulation, Photocycles of Channelrhodopsin-2, Phototransduction cascade in invertebrates. The research methodology is mainly theoretical.

More specifically, I created a model of the G-protein coupled cascade in Drosophila photoreceptors which revealed many interesting properties as well as the underlying mechanisms by which the system generates high quantum efficiency, single photon responses, huge signal amplification and fast recovery, as well as light adaptation to 11 orders of magnitude of light intensities. I am now exploring the feasibility of converting a cascade of biological amplifiers into electronic equivalents. These circuits can then be used in very sensitive imaging chips, uncooled infrared detectors and cameras, or for single photon detection, photon counters or for silicon photonics detectors and silicon retinas.

The work on neural stimulation using light has been done in collaboration with the Dr Degenaar's Group. My main contribution was the channelrhodopsin-2 (ChR2) photo-cycle modelling. ChR2 is a light-gated ion channel and the expression of ChR2 in neurons allows for optical stimulation of neurons. This field has the potential to be one of the most important new techniques in neuroscience for many years and has direct implications in future therapeutic strategies – we have filed for two patents in this area regarding retinal prosthesis. The modelling of the neural stimulation was extended to a Hodgkin-Huxley type of model for the action potential generation.

Key References

- C Koch, "Biophysics of Computation: Information Processing in Single Neurons (Computational Neuroscience)", Oxford University Press, ISBN: 0195104919, 1998.

Recent Publications

1. N Grossman, V Poher, M Grubb, G Kennedy, K Nikolic, M Neil, J Burrone, M Dawson, P Degenaar, "Matrix Photostimulation Technique", Journal of Neural Engineering, Vol. 7, No. 1, 2010.
2. K Nikolic, N Grossman, M Grubb, J Burrone, C Toumazou, P Degenaar, "Photocycles of Channelrhodopsin-2", Photochemistry and Photobiology, Vol. 85, pp. 400 – 411, 2009.
3. TG Constandinou, K Nikolic, C Toumazou, "Method and Apparatus for Optically Outputting Information from a Semiconductor Device", Patent pending filed Feb 2010.
4. N Grossman, V Poher, GT Kennedy, K Nikolic, P Degenaar, MAA Neil, "Opto-neural stimulation equipment", Patent pending filed May 2009.

9024 IMP AnnRep.indd 34 02/06/2010 16:02

OLIVER, Dr Nick

Research Focus: Bioengineering for Diabetes

Funding: The Wellcome Trust

Type 1 diabetes is caused by antibodies attacking the insulin-producing beta cells in the pancreas. Treatment is usually by regular insulin injections, informed by glucose measurements from finger prick blood samples. However, these do not mimic the normal behaviour of the beta cell and this leads to suboptimal blood glucose control and complications including kidney failure, blindness, nerve damage and heart disease. Intensive insulin treatment reduces the progression of these complications but increases the risk of disabling low blood glucose levels (hypoglycaemia). A closed loop insulin delivery system, comprising a continuous glucose sensor, an intelligent algorithm and an insulin pump, provides the potential to improve diabetes control while avoiding hypoglycaemia. The Imperial College artificial pancreas team is pursuing novel technology to form a closed loop system with clinical trials in the Imperial Healthcare Hospitals co-ordinated by Dr Oliver in collaboration with Professor Johnston.

Other current research includes glucose fluctuations in diabetes, looking specifically at the causes, associations and consequences of glucose changes in diabetes; wireless monitoring of physiological parameters such as heart rate, respiratory rate and temperature.

Key References

1. R Hovorka, "Continuous glucose monitoring and closed-loop systems", Diabetic Medicine, Vol. 23, No. 1, pp. 1 – 12, 2005.
2. P Georgiou, C Toumazou, "A Silicon Pancreatic Beta Cell for Diabetes", IEEE Transactions on Biomedical Circuits and Systems, Vol.1, No.1, pp. 39 – 49, 2007.

Recent Publications

1. J Valabhji, NS Oliver, D Samarasinghe, T Mali, RGJ Gibbs, WMW Gedroyc, "Conservative management of diabetic forefoot ulceration complicated by underlying osteomyelitis: the benefits of magnetic resonance imaging", Diabetic Medicine, Vol. 26, pp. 1127 – 1134, 2009.
2. NS Oliver, P Georgiou, D Johnston, C Toumazou, "A Benchtop Closed Loop System Controlled by a Bio-Inspired Silicon Implementation of the Pancreatic Beta Cell", Journal of Diabetes Science and Technology, Vol. 3, pp. 1419 – 1424, 2009.
3. S Mehdi, E Hatfield, A Dornhorst, NS Oliver, "Assessment of glycemic variability in continuous subcutaneous insulin infusion therapy in Type 1 Diabetes related to anthropometry and complication status", J Diabetes Science and Technology, Vol. 3, pp. 1227 – 1228, 2009.
4. E Alasaarela, NS Oliver, "Wireless Solutions for Managing Diabetes", Technology and Healthcare, Vol. 17, pp. 353 – 367, 2009.
5. E Alasaarela, R Nemana, S DeMello, NS Oliver, et al., "Wireless for managing Healthcare", International Journal of Healthcare Delivery Reform Initiatives, Vol. 1, pp. 52 – 73, 2009.
6. NS Oliver, et al., "Glucose Sensors: A Review of Current and Emerging Technology", Diabetic Medicine, Vol. 26, pp. 197 – 210, 2009.

9024 IMP AnnRep.indd 35 02/06/2010 16:02

PRODROMAKIS, Dr Themistoklis

Research Focus: Bio-inspired Devices: Methods and Applications

Funding: Corrigan Fellowship

The aim of this project is to utilise well-established technologies in an innovative way for developing architectures that imitate the functions of biological systems. Particularly, our cleanroom suite has played a catalytic role in enabling practical implementations of a number of bio-inspired devices/systems, through the development of prototyping specimens that are fabricated with standard micro/nano fabrication processing techniques.

The recent discovery of the memristor has marked a new era for the advancement of neuromorphic applications. Our group is the first within the UK that has made significant research contributions in this field through in-house fabrication, characterisation, modelling and application. So far we have been exploiting practical micro/nano fabrication techniques that are cost-effective and avail in most research environments for fabricating micro-scale memristive devices that are supported by analytical models. The memristor appeals to be fitting in a variety of applications, from non-volatile memory to programmable logic, however, its sensational property lies with the ability to perform analog computation while the product is locally stored. Individual memristors can thus be used to replicate the strength of different ionic channels, which is a more suitable alternative to CMOS log-domain circuits both in complexity and space. Particularly the latter is a critical parameter for integrating a large number of devices in memristive networks. Multiple interconnects between such devices could in principle allow associative indexing by altering the modulation weight of particular trails, similar to what has been demonstrated for cellular neural networks. Presently, we are developing nano-scale devices as well as complex memristive networks that could imitate synaptic networks and essentially the way the human brain functions in processing and storing of information perceived by our body's sensory network.

On-going research also includes the development of chemical sensors for linking biological functions with electronics. Substantial research is carried out for addressing issues as encapsulation as well as developing novel architectures. Commercially available CMOS technologies along with customized CMOS processes are exploited to enhance the performance of chemical sensors and particularly ISFETs. A showcase example is the recent development of the world's first stretchable bio-sensing platform that can recognise the environment and physical context within which the signal is sensed and conform to the shape of an organ for improving the adhesion between the sensor and the sensed area.

Key References

1. R Williams, "How we found the missing memristor," IEEE spectrum, Vol. 45, No. 12, pp. 28 – 35, 2008.
2. L Chua, "Memristor – the missing circuit element," IEEE Trans. Circuit Theory, Vol. 18, No. 5, pp. 507 – 519, 1971.

Recent Publications

1. T Prodromakis, et al, "Cost-effective fabrication of nanoscale electrode memristors with reproducible electrical response", IET Micro/Nano Letters, vol. 5, no. 2, pp. 91-94, 2010.
2. T Prodromakis, K Michelakis, C Toumazou, "Switching mechanisms in microscale Memristors", IET Electronic Letters, vol. 46, no. 1, pp. 63-65, 2010.
3. T. Prodromakis, K. Michelakis and C. Toumazou, "Fabrication and Electrical Characteristics of Memristors with TiO2/TiO2+x active layers", IEEE ISCAS 2010.
4. T. Prodromakis, K. Michelakis and C. Toumazou, "Practical micro/nano fabrication implementations of memristive devices", CNNA 2010.

9024 IMP AnnRep.indd 36 02/06/2010 16:02

REHAK, Dr Marian

Research Focus: ISFET modifications by means of surface chemistry and its integration into medical devices

Funding: Technology Strategy Board (TSB)

This broad topic embraces various projects within the Institute. Modifications of the surface properties of the ISFET chip itself and its integration with a fluidic component to create functional medical device results in alteration of the ISFET sensing properties.

SNP detection: A single-nucleotide polymorphism (SNP) is a variation in DNA sequence occurring at the level of a single nucleotide. As a result humans can have predispositions and can develop various diseases. pH sensitive, semiconductor technology of Ion Sensitive Field Effect Transistor (ISFET) discovered at the Institute is being developed into a point-of-care diagnostic tool for SNP detection.

Focus is on the transition from proof-of-principle and the pure research environment to the product development phase and integration of all aspects of technology to produce a point-of-care diagnostic platform for monitoring pharmacogenetically relevant single nucleotide polymorphism (SNP). Major long term tasks are:

Design, testing, optimisation and validation of a cartridge based DNA purification system
Integration of chip, DNA purification and amplification systems, and the detection assay into a disposable cartridge

DNA methylation detection: Recent advanced in epigenetic predetermined DNA methylation as one of extremely promising molecular biomarker. Abnormalities in DNA methylation in particular gene regions, can lead to changes expression, resulting in cancer development.

Proposed detection method is ISFET based analysis of DNA methylation as a real-time platform for early tumour detection.

Key References

1. DM Garner, H Bai, P Georgiou, TG Constandinou, S Reed, LM Shepherd, W Wong Jr, KT Lim, C Toumazou, "A Multichannel DNA SoC for Rapid Point-of-Care Gene Detection", Proceedings IEEE International Solid-State Circuits Conference (ISSCC), Pages: 492–494, 2010.
2. HH Cheung, TL Lee, OM Rennert, WY Chan, "DNA methylation of cancer genome," Birth Defects Research (Part C), Vol. 87, No. 4, pp. 335 – 350, 2009.
3. P Das, R Singal, "DNA methylation and cancer," Journal of Clinical Oncology, Vol. 22, No. 22, pp. 4632 – 4642, 2004.

9024 IMP AnnRep.indd 37 02/06/2010 16:02

SIDERIS, Dr Dimitrios

Research Focus: Development of Microfluidic Chip with very high resolution and throughput for DNA and Protein Analysis

Funding: London Development Agency (LDA)

Co-researchers/Collaborators: Reza Bahmanyar, Mishaal Almashan, Alex Iles, Richard Jackson

We are developing a revolutionary microfluidic system to analyse DNA and proteins with ultra high resolution, throughput and sensitivity.

The chip analyses the macromolecules using an innovative separation method that resembles electrophoresis but achieves resolutions, which are 100 times higher than conventional technology. The sensitivity in sample amount is also considerably increased.

The current bottleneck of separation systems is the relatively low resolution of identification of different molecular species. Our system removes this bottleneck by dramatically increasing the resolution of separation systems. This literally unlocks the power of microfluidic systems, which are especially affected by this bottleneck. Our technology has the potential to achieve fast and accurate DNA and protein analyses in a miniature cartridge.

Molecular separations are central in academic research, drug development and diagnostics. There are several other applications such as forensics (STR detection), identification of Single Nucleotide Polymorphisms and inorganic molecule analysis. 80% of the labs worldwide have a separation instrument in their possession.

Our system has already proved the operational principle achieving unprecedented resolutions. Currently we are working to further improve the functionality and develop real world applications.

The outcome of our project is the construction of an instrument that utilises the special microfluidic chip.

Key References

1. CP Fredlake et al, PNAS, Vol. 105, No. 2, pp. 476-, 2008.
2. RG Blazej, P Kumaresan, R Mathies, PNAS, Vol. 103, No. 19, pp. 7240-, 2006.
3. ES Mansfield et al., “Short Tandem Repeat”, Electrophoresis, Vol. 19, No. 1, pp. 101-, 1998.
4. SNP: Single Nucleotide Polymorphism, JJ Sanchez, Nature Protocols 1, 2006, 1370, 2006.

Recent Publications

- D Sideris, Patent Application US20080083621, 2010.

9024 IMP AnnRep.indd 38 02/06/2010 16:02

TRIANTIS, Dr Iasonas

Research Focus: Advanced Neural Interfacing

Funding: Engineering and Physical Sciences Research Council (EPSRC)

Since June 2005 I have been pursuing research in advanced neural recording and stimulation. My main research interest has been the investigation of alternative modalities in neural interfacing. My objectives include researching technologies and electrode topologies to increase selectivity in neural monitoring and stimulation and implementing intelligent closed-loop stimulation systems. Overall, I am currently pursuing interdisciplinary research in all three major areas of a closed-loop stimulation neuroprosthesis: the monitoring, the interface and the stimulation parts.

Within the Advanced Neural Interfaces (ANI) group - part of the Bionics Group - I am responsible for the Neuroprosthetic and Analytical Sensors (NAS) laboratory and establishing the neural interfacing part. I have formed collaborations with researchers working on sensors, microelectronics, chemistry, biology and medicine. I work along with researchers that have experience with cochlear and retinal prostheses. External collaborations include IMTEK in Freiburg, Br. and IBMT in Fraunhofer in Germany, the MEMS group in Cork, Ireland, PPCU and SZTAKI in Budapest, Hungary, UCY in Cyprus, the Metabolic Medicine group at Hammersmith Hospital, Imperial College London and the Neuroscience Division at the same hospital. I am routinely carrying out in-vitro and acute in-vivo experiments in collaboration with clinical researchers. The bioengineering context of the research is to transfer spinal cord injury neuroprostheses methodology to vagus nerve interfacing. The medical context of my research is vagal monitoring for assessing appetite control drugs and the use of stimulation for direct appetite control in conjunction with pharmacological treatment.

Specifically, my research tasks include: investigating chemical neural monitoring; developing a multi-electrode "matrix" cuff for selective interfacing; developing advanced neurostimulation strategies; and designing low power neural amplifiers.

Key References

- W. Horch and Gurpreet Dhillon, "Neuroprosthetics: Theory and Practice", World Scientific Publishing, ISBN: 9812380221, 2002.

Recent Publications

- S Sharma, A Radomska, IF Triantis, K Michelakis, J Trzebinski, BCT Field, C Toumazou, AEG Cass, "Ion-sensitive field effect transistor based micro-fluidic devices for monitoring physiological changes", 20th World Congress. Biosensors, 2010.

9024 IMP AnnRep.indd 39 02/06/2010 16:02

VILCHES, Dr Antonio

Research Focus: 3-Tier Bio-Communication Platform

Funding: Engineering and Physical Sciences Research Council (EPSRC)

I am applying semiconductor device engineering, the high-frequency modeling of electronic devices, analogue and microwave circuit design and the application of non-invasive microwave radar techniques to medical imaging. My specific interest is in span novel device design, especially ultrasonic transducers and surface acoustic wave devices, baseband to microwave circuit design and bio related EM propagation studies.

Current projects are focused on investigating methods to improve the long-term communications and powering / recharging of medical device implants using a variety of pressure wave and electromagnetic technologies, including ultrasonic pressure waves, inductive coupling, microwave RF and carrier-free / pulsed transmissions. Recent collaboration with Prof J Hand (Hammersmith Hospital) has involved the design of a system for the non-invasive characterisation of brain tumours and is currently focussed on the invention of a novel ultra-broadband monolithic antenna for use in bio-tissue imaging and spectroscopy.

These solutions can be used in a wide range of medical devices including – Implantable Devices, Hearing Aids, Glucose Monitors, Drug Delivery Systems, Pacemakers and implantable insulin pumps. The aim is a limitless lifetime performance in a safe that transmits the information to a distance location wirelessly to the health provider.

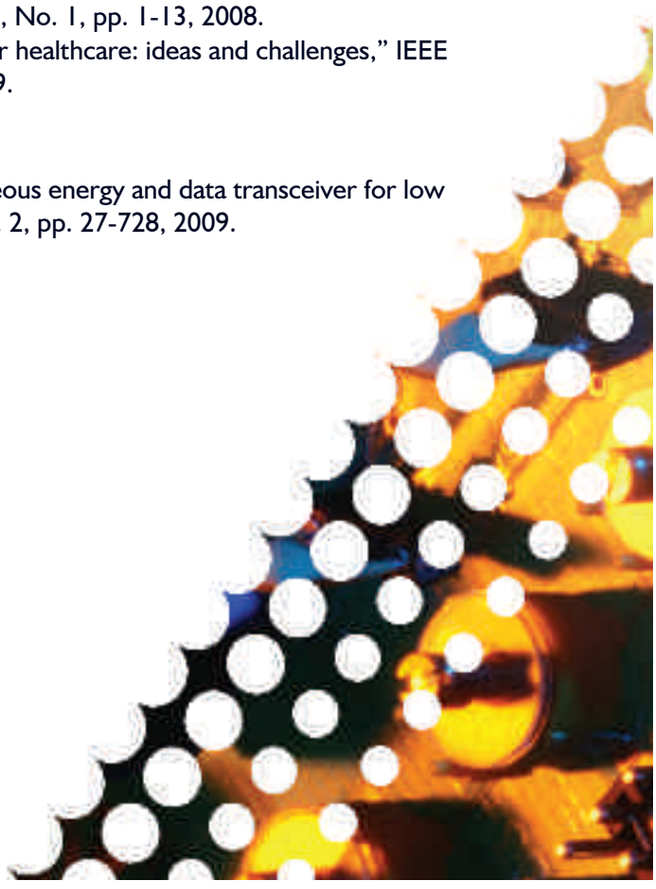
I have previously shown that the use of HMODFET Si/SiGe devices in micropower RF applications are more gain efficient under low-voltage, micropower operation than when operated at full power and this led to the publication of the first true micropower microwave small-signal model for Si/SiGe HMODFET devices and the first monolithic Si/SiGe HMODFET true RF capable micropower amplifier. We are now seeking to provide robust generic interfaces / platforms for medical device implants. These solutions will be available for use in a wide range of medical devices including Implantable Devices, Hearing Aids, Glucose Monitors, Drug Delivery Systems, Pacemakers and implantable insulin pumps.

Key References

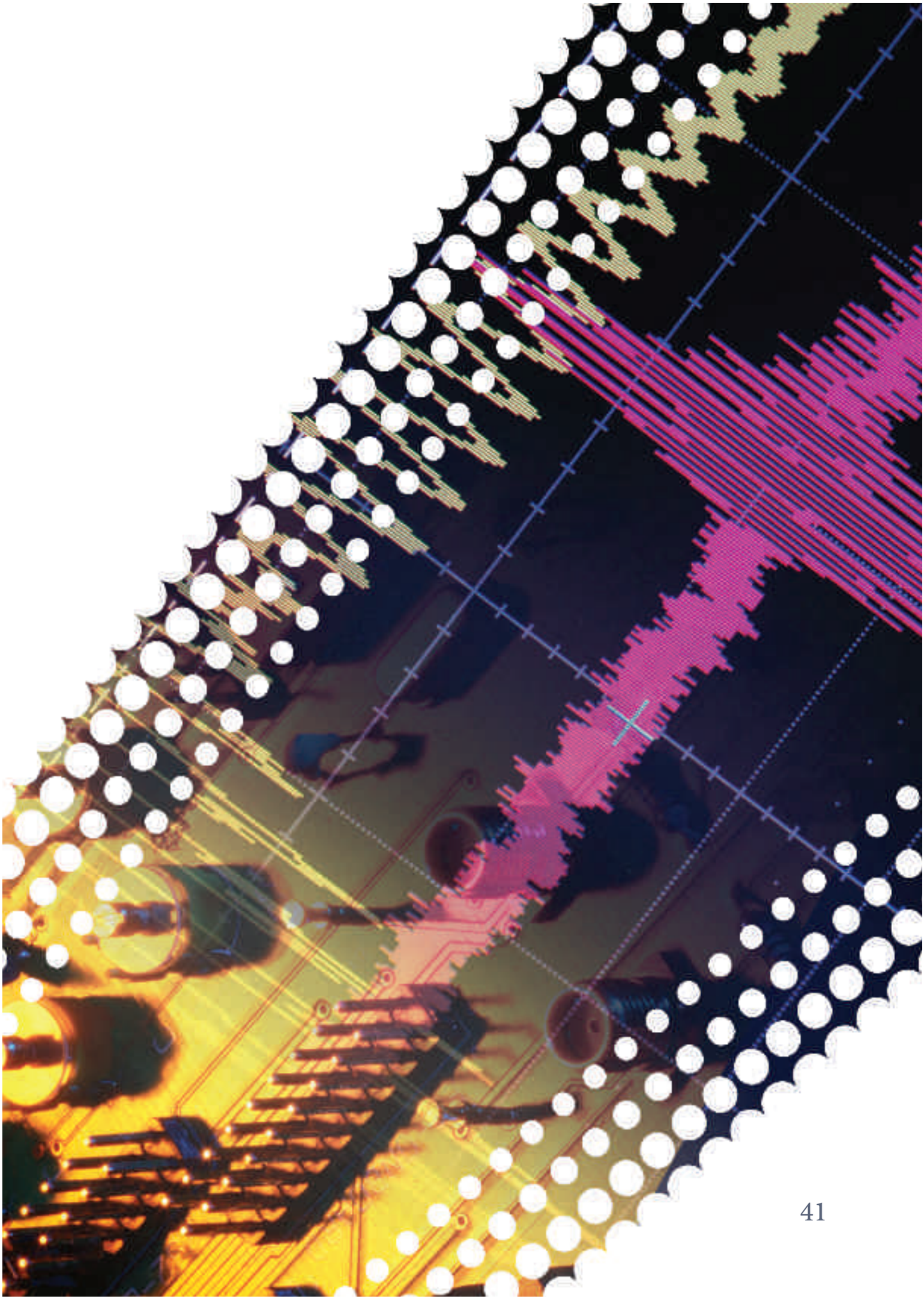
1. X Wei, J Liu, “Power sources and electrical recharging strategies for implantable medical devices, ” Frontiers of Energy and Power Engineering in China; Vol. 2, No. 1, pp. 1-13, 2008.
2. K Malasri, L Wang, “Securing wireless implantable devices for healthcare: ideas and challenges,” IEEE Communications Magazine, Vol. 47, No. 7, pp. 74 – 80, 2009.

Recent Publications

- A Vilches, A Sanni, C Toumazou, “Single coil pair transcutaneous energy and data transceiver for low power bio-implant use”, IET Electronics Letters, Vol.45, No. 2, pp. 27-728, 2009.



9024 IMP AnnRep.indd 40 02/06/2010 16:02



9024 IMP AnnRep.indd 41 02/06/2010 16:02

Research Students/Assistants Reports

AL-AHDAL, Mr Abdulrahman

Research Focus: ISFET based disposable Chemical inverter

Supervisor: Professor Christofer Toumazou

Generally all ISFETs were built for continuous time (analogue) measurement with analogue pre-processing circuits around them. In order to exploit the ISFET in the digital domain, one should start with the most basic building block that is an inverter. Successful implementation of a pH driven inverter opens the door for integrating digital signal processing with it in the same IC without the need for analogue parts. That is a new area to be exploited.

The work aims at building an inverter using an ISFET as a pH sensor. This can be used in arrays tailored for specific applications like DNA sequencing. One challenge here is to overcome the Vt mismatch of ISFETs. The work aims at using electron tunneling and hot electron injection to tackle this problem.

Key References

1. P Bergveld, "Thirty years of ISFETOLOGY What happened in the past 30 years and what may happen in the next 30 years", sensors and actuators B, Vol. 88, 2003.
2. Liu Yan, Pantalis Georgiou, Timothy G. Constandinou, David Garner, and Chris Toumazou, " An Auto-Offset-Removal circuit for chemical sensing based on the PG-ISFET", IEEE International Symposium on Circuits and Systems ISCAS 2009.
3. Chris Diorio, PhD thesis titled "Neurally Inspired Silicon Learning: From Synapse Transistors to Learning Arrays", California Institute of Technology Pasadena, California, 1997.
4. P. Georgiou and C. Toumazou," ISFET threshold voltage programming in CMOS using hot-electron injection", ELECTRONICS LETTERS, Vol. 45 No. 22, 22nd October 2009.

9024 IMP AnnRep.indd 42 02/06/2010 16:02

BUNGA, Mr Santos

Research Focus: Low Power Bio Sensing Solutions

Supervisor: Dr Antonio Vilches

This project will investigate current technologies and approaches used on active implantable medical devices (IMD), their processing, sampling data and transmission of data with a view to identifying state-of-the art technologies and methods to improve the long-term powering and recharging of an IMD in a highly safe, efficient and convenient way.

An implant is composed of four main parts: power source, sensor, data sampler and data transceiver. We aim to fabricate a suitable micro-power source and related low-voltage circuitry. Design will focus on low bit-rate data sampling and carrier-less transmission, with the final goal of integration into a sub-micron CMOS IC that operates on ultra low power.

These solutions can be used in a wide range of medical devices including – implantable devices, hearing aids, glucose monitors, drug delivery systems, pacemakers and implantable insulin pumps. The aim is a limitless lifetime performance in a safe, that transmits the information to a distance location wirelessly to the health provider.

Key References

1. X Wei, J Liu, "Power sources and electrical recharging strategies for implantable medical devices," Frontiers of Energy and Power Engineering in China, Vol. 2, No. 1, pp. 1 – 13, 2008.
2. J Barrett, RV Martinez-Catala, "A Modular Wireless Sensor Platform with Fully Integrated Battery," IEEE Transactions on Components and Packaging Technologies, Vol. 32, No. 3, pp. 617 – 626, 2009.
3. RG Griffin, "The Future of MEMS Microelectromechanical Systems in Transportation Engineering," TRANSPORTATION RESEARCH; Number E-C056, October 2003; ISSN 0097-8515

9024 IMP AnnRep.indd 43 02/06/2010 16:02

CHAN, Mr Wai Pan

Research Focus: Low Power CMOS Methodologies for ISFETs Instrumentation

Supervisor: Professor Christofer Toumazou

I have developed a robust design methodology in a 0.18μ commercial CMOS process to circumvent the performance issues of the integrated Ion Sensitive Field Effect Transistor (ISFET) for pH detection.

It is known that the ISFETs on unmodified CMOS chips are subjected to variation of threshold voltages due to the trapped charges. Few proposals existed in the literature to tackle the effect of the trapped charges; the most accepted solution to reduce the negative trapped charges found in p-typed ISFETs is to use UV radiation. Nonetheless, using UV radiation is expensive, as we have no prior knowledge to quantify the trapped charges. I have invented an integrated averaging amplifier [1] based on the current feedback opamp topology, in order to neutralize any trapped charges. The effectiveness of using the averaging, has to meet some assumptions, but the averaging technique does not involve any post CMOS processing. Thus, the design solution is served to suggest a low cost solution to circumvent the trapped charges.

My thesis on using the ISFETs is targeted on portable instrumental applications for pH detection; it is a 'system-on-chip' (SoC) solution, which is mass producible at low cost. There are only few ISFET-related works published in the literature about pH to digital conversion, and I have proposed using the reference-less sigma delta modulator as a pH to digital converter [2]. The system proposed in my thesis can manage mismatched ISFETs on chip for doing linear pH-to-digital conversions, with up to 8-bit accuracy, and under 80 microwatts static power consumption.

Key References

1. P Berveld, "Thirty years of ISFETOLOGY", Sensor and Actuators B, Vol. 88, No. 1, pp. 1 – 20, 1 2003.
2. F Cannillo, C Toumazou, "Subthreshold parallel FM-to-digital - converter with output-bit-stream addition by interleaving", IEEE Transactions on Circuits and Systems I (TCAS-I), Vol. 56, No. 8, pp. 1576 – 1589, 2009.

Recent Publications

1. WP Chan, B Premanode, C Toumazou, "64 pH-ISFET averaging array employing global negative current feedback", IET Electronics Letters, Vol. 45, pp. 536 – 537, 2009.
2. WP Chan, B Premanode, C Toumazou, "An Integrated ISFETs Instrumentation system in Standard CMOS Technology", IEEE Journal of Solid-State Circuits, 2010, in press.

9024 IMP AnnRep.indd 44 02/06/2010 16:03

EL-SHARKAWY, Mr Mohamed

Research Focus: Sensor instrumentation for Bio-inspired Artificial Pancreas

Supervisor: Dr Pantelis Georgiou

Funding: The Wellcome Trust

Current blood glucose measurement relies on the diabetic patient pricking his fingertip with a lancelet and allowing a test strip connected to a glucose reader to absorb the blood and display the blood glucose concentration. This is quite tedious, invasive and open loop, which makes it non-ideal for strict glyceamic control. In order to build a successful closed loop control system it is therefore necessary to take continuous glucose measurements and display them in real time.

My research involves designing low power instrumentation, which is needed to drive electrochemical based glucose sensors. In doing so acquisition of the necessary signals and signal processing on the raw signal data such as filtering and averaging is possible. This is needed to enhance signal to noise ratio and extract the necessary trends. At the core of this sensor front end is a low power potentiostat, which is required to control a three-electrode cell and allow the necessary electrochemical reactions to take place. It achieves this by keeping the potential between two electrodes known as the working and reference electrodes constant. The current which flows through the third electrode is then converted to a voltage using a trans-impedance amplifier and gives a measure of the glucose concentration.

In addition there exists a 10 minute lag between the glucose concentration in the blood and the interstitial fluid where the sensor is placed. As a result I am implementing regression techniques, which are used for forecasting and calibration. Finding the optimum calibration method and the number of times it needs to be performed in order to provide accurate measurements is crucial to the success of the whole system.

Key References

1. N Oliver, P Georgiou, D Johnston, et al, “A Benchtop Closed-loop System Controlled by a Bio-Inspired Silicon Implementation of the Pancreatic beta Cell”, J. Diabetes Sci Technol, Vol. 3, pp. 1419 – 1424, 2009.
2. A Mahdi, AJ Graham, “Current-mirror-based potentiostats for three-electrode amperometric electrochemical sensors”, IEEE Transactions On Circuits And Systems, Vol. 56, pp. 1339-1347, 2009.

Recent Publications

- M El-Sharkawy, P Georgiou, C Toumazou, “A Silicon Pancreatic Islet for the Treatment of Diabetes”, Proceedings of the IEEE International Symposium on Circuits and Systems (ISCAS), 2010, in press.

9024 IMP AnnRep.indd 45 02/06/2010 16:03

GUVEN, Mr Onur

Research Focus: Non-Invasive Blood Spectroscopy

Supervisor: Dr Dylan Banks

Funding: Engineering and Physical Sciences Research Council (EPSRC)

There is a strong clinical need to increase safety with an accurate and cheap continuous assessment of tissue oxygen to allow timely intervention in cases of hypoxia. The excess demand over supply of blood for transfusions ensures a strong clinical need to rationalise them, avoiding unnecessary interventions.

Hypoxia is currently indirectly calculated by intermittent sensing of total SpO2 and Hb with blood gas- haemacue- or frequent blood laboratory analysis.

The aim of this project is to produce a prototype non-invasive real-time blood measurement system, including the necessary optical, signal processing and analysis circuitry, and to test it in clinical trials.

The device works by passing light of multiple wavelengths, between the visible and near infrared, through the subjects body, at a point such as a finger, and measuring the absorption changes of the light wavelengths over time. Those changes are processed stored on hardware. This technique shows the patients' effective amount of oxygen available in their system including their carboxyhaemaglobin and methaemaglobin levels as well as their total haemaglobin concentrations. In addition to that, the energy efficiency of the designed hardware has a longer battery run than the current commercial products.

By doing this we hope to improve patient care, reduce costs, increase patient safety, rationalise blood transfusions and blood laboratory analysis and improve diagnostic tools within primary healthcare and surgical settings.

Further stages of development are intended to elucidate the concentrations of glucose in the blood, which will offer a significant improvement of real-time glucose monitoring systems.

Key References

1. United States Patent Application Publication. Pub. No.: US 2008/0242958 A1
2. United States Patent Application Publication. Pub. No.: US 2008/0221418 A1

9024 IMP AnnRep.indd 46 02/06/2010 16:03

JUFFALI, Mr Walid

Research Focus: ISFET-based Chemical Sensing Platform for Neurochemical Analysis

Supervisor: Professor Christofer Toumazou

The vast majority of information in operation, control and sensing of the body is carried by neural signals between the brain and the vital organs. A number of conditions can be linked to the impairment or malfunction of this neural link including: epilepsy, spinal cord injury, dystonia and pain. By directly monitoring and potentially intervening in the neural pathways one can aim to aid in diagnosis (early warning/detection) and treatment (electrical stimulation [1] or drug administration) for the above-mentioned conditions [2]. One of the vital central nervous system (CNS) communication pathways is the vagus nerve. The vagus nerve innervates most vital organs including the heart, oesophagus, gastrointestinal tract, liver and pancreas and has a key role in conveying sensory information about the state of the viscera (the internal organs) to the central nervous system.

Initially the aim is to develop an ISFET-based chemical sensing platform for general sensing but specifically targeted for vagus nerve neurochemical sensing. Further investigation will promote the translation of this technology to creotinine/urea sensing for renal failure. We aim to develop the chemFET on cuff technology, develop sensing front-end platforms and importantly analyse and correlate chemical and electrical responses. It is the long term perspective that the development of the sensing technology on cuff and in general can allow correlations of local chemical and electrical neural changes as well as vagus nerve activity to chemical responses and reactions in other areas of the body.

Key References

1. IF Triantis, "An Adaptive Amplier for Cuff Imbalance Correction and Interference Reduction in Nerve Signal Recording", in Electrical and Electronic Engineering, University College London, 2005.
2. JJ Struijk, et al., "Cuff electrodes for long-term recording of natural sensory information", IEEE Engineering in Medicine and Biology Society Magazine, 1999. Vol. 18, No. 3, pp. 91 – 98, 1999.
3. L Borovikova, et al., "Vagus nerve stimulation attenuates the systemic inflammatory response to endotoxin", Nature, Vol. 405, No. 6785, pp. 458 – 462, 2000.

9024 IMP AnnRep.indd 47 02/06/2010 16:03

KALOFONOU, Miss Melpomeni

Research Focus: Electrical detection of DNA methylation-based biomarkers in tumors using semiconductor technology

Supervisor: Professor Christofer Toumazou

My research focuses on the electrical detection of DNA methylation-based biomarkers in tumors using the well-established pH sensitive, CMOS based Ion Sensitive Field Effect Transistor (ISFET) technology. The aim is to develop a valuable tool for early detection of multiple cancer types using a minimally invasive approach.

In the earlier days of cancer research, genetic alterations were considered to be the molecular framework responsible for multistage carcinogenesis in humans. However, genetic events may not entirely explain the whole process of carcinogenesis. Events that do not follow the normal genetic principles of heritability can be described as "epigenetics", playing a leading role in multistage tumor progressions.

Epigenetics has evolved as a rapidly developing area of research, referring to heritable and potentially reversible alterations in the gene expression that are not coded in the DNA sequence itself. DNA methylation is one of the most common epigenetic events in the human genome and one highly promising molecular biomarker, playing a critical role in regulating the gene expression. Abnormalities in DNA methylation in particular gene regions, known as "CpG islands", can lead to inappropriate expression or silencing of genes, resulting in epigenetic disease development, notably cancer.

The analysis of DNA methylation-based biomarkers, being actively studied in multiple cancers, is rapidly advancing with the possibility of the methylation profile to distinguish tumor types and perhaps the response to chemotherapeutic agents. Therefore, the need for detection of DNA methylation in the promoter region of tumor suppressor genes appears to be one of the most important assays in early cancer diagnosis and so there is demand for prognostic and predictive markers.

Primarily I aim to develop a sensitive and specific system for detecting the methylation status of markers of interest in the presence of a strong background of DNA in remote media using the biocompatible ISFET technology. This system will work in a real-time continuous way utilising intelligent sensor design due to the integrative capability of ISFETs with standard circuit techniques.

Key References

1. HH Cheung, TL Lee, OM Rennert, WY Chan, "DNA methylation of cancer genome," Birth Defects Research (Part C), Vol. 87, No. 4, pp. 335 – 350, 2009.
2. P Das, R Singal, "DNA methylation and cancer," Journal of Clinical Oncology, Vol. 22, No. 22, pp. 4632 – 4642, 2004.
3. M Esteller, "CpG island hypermethylation and tumor suppressor genes: a booming present, a brighter future," Oncogene, Vol. 21, No. 35, pp. 5427 – 5440, 2002.
4. Y Kanai, S Hirohashi, "Alterations of DNA methylation associated with abnormalities of DNA methyltransferases in human cancers during transition from a precancerous to a malignant state," Carcinogenesis, Vol. 28, No. 12, pp. 2434 – 2442, 2007.

9024 IMP AnnRep.indd 48 02/06/2010 16:03

LEENUTAPHONG, Mr Jatgrarath

Thesis Topic: Development of an adaptive error correction for a high delay channel

Supervisor: Professor Christofer Toumazou

Funding: Royal Thai Scholarship

My project is focused on the modelling and the prediction of the error magnitude of data packets sent through terrestrial digital audio broadcasting (DAB-T) devices and infrastructure. Discrete time-series modelling techniques are used to capture the statistic properties of the sequences of error magnitude, and to produce input data for error magnitude prediction algorithms. The errors are then corrected by either adjusting the parameters of forward error correction, or requesting retransmissions from a sender.

The model's parameter learning algorithm is being developed in order to capture the dynamic nature of the error magnitude in real-time and on-line approach, as the amount of memory is limited in practice. Combination of the back tracking information with the model's parameters, providing likelihood values, which are used to perform an error magnitude prediction. This prediction is then weighted by the "cost of transmission" calculated from developed utility function, providing the decision for choosing optimum error control strategy and parameters.

An aim of this development is to integrate these algorithms and functions into a transmission protocol, which targets on improving the throughput of transmission over the very high delay channel while retaining the integrity of the data sent. It is has been proved that using ordinary transmission on erroneous high delay channel causes the significantly reduction on the throughput and quality of service compared to a shorter delay channel. As such erroneous high delay channel can be found on satellite channel and terrestrial digital broadcasting channel. These channels have advantages in very high bandwidth and long transmission range, which are considered to be useful in numerous applications.

With the implementation of the developed protocol on DAB-T, the benefit of this protocol is to be able to provide broadband quality and trustworthy communication channel for remote rural area such as mobile medical unit. An increasing of data transmission throughput and lower power consumption in an ordinary wireless channel, such as Bluetooth or body sensor network, is also expected.

Key References

1. EN, E., 300 401 Ver. 1.4. 1 "Radio Broadcasting Systems. Digital Audio Broadcasting (DAB) to mobile, portable and fixed receivers", 2006.
2. W Hoeg, T Lauterbach, "Digital audio broadcasting: principles and applications of digital radio", John Wiley & Sons, 2003.
3. H Balakrishnan, et al., "A comparison of mechanisms for improving TCP performance over wireless links", IEEE/ACM Transactions on Networking (TON), Vol. 5, No. 6, pp. 756 – 769, 1997.
4. D Eckhardt, P Steenkiste, "A trace-based evaluation of adaptive error correction for a wireless local area network", Mobile Networks and Applications, Vol. 4, No. 4, pp. 273 – 287, 1999.

9024 IMP AnnRep.indd 49 02/06/2010 16:03

LIU, Mr Yan

Thesis Topic: Engineering Robust CMOS ISFET Smart Sensor Systems

Supervisor: Professor Christofer Toumazou

Funding: DNA Electronics Ltd.

This project aims at understanding the characteristics, especially non-ideal behavior of this device, minimizing these effect by utilizing new device structure based on CMOS technology, and designing interface circuit and instrumentation system with low power consumption, hardware complexity and ability of correcting non-ideal behaviour of intrinsic sensors. This is intended to simplify the sensor and processing overhead, and ultimately lead to implement, Lab-on-chip, systems with large-scale sensor arrays.

The final target of this project is to design and fabricate a biochemical measurement system using chemical sensor, ISFETs and an electrical feedback system coupled with interface circuitry, in order to reduce nonlinear effect in the measurement. By feeding back the electrical signal to the chemical world using Sigma-Delta modulation, the measurement error and low frequency noise can be dramatically attenuated.

We've fabricated different chemical sensors with different structure and dimension, and investigated the drift and low frequency noise on these devices. Two types of circuits to enhance the measurement sensitivity and cancel the offset, has been proposed and designed. The components of Sigma-Delta feedback system has been realized in CMOS chip, and verified. The structure of measurement system has been designed, simulated and verified. The program to perform voltage to charge conversion has been designed and embedded into the test instruments. Initial tests have been performed to verify the components and program functionality. However the output is not the same as we expected.

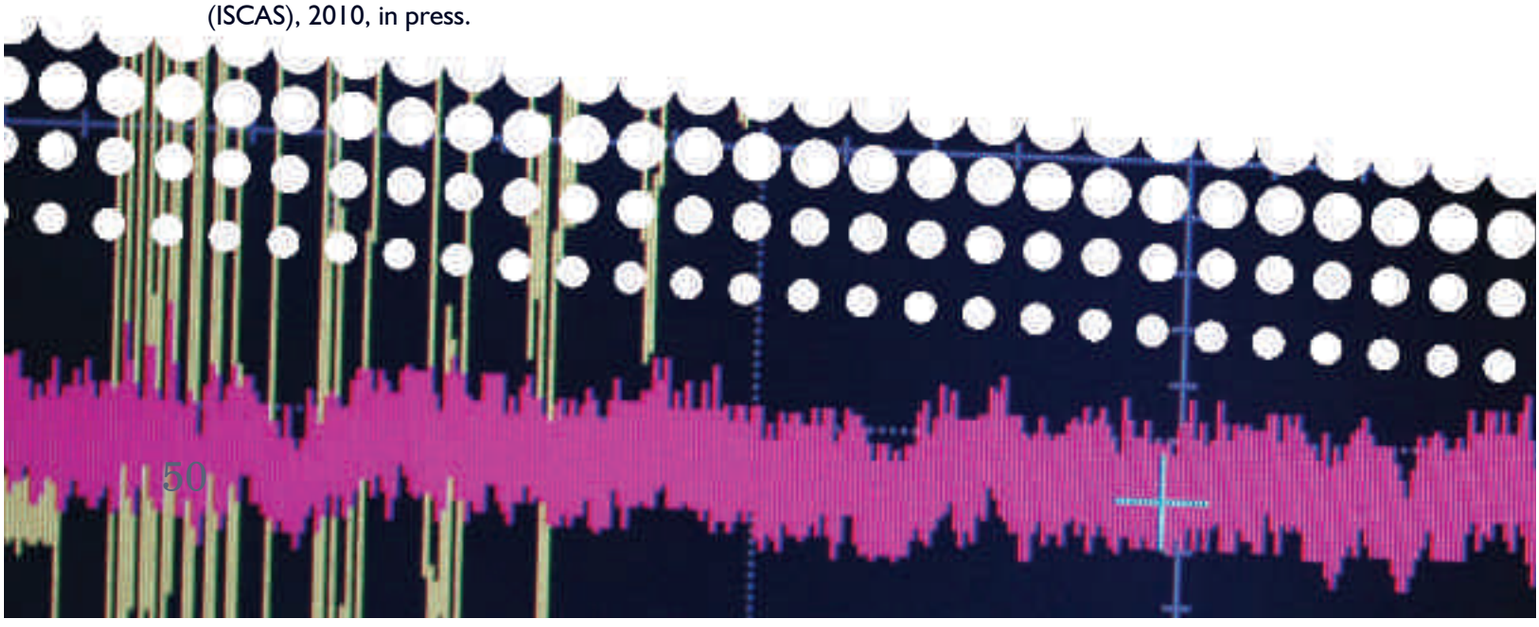
Currently, I'm focusing on the electrochemical interface between sensor and titrator, in order to extract correct compensation and PWM parameter for feedback system. Also further design of titrator is ongoing to give better coulometric titration performance. I'm also doing the experiments with titrator and feedback in order to reduce the noise and drift.

Key References

- P Berveld, "Thirty years of ISFETOLOGY", Sensor and Actuators B, Vol. 88, Issue. 1, pp. 1 – 20, 1 2003.

Recent Publications

1. Y Liu, P Georgiou, TG Constandinou, D Garner, C Toumazou, "An Auto-Offset-Removal circuit for chemical sensing based on the PG-ISFET", Proceedings of the IEEE International Symposium on Circuits and Systems (ISCAS), 2009.
2. Y Liu, C Toumazou, "An ISFET Based Sensing Array with Sensor Offset Compensation and pH Sensitivity Enhancement", Proceedings of the IEEE International Symposium on Circuits and Systems (ISCAS), 2010, in press.



9024 IMP AnnRep.indd 50 02/06/2010 16:03

LUI, Mr Kwok Wa

Thesis Topic: Energy Harvesting and Data Transmission system for Bio-implants using Non-traditional Antenna

Supervisor: Dr Antonio Vilches

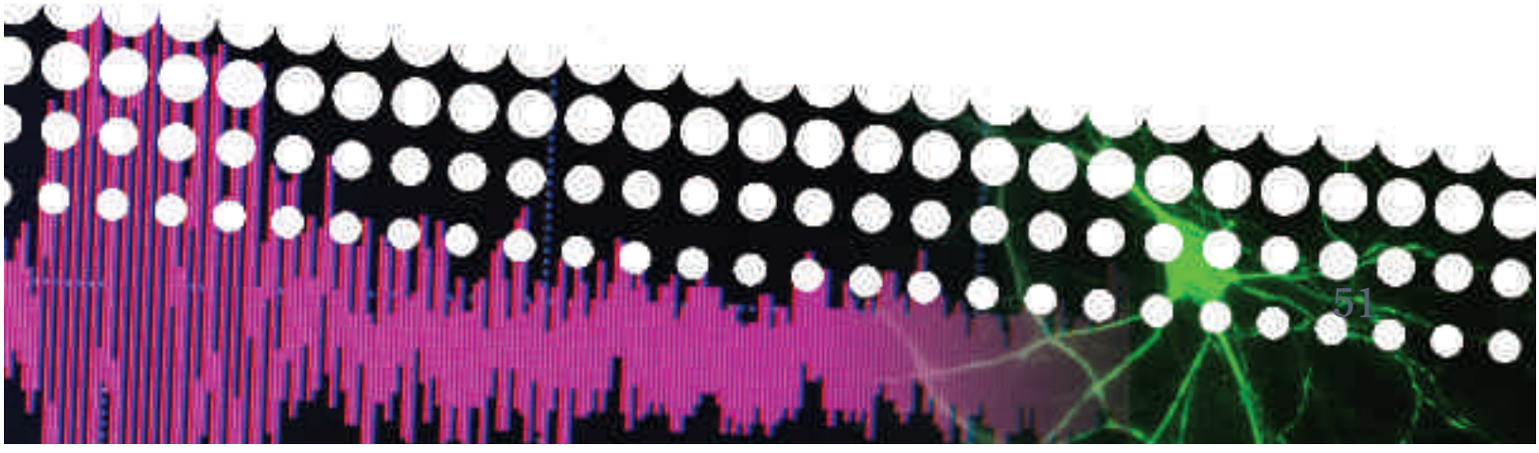
Funding: DNA Electronics Ltd.

This project will study the performance of the non-traditional antenna using conductive material for low-power medical device (IMD). In addition, we will investigate the application for the non-traditional antenna on energy harvesting for low-power operation [1] [2] [3]. A system will be built based on the non-traditional antenna and low-power electronics to transmit wirelessly data and/or energy to our bio-implant devices.

Our goal is to develop a wirelessly powered platform for real time body monitoring system without the need to change the battery because energy is recycled from the radiation of the environment or base station. By integrating the non-traditional antenna with state-of-the-art, low-power electronics, we can not only lower the system and maintenance cost but also increases the portability of our bio-implantable device.

Key References

1. T Paing, J Morroni, A Dolgov, J Shin, J Brannan, R Zane, Z Popovic, "Wirelessly-powered wireless sensor platform," European Microwave Conference, pp. 999 – 1002, 2007.
2. T Paing, J Shin, R Zane, Z Popovic, "Resistor Emulation Approach to Low-Power RF Energy Harvesting", IEEE Transactions on Power Electronics, Vol. 23, No. 3, pp.1494 – 1501, 2008.
3. EC Kohls, A Abler, P Siemsen, J Hughes, R Perez, D Widdoes, "A multi-band body-worn antenna vest", Proceedings of the IEEE Symposium on Antennas and Propagation, Vol.1, pp. 447 – 450, 2004.



9024 IMP AnnRep.indd 51 02/06/2010 16:03

MORRIS, Miss Christina

Thesis Topic: Investigating pancreatic alpha cell glucagon secretion

Supervisor: Professor Christofer Toumazou

Funding: Esmee Fairbairn Foundation and Winston Wong Centre for Bio-Inspired Technology.

Type 1 diabetes is a chronic condition in which the immune system attacks the insulin-secreting pancreatic beta cells. Insulin is a hormone that reduces blood glucose, preventing hyperglycaemia (high blood glucose).

Diabetic complications are correlated with hyperglycaemic events [1] and glucose variability [2] that result from inefficient treatment, and subsequently increases morbidity and mortality in Type1 diabetic individuals. It has been shown [3] that insulin-intensive treatments, such as the combination of a real time glucose sensor with a pump that delivers insulin, can improve blood sugar control. Common to these systems however is an increase in hypoglycaemic (low blood glucose) episodes [3]. The pancreatic hormone Glucagon acts to prevent hypoglycaemia by increasing low blood glucose. Knowledge of the mechanisms and processes by which glucagon is regulated within the alpha cells is unclear and inconsistent [4].

My research involves investigating pancreatic alpha cell glucagon secretion under different glucose and insulin conditions to build a model of glucagon regulation within the pancreas. This will assist artificial pancreas systems by allowing improved and more robust prevention of hypoglycaemia.

I am generating data using in vitro techniques on pancreatic mouse tissue called Islets of Langerhans in which the alpha and beta cells are located. This research includes the development of a perfusion system on a microscale that provides accurate, quantitative analysis of the dynamics of glucagon regulation.

Part of the project also involves the study of an intracellular enzyme adenosine monophosphate-activated kinase (AMPK). AMPK is found in all cells where it acts as a glucose sensor to help regulate low glucose levels. Using qualitative and quantitative techniques, the link between this enzyme's activity and glucagon secretion in alpha cells is studied.

Key References

1. M Brownlee, "Biochemistry and molecular cell biology of diabetic complications", Nature, Vol. 414, 2001.
2. F Moshin, M Craig, et al, "Discordant trends in microvascular complications in adolescents with type 1 diabetes from 1990 to 2002", Diabetes Care, Vol. 28, pp. 1974 – 1980, 2002.
3. DCCT Research Group, "The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus", NJEM, Vol. 329, pp. 977 – 986, 1993.
4. J Gromada, I Franklin, C Wolheim, "Alpha cells of the endocrine pancreas: 35 years of research but the enigma remains", Endocrine Reviews, Vol. 28, pp. 84 – 116, 2007.

9024 IMP AnnRep.indd 52 02/06/2010 16:03

PARASPEVOPOULOU, Miss Sivylla-Eleni

Thesis Topic: Ultra Low Power Implantable Platform for Next Generation Neural Interfaces

Supervisor: Dr Timothy Constandinou

External devices such as the electroencephalograph (EEG) record the general pattern of neuronal activity revealing the state of cognitive awareness. However the essential information, associated with sensation, thought, movement and act, is hidden in the electrical impulses, or spikes, produced by single neurons. In order to record the latest, a multiple electrode array must be inserted in the brain and to extract the useful information, signal processing is required. The goal of this project is to develop an implantable platform that will perform both the recording and processing. Potential applications include neuroscience basic research and neural prosthetics.

The two essential building blocks of the chip are the processing unit, which I am focusing on, and the wireless communication one. There are three main steps in processing the neural signals: spike detection, feature extraction and ultimately, spike sorting. Currently, the majority of implantable chips transmit raw data with few exceptions that include the spike detection stage; the rest of the stages are executed by off-line algorithms. The main reason is the power constraint 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 1C, major issue when dealing with valuable brain tissue.

Recent feasibility studies have proven that feature extraction and spike sorting can be implemented on hardware. The aim of my work is to design an all-inclusive platform that will severely reduce the amount of data to be transfer out of the brain, and thus the power dissipation of the communication unit. Elaborate algorithms perform very well in terms of accuracy; nevertheless their on-chip implementation can be quite power-hungry. We are seeking for the optimal compromise between complexity and accuracy. Already executed simulations in SIMULINK/MATLAB on analog low-power spike detection have given us encouraging results. Moreover, the group's expertise in delivering ultra-low power systems-on-chips reinforces our confidence in the development of this next-generation neural interface.

Key References

1. T Borghi, R Gusmeroli, A Spinelli, G Baranauskas. "A simple method for efficient spike detection in multiunit recordings," Journal of Neuroscience Methods, Vol. 163, pp. 176 – 180, 2007.
2. R Harrison, R Kier, B Greger, F Solzbacher, C Chestek, V Cilja, P Nuyujukian, S Ryu, K Shenoy, "Wireless neural signal acquisition with low-power integrated circuit," in Proceedings of the International Symposium on Circuits and Systems (ISCAS), pp. 1748 – 1751, 2008.
3. M Rizk, C Bossetti, T Jochum, "A fully implantable 96-channel neural data acquisition system", Journal of Neural Engineering, Vol. 6, pp. 1 – 14, 2009.
4. Z Zumsteg, C Kemere, S O'Driscoll, G Santhanam, R Ahmed, K Shenoy, T Meng, "Power Feasibility of Implantable Digital Spike Sorting Circuits for Neural Prosthetic Systems," IEEE Transactions on Neural Systems and Rehabilitation Engineering, Vol. 13, No. 13, pp. 272-279, 2005.

9024 IMP AnnRep.indd 53 02/06/2010 16:03

PESL, Mr Peter

Thesis Topic: Real-time intelligent smartphone platform for monitoring of Type 1 diabetes

Supervisor: Dr Pantelis Georgiou

Funding: Toumaz Technology Ltd

This research is part of the 'Artificial Pancreas' project, which aims to develop a novel closed-loop insulin delivery system for diabetes Type 1 patients centred around a silicon cell. The objectives are to develop a sensation-less glucose sensor, develop the silicon cell and provide a safe, accurate pump and then to integrate these components in a closed-loop system.

My research focuses on monitoring the patients' blood glucose profile and the wireless communication with a smartphone. Therefore, a real-time intelligent wireless platform is being developed. The system will receive patient glucose data from a continuous monitor, which will then be processed and transmitted efficiently for real time display of the subjects' glucose profile to a smartphone. In addition to this the system must be intelligent such that it predicts changes in blood glucose to give alarms of the event of hypoglycaemia in up to 30 minutes in advance as well is applying smoothing and fault detection filters to the sensor data and forecasting 10 minutes in advance to compensate for sensor lag. The platform will consist of a miniaturised PCB housing a microcontroller and an ultra low-power radio to communicate with the smartphone, which will display the data and run the algorithms. The microcontroller A/D will sample data from the glucose ensor, on which it will be filtered and then encoded for reliable transmission via the radio module.

Benefits: Patients will be able to keep track on their blood glucose profile in real-time and react on projected warnings provided by the system. Future work aims to develop a comprehensive mobile management tool for diabetes Type 1 patients.

Key References

1. N Oliver, P Georgiou P, D Johnston, et al, "A Benchtop Closed-loop System Controlled by a Bio-Inspired Silicon Implementation of the Pancreatic beta Cell", J. Diabetes Science and Technology, Vol. 3, pp. 1419 – 1424, 2009.
2. R Hovorka, "Continuous glucose monitoring and closed-loop systems", Diabetic Medicine, Vol. 23, No. 1, pp. 1 – 12, 2005.
3. P Georgiou, C Toumazou, "A Silicon Pancreatic Beta Cell for Diabetes", IEEE Transactions on Biomedical Circuits and Systems, Vol.1, No.1, pp. 39 – 49, 2007.

9024 IMP AnnRep.indd 54 02/06/2010 16:03

POOKAIYAUDOM, Mr Panavy

Thesis Topic: The Chemical Current Conveyor: Design, Development and Applications

Supervisor: Professor Christofer Toumazou

Funding: Royal Thai Scholarship

The ISFET is an extremely effective biomedical sensor and has been the subject of extensive development over more than 30 years [1]. Recent research work has focussed on development of integrated circuit sensors with an ISFET to form a biosensor microchip, generally with an on-chip operational amplifier to give the required analog system gain [2] [3]. In this research project a new approach is taken for an ISFET pH biosensor microchip, based on the integration of an ISFET input stage and an integrated current-conveyor type two, CCII+, [4], rather than the more common design which uses operational amplifier/s. We have called this new device concept the 'Chemical CurrentConveyor' because it exploits the very versatile CCII+ within the design, and the acronym CCCII+ reflects its origins.

Major advantages offered with this circuit topology are that the reference electrode can be grounded and feedback readily applied to the source of the ISFET, unlike other operational amplifier reported techniques where the ISFET forms part of the differential pair input stage and so feedback cannot be applied directly to the ISFETs source or gate [5]. Further advantages arise from using the CCII+ as the primary basis for the design, namely (i) it is a relatively straightforward circuit with a lower parts count than an operational amplifier, (ii) it does not require frequency compensation and is therefore inherently stable, and (iii) finally it can readily be configured to provide an output directly proportional to the time integral or time derivative of pH, which can be exploited to advantage to produce a measurement of buffer index, , of the sampled solution in addition to pH. Also, extending the design by adding an output voltage buffer creates the potential to produce a currentfeedback operational amplifier (CFOA) architecture to enable overall feedback to be applied, thus producing an accurate closedloop gain. A multitude of linear and nonlinear computational functions can be produced and so the concept can be used for excellent real time process bio chemistry.

Key References

1. P Berveld, "Thirty years of ISFETOLOGY", Sensor and Actuators B, Vol. 88, Issue. 1, pp. 1 – 20, 1 2003.
2. RA Rani, O Sidek, "ISFET pH Sensor characterization: towards Biosensor Microchip Application," IEEE Tencon 2004, Vol. 4, pp. 21-24, 2004.
3. L Shepherd, P Georgiou, C Toumazou, "A Novel voltageclamped CMOS ISFET sensor interface," IEEE Proc. ISCAS 2007, pp. 3331-3334, 2007.
4. Sedra, K Smith, "A second-Generation Current Conveyor and its Applications," IEEE Trans on Circuit Theory, Vol.17, pp.132-134, 1970.
5. F Chan and MH White, "Characterization of surface and buried channel ion sensitive field effect transistor (ISFET's)," IEDM Tech. Dig, pp. 651-653, 1983.

Recent Publications

1. P Pookaiyaudom, C Toumazou, FJ Lidgey, "The Chemical Current-Conveyor: a new microchip biosensor," IEEE Proc. ISCAS 2008, pp. 3166-3169, 2008.
2. P Pookaiyaudom, et al, "Chemical Current Conveyor (CCCII)…", Sensors and Actuators B: Chemical, 2010.

9024 IMP AnnRep.indd 55 02/06/2010 16:03

SANNI, Mr Ayodele

Thesis Topic: A 3-Tier Bio-Implantable Sensor Monitoring Platform

Supervisor: Dr Antonio Vilches

Funding: Engineering and Physical Sciences Research Council (EPSRC)

A major hindrance to the advent of novel, potentially bio-implantable sensor technologies is the urgent need for a reliable data communications platform capable of continuously monitoring deeply implanted medical devices. A generic and reliable bio – implantable communications platform (electronics network) capable of remotely and wirelessly monitoring deeply implanted sensors is proposed.

The proposed solution employs a three-tier approach to transfer energy wirelessly to the implant device and consequently transmit sensed data captured by the energized implant to the outside.

Energy, from an externally worn battery, is wirelessly transferred through the skin by a single pair of inductor coils via inductive coupling to the subcutaneous ultrasound transponder –removing the need to place batteries on any implanted circuitry.

The abundant liquid medium in a living bio-system (humans: 60 – 70% volume) presents an efficient "ready-made transmission medium for ultrasonic signals. Sensed data from the implanted medical device (comprising the bio-sensor with an Ultrasonic transducer) is modulated into digital format and transmitted as a series of ultrasonic pulses, which propagate easily through the medium.

The pulsed data is then detected by a circuit on the subcutaneously implanted ultrasound transponder and retransmitted by the same coil pair via amplitude modulation to the externally worn transponder that would then retransmit the data to air via radio frequencies to be received by a hand-held personal device, laptop computer.

Key References

1. K Malasri, L Wang, "Securing wireless implantable devices for healthcare: ideas and challenges," IEEE Communications Magazine, Vol. 47, No.7, pp. 74 – 80, 2009.
2. D Panescu, "MEMS in medicine and biology," IEEE Engineering in Medicine and Biology magazine, Vol. 25, No.5, pp.19-28, 2007.
3. U Jow, M Ghovanloo, "Design and optimization of printed spiral coils for efficient transcutaneous inductive power transmission," IEEE Transactions on Biomedical Circuits and Systems, Vol.3, No. 2, pp. 339 – 347, 2007.
4. S Arra, J Leskinen, J Heikkila, J Vanhala, "Ultrasonic power and data link for wireless implantable applications," Wireless Pervasive Computing, 2nd International Symposium on, pp.259 – 262, 2007.

Recent Publications

- A Vilches, A Sanni, C Toumazou, "Single coil pair transcutaneous energy and data transceiver for low power bio-implant use", IET Electronics Letters, Vol.45, No. 2, pp. 27-728, 2009

9024 IMP AnnRep.indd 56 02/06/2010 16:03

SAREMI-YARAHMADI, Mr Siavash

Thesis Topic: Radio Frequency Inductive Sensors for the Evaluation of the Conductivity of Liquid Samples

Supervisor: Professor Christofer Toumazou

The main aim of this research is to employ planar inductors to deploy a contact free eddy current sensor that uses RFID technology for its readout unit. The sensor is used for detection of change in the conductivity of a liquid sample when a particular reaction takes place. This leads to a modification free and tag free sample analysis method; hence no external material is added to the solution in order to amplify the effects of a particular reaction or species. Different packaging materials are also used and their effect on the properties of the inductive coil is being investigated. The interactions between the packaging materials and the solution under test are also of great interest, and the degree of exposure of the packaging to different liquid sample and its effect on the overall response of the sensor is being studied.

Near field coupling of the sensor with an antenna for RFID readout will be investigated. Optimum designs for maximum sensitivity of the sensor to the RFID readout unit and changes in the sample under test will be found. Finite Element (FE) analysis will be used in order to model the behaviour of the sensor and its RFID response and the solutions obtained using FE, alongside experimental data, will be used to optimize the design. The coupling between multiple sensors with one another and with the readout antenna will also be investigated to find the optimum distance and readout sensitivity for closely packed sensors.

This research has applications in the fields of proteomics, DNA amplifications and gastric juice monitoring. As part of this research, evaluation studies are taking place to exploit all features offered by this sensory system for each of the respective applications.

Key References

1. JE Pandolfino et al. “Ambulatory Esophageal pH Monitoring Using a Wireless System” The American J. Gastroenterology, 2003.
2. SE Woodard and BD Taylor, “Measurement of multiple unrelated physical quantities using a single magnetic field response sensor”, Meas. Sci. Technol., 2007.
3. G Laurent et al. “DNA Electrical Detection Based on Inductor Resonance Frequency in Standard CMOS Technology”, IEEE, 2003.

Recent Publications

- S Saremi-Yarahmadi, OH Murphy and C Toumazou, “RF Inductive Sensors for Detection of Change in the Ionic Strength and pH of Liquid Samples”, Proceedings of the IEEE International Symposium on Circuits and Systems (ISCAS), 2010, in press.

9024 IMP AnnRep.indd 57 02/06/2010 16:03

SERB, Mr Alexandru

Thesis Topic: A bidirectional power/data transfer platform based on electro-optical effects in standard CMOS

Supervisor: Dr Timothy Constandinou

Funding: Engineering and Physical Sciences Research Council (EPSRC)

This project aims to develop the necessary technology that will enable integrated circuits to communicate between themselves and with the outer environment wirelessly. This will be achieved by means of optical interconnects, which shall, however, not be physical objects but rather consist of dedicated receiver and transmitter areas on the integrated circuit.

A successful finish to the project will be the fabrication of such communications system on an IC that can perform a practical task. More specifically, the aforementioned IC must be able to receive data and power wirelessly, process the data in, and transmit the data out also wirelessly.

The use of such technology would be extremely wide ranging. Although originally conceived with applications in microfluidics, where sensor ICs currently need to be planarised before use a problem eliminated by this technology, other applications may include 3D, modular IC design. In the latter application ICs will be manufactured in a fractured form (e.g. different modules that do different tasks rather than the entire IC together) and subsequently fitted together much like a large 3D puzzle. The advantage of such technique is that the typical problem whereby if any part of the entire IC is dysfunctional, it must be thrown away, suddenly disappears. Moreover, there is hope that future lab experiments in the framework of this project shall demonstrate that this method of communication is more robust against noise. Finally, it is another building block in the large edifice of optoelectronics, which is likely to be the next radically different generation of computers.

At the moment, and to my best of knowledge, there is nobody attempting to build such system, however the optical properties of silicon and other semiconductors are being closely studied. People around the globe have studied the fundamental properties of silicon [1] [2], attempted to use it as a switchable waveguide [3] and even attempted to make it emit light efficiently with various degrees of success [4], not to mention the extremely wide variety of publications on silicon solar cells. As such, this project integrates well in a solidly understood part of physics and an active, hot research area.

Key References

1. RA Soref et al., “Electro optical effects in silicon”, Vol. 23, No. 1, IEEE Trans. Quantum Electr., pp 123 – 129, 1989.
2. RA Soref, “Silicon-based optoelectronics”, Vol. 81, No. 12, Proc. of the IEEE, pp 1687 – 1706, 1993.
3. A Cutollo et al., “Silicon Electro-Optic Modulator Based on a Three Terminal Device Integrated in a Low-Loss Single-Mode SOI Waveguide”, Vol. 15, No. 3, Journal of Lightwave technology, pp. 505 – 518, 1997.
4. M Milosavijevic et al., “Optimising dislocation-engineered silicon light-emitting diodes”, Applied Physics B, 2006.

9024 IMP AnnRep.indd 58 02/06/2010 16:03

THANAPITAK, Mr Surachoke

Thesis Topic: Towards a Bionics Chemical Synapse

Supervisor: Professor Christofer Toumazou

Funding: Royal Thai Scholarship

The term bionic was formed from "biology" and "electronics". Nowadays, there are various attempts inspired by this term to produce devices which have the same function as a biological system. A synapse is one of the crucial parts in the communication path between neurons. The operation of the central and peripheral nervous system could not be carried out without it.

This project presents an analogue current mode VLSI circuit which implements four particular receptors of the chemical synapse: AMPA, NMDA, GABAA and GABAB. The dynamics of the postsynaptic receptor is mathematically implemented in a CMOS current mode circuit.

Furthermore, with chemical sensor advancement, the possibility of realising a complete synapse which models the non-linear electrochemical behaviour of the synapse is now feasible. Therefore, this work also involves a study in sensors which can sense the fast chemical stimuli required for realising a chemical synapse. Specifically, an ISFET sensor, reported as a sub-millisecond sensor, is used in this work. In order to understand an ISFET's speed capabilities, an experimental setup involving rapid titration is investigated.

Key References

- P Berveld, "Thirty years of ISFETOLOGY", Sensor and Actuators B, Vol. 88, Issue. 1, pp. 1 – 20, 1 2003.

Recent Publications

- S Thanapitak, C Toumazou, "Towards a bionic chemical synapse", Proceedings of the IEEE International Symposium on Circuits and Systems (ISCAS), pp. 677 – 680, 2009.

9024 IMP AnnRep.indd 59 02/06/2010 16:03

WONG, Mr Winston Jr

Thesis Topic: Towards ISFET based DNA logic for rapid nucleic acid detection

Supervisor: Professor Christofer Toumazou

This work investigates a novel configuration for Ion sensitive Field Effect Transistors (ISFETs) to be used as a threshold-based logic function for Single Nucleotide Polymorphism (SNP) detection. ISFET-based inverters are used as reaction threshold detectors to convey the chemical reaction level to a logic output once a threshold has been reached. Using this, DNA logic functions are derived for nucleotides allowing identification of multiple SNPs. This logic is extended to facilitate a combination of SNPs, deriving gates, which give a simple Yes/No answer to their presence. A DNA logic 'NOR' gate is derived for an application where two SNPs need to absent in order to determine drug delivery.

In the recent decades ISFETs have advanced to the point were we can fabricate them in a commercially available CMOS technology and therefore integrate them with other circuits on a single chip. Use of an n-type ISFET with its complimentary p-type MOS equivalent results in a chemical inverter which switches once the reaction occurring on the ISFET causes its threshold voltage to exceed a certain level. When used for nucleic acid detection by monitoring a base pair match during primer extension, this acts as a DNA logic function, giving a Boolean output from chemical input. This is used to give a Yes/No answer when looking for a particular SNP in a cheap, rapid and reliable way. Furthermore, DNA logic blocks can be combined enabling the detection of multiple SNPs and therefore the combination of different logic outputs.

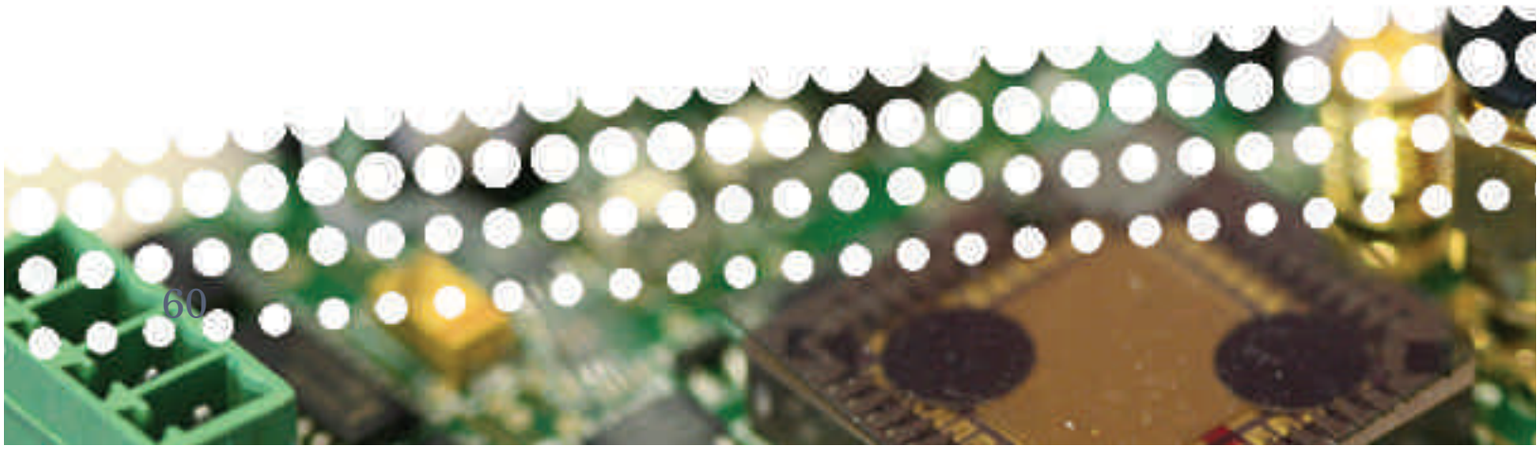
Some SNPs are linked to drug metabolism and therefore can be used to predict whether a patient should take a high or low dose of certain prescription drugs. In the case of warfarin, a blood-thinning agent, a high dose in people with certain SNPs could cause excessive bleeding. Two SNPs in particular have been found to correspond with lower dose requirements, due to the fact that they indicate slower metabolism of the drug. These SNPS are on the "CYP2C9*2" and "CYP2C9*3" alleles, and a patient with either orboth of these SNPs will require a lower dose of warfarin.

Key References

1. WH Koch, "Technology Platforms for Pharmacogenomic Diagnostic Assays," Nature Rev. Drug Discovery, Vol. 3, No. 9, pp. 749 – 761, 2004.
2. M Amos, "Cellular Computing", Oxford University Press, 2004.
3. AC Syvanen, "Toward genome-wide SNP genotyping", Nature Genetics, Vol. 37, 2005.

Recent Publications

1. W Wong Jr, P Georgiou, L Shepherd, C Toumazou, "Towards ISFET based DNA logic for rapid nucleic acid detection", Proceedings of IEEE Sensors Conference, 2009.
2. W Wong Jr, P Georgiou, CP Ou, C Toumazou, PG-ISFET based DNA-logic for reaction monitoring, IET Electronics Letters, Vol. 46, No. 5, 2010.
3. DM Garner, H Bai, P Georgiou, TG Constandinou, S Reed, LM Shepherd, W Wong Jr, KT Lim, C Toumazou, "A Multichannel DNA SoC for Rapid Point-of-Care Gene Detection", Proceedings IEEE International Solid-State Circuits Conference (ISSCC), Pages: 492–494, 2010.



9024 IMP AnnRep.indd 60 02/06/2010 16:03

WOODS, Mr Stephen

Thesis Topic: Swallowable Capsule for Microscale Diagnosis and Targeted Therapy

Supervisor: Dr Timothy Constandinou

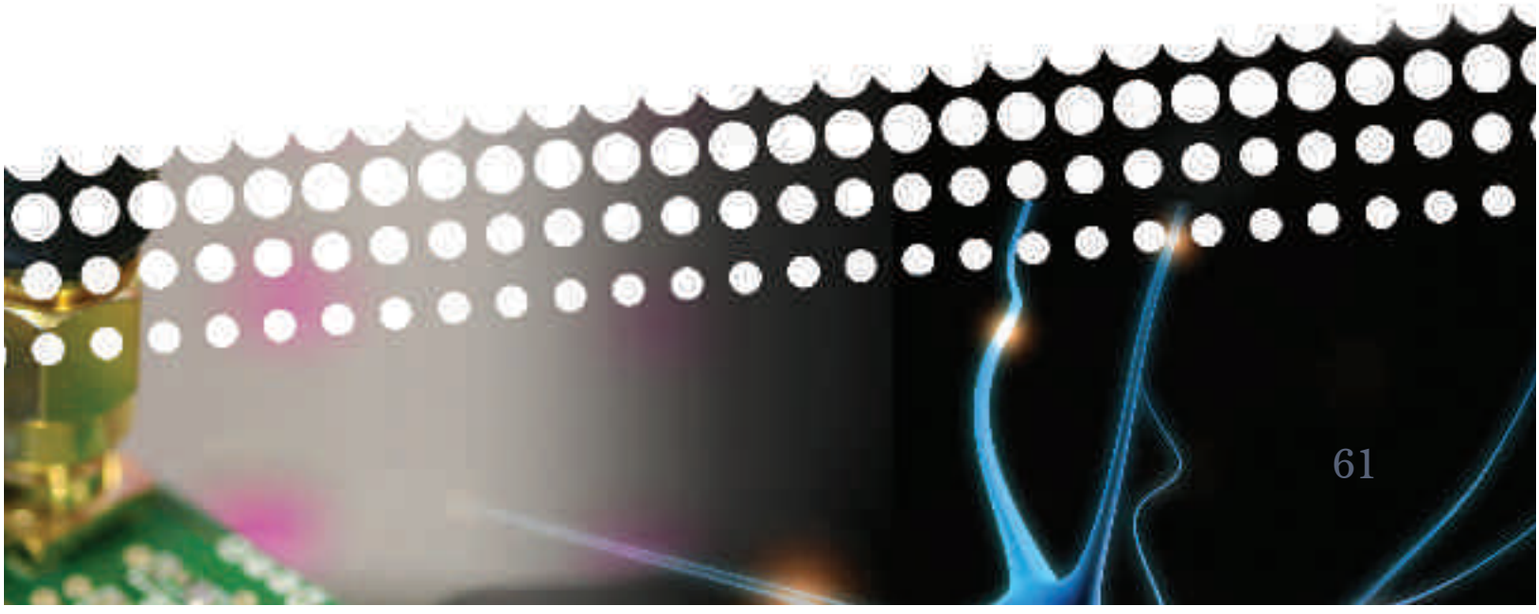
Capsule endoscopy is widely used in medicine for imaging of the gastro-intestinal tract.The limitation of these systems is that they do not offer the ability to perform therapy to the affected areas leaving only the options of either administering large quantities of drugs or surgical intervention. Although there are minimally invasive surgical techniques which can be performed that are less traumatic for the patient, minimally invasive surgery (MIS) can present problems for the surgeon. One such problem is limited access, which impacts the surgeon's ability to manipulate the tools limiting the number of degrees of freedom (DOF) the tools can perform through. The problem of accessibility in MIS can potentially be overcome by the application of a micro robot [2]. Introducing a micro robot into the body through a natural orifice can offer greater DOF to the surgeon who can now perform therapy remotely using the micro robot.

The aim of the project will be to develop a swallowable micro robotic platform which has novel functionality such as a targeted drug delivery system combined with constant pH monitoring and an onboard CMOS camera. The first stage of the project which is underway is to develop the drug targeting system.

There will be great benefits to patients and surgeons if a system for diagnosing and treating patients remotely with a micro robot could be realised [3]. The onboard camera would allow the surgeon to visibly target a site with the drug delivery system which when operated would allow a lower dose of medication to be delivered this in turn could improve the patient's recovery time.

Key References

1. GD Meron, "The development of the swallowable video capsule (M2A)," Gastrointest Endosc, Vol. 52, pp. 817 – 9, 2000.
2. MC Carrozza, P Dario, LPS Jay, "Micromechatronics in surgery," Transactions of the Institute of Measurement and Control, Vol. 25, pp. 309 - 327, 2003.
3. K Twomey, JR Marchesi, "Swallowable capsule technology: current perspectives and future directions," Endoscopy, Vol. 41, pp. 357-62, 2009.



9024 IMP AnnRep.indd 61 02/06/2010 16:03

WOODS, Miss Virginia M

Thesis Topic: The Role of the Electrode-Electrolyte Interface in the Design of Stimulus Waveforms for Selective Nerve Activation

Supervisor: Professor Christofer Toumazou

Funding: The Whitaker Foundation and Esmee Fairbairn Foundation

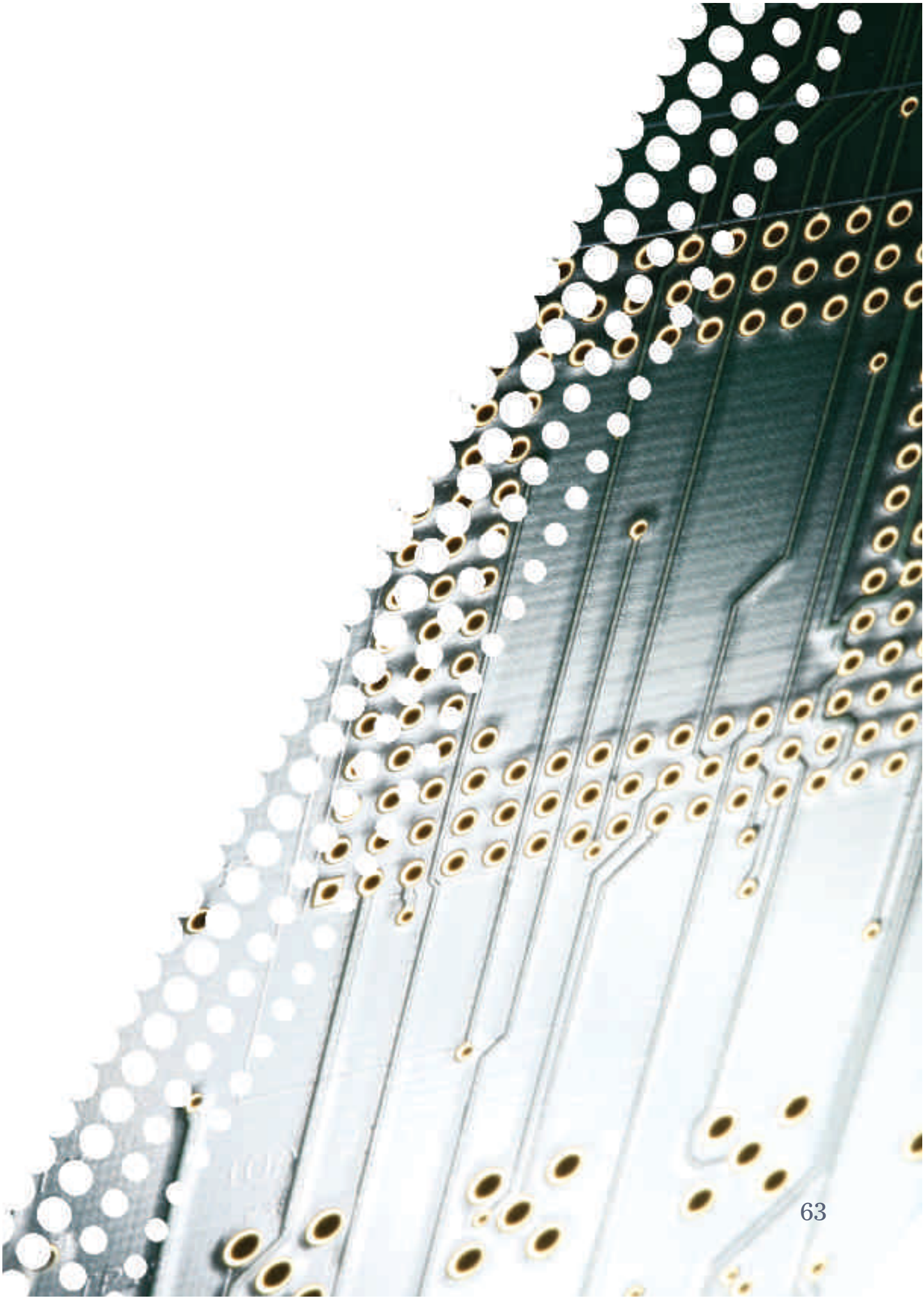
Stimulation with cuff electrodes has been used as a part of several neurorehabilitative applications, such as upper and lower limb prosthetics, diaphragm pacing, bladder control and chronic pain management. Excitation of the nervous tissue relies on the injection of charge from the electrode into the extracellular fluid, where it then diffuses towards the nerve and depolarizes the cellular membranes. The stimulus signal can be realised either by applying a voltage across the stimulus electrodes ("voltage-mode") or by injecting a current to flow between them ("current-mode"). In many clinical stimulators, waveform specifications are defined in the current mode as current stimulation allows for a controlled amount of charge injection irrespective of changes in electrode-tissue impedance [1]. However, not all of the charge injected during a stimulus pulse is available for neural activation because of the biophysical processes involved in translating the charge carrier [2]. Charge injection is safe and reversible when current flows through a surface capacitance or through the chemical reactions within a material-specific potential range [3]. Irreversible surface reactions while stimulus pulsing alters the surface properties of the electrode resulting in metal dissolution and adverse by-products which can damage to the surrounding tissue [3, 4]. Failure to consider the charge losses at the electrode-electrolyte interface leads to reduced biocompatibility, shorter implant lifespan and ultimately cell death.

This work aims to reverse engineer stimulus waveforms by circumventing the harmful surface processes and interfacial charge losses. We have developed an equivalent electrical model of the electrode-electrolyte impedance based on the electrode's surface chemistry, which is appropriate for implantable stimulation conditions. Simulations, stimulation tests in extracellular saline and electrophysiology experiments have shown that the use of these novel stimulus waveforms results in improved electrode longevity without compromising targeted nerve activation.

Key References

1. WM Grill, JT Mortimer, "Stimulus waveforms for selective neural stimulation," IEEE Eng Med Biol Mag, Vol. 14, pp. 375 – 385, 1995.
2. DR Merrill, M Bikson, JGR Jefferys, "Electrical stimulation of excitable tissue: design of efficacious and safe protocols," J Neurosci Methods, Vol. 141, pp. 171-1932005.
3. HP Schwan, "Alternating current electrode polarization," Biophysik, Vol. 3, pp. 181-201. 1966.
4. SB Brummer, MJ Turner, "Electrochemical considerations for safe electrical stimulation of nervous system with platinum electrodes," IEEE Trans Biomed Eng, Vol. 24, pp. 59 – 63. 1977.
5. TL Rose, LS Robblee, "Electrochemical guidelines for selection of protocols and electrode materials for neural stimulation", in Neural Prostheses, Agnew WF and McCreery DB, Eds. Englewood Cliffs, NJ: Prentice Hall, pp. 25 – 66, 1990.

9024 IMP AnnRep.indd 62 02/06/2010 16:03



9024 IMP AnnRep.indd 63 02/06/2010 16:03

Centre for Bio-Inspired Technology
Institute of Biomedical Engineering
Imperial College London, South Kensington, London SW7 2AZ

T 020 7594 0701
F 020 7594 5196
E bioinspired@imperial.ac.uk
W www.imperial.ac.uk/biomedeng/research/bioinspired

9024 IMP AnnRep.indd 64 02/06/2010 16:03