The 6th UK and RI Postgraduate Conference in Biomedical Engineering and Medical Physics

14th—16th August, IET Teacher Building, Glasgow
Proceedings of the

6th UK & Republic of Ireland Postgraduate Conference in Biomedical Engineering and Medical Physics

PGBIOMED 2011

14th – 16th August 2011

IET Teacher Building, Glasgow

Editors: Abeer Syed and Christopher Hamilton
ORGANISING COMMITTEE

William Sandham (Faculty Advisor)  
Scotsig/University of Strathclyde  
Email: w.sandham@scotsig.co.uk

Christopher James (Faculty Advisor)  
Univerisity of Warwick  
Email: e.james@warwick.ac.uk

Natalie Nimmo (Conference Chair)  
University of Strathclyde  
Email: natalie.nimmo@strath.ac.uk

April Dunham (Conference Vice-Chair)  
University of Strathclyde  
Email: april.dunham@strath.ac.uk

Christopher Hamilton (Publicity Chair)  
University of Strathclyde  
Email: christopher.hamilton@strath.ac.uk

Matthew Banger (Publicity Vice-Chair)  
University of Strathclyde  
Email: matthew.banger@strath.ac.uk

Alejandra Aranceta-Garza (Social Programme Chair)  
University of Strathclyde  
Email: alejandra.aranceta-garza@strath.ac.uk

Claire Harrison (Exhibitions Chair)  
University of Strathclyde  
Email: claire.harrison@strath.ac.uk

Abeer Syed (Technical Programme Chair)  
Glasgow University  
Email: a.syed.1@research.gla.ac.uk

Colm Craven (Finance Chair)  
Glasgow University  
Email: ccraven@eng.gla.ac.uk

Kit Mei-Tan (Finance Vice-Chair)  
University of Strathclyde  
Email: kit.tan@strath.ac.uk

Copyright © 2011

Edited by Abeer Syed and Christopher Hamilton

No partial or complete copy of the material in this proceeding is allowed without specific permission of the publishers and authors.
FOREWORD

Welcome to PGBioMed 2011, the 6th Postgraduate Biomedical Engineering and Medical Physics event in the UK and Republic of Ireland. The organising committee are delighted to bring what has proven to be a highly successful event in the past to Glasgow in 2011.

The idea behind PGBioMed is to give postgraduate students the opportunity to share their work with fellow students in similar fields of study and at similar stages of research. We encourage you to share your ideas and learn from those around you, the links you forge here may benefit you in years to come and grant you an opportunity to interact with tomorrow’s leading specialists.

We aim to provide a friendly and relaxed environment for early stage researchers to present their work. As such we find ourselves situated within the IET Teacher building here in Glasgow, supported by the three Glasgow universities (Glasgow, Strathclyde and Glasgow Caledonian). We hope you will find your surroundings comfortable and feel at ease during the event.

We are very pleased to welcome Prof Jon Cooper from Glasgow University and Mr Bill Spence from the National Centre of Prosthetics and Orthotics at Strathclyde University, each of whom will give an invited presentation. Our speakers all have a wealth of experience in biomedical engineering and medical physics and will bring practical insights into the work they have undertaken.

We are also delighted to welcome Mr Andrew Whitton from Boots Ltd, who will give an invited talk on making the jump into industry after completing an EngD in Bioengineering at the University of Strathclyde.

We are very grateful to all our sponsors for their generosity: IEEE EMBS UK and RoI chapter and IEEE EMBS, the IET Healthcare Professional Network, Vascutek, the University of Strathclyde, in particular Prof. Bernard Conway, the University of Glasgow, in particular Prof. John Cooper and Glasgow Caledonian University, in particular Prof. Malcolm Granat. The help and support given by the reviewers was also essential and is also acknowledged. I am grateful to the committee who has worked tirelessly to make this event enjoyable for all concerned.

I hope that you will enjoy your time in Glasgow and more importantly gain something from your experience, be that information or inspiration.

Prof Christopher J. James
Chairman IEEE UKRI Section
GUEST SPEAKER

Prof. Jonathan M. Cooper

Professor Jon Cooper holds the Wolfson Chair in Bioengineering. He has developed a range of technologies associated with Lab-on-a-Chip for diagnostics, cell measurements and proteomics. The primary focus of his work has been the demonstration of the analytical advantages of studying biological systems at the micro- and nanoscale. His work is recognised by many invited/plenary lectures at leading conferences including, including most recently, Microfluidics and Nano-fluidics (2008), the European Congress of Lab-on-a-Chip (2009), micro-Flu (Toulouse, 2010), European Congress of Lab-on-a-Chip (Dublin, 2009) and Asia Pacific Congress on Lab-on-a-Chip (Singapore, 2011). He has published more than 180 research papers and 15 refereed books, book chapters and reviews, in the field. He is currently on the International Advisory Panel for Lab-on-a-Chip. He was elected as a Fellow of the Royal Society of Edinburgh in 2001 and a Fellow of the Royal Academy of Engineering in 2004.

GUEST SPEAKER

Mr. Andrew Whitton

Andrew Whitton is the Medical Devices Advisor for a leading international pharmacy-led health and beauty group, Alliance Boots. He has technical and regulatory responsibility for in excess of 300 medical devices in the recently launched Boots Pharmaceuticals brand, which has the widest range of healthcare products in the UK. He has worked to develop over 50 of these products including the Allergy Relief Device. Andrew has recently completed research for his EngD in Medical Devices at the University of Strathclyde. The focus of his work was the development of experimental models for testing vascular graft materials which received recognition at the University of Strathclyde’s annual Research Day in 2009. He subsequently presented his research at two international conferences in 2010; ASME Biomed and the Macro World Polymer Congress.
GUEST SPEAKER

Mr. Bill Spence

Bill Spence is a State Registered Prosthetist/Orthotist who spent most of his career working in the Bioengineering Unit of the University of Strathclyde as a member of Academic staff. He also spent some time as a lecturer in the Norwegian School for prosthetics and orthotics. His research interests lie predominantly, but not exclusively, in the field of lower limb amputee work and pathological gait. He has been the recipient of several awards for his work including the ISPO George Murdoch medal.

Some time as head of prosthetic research for the commercial company Chas. A Blatchford & Son and a period of work in the USA provided sufficient spark for him to establish a company in Scotland to supply the NHS with a prosthetic service in the late eighties.

He now owns and operates the only private, prosthetic company in Scotland providing medico-legal services and more importantly ‘high-end’ prosthetic care to many amputees.
<table>
<thead>
<tr>
<th>Page No.</th>
<th>Platform Session 1.1</th>
</tr>
</thead>
</table>
| 1       | Modelling Patient Vital-Sign Deterioration Trajectories using Bayesian Inference  
S. Khalid, D. A. Clifton, and L. Tarassenko |
| 2       | Low Cost Diagnostic Device using Mobile Phone Technologies  
Y. Bourquin, J. Reboud, R. Wilson, Y. Zhang and J.M. Cooper |
| 3       | Augmented Reading Utilizing Edge Detection for the Visually Impaired  
| 4       | Highly-Curved Microchannel for Particle Separation  
C. Wang and Y. Ventikos |

**Poster Session 1**

<table>
<thead>
<tr>
<th>Page No.</th>
<th>Poster Session 1</th>
</tr>
</thead>
</table>
| 5       | Global Health Initiative through EWH-Oxford Student Organization  
B. Joachim, G. Milandri, A. Raghu, S. Fathima and G. D. Clifford |
| 6       | Determination the Age of Saliva Stain using RT-PCR  
M. Alrowaithi and N. Watson |
| 7       | Development of a Microfluidic Biochip for Absorption, Distribution, Metabolism and Excretion Toxicology Studies (ADME-Tox)  
N. Macdonald and J. M. Cooper |
P. D. Dowd, J. O. Karolin, C. Trager-Cowan, D. J.S. Birch and W. H. Stimson |
| 9       | RNA Stability in Frozen/Thawed Clinical Samples  
O. M. Posada, R. J. Tate and M. H. Grant |
| 10      | The Total Design Method as Applied to pProsthetic Foot Design  
P. Connolly, A. Buis and S. Solomonidis |
| 11      | Miniature wireless deep-brain stimulation and eeg recording device for the treatment of cognitive deficits in schizophrenia  
R. Pinnell |
| 12      | Microrheological Study of Biopolymers using Optical Tweezers  
E. Chambers, M. Tassieri and J. Cooper |
Platform Session 1.2

13  A New Light in Amyloid Oligomerisation
M. Amaro, D. J. S. Birch and O. J. Rolinski

14  Design of a Shoe Platform to Simulate Ground Reaction Force
J. Fang and A. Vuckovic

15  Local Pressure Fluctuations in an Occluded Artery
O. Korolkova, J. Alastruey, A. Lowe, J. E. Davies, A. D. Hughes, K. H. Parker and J. H. Siggers

16  Breathing Pattern Detection for an Abdominal Functional Electrical Stimulation System for Tetraplegics
E. J. McCaughey, A. J. McLachlan and H. Gollee

Platform Session 1.3

17  Atomic Force Microscopy of Bovine Articular Cartilage
M. Austin, A. Herbert, R. Black and P. Riches

18  Inhalation Drug Delivery using Surface Acoustic Wave Nebulisation
M. H. Ismail, J. Reboud, R. Wilson and J. M. Cooper

19  Interaction of Antimicrobial Peptides with Biomimetic Membranes by Broadband Optical Tweezer Microrheology
D. Paterson

20  Patient Oriented Electrochemically Structured Titanium Implants
J. Varia, S. Roy, J. Portoles, A. McCaskie and M. Birch

Platform Session 2.1

21  Investigating Core Nets and Stability of Periodic Random Boolean Networks
Yanika Borg

22  A Multi-Paradigm Modelling Framework to Capture Dynamic Reciprocity
H. Kaul, Z. Cui and Y. Ventikos

23  Improved Diagnostics for Human African Trypanosomiasis
C. Kremer

24  Chemically Modified Scaffolds for Primary Hepatocytes
C. Hamilton, R. V. Ulijn and M. H. Grant
Platform Session 2.2

25 Nano-Scale Hydrogels for Stem Cell Differentiation: The Influence of Mechanical Stimuli on Cell Behaviour and Function
V. Jayawarna, M. J. Dalby, R. V. Ulijn

26 An Investigation into the Compatibility of 5 Potential Binders for the Production of Artificial Bone Scaffolds
A.F.L. Dunham, X.T. Yan and M. H. Grant

27 Fabrication of 3D High Throughput Cell Screening Topographies using Plasma Polymerized Gradients as a Secondary Etch Mask
P. M. Reynolds, R. H. Pedersen and N. Gadegaard

28 Spectrometer-on-Chip for Fluorescence Bio-Sensing

Poster Session 2

29 Saw-ing into Cells: Porating Cells with Surface Acoustic Waves
S. E. Thurlow, J. Reboud, R. Wilson and J. M. Cooper

30 Investigating Ground Contact Information for use in Neuro-Prosthetic Control of FES Assisted Gait in Patients with Spinal Injuries
C.A Macleod, B.A Conway and B. Porr

31 The Effects of Transcranial Stimulation on Enhanced Physiological Tremor: A Pilot Study
P. Axford, H. Lakany and B. Conway

32 Micropolar Properties of Bone
J. Frame, M. Wheel and P. Riches

33 A Combined AFM and Immunofluorescence Study of Cell Elasticity as Affected by Topography
C. Fyfe, G. McPhee, M. Dalby, M. Riehle and H. B. Yin

34 Characterisation of Metal Nonoparticles for the Development of a Novel Immunocontraceptive Device
N. Nimmo, O. Sutcliffe, A. B. Mullen and V. A. Ferro

35 Microfluidic Devices for Single Cell Division and Migration
M. Chanasakulniyom, A. Glidle and J. M. Cooper

36 Shaping Hydrodynamic and Acoustic Forces for Fluid Manipulation using Microstructured Arrays
L. A. Alvarez and J. M. Cooper
Platform Session 2.3

37  Development of a Reinforced Synthetic Heart Valve for Percutaneous Delivery
    M. Rozeik

38  Droplet-Based Microfluidic System for Intracellular Protein Quantification
    C. Martino, M. Zagnoni, M. E. Sandison, M. Chanasakunyiyom, A. R. Pitt and J. M. Cooper

39  A Non-Invasive System for Real-Time Detection and Treatment of Sleep Apnea Episodes
    A. M. Aird and W. Sandham

40  Patient Specific Modelling of the Hybrid Procedure: The Clinical Need & Challenges in using Patient Specific Data
    A. Young, M. Danton, S. McKee and T. Gourlay
MODELLING PATIENT VITAL-SIGN DETERIORATION TRAJECTORIES USING BAYESIAN INFERERENCE

Sara Khalid¹, David A. Clifton¹, and Lionel Tarassenko¹

¹Institute of Biomedical Engineering, Dept. of Engineering Science, University of Oxford, OX3 7DQ, U.K.

Abstract – Vital signs recorded at the hospital bedside manually by clinical staff are key indicators of patient physiology and may be used to track patient deterioration. The low frequency of vital-sign observations by clinical staff (every 4, 8 or 12 hours) makes it difficult to determine the underlying distribution for each vital sign. In this paper we demonstrate how a Bayesian approach may be used to estimate the unknown parameters of vital sign data.

INTRODUCTION
Vital signs such as heart rate (HR), breathing rate, blood pressure, oxygen saturation, and temperature, are key indicators of patient condition. Understanding the behaviour of vital signs, individually and collectively, prior to an episode of patient deterioration (which can lead to an emergency admission to the Intensive Care Unit) is vital to alerting clinicians early to the impending deterioration. Typically, vital-sign data are sampled and recorded manually every four to twelve hours by nursing staff on hospital wards, and may be used to construct a model for identifying and predicting deterioration. However, the low sampling frequency makes it difficult to estimate the underlying distribution accurately. We propose to take a Bayesian approach for model parameter inference, such that the uncertainty in estimation is accounted for in a principled manner.

ESTIMATING THE UNKNOWN DISTRIBUTION
We initially assume the underlying distribution of a window of 5-dimensional vital-sign data, \( \mathbf{X} = \{ x_1, x_2, ..., x_N \} \), to be Gaussian, which is fully described by its mean and variance. The Bayesian approach to estimating a Gaussian distribution with unknown mean (\( \mu \)) and precision (\( \lambda \)), the inverse of the variance, is described by the conjugate pair of prior \( p(\mu, \lambda) \) and posterior \( p(\mu, \lambda | \mathbf{X}) \) distributions, which for the case of a univariate Gaussian distribution with unknown mean and variance, follows the ‘normal-gamma’ distribution, defined as [1]:

\[
\text{Normal Gamma} (\mu, \lambda | \mu_{\text{a}}, \beta_{\text{a}}, \alpha_{\text{a}}, \beta_{\text{a}}) \sim \\
\text{Normal} (\mu | \mu_{\text{a}}, (\beta_{\text{a}})^{-1}) \text{ Gamma} (\lambda | \alpha_{\text{a}}, \beta_{\text{a}})
\]

DISCUSSION AND CONCLUSION
The preliminary results introduced in this paper suggest that HR deterioration can be a gradual phenomenon occurring over several days. In future, we intend to use multivariate extensions to investigate deterioration in combinations of vital signs, with more complex, multi-modal distributions.

REFERENCES
LOW COST DIAGNOSTIC DEVICE USING MOBILE PHONE TECHNOLOGIES

Y. Bourquin1, J. Reboud1, R. Wilson1, Y. Zhang1 and J.M. Cooper1

1Division of Biomedical Engineering, University of Glasgow, Glasgow, UK

y.bourquin.1@research.gla.ac.uk

Abstract - The diagnosis of infectious diseases in the Developing World is technologically challenging, requiring assays achieving high analytical performance at minimal cost. Here we show how components commonly found in mobile phone technologies (surface acoustic wave (SAW) transducers, CMOS camera, LED) were integrated into an opto-acoustic immunoassay platform. Antibody functionalised microparticles were manipulated on a low-cost disposable cartridge using SAW and detected optically. Interferon-γ, a biomarker used for the diagnosis of tuberculosis, was detected at pM concentrations, within only few minutes.

INTRODUCTION

The diagnosis of infectious diseases in the Developing World requires the full integration of complex assays in easy-to-use platforms, as well as strong analytical performance at minimal cost. Mobile phones are widespread around the world, even in resource-limited countries. Their components comprise the technology required for a Point-of-Care (POC) diagnostic device such as the Surface Acoustic Waves (SAWs) device, CMOS camera and LED. SAWs recently showed the ability to perform complex microfluidic actuations [1]. CMOS camera has been recently turned into powerful lensfree devices to observe micrometer particles and cells [2].

Combining SAW microfluidics with lensfree optical detection, we demonstrate here an integrated immunoassay for the detection of interferon-γ, a biomarker used in the diagnosis of tuberculosis, on a low cost disposable chip, using mobile phone technologies.

MATERIALS AND METHODS

The device comprised a slanted interdigitated transducer (IDT), fabricated using standard photolithography on a lithium niobate wafer (Figure 1a), where the position of the generated waves is tuneable by the input frequency [1]. The acoustic waves were coupled into a disposable chip covered with monoclonal antibody (Figure 1a). 2 µm latex beads, functionalised with a second monoclonal antibody, were rapidly mixed with the analyte, bound to the surface and washed away all using SAW streaming. The remaining beads, specifically attached to the surface, were then observed with a CMOS camera positioned directly underneath the superstrate and counted using ImageJ software.

RESULTS AND DISCUSSION

A dose-response curve for interferon-γ, is presented in Figure 1b. The limit of detection was situated around 1 pM, which is the limit required for the diagnostic of tuberculosis in the interferon-γ release assay and the dynamical range spanned three order of magnitude (1-1000 pM). The use of SAW streaming enhanced the binding kinetics while reducing non-specific binding of beads [4].

CONCLUSION

We have demonstrated a low cost diagnostic device based on mobile phones technologies.

REFERENCES

AUGMENTED READING UTILIZING EDGE DETECTION FOR THE VISUALLY IMPAIRED

R.M. Gibson¹, S.G. McMeekin¹, A. Ahmadinia¹, L.M. Watson², N.C. Strang², V. Manahilov²

¹School of Engineering and Computing & ²School of Life Science
Glasgow Caledonian University
Ryan.Gibson@gcu.ac.uk

Abstract - Image processing can be applied to provide augmented vision, where novel techniques such as object detection, contrast modulation and text to speech synthesis can aid the visually impaired. The image processing technique of detecting an image edge with the Sobel method is utilized to augment text for simulated low vision to demonstrate the effectiveness of applied image processing in aiding the visually impaired.

INTRODUCTION
It is estimated that in the U.K. there are 1.8 million people who suffer from visual impairments that cannot be treated [1]. Recent work has developed digital image processing techniques to aide visually impaired individuals through contrast enhancement, magnification, and object detection [2]. Advances in the image processing power of embedded programmable platforms are enabling further development to provide real time augmented vision to combine into a portable system consisting of a wearable head mounted display (HMD). In this paper we analyse the effectiveness of the Sobel edge detection method [3] for enhancing reading text in simulated low vision and propose a novel edge detection technique suitable for future embedded augmented vision applications.

METHODS
The effectiveness of the Sobel edge detection was analysed using words of three to six characters in length randomly generated from the Legge word database [4] on a 50% luminance contrast background. Sobel edge detection was utilised to detect the edges that were then superimposed over the original image as shown in Figure 1. Sixteen subjects with normal vision read the randomly generated words and the percentage of correct words were recorded. This process is completed for unenhanced text and augmented text, and then repeated with frosted glasses to simulate a visual impairment with only low spatial frequency information available.

RESULTS
The application of the text edge enhancement produced a significant (P<0.001, paired t-test) increase from 36% to 63% in the number of words correctly identified for the simulated low vision subjects.

DISCUSSION
The results indicate that overlaying detected edges with the original image in simulated low vision can achieve a significant improvement in the ability to correctly identify the word. However when applied to complex real world images the Sobel technique suffers from background texture and noise that will limit effectiveness for augmented vision. A more robust edge detection technique based on a statistical analysis of the image has therefore been developed and optimised [5] to provide a significant improvement in the image quality within real time environmental constraints of an FPGA. (See figure 2).

CONCLUSION
The application of edge detection can provide a significant improvement in the ability of subjects with low vision to correctly identify words. The development and optimisation of the edge detection algorithm can enable the technique to operate within real time hardware constraints to realise a wearable embedded technology that can provide a new aide to low vision individuals.

REFERENCES


HIGHERLY-CURVED MICROCHANNEL FOR PARTICLE SEPARATION
Chao Wang, Yiannis Ventikos

Department of Engineering Science, University of Oxford
yiannis.ventikos@eng.ox.ac.uk

Abstract—We investigate computationally the feasibility of using curved microchannels for microparticle manipulation and size-based separation. Utilising 3D flow solution coupled with detailed particle trajectory estimations, we show that such methodologies offer promise for such fractionation processes.

INTRODUCTION
Particle manipulation represents an important field of process engineering, including particle focusing, sorting and separation. Continuous manipulation of microparticles is especially significant for the analysis of bio-particles detection and separation. Microfluidics offers the advantage of small volume and thus low analyte and reagent consumption. More importantly, it also offers unique hydrodynamic effects and more intensive exploitation of external field forces due to the scaling down. Microscale curved channels have been reported as efficient devices for microparticle focusing and separation [1]. However investigations to-date have been mostly restricted to semi-empirical analysis and to experimental approaches. In this work, we adopt a comprehensive numerical model to reveal the effects of a highly-curved microchannel, (Fig. 1), on the behaviour of different sized microparticles.

METHODS
The flow field is governed by the continuity equation and Navier-Stokes equation. A pressure correction method over structured multi-block grids is implemented in the CFD-ACE+ suite (ESI Group, Paris, France). Detailed grid independence analysis has been conducted to verify that the meshes utilised resolve the flow (Fig. 2).

An individual particle is represented by a centre of mass location and a number of marker points defining its surface. The particle holds tangential no-slip and zero normal flux boundary conditions. Particle tracking is achieved by solving the equation of motion in a Lagrangian frame of reference:

$$F_{p,i} = \sum_{i=1}^{n}(-p_i n_i + \tau_i \cdot n_i) \Delta S_i$$

where $N$ denotes the total number of marker points; $p_i$ is the pressure imposed on the marker point $k$; is the stress tensor at the $\tau_i$ marker point $k$; is the outward normal vector at the marker point $k$; $\Delta S_i$ is the surface area attached to marker point $k$.

RESULTS AND DISCUSSION
The axial velocity along a probe line defined in Fig. 1 is shown in Fig. 2 for the grids tested, demonstrating grid independence.

CONCLUSION
Purely hydrodynamic forces in microfluidic channels offer a promising option for continuous microparticle manipulation that warrants detailed further investigation.

REFERENCES
Global Health Initiative through EWH-Oxford Student Organization
Behar Joachim¹, Giovanni Milandri¹, Arvind Raghu¹, Sana Fathima¹, Dr Gari D. Clifford¹
for the EWH-Oxford team

¹Department of Engineering Science, Oxford

joachim.behar@gmail.com

Abstract - EWH-Oxford [1] is a group of students, researchers and faculty at the University of Oxford working on projects related to healthcare in resource-poor regions. It is a chapter of Engineering World Health (EWH) mobilizing the biomedical engineering community to improve the quality of healthcare in vulnerable communities of the developing world [2]. The recently created EWH-Oxford chapter focuses on telemedicine, mHealth, data mining, artificial intelligence and signal processing.

INTRODUCTION
The recent global explosion of cellular telecom usage has provided an extensive supply chain for hardware as well as rapid communication and data transfer. Nowadays there are over five billion mobile phone connections worldwide, which represent about 73% of the population [3] and around 90% of humanity lives within the range of a telecom transmitter [4]. The provision of an intelligent communication device to the relatively abundant untrained or semi-trained workers around the globe allows for an integrated approach for capturing diagnostic data and enables experts to rapidly review and diagnose. At EWH-Oxford we have focused on the use of mobile technology to increase health access in resource-poor regions. Our products are designed to be disposable, robust (potted), battery-free and environmentally friendly (using recycled enclosures).

PROJECTS
Multiple projects have started during this academic year (2010/11) and more will be starting for the coming year. These include:
- Blood Pressure (BP) Monitoring Device [5,6]: A low cost, easy-to-use device to assist a minimally-trained person to take BP has been developed. It uses a cuff and a mobile that are connected by a small signal acquisition box. A functional prototype has been developed which runs on Android and costs less than £10.
- Pulse Oximeter for Sleep Apnea: This project aims to develop a low-cost pulse oximeter that can process heart rate and blood oxygen saturation level measurements and transmit these signals to a mobile phone for remote evaluation, or further processing. This project focuses on the clinical application to apnea monitoring, but can be used for more general monitoring as well. The development of a prototype is in progress.
- mHealth Open Source Platform for Diabetic Foot Ulcers Tele-consultations: This is a collaborative project with SANA mobile [7] and the University of Thessaly in Greece.
- Cardiovascular disease (CVD) Risk Assessment tool: This involves an Android application which integrates data from various devices such as the BP cuff, pulse oximeter and blood glucose to generate a 5-year CVD risk score. The application considers key aspects such as population-based variability based on country-specific guidelines. Given the high propensity for chronic diseases such as diabetes (that ultimately increase CVD risk) in developing countries, this tool is expected to be of significant interest. A prototype has been developed and the tool is expected to be versioned for use by GPs and also for self-monitoring.
- Sleep Diagnostic System: Preliminary work has been performed to create an Android-based prototype for evaluating sleep disturbances using audio and accelerometer sensors on the phone.

CONCLUSION
Through EWH-Oxford we have created an environment for development using mobile technology to enhance healthcare in resource poor regions. Several promising projects have been started this year and more are planned.

REFERENCES
DETERMINATION THE AGE OF SALIVA STAIN USING RT-PCR

M. Alrowaithi1 and N. Watson1

1CFS, University of Strathclyde, Glasgow, UK

majid.alrowaithi@strath.ac.uk

Abstract - Although the great development in the forensic genetics has been DNA analysis, it does not provide any information about the time of the deposition of biological stain. Time since deposition could exclude potential suspects from the investigation as well as determination when the crime occurred. In this study the relative expression ratio (RER) of the β-actin mRNA to 18S rRNA in saliva samples that were aged over 42 days was monitored by using RT-qPCR assay. The results show that there is a correlation between the age of saliva and the RER and the age of the sample can be approximated.

INTRODUCTION

Time since deposition of the biological stain is important in many forensic cases. It becomes more important in crimes where there is a close personal tie between the victim and the suspect [1]. Many techniques, ranging from simple visual examinations to more complicated techniques, were used to determine the age of biological stain [2]. Unfortunately, the results of studies depending on the changes in the physical and chemical features of the stain were approximate at best.

The most promising studies were those involved RNA degradation. Anderson et al [3] developed a reverse transcription quantitative polymerase chain reaction (RT-qPCR) assay where two RNA molecules from different RNA types extracted from blood stains were analysed and the ratio between them was used as an indicator of the ageing of the bloodstain over the course of 150 days. This approach offers a number of potential advantages; such as the precision and the accuracy of the results, a small quantity of the sample is needed for the test and the analysis is not affected by the size of the sample because it examines the RNA ratio. Moreover, this approach could be applied to tissue types other than blood. Hampson et al [4] carried out this approach to determine the age of hair aged over a period of three months.

This study was conducted to test the assumption of the suitability of the approach, carried out by Anderson et al, using another stain (saliva) which is one of the common crime body fluids and not tested in this way before. In this study RNeasy micro kit was used instead of the phenol chloroform extraction method which was used in previous studies. RNALater was also used to stop RNA degradation when each sample reached the desired ages.

METHOD

Saliva was collected from 6 volunteers (3 males and 3 females). The samples are aliquoted and stored at room temperature in a dry place to simulate natural aging until they reach the desired ages (1, 2, 3, 7, 14, 21, 28, 35, 42 days). Real-time reverse transcriptase PCR was used to determine the Ct value of the β-actin mRNA and the 18S rRNA.

RESULTS

The preliminary results of this study show that there is a correlation between the time since deposition of the saliva samples and the relative expression ratio of the β-actin mRNA to 18S rRNA.

DISCUSSION AND CONCLUSION

The relation between the age of saliva samples and the RER of the β-actin mRNA to 18S rRNA is due to the faster degradation of the β-actin mRNA than 18S rRNA. This difference in degradation rate resulted from the differences between these two RNAs [3].

In conclusion, the preliminary results of this study demonstrate the relation between the age of saliva samples and RER which can be used as indicator to predict the age of the sample. Moreover, the correlation between the age of saliva samples and the RER of β-actin mRNA to 18S rRNA confirms the hypothesis of the suitability of the approach to other tissue types other than blood [3].

REFERENCES


DEVELOPMENT OF A MICROFLUIDIC BIOCHIP FOR ABSORPTION, DISTRIBUTION, METABOLISM AND EXCRETION TOXICOLOGY STUDIES (ADME-TOX)
Niall Macdonald¹, Jon Cooper¹

¹Biomedical Engineering, Glasgow University, Scotland, G12 8LT
n.macdonald.1@research.gla.ac.uk

Abstract - Absorption, Distribution, Metabolism and Excretion Toxicology studies (ADME-Tox) of Foods and Household Personal Care (HPC) products are carried out systematically under regulation to rule out any health effects. Here we show the development of a microfluidic strategy to provide a more realistic in vitro environment for tests that will result in more meaningful toxicological conclusions. The microfluidic systems enabled dynamic and high-precision control over fluidic behaviour, such as shear-stress, flow rate and nutrient perfusion.

INTRODUCTION
In 2013 there will be a complete ban of animal testing for ingredients in the EU, calling out for robust in vitro equivalents. Because the liver is the principal site of xenobiotic metabolism, it is the best enzyme source to perform the first primary screening of metabolism. [1] It is also the most common organ where toxicity manifests itself. [2] This project aims to render the in vivo physiological environment of the liver within in vitro microfluidic structures to yield more accurate toxicity data than is currently available in a high-throughput in vitro format.

TECHNICAL INFORMATION
The biochip design consists of a growth medium dispensing system fabricated with a 3D printer connected to a PDMS micro fabricated microfluidic network, all mounted on a glass slide for ease of inspection. [Fig 1] Contrary to most microfluidic systems, which tend to use syringe pumps, here a pumpless, gravity based system is integrated with a microfluidic channel network.

Hepatocytes (HepG2/C3A) were cultured in hydrogel on a microfluidic chip. The microfluidic system did not show any detrimental effects on the cells, which were kept alive over a period of days [Fig 2], as shown by fluorescence imaging (live/dead stain, Invitrogen).

In future, we will use data from mathematical modelling of circulation in the liver [3], to design microfluidic structures that supply nutrients and shear stresses found in-vivo. Compounds with known toxicity (acetaminophen, fialuridine, anethole) will be used to assess the system.

REFERENCES
INTRODUCTION

The homogeneous assay format is expected to make a profound impact in the point-of-care (POC) diagnostic sector by eliminating the need for multiple washing steps [1]. In addition, fluorescence polarisation immunoassays (FPIs) offer a sensitivity and potential for miniaturisation that is well suited to POC devices. In this study we aim to design and characterise a homogeneous time-resolved FPI to detect the decapptide gonadotropin-releasing hormone, type 1, (GnRH-1).

METHODS

A synthetic labelled 9-amino acid ‘fragment’ (LF) is introduced to compete with GnRH-1 for the two binding sites on the GnRH-1 specific antibody, 7B10.1D10, (Ab) thus providing an extrinsic fluorescence measurement for time-resolved fluorescence experiments.

In single photon counting experiment the anisotropy of a macromolecule is often described by a bi-exponential law with the overall rotational diffusion evident as a plateau value \( r_\infty \). Restricting the data analysis to a region in the plateau phase of the anisotropy decay curve yields the potential detection parameters \( \Delta r \) and \( r_p \).

Time-resolved fluorescence lifetime and anisotropy measurements were performed using the time-correlated single photon counting technique (TCSPC) on a FluoroCube (Horiba Jobin Yvon IBH Ltd, Glasgow) [2].

RESULTS & DISCUSSION

When comparing the sample of LF with a sample of LF in the presence of Ab (Ab-LF) there is a clear difference in the both the time- resolved lifetime decay values and anisotropy decay curves. However when GnRH-1 is added to the Ab-LF mixture a distinct change is only revealed in the anisotropy measurements (Table 1).

Abstract – In this report we employ time-resolved fluorescence techniques to describe the presence of GnRH-1 in a homogeneous solution. Furthermore, we propose the parameter \( r_p \), which is derived from the time-resolved fluorescence anisotropy, as a descriptor of the concentration of GnRH-1 in solution.

### Table 1: Lifetimes resolved into two components \( \Delta r \) and \( r_p \). The anisotropy \( r_p \) and the correlation time \( \Delta r \) extracted from the plateau region of the anisotropy decay curves.

<table>
<thead>
<tr>
<th><em>set</em> ( f_1 )</th>
<th>( \Delta r_1 ) (ns)</th>
<th>( f_2 )</th>
<th>( \Delta r_2 ) (ns)</th>
<th>( r_p ) (ns)</th>
<th>( \Delta r_p ) (ns)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>90.8</td>
<td>3.82</td>
<td>9.2</td>
<td>0.95</td>
<td>1.16</td>
</tr>
<tr>
<td>0.5</td>
<td>94.1</td>
<td>3.71</td>
<td>5.9</td>
<td>0.49</td>
<td>1.29</td>
</tr>
<tr>
<td>1.0</td>
<td>94.8</td>
<td>3.79</td>
<td>5.2</td>
<td>0.58</td>
<td>1.16</td>
</tr>
<tr>
<td>1.3</td>
<td>95.2</td>
<td>3.78</td>
<td>4.8</td>
<td>0.49</td>
<td>1.12</td>
</tr>
<tr>
<td>2.0</td>
<td>94.6</td>
<td>3.76</td>
<td>5.4</td>
<td>0.54</td>
<td>1.21</td>
</tr>
<tr>
<td>3.0</td>
<td>94.0</td>
<td>3.64</td>
<td>6.0</td>
<td>0.41</td>
<td>1.34</td>
</tr>
<tr>
<td>LF</td>
<td>91.6</td>
<td>2.77</td>
<td>8.4</td>
<td>0.53</td>
<td>1.21</td>
</tr>
</tbody>
</table>

*each ‘set’ describes a sample in terms of the ratio GnRH-1 molecules to antibody binding sites, with the exception of ‘LF’ which refers to a sample containing the labelled fragment only.

The anisotropy term \( r_p \) is reduced as LF spends more time unbound due to Ab sites being occupied by GnRH-1. The rotational correlation time associated with the plateau region, \( \Delta r_p \), is influenced by the complex motion of the flexible Ab molecule and does not, in this form, offer a simple quantitative measure of the concentration of GnRH-1 in solution.

CONCLUSION

In this study we highlight the use of time-resolved fluorescence techniques to evaluate an immunoassay for the detection of GnRH-1 with the intention of applying these techniques to the design of homogeneous immunoassays for point-of-care applications.

REFERENCES

RNA STABILITY IN FROZEN/THAWED CLINICAL SAMPLES
Olga M. Posada1, Rothwelle J. Tate2, Helen Grant1

1Bioengineering Unit, 2Strathclyde Institute for Pharmacy & Biomedical Sciences, University of Strathclyde, Glasgow G4 0NW
olga.posada-estefan@strath.ac.uk

Abstract - The main challenge of RNA extraction from frozen blood samples is to obtain sufficient RNA of acceptable quality for gene expression analysis. In this trial we compared the RNA stability in clinical blood samples with and without a RNA stabilizer, RNAlater. Results show that high quality RNA can be extracted from blood with RNAlater that has been frozen and thawed several times before the extraction.

INTRODUCTION
Gene expression analysis of blood cells allows minimally invasive repeated measurements [1]. Archived frozen blood represents a robust and invaluable source of human tissue for gene expression research [2]. The main challenge of RNA extraction from frozen blood samples is to obtain sufficient RNA of acceptable quality for molecular studies. The freezing of blood destroys a large fraction of blood cells, exposing the RNA to released enzymes, including RNases, and subsequent RNA degradation [1]. We tested the RNA stability in clinical blood samples with and without the RNA stabilizer, RNAlater (Ambion), after freeze/thaw cycles.

METHODS
On arrival in the laboratory, 500μl of fresh whole blood were added to eight 2ml microcentrifuge tubes. Four of these tubes contained 1.3ml of RNAlater. Multiple freeze/thaw cycles were carried out freezing the samples at -80ºC for 10min and thawing them at room temperature for 15min. RNA extractions were performed after 0, 3, 6, and 10 freeze/thaw cycles using the commercial kit RiboPure Blood (Ambion), according to the manufacturer’s recommendations. RNA concentration and purity (A260/A280 Absorbance ratio) were determined using a NanoDrop 2000C spectrophotometer (NanoDrop Technologies), and RNA quality was assessed by determining the RNA quality indicator (RQI) using the Experion™ Automated Electrophoresis System (Bio-Rad).

RESULTS
RNA yield, purity and quality were compared. We observed similar yields and purity for all samples. Higher RQI numbers were found in all the samples with RNAlater. Results are summarized in table 1.

DISCUSSION AND CONCLUSION
It has been demonstrated that RNA quality has a large influence on gene expression data [1]. This trial suggests that RNA from whole blood samples treated with RNAlater can be frozen and thawed several times before RNA extraction, and still extracted in quantities and qualities required for molecular studies.

REFERENCES

<table>
<thead>
<tr>
<th>Sample</th>
<th>RNA Yield (μg)</th>
<th>A260/A280 Absorbance Ratio</th>
<th>RNA Quality (RQI: 1=poor, 10=high)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNAlater +, 0 freeze/thaw cycles</td>
<td>6.88</td>
<td>1.92</td>
<td>7.2</td>
</tr>
<tr>
<td>RNAlater -, 0 freeze/thaw cycles</td>
<td>3.17</td>
<td>1.96</td>
<td>6.6</td>
</tr>
<tr>
<td>RNAlater +, 3 freeze/thaw cycles</td>
<td>4.98</td>
<td>2</td>
<td>7.6</td>
</tr>
<tr>
<td>RNAlater -, 3 freeze/thaw cycles</td>
<td>4.97</td>
<td>2.02</td>
<td>3.4</td>
</tr>
<tr>
<td>RNAlater +, 6 freeze/thaw cycles</td>
<td>4.79</td>
<td>2.01</td>
<td>8.9</td>
</tr>
<tr>
<td>RNAlater -, 6 freeze/thaw cycles</td>
<td>6.2</td>
<td>1.94</td>
<td>3.6</td>
</tr>
<tr>
<td>RNAlater +, 10 freeze/thaw cycles</td>
<td>4.59</td>
<td>1.89</td>
<td>8.7</td>
</tr>
<tr>
<td>RNAlater -, 10 freeze/thaw cycles</td>
<td>6.2</td>
<td>1.96</td>
<td>2.8</td>
</tr>
</tbody>
</table>

TABLE I: RNA yield, purity and quality.
THE TOTAL DESIGN METHOD AS APPLIED TO PROSTHETIC FOOT DESIGN

Philip Connolly¹, Dr. Arjan Buis², Mr. Stephanos Solomonidis¹

¹Bioengineering Department, Wolfson Building, University of Strathclyde, Glasgow, G4 0NW
²National Centre for Prosthetics and Orthotics, University of Strathclyde, Glasgow, G4 0LS

Philip.A.Connolly@strath.ac.uk

Abstract – Total Design is a process for design where all relevant factors are considered and defined prior to design commencing. The method is highlighted and examples of applications in the field of prosthetic foot design are used. After highlighting the factors involved a product design specification (PDS) is formed and then concepts generated and evaluated based on the PDS. Further sets of design and evaluation are carried out leading to a single concept for design to completion, including the manufacture and sale.

INTRODUCTION

Stuart Pugh published the ‘Total Design’ method in 1990 [1]. What it set out is a systematic process for taking the design of any product from initial conception and definition through to sale. Historically prostheses have been developed through iterative methods however in the modern market, particularly in the case of prosthetic feet, the wide range of options and competition mean iterative design methods are unsustainable. The aim here is to apply this method to prosthetic foot design specifically and raise awareness to a wider audience.

TECHNICAL INFORMATION

Pugh’s method of Total Design consists of evaluating the market through three distinct techniques, parametric analysis, customer needs analysis and a matrix analysis. In evaluating the market successful competitors may be identified and reasons for success highlighted. This analysis also helps to illuminate niches in the market where it may be possible to place a new product.

From having evaluated the market a thorough product design specification (PDS) may be drawn up. This includes thirty-two subsections in order to cover all relevant areas. Examples are to be given with emphasis on prosthetic foot design. Once a PDS has been fully specified then concept genesis and evaluation can proceed. A method of controlled convergence is applied where concepts are generated then evaluated against the PDS, and then further developed and re-evaluated until a single concept remains.

At this stage the specific design can proceed at the same time as the design for manufacture. This is important in that it saves time and effort by not designing a product which cannot be manufactured and so avoids redesign and modification.

In this particular case the foot being designed is suitable for trans-tibial amputees, that is, where amputation has occurred between the knee and ankle. The aim is to produce a low cost, effective prosthetic foot for use in developing countries. Through using the Total Design method all relevant factors may be included to produce a foot unit with this specific market in mind with considerations including materials, functions and costs.

CONCLUSION

Total Design provides a comprehensive design guide which may be used to more effectively design a range of products and is applicable to prosthetic feet.

REFERENCES

As deep-brain stimulation (DBS) gains momentum in both the clinical and research areas, new experimental strategies are required to further elucidate its mechanisms of action. In exploring novel experimental approaches, this study presents a miniature wireless system designed to simultaneously record multichannel EEG and perform DBS in freely-moving rodents. Initial testing of this device looks promising and forms a pre-requisite for its forthcoming application in studying the effects DBS has on the cognitive deficits in schizophrenia.

INTRODUCTION

With its origins in ablative neurosurgery, the success of DBS in motor-neuron diseases such as Parkinson’s has led to further avenues of research into other neurological disorders, such as depression and obsessive-compulsive disorder [1-2]. This study looks at its application in the cognitive symptoms of schizophrenia, which are widely considered to be implicated in the primary pathology of the disease.

At present the exact causes of schizophrenia are yet to be determined. This study focuses on the loss of neural coordination between the hippocampus and prefrontal cortex that occurs in schizophrenic patients and animal models. In the latter case this can be observed via local field potentials (LFPs) and is known to be directly analogous to deficits in learning and working memory [3]. Using sub-chronic phencyclidine (PCP) treated rats as a schizophrenia model; DBS is currently being investigated as a possible means of correcting this corticocortical coordination deficit. At present there is a lack of commercial miniature wireless systems capable of simultaneous DBS and EEG recording. Attempts by researchers to create such devices have resulted in systems inadequate for this study both due to their large size and limited functionality. As such a novel system is developed to allow these experiments to take place.

METHODS

A miniature wireless system is developed for head-mount operation in rats using off-the-shelf components. Featuring 2-channels of DBS and 4-channels of EEG recording, it’s designed to transmit continuous EEG up to 10 meters, as well as being configurable in real-time. Initial verification of the system performance is made through human scalp-recorded EEG, and measurement of DBS pulses are made through custom-made electrodes immersed in saline.

RESULTS

The system performs as expected, reproducing EEG to a high accuracy as well as delivering well-defined DBS pulses that change parameters immediately following user-input at the computer. Using a CR2032 battery the system can record and stimulate continuously for over 2 hours, and 3 days, respectively - depending on DBS and transmission settings. Excluding the battery the system measures approximately 15x25x10mm and weighs 4.7g.

CONCLUSION

The current phase of this study has seen the completion of the system and subsequent testing with scalp-recorded EEG against a commercial EEG recording system. The system is able to maintain an efficient balance between performance, functionality and battery life, and is significantly smaller and more functional than similar devices of its kind. The next phase of this study involves recording and stimulation pilot studies in vivo using freely moving rodents.

REFERENCES


MICRORHEOLOGICAL STUDY OF BIOPOLYMERS USING OPTICAL TWEezERS
Eleanor Chambers, Manlio Tassieri, Jonathan Cooper
Division of Biomedical Engineering, University of Glasgow
0909335c@student.gla.ac.uk

This project aims to develop new methodologies for the observation of the rheological properties of biopolymers. Current work includes investigating the variety in rheological characteristics of Cryptococcus neoformans polysaccharide capsules taken from different patients.

INTRODUCTION
Rheology is the study of the flow and deformation of matter. Traditionally, rheology has been investigated at the macroscale using bulk rheometers, but in recent years the potential of rapidly developing microrheological methods has attracted increasing attention.

The basis of most microrheological techniques (with the exception of atomic force microscopy) is to track the motion of micron-sized probe particles in a viscoelastic medium and to relate this motion to the medium's rheological properties. This enables the analysis of smaller scale interactions than in bulk rheology, as well as having the ability to probe a sample's local heterogeneity. Another advantage of microrheology over macrorheology is that it does not require so large a sample volume, which is especially relevant to biological specimens where the amount of sample may be very limited.

Optical Tweezers, as applied to microrheology, make use of a high intensity beam of light (usually a laser) to confine a probe particle in a potential well where the Brownian motion of the particle can be observed. This motion can then be related to the viscoelastic properties of the fluid in which the particle is embedded by relations pioneered by Mason and Weitz in 1995 [1].

METHODS
Part of this project includes the construction of a microfluidic platform in which one can observe rheological changes within biological samples in real-time.

CURRENT WORK
Cryptococcus neoformans is the fungus responsible for cryptococcosis, a major cause of death in Sub-Saharan Africa. It has a polysaccharide capsule which makes C. neoformans a particularly virulent fungus [2]. We took Optical Tweezer measurements of the motion of silica probes particles which had been added to samples of the capsular polysaccharide taken from four different patients.

RESULTS
Figure 2 shows that for each patient, PH4, 9, 13 and 14, a distinct data set with closely matched scaling laws can be observed.

The scaling laws indicate rod-like molecules in solution [3], which is backed up by SEM images of the sample (Figure 3).

REFERENCES

FIGURE 1: Diagram of prototype device. The observation chamber contains the sample of interest and the contents of the chamber above can be changed to affect the sample in the observation chamber by diffusion of salt, for example, across the membrane separating the two chambers. Rheological changes can be observed in real-time through the use of the Optical Tweezers.

FIGURE 2: Graph showing the complex viscosity of the polysaccharide sample versus its concentration. Dotted lines show scaling laws, indicating different regimes of behavior as the sample concentration is varied.

FIGURE 3: SEM images of the capsular polysaccharide sample at a low concentration, surrounded by probe beads.
A NEW LIGHT IN AMYLOID OLIGOMERISATION
Mariana Amaro\(^1\), David JS Birch\(^1\) and Olaf J Rolinski\(^1\)

\(^1\)Centre for Molecular Nanometrology, Department of Physics, Scottish Universities Physics Alliance, University of Strathclyde, Glasgow G4 0NG, UK
mariana.amaro@strath.ac.uk

Abstract - Alzheimer disease, the most common of the neurodegenerative diseases, is thought to be associated with β-amyloid (Aβ) peptide aggregation. Despite extensive research still little is known about the early stages of aggregation where neurotoxic oligomers are formed. We report on the advantages of using Aβ intrinsic fluorescence to detect and monitor the stages of oligomerisation.

INTRODUCTION
Over 60\% of dementias are caused by Alzheimer disease (AD), a neurodegenerative amyloidosis \([1]\). Amyloidoses essential feature is the aggregation of proteins and their deposition in the body. In AD the aggregation of β-amyloid (Aβ) peptides is believed to play a central role. In the early stages of Aβ aggregation cytotoxic oligomers are formed. It is important to fully understand these early stages as it can help in designing more effective therapeutics.

Our approach explores the sensitivity of fluorescence which enables monitoring interactions of individual biomolecules. It reveals crucial information on early stages of aggregation which is not achieved by other commonly used techniques \([2]\). The method eliminates the drawbacks of extrinsic fluorophore-based techniques and can be used to monitor oligomerisation non-invasively.

Here the aggregation of single Aβ peptides is monitored in vitro by detecting fluorescence lifetimes of Aβ’s intrinsic fluorophore (Tyrosine) and is shown how its fluorescence behaviour tracks the process of oligomer formation \([3]\).

METHODS
Fluorescence decays were recorded using the time-correlated single-photon counting technique and measurements executed at 37°C. Data analysis was performed using a discrete three-exponential decay model:

\[
I(t) = \sum_{i=1}^{3} \alpha_i \exp \left[-t/t_{\alpha_i}\right]
\]

RESULTS
As is expected that the aggregation process might depend on the initial concentration of peptides, two samples were followed over time: one sample of 5μM concentration of Aβ monomers and another of 50μM.

A. Low concentration sample
Lifetime values are stable during the course of the 210h of experiment and the fractional contributions of decay lifetimes also show no significant changes throughout. These suggest the sample is fairly stable and aggregation does not occur or occurs at a slow rate and is unnoticeable during the 210h of experiment. This is confirmed by the ratio of \(f_1\) to \(f_2\) values, which can be used as an indicator of aggregation \([2]\), whose value is scattered around 0.864 ± 0.018.

B. High concentration sample
Lifetimes show a very slow increase with time, while changes in fractional contributions are quite significant. This may indicate a new process, not observed in the low concentration sample, likely the effect of Aβ spontaneous aggregation. We propose this result is a signature of oligomerisation. The ratio \(f_1/f_2\) can be fitted to the exponential function

\[
(f_1/f_2)(t) = (A_1 - A_0) \exp \left[-t/t_{\text{agg}}\right] + A_0
\]

where the characteristic “aggregation time”, \(t_{\text{agg}}\), achieved a value of 33.3±3.1 h. Such kinetics may reflect high “consumption” of monomers to form small oligomeric species at the beginning of aggregation. As oligomers get bigger and diffuse slower, and monomers become sparser the initial rate of aggregation slows down.

CONCLUSIONS
Here was shown how the intrinsic fluorescence of Aβ can be useful for monitoring the early stages of single peptide-peptide aggregation. It was also demonstrated that the initial monomer concentration determines the oligomerisation rate. The results are of fundamental importance because no other technique enables detection of single peptide binding non-invasively. The method can be used in the search for factors interfering with oligomerisation. Such research may lead to drug discoveries that will allow preventing, controlling or even reversing the aggregation that leads to the AD.

REFERENCES
\([1]\) World Alzheimer Report 2010
\([3]\) M. Amaro, et al., PCCP, 13, 2011, pp.6434-6441
DESIGN OF A SHOE PLATFORM TO SIMULATE GROUND REACTION FORCE
Juan Fang, Aleksandra Vuckovic

Abstract - This paper presents results of experimental testing of a shoe platform designed to mimic the ground reaction forces during walking for bedridden patients. The shoe platform was tested on healthy volunteers. It is envisaged that the platform would stimulate the mechanoreceptors on the foot, which provides important sensory information during rehabilitation process of patients with impaired lower limb functions.

INTRODUCTION
Patients with impaired lower limb functions should start rehabilitation as soon as possible. A stepping device has been designed for acute patients who are restricted to bed to promote early rehabilitation [1]. One of the challenges of such a device is how to generate a ground reaction force to the foot for users that are still in bed, without eliciting a reflex response. This paper describes the development of a dynamic shoe platform designed to deliver mechanical stimulation on the foot.

METHODS
The platform, made of a foot plate and two pressure plates (under the heel [5 2 cm$^2$] and the forefoot [63 cm$^2$]) was driven by pneumatic cylinders. A control system was developed in Matlab/Simulink. Ten healthy volunteers wore the shoe platform while lying on a bed. In order to test the reflex responses, single pulse was applied with varying pressures (2, 2.5, 3 and 3.5 bar) and different rising speeds of force (fast: 0.5m/s and slow: 0.01m/s). Random order pulses were repeated 4 times. With respect to volunteers’ body weight, a pressure of 3.5 bar on the heel was between 30% and 60%, and was similar to a body weight experienced by patients practicing treadmill walking with a body-weight support. Then the foot was stimulated with a series of synchronised heel and forefoot pulses (3.5 bar, slow speed) which mimicked walking at 3 Km/h.

RESULTS
Stimulation with fast single pulses induced reflexes in SOL and/or TA in 8 out of 10 subjects. Mean latencies of the reflex response were 30-87 ms for SOL and 27-84ms for TA. Mean ankle angle change was 1.22° with force on the heel and 0.84° with force on the toe, independent on reflexes. Frequency of reflex occurrence increased with an increase of the pressure. There was no correlation between the frequency of response and volunteers’ body weight. Slow stimulation did not elicit any reflexes. Fig.1 shows mechanical force applied on the heel and the forefoot during simulated walking. A stance phase was 60% of the gait cycle (GC) and stimulation of the heel preceded stimulation of the forefoot by 20% of GC. Fig.2 shows muscle response during simulated walking in one subject. Small modulation of the background EMG activity can be noticed, accompanied by changes in the ankle angle by 2°. The volunteers reported that the platform was comfortable to use and they felt walking-like pattern force.

DISCUSSIONS
The shoe platform applied mechanical force on the foot, which stimulates the load receptors by pressing and stretches the muscle by changing the ankle angle. The reflexes recorded in the current study might be a combination of cutaneous reflex and stretch reflex. During the walking simulation, reflex response was avoided by reducing the speed of the mechanical force. The platform induced change in the EMG and small perturbation of the ankle angle produced sensation similar to those during walking.

CONCLUSIONS
The study shows feasibility of a dynamic shoe which achieves walking like mechanical stimulation on the insole of users in a supine posture.

REFERENCES
[1] J.Fang et al. 17th ESB.
LOCAL PRESSURE FLUCTUATIONS IN AN OCCLUDED ARTERY

O. Korolkova¹, J. Alastruey¹, A. Lowe², J. E. Davies¹, A. D. Hughes¹, K. H. Parker¹ and J. H. Siggers¹

¹Department of Bioengineering, Imperial College London, London, UK
²PulseCor Ltd, Auckland, New Zealand
o.korolkova09@imperial.ac.uk

Abstract - The effect of occlusion of the brachial artery on pressure waveforms was investigated using a 1D model of the human arterial system. Pressure waveforms were calculated with and without brachial occlusion using aortic blood flow as an input. The results show that an occlusion generates additional oscillations in the brachial pressure. Changing the lengths or compliances of the arteries in the model or the position of the occlusion suggests that any arterial occlusion affects the local pressure waveform.

INTRODUCTION

We investigate changes in the pressure waveform in the brachial artery when it is occluded during, for example, a cuff-based measurement of blood pressure. To generate the pressure curves in the brachial artery, a simplified 1D model of the arterial network is used, in which the arteries are treated as tapered segments with viscoelastic walls and the flow to be unidirectional and uniform [1]. Mass and momentum conservation are used, together with a tube law to relate the blood pressure and cross-sectional area. The system of equations is hyperbolic and shows that information propagates at speed $U \pm c$, where $c$ is the wave speed and $U$ is the mean velocity along the vessels. The occlusion of the artery causes local changes in pressure and cross-sectional area of the artery [1] [2], as well as the changes in the wave speed. The effect of several parameters are tested, including the lengths of vessels in the arterial network, the compliance of the vessel walls, and the position of the point of occlusion of the brachial artery.

METHOD

To account for the effect of the cuff we adapt the model by setting the velocity of the blood to zero at 26 cm from the upstream brachial bifurcation (thus the distal blood vessels in the left arm are excluded from the model). We compare the pressures calculated in this case with those calculated with no occlusion. To investigate the influence of other parameters in the model, the length and elasticity of vessels in the network are increased or decreased by 10%.

RESULTS

The pressure curves within the occluded brachial artery exhibit superposed oscillations of variable amplitude and frequency (Fig 1), with the largest amplitudes obtained during systole. The oscillation is either much smaller or not observable even in nearby arteries: there are no changes from the non-occluded case in the left subclavian artery and only slight oscillations in the left vertebral artery. The oscillations are not caused by either arterial taper or viscosity of the blood, and actually increase in amplitude when taper and viscosity are removed. If either the length or the elasticity of the vessels is changed by 10%, there are slight changes in the pressure waveform in the aorta and brachial artery during diastole, but nothing significant during systole.

CONCLUSIONS

We conclude that occlusion of the brachial artery leads to relatively large superposed temporal oscillations in local brachial blood pressure. These oscillations are present in all cases considered in this study: we considered the effects of removal of arterial taper and viscosity, and also changes in patient height, arterial compliance and cuff position. We therefore conclude that the oscillations are solely due to arterial occlusion and not to the interaction of the occlusion with other phenomena. Further tests are planned to see if these oscillations are present in vivo.

REFERENCES

BREATHING PATTERN DETECTION FOR AN ABDOMINAL FUNCTIONAL ELECTRICAL STIMULATION SYSTEM FOR TETRAPLEGICS

E. J. McCaughey¹, A. J. McLachlan¹ and H. Gollee¹

¹Centre for Rehabilitation Engineering, University of Glasgow, Glasgow, Scotland
e.mccaughey.1@research.gla.ac.uk

Non intrusive real time detection of breathing patterns is an essential step in the development of a stand alone Abdominal Functional Electrical Stimulation (AFES) system for the tetraplegic population. In this study we recruited 10 able bodied volunteers and asked them to perform different breathing modes, which were recorded using a number of sensors. These results were then analysed and from these results the optimum sensor for use as the input to a novel stand alone abdominal FES system will be established.

INTRODUCTION

Abdominal Functional Electrical Stimulation (AFES) has been shown to improve respiratory function in tetraplegic subjects [1]. In such a system stimulation must be applied only during exhalation in order to achieve the greatest benefit for the user. Additionally generation of a cough requires a greater intensity of stimulation than a quiet breath. Therefore, a standalone AFES system must be capable of real time breathing pattern detection to enable the correct stimulation to be applied at the correct point in the breathing cycle.

A spirometer measures air flow at the mouth and is currently regarded as the ‘gold standard’ for measuring breathing patterns of the tetraplegic population [2,3]. Unfortunately a spirometer is intrusive, leaving the user unable to eat, drink or verbally communicate effectively while in use. An alternative, non intrusive, method of breathing pattern detection would enable the use of an AFES system for a greater duration with less discomfort for the user.

In this study a number of sensors were used to measure different breathing patterns in able bodied subjects. The signals from these sensors will be analysed and combined to give the optimum signal. The signals will then be compared to the spirometer and the optimum non intrusive sensor for breathing pattern detection established. This sensor will then be used as the input to a standalone AFES device.

METHODS

This study was approved by the Faculty of Biomedical and Life Sciences ethics committee, University of Glasgow. 10 able bodied subjects gave informed consent and attended 2 sessions. Subjects were asked to undertake various breathing modes including quiet, rapid and deep breathing as well as coughing, all with and without AFES. The non intrusive detection sensors used were: accelerometers, piezoelectric belts, and a nasal thermistor. An ultrasound measurement system and a spirometer were used as a reference.

RESULTS

Preliminary analysis has shown that accelerometers, piezoelectric belts and a nasal thermistor are all non intrusive methods capable of real time breathing pattern detection as can be seen in Figure 1. Further results will be presented at the conference.

Fig. 1 Spirometer, integrated signal of accelerometer on abdomen, nasal thermistor and abdominal belt signals for 3 coughs and 2 quiet breaths.

DISCUSSION AND CONCLUSIONS

This study describes the optimum sensor for the detection of breathing patterns. This sensor will then be suitable to be used as the input to a novel standalone AFES device.

REFERENCES

ATOMIC FORCE MICROSCOPY OF BOVINE ARTICULAR CARTILAGE
Megan Austin\(^1\), Anthony Herbert\(^1\), Richard Black\(^1\) & Philip Riches\(^1\)

\(^1\)Bioengineering Unit, University of Strathclyde, 106 Rottenrow, Glasgow, G40NW
megan.j.austin@strath.ac.uk

Abstract – Articular cartilage is notoriously difficult to image using standard AFM techniques. We have imaged the surface of bovine articular cartilage using a magnetically actuated cantilever allowing these samples to be imaged in physiological conditions. This methodology has identified microstructures that are likely to be collagen fibrils oriented parallel to the surface. Further, images suggest that subsurface fibrils are oriented in an alternate direction.

INTRODUCTION
Articular cartilage covers the end of long bones, optimising load support and joint lubrication. Articular cartilage is composed of water and a solid phase which consists of a proteoglycan matrix, collagen fibres and chondrocytes. Cartilage has no blood supply, repair is very slow and degeneration can lead to osteoarthritis.

Atomic Force Microscopy (AFM) is a scanning probe microscopy technique that has a resolution in the order of nanometres and, uniquely among imaging techniques, can provide surface property characteristics. Previous studies have imaged the surface of human and animal cartilage [1, 2] but, possibly due to its compliant nature, the tissue’s microstructure is has not been well resolved under fluid.

We aim to use the iDrive\(^\text{TM}\) capability if the Asylum Research MFP-3D AFM, which uses a magnetically actuated cantilever, to improve the sensitivity of the technique in fluid in order for microstructural features of the surface to be identified.

TECHNICAL INFORMATION
Fresh bovine articular cartilage plugs (5mm x 5mm) were removed from the medial condyle of the caudal knee using an oscillating autopsy saw and scalpel. Sections, 20 µm thick and parallel to the surface, were subsequently cryotomed. Samples were secured to glass slides and submerged in PBS before and during testing.

AFM images were collected with the Asylum Research MFP-3D AFM fitted with an iDrive\(^\text{TM}\) magnetically actuated cantilever and operated in AC (oscillating) mode. The iDrive\(^\text{TM}\) simplifies fluid imaging potentially making it suitable for AC imaging of soft samples under fluid conditions. A scan rate of 0.10 Hz was used for all samples.

RESULTS
Figures 1 and 2 demonstrate the typical topography of the articular cartilage surface. A corrugated surface of about 100nm in amplitude is evident. These images also show continuous fibre-like structures running parallel to the surface, with subsurface structures oriented in an alternate direction.

CONCLUSION
Using AFM, we have identified microstructures that are likely to be collagen fibrils on the surface of articular cartilage, although the typical banding pattern associated with these structures is not evident. The observed microstructure is consistent with known anatomy and suggests that fibrils are oriented to resist tensional forces associated with the swelling pressure of cartilage.

REFERENCES
INHALATION DRUG DELIVERY USING SURFACE ACOUSTIC WAVE NEBULISATION

Mohd Hafiz Ismail1, Julien Reboud1, Rab Wilson1 and Jonathan M. Cooper1

1Division of Biomedical Engineering, University of Glasgow, Oakfield Avenue, Glasgow, G12 8LT, UK
m.ismail.1@research.gla.ac.uk

Abstract – Targeted delivery of medication to a specific location in the body can be achieved effectively via non-invasive routes, and most commonly through inhalation of drugs in a droplet form. However the efficiency of the delivery depends heavily on the size of the droplets. In this paper, we demonstrate a surface acoustic wave (SAW) device as a nebuliser for drug delivery applications. Nebulisation was enabled by SAW generated by uniform interdigital transducers (IDT) on a piezoelectric substrate. The droplet size of various nebulised liquids were measured using Malvern Spraytec, a technique based on the laser diffraction. Droplet size was found to be inversely proportional to the excitation frequencies as expected from Kelvin, Rayleigh and Lang equations. The mean diameters of droplets range between 0.87 and 2.15µm proved that SAW devices are capable of generating droplets within the optimum sizes for drug delivery with controllable dosage at low input power of less than 2W.

INTRODUCTION

The droplet size distribution of aerosols generated by nebulisers is the main factor determining the efficiency of the penetration of the drug in the targeted organ. Pulmonary drug delivery requires droplets with diameters between 1 and 5µm[1]. Below that range, drops evaporate too quickly to reach the targeted area, while above, they tend to be deposited on the tissue lining before reaching the lungs SAW device have the capability to generate aerosols with a controlled droplet size at a high delivery efficiency and low power[2].

METHODS AND MATERIALS

Interdigital transducers were fabricated on 127.8° Y-cut lithium niobate (LiNbO3) substrate using the standard lithography and lift-off process[3]. The droplet sizes of four different nebulised liquids and four excitation frequencies were measured using Spraytec (Malvern Instrument Limited).

RESULTS AND DISCUSSIONS

Figure 1 shows the droplet size distribution obtained for different solutions. Pure ethanol used as a solvent that evaporates quickly showed a droplet size around 0.8µm. Bovine serum albumine (BSA) 5% in Phosphate buffer (PBS) that represents a protein solution widely used in drug delivery was nebulised at 0.9µm. Glycerol, more viscous and used when evaporation is not desired, created drops of 1.1µm. Finally water as a control produced droplets with a mean diameter of 1.6µm +/- 0.15µm. These diameters fall in the appropriate range for an efficient delivery of drugs to the lungs (1-5µm). Using these different solutions we demonstrated that droplet size increases linearly with surface tension, while viscosity does not play a significant role. Another handle that SAW nebulisation provides to control the droplet size is the excitation frequency. Droplet size is inversely proportional to the excitation frequency. Together with the solution composition, the frequency response will be used to design SAW-based nebulisers for efficient drug delivery to the lungs.

CONCLUSION

Our investigations of the effect of different parameters on the droplet size have shown that the excitation frequency was also powerful handles to control the droplet size efficiently in a range between 0.8 and 2µm at a low input power of approximately 2W. In future, phononic structures will be used to focus the waves into specific areas and suppress the generation of larger droplets.

REFERENCES

INTERACTION OF ANTIMICROBIAL PEPTIDES WITH BIOMIMETIC MEMBRANES BY BROADBAND OPTICAL TWEEZER MICRORHEOLOGY
David Paterson, Manlio Tassieri and Jon Cooper
Division of Biomedical Engineering, University of Glasgow, 0905807p@student.gla.ac.uk

Abstract - Linear, cationic antimicrobial peptide (LCAMP) family exert bactericidal effects by the formation of membrane-spanning pores, although the exact mechanism is poorly understood. Biomimetic giant unilamellar vesicles (GUVs) present versatile test-beds for investigation of the lipid-peptide interactions governing these peptides. Multiple analytical platforms gathering data from single GUVs in response to LCAMP binding, will generate large, comparable data sets, and potentially elucidate the complex behaviour of LCAMPs. This report presents the first part of this strategy: proof of concept for a novel optical tweezer broadband microrheology method, investigating effects of LCAMP binding on GUV viscoelastic properties.

INTRODUCTION
Antimicrobial research has undergone a recent resurgence, due to the pandemic of multidrug-resistant pathogens currently underway in developed world hospitals. LCAMPs show potential for development as novel therapeutics, showing much lower rates of acquired resistance in exposed bacteria than conventional antibiotics (2). Bacterial death occurs by leakage of intracellular contents and dissipation of ionic gradients, due to membrane-spanning toroidal pores formation (fig. 1) [3]; LCAMPs must produce changes to the viscous and elastic properties of bilayers, due to the high degree of membrane distortion induced during pore formation.

METHOD
Electroformation was used to produce biomimetic GUVs with bacterial and mammalian lipid compositions (1). By confining GUVs between optically-trapped silica beads (fig. 2a), particle tracking microrheology can determine inter-bead distance fluctuations (in the plane of the GUV), the viscoelastic moduli of the GUV can be derived.

RESULTS
Fig. 2(b) shows the mean-square displacement autocorrelation function generated, and fig. 2 (c and d) a comparison of moduli calculated for a free bead and an entrapping bead.

The autocorrelation curve shows a clear difference in the plane containing the entrapped bead, and the entrapping bead records an elasticity modulus, absent in the free bead.

CONCLUSIONS
The results provide proof of concept evidence that broadband microrheology is a suitable technique for the investigation of LCAMP induced changes in GUV viscoelastic properties. Calibration of the method using a known system will allow quantitative information to be determined.

REFERENCES
PATIENT ORIENTED ELECTROCHEMICALLY STRUCTURED TITANIUM IMPLANTS

J. Varia1, S. Roy1, J. Portoles1, A. McCaskie1, M. Birch1

1School of Chemical Engineering and Advanced Materials, University of Newcastle upon Tyne
2School of Mechanical & Systems Engineering, University of Newcastle upon Tyne
3Institute of Cellular Medicine, University of Newcastle upon Tyne

jeet.varia@ncl.ac.uk

Abstract – The application of electrochemical microfabrication of titanium alloys with enhanced osteointergration for medical bone related implants, within an overall paradigm of translational medicine. Our aim being the design of an electrochemical reactor for the micro-fabrication of 3D structured implants for application in the wider medical community.

INTRODUCTION

Translational research has the potential to deliver many practical benefits for patients and justify the extensive investments placed by the private and public sector in biomedical research [1]. For academia, translational research represents a general desire to test novel ideas generated from basic investigations with the hope of turning them into useful clinical applications. Of particular interest here is the application of electrochemical techniques for the enhanced fabrication of titanium materials for implants and design of novel reactors with reproducible 3D electro-microfabrication. Missing teeth, fully edentulous jaws, osteoporotic femoral neck fractures, and degenerative changes of hip and knee joints is just some application of titanium load bearing endogenous implants [1]. In the UK alone the need for hip replacements could near double in the next 30 years with a rise of replacement operations from 46,000 in 1996 to 65,000 in 2026 [ii].

TECHNICAL INFORMATION

Titanium and titanium alloy are widely used biomedical materials for biocompatibility, excellent corrosion resistance [iii] and chemical stability due to a dense oxide layer formed on exposure to the atmosphere; and good mechanical properties of lightness. Their application hitherto as endogenous load bearing anchors is directly dependent on the heterogeneous osteointegration of cells upon the surface. Here electrochemical anodic dissolution in non-aqueous methanol sulphuric electrolytes has shown to produce surface structures in the micro and nanometre range which significantly influence the attachment and growth of bone tissue [iv]. The phenomenon of surface integration of osteoblast cells (osteointergration) to titanium alloys is a

REFERENCES

INVESTIGATING CORE NETS AND STABILITY OF PERIODIC RANDOM BOOLEAN NETWORKS
Yanika Borg and Joseph Muscat

13, Triq il-Qighan, Mellieha, MLH 1813, Malta.
akinay.b@gmail.com

Abstract - Gene networks are often modelled as Boolean networks. We report an investigation on periodic random Boolean networks, where a genetic algorithm was used to evolve networks with a given period. In most cases, a core network with about half the nodes was found to be driving the periodicity. The cores tend to belong to a small set of networks which are large and irregular enough to be stable.

INTRODUCTION
When working with oscillatory circuits in biological systems, a property which is often considered is stability. It has been shown that random feedback networks “behave with stability comparable to that in living things”; even though biological networks are not random [1]. Boolean networks have also been used to model plant synthesis regulating conditions and protein production [2] [3].

A random Boolean network (RBN) is a directed graph where the nodes are inhibited or activated by their input neighbors and the relations between the nodes are set randomly. The objective of this study is to analyse a set of RBNs with a particular periodic length, by finding which nodes are causing the periodicity and which network setups are more stable. In this study, a stable network is defined as a network which evolves to the same periodic behaviour under different initial conditions. The aim of this paper is to get a clearer picture of the foundation of periodic RBNs.

METHODS
A genetic algorithm was used to collect RBNs with a period of length four. Nodes and relations which were causing the network to be periodic were then located. Thus, an itinerary of ‘core nets’ was built for the different periodic RBNs considered. A check for stability was then carried out, by seeing whether the periodic behaviour was emulated by a core net under different initial conditions. Results were visualised using phase diagrams.

RESULTS AND DISCUSSION
In most cases, the RBN considered was reduced to a net roughly half its original size. Fig. 1 shows one such core and its phase diagram. The smallest core consisted of a pair (A,B) with A activating B, and B inhibiting A. It was also observed that some networks which appeared to have nothing in common were reduced to the same core net.

Analysis carried out to examine stability of cores showed that the least stable nets were regular or quasi-regular. In some cases, the phase diagram showed up to six attractor cycles. It is interesting to note that one extra relation was sufficient to make these nets more stable. Larger nets were generally more stable.

CONCLUSION
This study on RBNs gave indications on the number of nodes and type of Boolean relations which allow a network to evolve a periodic behaviour. This study was limited to analysis of small networks. It would be interesting to carry out investigations on larger networks, and see if similar results are observed. Additional studies can be carried out to look into the predictive properties of the core nets; given an unknown net, can its behaviour be predicted using knowledge from known nets? This study has indicated that complicated cycles can be somewhat simplified. It is intended to apply a similar analysis to real biological networks and find if their core networks are among the ones we found.

REFERENCES
A MULTI-PARADIGM MODELLING FRAMEWORK TO CAPTURE DYNAMIC RECIPROCITY

Himanshu Kaul¹, Zhanfeng Cui¹, Yiannis Ventikos¹

¹Institute of Biomedical Engineering and Department of Engineering Science
University of Oxford, Parks Road Oxford, OX1 3PJ
himanshu.kaul@eng.ox.ac.uk

Abstract – A major challenge that computational approaches encounter when attempting to model cellular behaviour is capturing the dynamic interplay that exists between cells and their local microenvironment [1]. This paper presents a novel multi-paradigm modelling platform capable of capturing not only the impact of a system’s internal mass transport on the encapsulated cells but the manner in which cell growth influences the mass transport as well. Simulation results confirming this capability are presented.

INTRODUCTION
Computational techniques have been used, especially in the last few years, as a tool to investigate and predict, given the model assumptions and boundary conditions, cellular behaviour. Although such techniques have had their share of success in explaining the internal dynamics of systems under observation, they remain far from giving us an adequately comprehensive idea of the processes that govern these systems. The main conceptual hindrance is the lack of computational tools that can capture not only the impact of microenvironmental transport phenomena on cellular behaviour but also the cellular activity that alters that very same local mass transport, thereby influencing overall cell growth – in short dynamic reciprocity.

TECHNICAL INFORMATION
The models applied to investigate cell behaviour can be classified as continuum or discrete. Whereas the continuum approach works well to model bulk phenomena, it fails to capture cell behaviour in its detail and specificity. This is because continuum approaches assume cell populations as continua and therefore ignore the variations that may exist between identical cells within a population, which may cause them to behave in a non-identical manner [2]. Discrete approaches are utilised to model this very lack of resolution. However, they are recommended only when the number of individuals to be modelled is relatively low, and therefore are ineffective in accurately simulating bulk phenomena. A multi-paradigm modelling platform was therefore developed by bringing together, for the first time, two conceptually and functionally diverse ideas: computational transport phenomena and agent-based modelling. In order to assess the platform a series of in virtuo test cases were simulated. Briefly, 3D virtual models of bioreactors seeded with virtual cells were constructed. The virtual cells were assigned a set of logical rules that dictated their behaviour; such as apoptosis, growth, differentiation, and chemotaxis. The rules governing the cells involved constants as well as variables, for example glucose concentration gradients – the latter emerging as a result of the dynamic interplay between the cells and their microenvironment. The results show differences in cell proliferation between each of the different cases simulated in virtuo, also capturing the dynamic variation in the concentration of the scalar quantity, unique to each test case that arises due to the growth of scalar consuming cell populations: dynamic reciprocity.

CONCLUSION
We conclude that the modelling platform can be used as an analytical tool to investigate biological systems in a more relevant detail than previously attainable. Furthermore, it can also be used as a concept selection tool during the bioreactor design process and as a guiding tool to fine tune the ‘design of experiment’ phase of projects that involve gathering biological data.

REFERENCES
IMPROVED DIAGNOSTICS FOR HUMAN AFRICAN TRYPANOSOMIASIS

C. Kremer¹, A Menachery¹, S L Neale¹, M P Barrett² and J M Cooper¹

¹School of Engineering, University of Glasgow, Glasgow, UK
²Wellcome Trust Centre for Molecular Parasitology, College of Medical, Veterinary and Life Sciences, University of Glasgow

c.kremer.1@research.gla.ac.uk

Human African trypanosomiasis (HAT), or sleeping sickness is a deadly disease that kills tens of thousands of people each year with millions at risk of infection [1]. Current methods of detection are expensive or lack the necessary sensitivity to reliably diagnose HAT [2]. We used dielectrophoresis to demonstrate a novel approach toward detection of sleeping sickness.

INTRODUCTION

Human African trypanosomiasis is a deadly disease found in sub-Saharan Africa. It is caused by a single cellular parasite, Trypanosoma brucei, which infects a human blood stream through the bite of the Tsetse fly. Sleeping sickness is always fatal in not treated.

Detection of the disease is only possible through the visual confirmation of a parasite in a blood sample. This is difficult due to the small number of parasites compared to the number of blood cells. A method to separate out trypanosomes from RBCs is hence mandatory to accomplish a sensitive method of detection that will work in a timely manner. The methods used in the field today were established decades ago and very little has been done to improve detection since then. It is vital for the control of HAT, that new approaches for diagnostics are investigated.

In this work we study the biophysical properties of T. brucei and try to use them to develop a novel detection method. Little work has been done to define these properties in the past and no data could be found in the literature describing the dielectrophoretic properties of trypanosomes. Dielectrophoresis describes the movement of particles with no net charge in a non uniform electric field. It was first defined by Pohl [3] and has since seen an increasing amount of applications for the manipulation of cells.

A method related to traditional DEP is travelling wave DEP. This method can be used to move particles over large distances based on their DEP properties without the need to manipulate the liquid around them (for example with a pump driven flow system).

Traditionally a non uniform electric field is created through solid electrodes, for example metal films that are patterned on a glass substrate. This kind of setup is by its nature static and makes individual manipulation of cells difficult. A new and more flexible method is called opto electronic tweezers (OET) and uses a photoconductive material to create virtual electrodes. The photoconductive material changes drastically in conductivity when exposed to light. This allows the creation of an electrode by simply exposing a certain area of the substrate to light. The intensity needed to induce this change in conductivity is comparatively low and can be achieved with a simple data projector.

METHODS

Metal electrodes were patterned on glass using standard procedures. Blood samples of mice and humans and in vitro cultures of T. brucei were used. Cells were washed in buffer solution to control the conductivity during experimentation. A self-made optoelectronic tweezers setup was used for experiments with amorphous silicon patterned on glass as the photoconductor.

RESULTS

Dielectrophoretic properties like crossover frequencies were determined for human and mouse blood cells as well as trypanosomes. Separation of red blood cells and trypanosomes was demonstrated using DEP and large scale spatial separation was demonstrated using travelling wave DEP.

Individual single cell manipulation was demonstrated using OET and selective lysis of red blood cells was also demonstrated using OET.

Results were examined for different conductivity media and the limit of detection for lower parasitaemia was determined.

DISCUSSION AND CONCLUSION

Dielectrophoresis offers a novel tool to develop a diagnostic device for sleeping sickness. The results presented in this work show that DEP has the potential to improve on existing methods of detection. The technique potentially allows for the construction of a small hand held point-of-care device.

REFERENCES
INTRODUCTION
The use of primary hepatocytes (liver cells) could potentially be of great benefit to pharmaceutical companies in the screening of new candidate drug compounds. Currently, however, it is difficult to maintain cultures of metabolically active hepatocytes [1]. Hepatocytes are anchorage dependent cells; it is well documented that they are capable of binding both the RGD (Arginine-Glycine-Aspartic Acid) peptide sequence and the carbohydrate galactose, via the αvβ3 integrin and the asialoglycoprotein receptor (ASGPR) respectively. To fully investigate the usefulness of these ligands in improving hepatocyte adhesion and subsequent survival, focus was turned to poly (ethylene glycol) (PEG) coated cover-slips. These PEG monolayers were modified to incorporate both the RGD sequence and galactose using already established techniques [2]. These new materials were characterised using fluorescence and water contact angle measurement. They were subsequently tested for suitability as a cell culture surface using live/dead fluorescent staining.

METHODS
Surfaces were prepared using established protocols [2]. Peptide coupling is monitored using Fluorescence Spectroscopy. All measurements were taken using a Jasco FP6500 spectrofluorometer.

Primary hepatocytes were prepared by perfusion of rat liver with collagenase. Viability was determined using the Trypan Blue exclusion test, and was typically found to be greater than 70%. Cells were stained with Carboxyfluorescein Diace-diamine coated surfaces (Figure 2A), likewise there are few cells present on surfaces coated with random peptides (not shown). The presence of the RGD sequence, however, produces a significant increase in cell number (Figure 2B). The PEG-diacid treated surfaces show a slight increase in cell number compared to the PEG-diamine (Figure 2C), subsequent attachment of galactose greatly increases cell numbers (Figure 2D).

RESULTS
Fluorescence spectra show the successful step-wise build-up of the GRGDS peptide sequence (Figure 1).

Live/Dead staining clearly shows that the incorporation of both the RGD sequence and the galactose molecule improves the adhesion of primary hepatocytes within a 24h period (Figure 2). There are no cells remaining on the PEG-diamine coated surfaces (Figure 2A), likewise there are few cells present on surfaces coated with random peptides (not shown). The presence of the RGD sequence, however, produces a significant increase in cell number (Figure 2B). The PEG-diacid treated surfaces show a slight increase in cell number compared to the PEG-diamine (Figure 2C), subsequent attachment of galactose greatly increases cell numbers (Figure 2D).

CONCLUSION
It has been well documented that the inclusion of both the RGD sequence and the galactose molecule to synthetic scaffolds improves the adhesion of anchorage dependent cells. Initial results indicate that the PEG surfaces have been successfully modified to include the GRGDS peptide sequence. Cell culture experiments suggest that both molecules provide suitable anchors for hepatocyte adhesion. Work will now focus on determining the long term benefits of using these molecules. Further surface characterisation will also be carried out to ensure a homogeneous monolayer is being produced during peptide build-up.

REFERENCES
NANO-SCALE HYDROGELS FOR STEM CELL DIFFERENTIATION: THE INFLUENCE OF MECHANICAL STIMULI ON CELL BEHAVIOUR AND FUNCTION

Vineetha Jayawarna¹, Matthew J Dalby², Rein V Ulijn¹

¹WestCHEM, University of Strathclyde, Cathedral Street, Glasgow G1 1XL, UK.
²Centre for Cell Engineering, Joseph Black Building, University of Glasgow, Glasgow, G12 8QQ, UK.
vineetha.jayawarna@strath.ac.uk

INTRODUCTION

There is a growing consensus among researchers that many advances in medical field could be realised through adult mesenchymal stem cells (MSCs). These cells have the remarkable potential to develop into many different cell types in the body and therefore act as a source of replacement cells to regenerate numerous tissues and treat a myriad of diseases. Number of surface parameters of the biomaterial substrate that mimic the ECM for MSCs, including surface chemistry, topography and stiffness have been explained as modulating the cell function and behaviour patterns. The existing research has demonstrated the need for optimising matrix elasticity to respond to the mechano-sensitivity of the adult stem cells¹. In this paper we report the first examples of a rationally designed self-assembling short peptide non-coated elasticity tuneable hydrogel model (Fmoc-F2/S) that differentially modulates MSC differentiation while maintaining the same surface chemistry.

MATERIAL AND METHODS

A mixture of Fmoc-di-phenylalanine and Fmoc-serine (Fmoc-F2/S) was subjected to self-assembly by varying the pH of the pre gelation peptide mixtures. Pre gelation peptide mixtures, formed into stable hydrogels at around neutral pH (7.8) in the presence of cell culture media. Upon studying the mechanical and physical characteristics, the hydrogels were subjected to stem cell culture and cells were studied using immunostaining of cytoskeletal markers and gene expression.

RESULTS AND DISCUSSION

All three hydrogels formed a fibrous structure (Fig 1C) and have mechanical profiles of viscoelastic materials with elastic moduli varying between 1 and 38 KPa. While the sample with the least pH in pre gelation mixture reported the lowest stiffness measures (G~1.72 KPa), the sample with the highest pH reporting the highest values, with values taking up to an order of 37 magnitude higher compared to the lowest. (Fig.1B).

Immunostaining results revealed how MSCs pregulate the transcription factors in accordance to the mechanical character of the hydrogel. While soft gels largely support the expression of Nestin and SOX9, hard gels have a higher tendency to express SOX9, Osteopontin, RUNX2. Interestingly cells on stiff hydrogel express all most all specific markers tested (fig 1D).

FIGURE 1: A: chemical structures of Fmoc-FF, Fmoc-S and Fmoc and photograph of three pre gelation mixtures and three hydrogels. B: Elastic and Viscous modulus spectra for three gels. C: AFM images for pre gelation mixtures which showing fibrous morphology. D: immunostaining results for nestin, SOX9, Runx2 and OPN markers.

CONCLUSIONS

The results highlight the potential of short peptide hydrogels as a media for MSC differentiation and suggest that stiffness characteristics of the microenvironment for MSCs are critical for the design of biomaterials for stem cell-based regenerative medicine

REFERENCES

AN INVESTIGATION INTO THE COMPATIBILITY OF 5 POTENTIAL BINDERS FOR THE PRODUCTION OF ARTIFICIAL BONE SCAFFOLDS

A.F.L. Dunham¹, X.T. Yan², M.H. Grant¹

¹Bioengineering Unit, University of Strathclyde
²Department of Design Manufacture and Engineering Management, University of Strathclyde

Current practice of facial reconstruction is often below patients’ expectations. This could be improved by the use of 3D printed personalised bone scaffolds. In this study the biocompatibility of 5 potential binders for this process was investigated in vitro. None of the binders showed an overt toxic effect. However, all potential binders except for sodium trisilicate solution showed a cytostatic effect at concentrations of 100µM suggesting their use could result in an inhibitory effect on wound healing in vivo.

INTRODUCTION

The human face is highly individualised enabling us to distinguish one human being from another. Consequently, if disfigured the patient often suffers from severe psychosocial effects [1] and strongly desires a functional and aesthetic restoration. However, current practice of facial reconstruction is frequently below the patients expectations [2]. This could be improved by 3D printing of artificial bone scaffolds personalised to the patient.

This process requires a liquid binder to stick together ceramic powder one layer at a time and it is essential that the materials used have no adverse effect. In this study the biocompatibility of 5 potential binders was investigated in vitro.

METHODS

Alkaline Phosphatase (ALP) activity was measured and an MTT assay carried out on immortalised rat osteoblasts after being exposed to the 5 potential binders (Polyacrylic acid (PAA), maltodextrin (MD), sodium trisilicate solution (STS), citric acid (CA) and malic acid (MA)) at concentrations of 10µM and 100µM in Complete Dubecco’s Minimum Essential Medium for 24 and 48 hours.

RESULTS

The MTT assay showed no significant difference between cells exposed to any of the binders compared to the control cells at both 24 and 48 hours except for the cells exposed to 100µM citric acid for 24 hours which showed 80% of the activity of the control.

DISCUSSION

At 48 hours none of the cells exposed to any of the binders showed a significant difference in the ability to reduce MTT showing that none of the binders had an overt toxic effect on osteoblasts and suggesting any would be suitable for use in future development of bone scaffolds. However, at 24 hours the ALP activity of the cells exposed to all of the binders at a concentration of 100µM, except STS, was significantly lower than the control. By 48 hours there was no significant difference suggesting those binders may be cytostatic and affect cell division only at the rapid log phase of growth. Although this may result in an inhibitory affect on wound healing in vivo, the ALP activity of the cells exposed to these binders was still more than 75% of the control suggesting they are still suitable for future work.

REFERENCES


FABRICATION OF 3D HIGH THROUGHPUT CELL SCREENING TOPOGRAPHIES USING PLASMA POLYMERISED GRADIENTS AS A SECONDARY ETCH MASK

P. M. Reynolds, R. H. Pedersen, N. Gadegaard

Division of Biomedical Engineering, School of Engineering, University of Glasgow, Glasgow, 0602340r@student.gla.ac.uk

Abstract - We present gradients of plasma polymerized hexane (ppHex) for use as etch masks, enabling asymmetric etching and the fabrication of grooves of variable depth. This gradient of groove depth is created orthogonal to a further gradient of groove pitch, allowing a multidimensional analysis of cellular response to two distinct surface parameters: feature depth and pitch. The localisation of favourable cellular response to the surface is a high throughput technique for optimising surface parameters.

INTRODUCTION

Studies investigating cell-surface interactions are often limited to just a few variable parameters, and are complicated by inter sample variation. Gradients of topography and chemistry offer a high throughput alternative, whereby the position of a certain cellular response allows high resolution determination of favorable surface properties for the future design of implantable medical devices [1]. Plasma polymerization is a versatile technique which allows the deposition of ultra-thin polymer films on both planar and non-planar substrates [2]. Such deposits have been shown to exhibit a high degree of conformity and stability, making them ideal for further processing, and leading to practical applications in surface functionalization [3] and protective coatings amongst others. Gradients of both film thickness and chemistry[4,5] have been demonstrated by allowing the gas phase monomer to diffuse along a channel whilst undergoing polymerization. The properties of such gradients are tunable based on deposition parameters such as power, pressure, monomer flow rate and channel geometry [4]. Here we present gradients of plasma polymerized hexane (ppHex) for use as a secondary etch mask, enabling asymmetric etching and the fabrication of grooves of variable depth. This gradient of depth is created orthogonal to a further gradient of pitch, Figure 1, allowing a multidimensional analysis of cellular response to two distinct surface parameters, i.e. feature depth and pitch, which have already been shown to influence cell behaviour [6].

MATERIALS AND METHODS

Silicon substrates were patterned using photoreisist as a primary etch mask, defining 8μm wide grooves with pitch ranging from 8μm to 100μm across a 10nm square pattern. ppHex gradients were deposited as a secondary mask in a custom-built borosilicate plasma chamber. These gradients ranged from 120nm to 10nm in thickness, Figure 2. The substrate was then etched in an ICP RIE, transferring the ppHex thickness gradient into the micro-patterned grooves. It has been observed that ppHex exhibits a selectivity of 1.8:1 against silicon. Subsequent plasma deposition and etching cycles are repeated until the groove depth ranges from 1μm to 10nm across the pattern. Finally, the primary mask is removed in acetone.

CONCLUSION

The silicon masters described here are currently being used in an embossing process to create constructs for high throughput screening of cell-surface interactions, focusing on epithelial cells for wound healing applications. A gradient of feature depth spanning two orders of magnitude offers a unique approach compared with previously reported studies, allowing a vast improvement in the rate at which cellular response to topographical motifs can be screened.

REFERENCES

SPECTROMETER-ON-CHIP FOR FLUORESCENCE BIO-SENSING
Zhixiong Hu1, Andrew Glide2, Charles N. Ironside3, Marc Sorel1, Michael Strain1, Jonathan M. Cooper1, Huabing Yin1

1School of Engineering, University of Glasgow, Glasgow, UK
huabing.yin@glasgow.ac.uk

Abstract – A visible Arrayed Waveguide Grating (AWG) spectrometer was designed and fabricated, for the first time, to detect fluorophores commonly used in biological assays. This concept of on-chip spectrometer was proved by detection of Cy5 fluorescence spectrum.

INTRODUCTION
Arrayed Waveguide Grating (AWG) devices were initially proposed as optical multiplexing routers for communication network [1]. Here, we transferred the AWG technology to the field of bio-sensing and developed a visible on-chip spectrometer to perform fluorescence spectroscopy, the most commonly used technique in biochemical analysis and medical diagnosis [2].

METHODS
Based on design in visible range instead of infrared region, an 8-channel flame hydrolysis deposition (FHD) silica AWG device was fabricated to realize a miniature spectrometer. Figure 1 shows the realisation of the device and the small size is illustrated.

RESULTS AND DISCUSSION
Optical characterisation of the AWG spectrometer was performed with a white light source and Figure 2 gives the output spectrum from different channels. Integrated with a microfluidic channel, the AWG device was employed to detect Cy5 emission spectrum. As shown in Figure 3, wavelength positions and intensity levels of light detected from different output channels were in good agreement with the envelope of Cy5 emission spectrum.

CONCLUSION
A visible on-chip spectrometer for fluorescence bio-sensing was realized based on Arrayed Waveguide Grating (AWG) technology. To prove this concept, Cy5 emission spectrum was detected.

REFERENCES
SAW-ING INTO CELLS: PORATING CELLS WITH SURFACE ACOUSTIC WAVES
Sophie E Thurlow*, Dr Julien Reboud, Dr Rab Wilson, Prof Jon Cooper*
Department of Electronics and Electrical Engineering, University of Glasgow
*1004959t@student.gla.ac.uk, jon.cooper@glasgow.ac.uk

Transfection of cells with DNA and RNA is a common technique to elicit specific phenotypes. Here we show that surface acoustic waves (SAWs) have a great potential to be used to porate cells and could facilitate transfection of mammalian cells. SAWs have been used in microfluidic applications, where sound activates liquids and particles within them. Microstructures patterned on microchips can be used to manipulate the propagation of the waves altering the motions of fluid streaming in a droplet placed in their path, creating pressures and strain that open membrane pores.

INTRODUCTION
Transfection of small interfering RNA (siRNA) in biological cells allows the knocking down of specific proteins, thereby mimicking abnormal cell states such as disease. This has been achieved using a number of techniques including sonoporation, which makes use of ultrasonic waves to cause acoustic cavitation giving rise to the formation of transient pores in the cell membrane [1].

Surface acoustic waves (SAWs), generated by interdigitated transducers (IDTs), are mechanical waves propagating along the surface of a material. Along with nanostructures, capable of manipulating wave propagation, SAWs can be used to control the streaming of fluids [2]. In a cell suspension droplet, the fluid streaming as well as the pressure waves induced by the SAWs will cause transient pore formation facilitating the passive uptake of siRNA.

MATERIALS AND METHODS
An IDT consisting of gold electrodes was patterned on lithium niobate (LiNbO₃), FIGURE 1. The IDT was operated at 9.54 MHz. The silicon superstrate was coupled to the LiNbO₃ wafer using KY Jelly.

RESULTS AND DISCUSSION
Figure 2 shows that SAWs can be used to open up the cells, which lets Trypan blue stain inside them. Increasing the power increases the efficiency of the poration. Future work will determine the extent to which the poration is transient and if transfecting cells using SAW results in functional changes in the cells for example the ability of cells to proliferate after exposure to SAW will be examined.

CONCLUSION
These results indicate that SAWs are capable of porating cell membranes and provide a promising approach for the transfection of cells with nucleotides such as siRNA.

REFERENCES
INVESTIGATING GROUND CONTACT INFORMATION FOR USE IN NEURO- PROSTHETIC CONTROL OF FES ASSISTED GAIT IN PATIENTS WITH SPINAL INJURIES

C.A Macleod1, B.A Conway1, B Porr2
1Bioengineering Unit, University of Strathclyde
2School of Engineering, University of Glasgow
c.a.macleod@strath.ac.uk

Abstract - Investigating load dependent reflexes and their role in the control of normal human walking will determine whether a walking pattern can be generated using a feedback loop driven by ground contact information from the feet. Finding a causal relationship between plantar pressure and leg muscle activity (EMG) during walking has potential in spinal cord injury rehabilitation. Measurements will be taken of plantar pressure and EMG in healthy human subjects while they walk on a speed controlled treadmill. A previous study using a constant speed treadmill found that a causal relationship does exist between heel plantar pressure and muscle activity.

INTRODUCTION
This project has developed from observation of RunBot, a biped robot which operates through reflexes without using a central pattern generator. Touch information from the feet is used to drive motors in the opposite leg, generating walking [1]-[2]. Finding a causal relationship between ground contact information and leg muscle activity during normal human walking will enable transfer functions to be determined. The aim is the development of a functional electrical stimulation (FES) device to assist in a spinal cord injury (SCI) patient’s gait capability. Currently, accurate control of FES cannot be achieved in an open-loop system due to difficulties in predicting the correct timing of a stimulus, non-linearity of the neuromuscular skeletal system and inability for modulation during deviations from an ideal gait cycle. A system which incorporates feedback control will allow gait cycle modifications to suit loading conditions; the stimulation pattern will be modulated by the walking itself, Fig. 1.

METHOD
Healthy volunteers were recruited for the initial study which involved recording leg muscle EMGs and foot pressure during average speed walking on a treadmill.

DISCUSSION
In the initial study, a correlation was identified between heel pressure and muscle activity, Fig. 2. This suggests that foot touch information has the potential to be used with FES for walking pattern generation.

REFERENCES
THE EFFECTS OF TRANSCRANIAL STIMULATION ON ENHANCED PHYSIOLOGICAL TREMOR: A PILOT STUDY

Pauline Axford¹, Heba Lakany¹, Bernard Conway¹

¹Bioengineering Unit, University of Strathclyde, Glasgow G4 0NW
pauline.axford@strath.ac.uk

Abstract – Anodal transcranial direct current stimulation (+tDCS) and 5Hz anodal transcranial sinusoidal stimulation (+tSS) were applied to the motor cortex of one subject who displayed enhanced physiological tremor (EPT). The effects of the interventions on the subject’s tremor were evaluated using inter-muscular coherence (IMC). Direct current stimulation enhanced the tremor and 5Hz sinusoidal stimulation reduced it. The inhibitory effect of the tSS was also shown to be dependent on the current intensity. This short pilot study suggests that transcranial stimulation to the motor cortex can alter tremor in EPT.

INTRODUCTION

A number of pathological tremors, such as essential physiological and Parkinsonian tremor, are treated with deep brain stimulation. EPT is a benign tremor which, depending on its severity, can be debilitating to the individual. Anodal tDCS is a type of non-invasive, low current brain stimulation that enhances excitability in the cortex [1]. Here we applied +tDCS and a novel 5Hz +tSS to the motor cortex of one subject who displayed EPT. IMC represents the degree of correlation, in the frequency domain, between two EMG signals, and was used to investigate neuronal excitability. We hypothesised that tDCS would enhance the tremor by increasing excitability, and 5Hz +tSS would alter the tremor by interfering with central oscillations.

METHODS

Both +tDCS and 5Hz +tSS were applied at 0.5mA for 5 minutes; the tSS paradigm was also repeated at 1mA. The oscillations for tSS were 10% of the maximum current. EMG was recorded, in four co-contracting muscles, for one minute before, during and after the intervention. The IMC was generated from the raw EMG data in the Matlab toolbox Neurospec [2].

RESULTS & DISCUSSION

The change, from baseline, in the total IMC of the tremor component was averaged over the six muscle pairs, and the standard deviation was obtained, for each time point (represented in Fig. 1). The literature suggests that +tDCS enhances cortical excitability; here we have shown that when applied to an EPT subject it enhanced the tremor. There is evidence to suggest that the neurogenic component of EPT originates as 8-12Hz oscillations between the basal ganglia and cerebellum [5]. Our observations, therefore, suggest that +tDCS is also capable of altering oscillations in deeper structures of the brain. Sinusoidal stimulation at 5Hz reduced the tremor during both the 0.5mA and 1mA interventions. The tremor returned to baseline following the 0.5mA paradigm, but the 1mA paradigm resulted in a persistent reduction. The persistence, and the reduction in the variance, observed for 1mA stimulation is in agreement with the current dependency of tDCS discussed in the literature [3]. Our results suggest that the new tSS paradigm is capable of interfering with oscillations in deeper structures of the brain. This may prove to be relevant in treating EPT and may have analogues in other types of pathological tremors potentially removing the requirement for invasive treatments.

CONCLUSION

The study suggests that tremor in EPT can be inhibited by non-invasive tSS, this may point to a new, non-invasive treatment of tremor. This was a small pilot study, and so conclusions must be drawn with caution; however, it does provide justification for an additional, more thorough investigation.

REFERENCES

MICROPOLAR PROPERTIES OF BONE
Jamie Frame¹ Dr Marcus Wheel¹ Dr. Phil Riches¹

¹University of Strathclyde
Jame.frame@strath.ac.uk

Abstract – Cortical bone is a heterogeneous material with a hierarchical microstructure. The influence of the microstructure on the macro structural material properties is not fully understood. Micropolar elasticity can describe materials with a microstructure. Finite Element analysis and experiments on bovine cortical bone have attempted to analyse the microstructure of bone and quantify the degree of micropolar behaviour observed. Results show a slight micropolar trend in bovine cortical bone. However the results show a high degree of variance and further experimentation is required to validate the results.

INTRODUCTION
Cortical bone is a heterogeneous material consisting of a hierarchical microstructure characterised by fibrous, porous and particulate features. Consequently, this has an impact upon the macroscopic material properties [1,2]. Bone prostheses are typically modelled using Classical Continuum Elasticity. However, this model may not adequately describe the stress concentrations produced by procedures such as a hip arthroplasty or femoral head resurfacing. Resultantly a material model which considers the microstructure of bone may better describe such situations.

Micropolar Elasticity is a Generalized Elastic Continuum Theory which incorporates a local rotation of points (a couple stress) into the formulation, as well as the direct stress. This has the net effect of producing four extra elastic constants (six in total) compared with those produced by classical elasticity. The micropolar behaviour can be analysed by the observation of a size effect in 3-point bending or torsion tests. Previous testing has revealed Micropolar behaviour in both cortical and cancellous bone [3].

TECHNICAL INFORMATION
By creating computational models of idealised heterogeneous materials with regularly arranged voids micropolar behaviour has been simulated as a size effect in 3-point-bending. The results show that the micropolar characteristic length is of the order of the diameter of the voids and the micropolar Young’s modulus is equivalent to the axially loaded Young’s modulus on the same heterogeneous material. Moreover, simulations have also demonstrated that the influence of surface effects has an important impact on the behaviour of such materials.

The microstructure of bone can be compared to an idealised heterogeneous material. A series of experiments have been undertaken to determine if micropolar behaviour is observed in cortical bone. Samples were prepared from the diaphysis of a bovine femur and loaded under 3-point-bending. Qualitatively the experimental results follow the trend shown computationally of micropolar materials. The results show a characteristic length of 0.15mm, in the region of the diameter of a Haversian canal, and the micropolar Young’s Modulus of 16.55 GPa. Both comparable to the Young’s Modulus of bone and the diameter of an osteon in cortical bone. There is, however, a high degree of variance in the results and further experimentation is required to validate the results.

CONCLUSION
Micropolar elasticity may be more effective for analysing stress concentrations around bone prosthesis than classical elasticity. Further experimentation is required to fully validate and quantitatively determine the scale of micropolar behaviour seen in bone.

REFERENCES
A COMBINED AFM AND IMMUNOFLUORESCENCE STUDY OF CELL ELASTICITY AS AFFECTED BY TOPOGRAPHY

C. Fyfe¹, G. Mcphee¹, M. Dalby², M. Riehle², H.B. Yin¹

¹ Division of Biomedical Engineering, University of Glasgow, UK
² The Centre for Cell Engineering, University of Glasgow, UK

*1000699f@student.gla.ac.uk

Abstract - Topography has been shown to influence cell fate and function. Using microfabrication techniques to mimic in vivo conditions enables researchers to gain a better understanding of cell behaviour. The influence of topography can result in changes in stiffness and lead to differentiation. This has been demonstrated by AFM measurements and immunofluorescence studies. Here we present an investigation of the links between topography induced biophysical cues and cell transcriptional changes. To achieve this, we hope to use siRNA techniques to knock down proteins involved in the communication between the cell cytoskeleton and the nuclear matrix.

INTRODUCTION

It has been shown that topographical cues can influence the differentiation of Osteoprogenitor cells and Mesenchymal Stem Cells (MSC) [1]. A substrate of pits with displaced placement results in MSCs forming bone nodules [1]. Further work has also shown that the topography can significantly influence the stiffness of a cell [2]. As seen in figure 1 the growth of cells in grooves results in significantly stiffer cells compared to grown on flat Poly (dimethylsiloxane) (PDMS) substrate.

METHODS

Cells are transfected with siRNA targeting nuclear lamins A/C and B using the Nucleofector device following recommended protocols. Transfected cells and controls are cultured on topographical features on PDMS before stiffness measurement and immunofluorescent staining is carried out.

RESULTS AND DISCUSSION

Here we report our preliminary results on the variations of cell stiffness pre/post-transfection with siRNA, which is correlated with the immunofluorescence staining of transcription factors and cell cytoskeleton.

REFERENCES


CHARACTERISATION OF METAL NANOPARTICLES FOR THE DEVELOPMENT OF A NOVEL IMMUNOCONTRACEPTIVE DEVICE

N. Nimmo¹, O. Sutcliffe², A.B. Mullen², V.A. Ferro²

¹Department of Bioengineering, University of Strathclyde, 106 Rottenrow, Glasgow G4 0TE.
²Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, 161 Cathedral Street, Glasgow
Natalie.nimmo@strath.ac.uk

We propose a long-term non-steroidal contraceptive device based on metal nanoparticles (NPs) with hydrophobic coatings, which will enable attachment of reproductive antigens to the NPs for further development. In this study, NPs were characterised by determination of particle size, electron microscopic imaging and determination of viable concentrations and immune response to human monocytic cells (THP-1). Preliminary investigations have shown substantial promise for future applications in both a contraceptive to replace existing steroidal methods and a novel immunocontraceptive to advance the field, with the long-term aim of developing a gel formulation and applicator design that makes the contraceptive cheap to manufacture and easy to self-administer.

INTRODUCTION

Development of a viable, non-steroidal human immunocontraceptive device could give a long-lasting reliable option that is less invasive than intrauterine devices, and could bypass side-effects, such as thrombosis, seen in steroidal methods [1]. The proposed device is based on metal nanoparticles (NPs) synthesised with one of two hydrophobic coatings, which will enable attachment of suitable antigenic proteins. This study characterises the NPs in order to determine their feasibility for use in a human vaccine device to prevent contraception.

METHODS

A. Synthesis, Sizing and Imaging

Synthesis of coated NPs was based on a method derived from Khanna et al (2008) [2]. Sizing was performed on dispersed NP solutions using a Malvern Zetasizer ZS for small particles, and a Malvern Mastersizer 2000 for large particles. Images of NPs were obtained using transmission electron microscopy (TEM) and scanning electron microscopy (SEM).

B. In Vitro Studies

Cell viability was determined by exposing dispersed NP solutions (0.5mg/ml-0.24µg/ml in serial dilution) to THP-1 cells, alongside a 10% (w/v) resazurin salt solution, for 48 hours before determining % cell viability by spectrophotometry (wavelengths: 570nm and 600nm). The potential response of immune cells was determined by monitoring THP-1 cell interactions with NPs using inverted light microscopy.

RESULTS AND DISCUSSION

FIGURES 1 AND 2. TEM (figure 1) and SEM (figure 2) images of NPs.

FIGURE 3. Light microscope images of control cells (A), and cells incubated with NPs (B and C)

A. Synthesis, Sizing and Imaging

NPs synthesised varied in size from 30-1000nm, independent of solvents used and concentration of NPs analysed. Imaging showed typical particle sizes of 200-300nm overall (Figures 1 and 2), with a coating depth of 130nm.

B. In Vitro Studies

Cell viability assays determined the 3 highest non-toxic concentrations to be 3.9µg/ml, 2µg/ml and 1µg/ml. On exposure to NPs, the THP-1 cells appeared to gravitate towards, and aggregate around, the NPs, and after approximately an hour, fragments of NP aggregates were found inside the cells. So far, preliminary studies have determined a method of NP synthesis and concentration of NPs potentially suitable for use in an immunocontraceptive device. Further testing is ongoing.

REFERENCES

MICROFLUIDIC DEVICES FOR SINGLE CELL DIVISION AND MIGRATION

Mayuree Chanasakulniyom*, Andrew Glidle and Jonathan M Cooper

Division of Biomedical Engineering, School of Engineering, University of Glasgow, Glasgow, G12 8LT, UK

*m.chanasakulniyom.1@research.gla.ac.uk

A micro plug-hole like device has been fabricated to trap cells and address how they migrate and divide. The device consists of three PDMS layers in which the bottom layer contains a network of submerged channels that link cavity-like plug holes and through which cells can migrate. Preliminary results show that cells both migrate from one cavity to another via the channel network and can divide within individual plug holes.

INTRODUCTION

Microfluidic techniques have become an invaluable tool for single cell analyses. By studying one cell at a time, its division or migration, rate of division and direction of migration can be monitored. This study used the micro plug-hole like device in order to address how single cells migrate and divide.

TECHNICAL INFORMATION

A. Microfluidic device fabrication

The micro plug-hole like device consists of three layers, each fabricated using photolithography. The bottom layer contains a network of submerged channels that link cavity-like plug holes. The middle layer consists of an array of circular holes used to organise single cells so that they are directly above the cavities of the lower layer. The top layer is a PDMS chamber for cell loading and cell culture medium perfusion (Figure 1).

![Figure 1 Schematic of the micro plug-hole like device. (A) a cross section (B) SEM image of the micro plug-hole like device (C) an overview](image)

B. Cell division and migration study

Human breast cancer cells MCF-7 expressing GFP-actin were trypsinized and resuspended in culture media. The MCF-7 cells suspension was introduce into the devices via tubing and microsyringe pumps starting with a fluid flow rate of 0.5 μl/min and then reducing it to 0.1 μl/min, after cells had entered the device. When cell loading was complete the fluid flow was stopped and the device placed in an incubator (37°C, 5% CO₂) for about 2 hours. This allowed cells to settle and attach, before perfusion with culture media at a flow rate 50 nl/ min. Cell proliferation and migration over the following three days was monitored using time lapse fluorescence microscopy.

RESULTS

As the images in Figure 2 show, in this device cells can extend their pseudopods and migrate from one cavity to another via the subterranean channel network. Besides that, division within individual plug holes was also observed.

![Figure 2. MCF7 cell behavior in microhole device after 24, 40 and 70 hours.](image)

CONCLUSION

A practical fabrication strategy has been devised to create a three tiered micro plug-hole like device. Using this and time-lapse microscopy, cell migration and division events can be observed over extended incubation times. Further studies of cell responses to patterns of stimuli will be performed to gain knowledge about the factors affecting cell migration and proliferation.
**SHAPING HYDRODYNAMIC AND ACOUSTIC FORCES FOR FLUID MANIPULATION USING MICROSTRUCTURED ARRAYS**

Liliana Acosta Alvarez¹ and Jonathan M. Cooper¹

Division of Biomedical Engineering, Rankine Building, University of Glasgow, G12 8LT

l.acosta-alvarez.1@research.gla.ac.uk

Deterministic Lateral Displacement (DLD) is a technique that allows separation with an exceptional resolution of down to 20 nm in particle diameter and provides low cost fabrication. DLD devices have other advantages such as being capable to be combined with Surface Acoustic Waves (SAW) to take advantage of both techniques to create a new method for fluid manipulation and particle separation.

**INTRODUCTION**

Pillar arrays have been used in the past as a blood separation technique invented by Huang et al. This technique is known as Deterministic Lateral Displacement and consists in a microarray of pillars constructed in a rigid material like silicon to sort particles based on size [1]. This technique has been shown to differentiate between micrometer-sized particles with a resolution in diameter on the order of 20 nm. The based sorting mechanism has been described for the devices used experimentally: particles smaller than a critical radius \( r_c \) follow streamlines through the array, while larger particles are systematically displaced laterally during each interaction with a post.

**TECHNICAL INFORMATION**

Additionally the array can be altered in shape and distribution to affect the flow direction. The hydrodynamics happening in a pillar array is a matter of interest because it has been demonstrated that depending on the geometry of the obstacles, particles disperse in fluid will change their trajectory [2].

Phononic crystals are synthetic fabricated materials which have different elastic properties that can have the ability to manipulate elastic wave propagation in certain frequencies depending on their characteristics. For this reason Surface Acoustic Waves can be used with micropillar arrays due to the periodic variation of density and elastic properties that make changes in the speed of sound in the crystal and therefore form a phononic band gap. [3]

Phononic crystals are nowadays an important subject for study due to its possible applications in the field of telecommunications and recently in biotechnology. These structures have been demonstrated to have the ability to create full band gaps, waveguides, sonic lenses and reflectors for Surface Acoustic Waves, to use them for fluid manipulation [3].

All the microstructured arrays were made on silicon and then coupled with a piezoelectric actuator.

Figure 1. An example of the velocity field solved with a finite element analysis model in COMSOL Multiphysics. The 2D array consists of 10 micron pillars and 10 micron gaps. A difference in pressure is applied from left to right of the array and velocity is measured at each element. The velocity profile shows that the pillars create regions of slow and fast fluid movement, being blue and red respectively. As it can be seen the highest velocity is achieved between the gaps.

**CONCLUSION**

This method for particle sorting not only will simplify fabrication, but also creates a more portable and cheaper device that can be changed according to particle size. In addition, this brings not only a sorting technology based on size but also on acoustic properties, that can be achieved depending on the design of the DLD device that acts as a phononic structure. Further investigation is needed into how these parameters, together with the geometry of the pillar array, can be optimized for the separation of biological particles such as cells, with regards to size and acoustic properties.

**REFERENCES**


DEVELOPMENT OF A REINFORCED SYNTHETIC HEART VALVE FOR PERCUTANEOUS DELIVERY

Monica Rozeik1, David Wheatley1, Fraser Sutherland2, Terence Gourlay1

1Bioengineering Unit, University of Strathclyde, 106 Rottenrow East, Glasgow
2 West of Scotland Regional Heart and Lung Centre, Golden Jubilee National Hospital, Glasgow
monica.rozeik@strath.ac.uk

Percutaneous heart valves (PHV) enable a trans-catheter delivery of a heart valve without the need for open heart surgery. It is the aim of this project to reduce the thickness of PHVs in order to provide a low delivery profile through a super-peripheral access site. Thin medical grade polyurethane films incorporated with carbon fibers were developed and mechanically tested. Results show improvement in tensile properties following reinforcement.

INTRODUCTION

It is desirable to reduce the thickness of percutaneous heart valves in the aim to achieve trans-catheter delivery through a super-peripheral access site. Polymeric valves combine the durability of mechanical valves with the hydrodynamic function of bioprosthetic valves [1]. It has been established that mechanically reinforcing the leaflets reduces the stresses that the heart valve is subjected to during cyclic loading [2].

In this study, various medical grade polyurethanes were reinforced with carbon fibres to produce thin (≤ 50 µm) films without compromising their mechanical integrity. It is envisaged that by reinforcing the leaflets, tear strength and resistance to fatigue will also be improved.

EXPERIMENTAL METHOD

Carbon fibers having wide and thin diameters were subjected to acid refluxing and calcination to remove the metallic impurities left from their synthesis. 1% w/w of fibers were then incorporated into medical grade polyurethane solutions of Carbothane® and Elast-Eon™ and solvent cast into thin films having thicknesses of approximately 40 µm.

Thin strips of each film were subjected to tensile testing to obtain the elastic modulus, stress relaxation and creep modulus. The tear strength was obtained from trouser specimens of the same composites. A two-sample t-test with a 95% confidence interval was conducted to determine statistical significance. The results for one of the Carbothane® polymers are shown in Figure 1.

RESULTS

The elastic modulus, was seen to improve significantly (p<0.05) for both polymers. For the wide fibres, improvement in modulus was as high as 76.9% compared to the thin fibres which had a maximum improvement of 36.1%. Tear strength was seen to improve proportionally to the stiffness.

Although the thinner fibres would have had a higher aspect ratio and were expected to provide a greater reinforcement, it is likely that they were more prone to agglomerating, reducing their aspect ratio.

CONCLUSION

Based on the findings from the mechanical tests, tri-leaflet heart valves will be dip-coated using the best composite material and tested for hydrodynamic and durability purposes.

REFERENCES

DROPLET-BASED MICROFLUIDIC SYSTEM FOR INTRACELLULAR PROTEIN QUANTIFICATION

Chiara Martino¹, Michele Zagnoni¹, Mairi E. Sandison², Mayuree Chanakulniyom¹, Andrew R. Pitt² and Jonathan M. Cooper¹

¹ Division of Biomedical Engineering, School of Engineering, University of Glasgow, Glasgow, G12 8LT, UK
² Institute of Molecular, Cell and Systems Biology, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow, G12 8QQ, UK
c.martino.1@research.gla.ac.uk

Abstract – This paper presents an original droplet-based microfluidic system used for the capture and quantification of cytoplasmic proteins from on-chip electrically lysed cells. This semi-automated method produced results comparable to those from Western blots, in faster times and using a much smaller number of cells.

INTRODUCTION

The capture and quantification of proteins expressed by cells constitute an important goal of modern biology for understanding cellular behaviours and represent a key requirement for elucidating intracellular signalling pathways [1]. In the last 10 years, the use of emulsions (i.e. water in oil droplets) formed using microfluidic technology has led to the development of increasingly complex biological assays, characterised by faster analysis times and reduced sample volumes. This paper presents the experimental results obtained from on-chip detection and quantification of RAS protein. An original schematic of the microfluidic design used for this goal is presented in Fig. 1.

FIGURE 1: Device architecture generating microdroplets with mean diameter of 80 μm produced at a frequency of 20 Hz [2].

The device consisted of a microdroplet generator permanently bonded to a glass slide, onto which microelectrodes were fabricated and used for electrically lysing cells. The chip comprised three inlets (A, B and C) for the oil, bead suspension and cell/protein solutions, respectively. Fluids entering from B and C merged at the Y-junction (D) and further downstream water-in-oil droplets were generated at the T-junction (E). Finally, droplets were stored in a chamber (F) where fluorescence imaging was performed.

TECHNICAL INFORMATION

The device was made using photolithographic, dry etching and lift off processes. Anti-H-Ras antibody was biotinylated and conjugated to superavidin beads. Six dilutions of a fluorescent secondary antibody solution containing FITC-conjugated anti-mouse IgG were prepared for calibration experiments. Data were processed and analysed using Matlab (version 7) and ImageJ.

Few hundreds of HEK-293 cells, expressing HRas-mCitrine, were injected from inlet C and electrically lysed over the electrode (20 V, 1 MHz). HEK-293 cells were susceptible to lysis under mechanical stresses therefore capture experiments were carried out with and without electrical lysis, in order to enable a comparative measurement (Fig. 2a). Intensity values for the non-lysed case corresponded to a HRas-mCitrine concentration of 3.5 nM, whilst the value obtained when lysing the cells was 13 nM, giving a value of approximately 10 nM for the contribution due to the cells lysed on-chip (Fig. 2b). This was in close agreement with the value from the Western Blot data (10.14 nM).

CONCLUSION

Compared to conventional methods, this system showed promising results in reducing the times of quantification of cellular proteins.

REFERENCES

A NON-INVASIVE SYSTEM FOR REAL-TIME DETECTION AND TREATMENT OF SLEEP APNEA EPISODES

Alison M. Aird¹, William Sandham¹,²

¹Dept of Bioengineering, University of Strathclyde, Glasgow, UK
²Scotsig, Glasgow, UK

Abstract - In obstructive sleep apnea, a person's airway becomes repeatedly blocked during sleep, and they awaken many times per hour to restore their breathing. Diagnosis is traditionally performed overnight in a sleep laboratory, which is expensive and uncomfortable. Treatment often involves wearing a pressurized mask to keep the airway open. The present authors are developing a new detection/treatment system, using a pressure sensitive mat located under the patient's mattress to monitor breathing movements in real time. Absence of a breathing signal triggers a vibrating device located under the patient's pillow, inducing them to move and resume breathing without awakening.

INTRODUCTION

Sleep apnea is a sleep disorder affecting about 3% of the population. A person's airway becomes blocked during sleep, and they awaken many times per hour to restore their breathing. This can result in excessive tiredness, cardiac problems and other health issues [1]. The standard treatment is continuous positive airway pressure therapy (CPAP), where the patient wears a pressurized mask to keep their airway open. However, this is uncomfortable and is not successful for all patients [2]. Diagnosis of sleep apnea is achieved by polysomnography, which measures multiple parameters overnight in a sleep laboratory, including nasal airflow, body movement, EEG and ECG. An alternative for home monitoring is pulse oximetry [3], but it is not suitable for real-time monitoring, due to a detection time lag of up to several minutes. There is a need for better methods of real-time detection and treatment.

METHODS

Monitoring a baby's breathing with a pressure sensitive mat below the baby's mattress is well-established [4]. A piezoelectric sensor in the mat detects pressure changes resulting from breathing movements. If the movements stop, an alarm is sounded. A key advantage is that it is non-intrusive, making no physical contact with the baby. The present authors are developing a device for real-time sleep apnea detection and intervention in adults, based on a piezoelectric sensor mat. Digital signal processing is used for improved breathing signal detection. A vibrating device under the patient's pillow is activated if the breathing signal disappears, inducing the patient to start breathing again, preferably without waking up. Preliminary testing was carried out using a pressure sensitive mat taken from a Babysense™ II baby monitor kit, manufactured by Hisense. The mat was placed under a large, thick cushion (equivalent to a thin mattress), with a person lying on top of it and breathing normally for a period, holding their breath for about 30 seconds, and resuming normal breathing. The voltage from the piezoelectric sensor was recorded to a computer at a 1kHz sampling rate using a Picoscope USB oscilloscope, and imported into MATLAB for processing and filtering.

RESULTS

The measured data was very noisy without filtering, with heartbeats and 50Hz mains hum. Noise was greatly reduced using a 5th order low pass Butterworth digital filter with 0.5Hz cut-off. In figure 1, the filtered signal is superimposed on the measured voltage data. A clear breathing signal is seen at a rate of one cycle about every 5 seconds, leveling off during the breath-holding period and resuming when the breathing re-started.

FIGURE 1: Graph of original and filtered pressure measurements from the mat.

A key challenge is to configure the vibrating device to be sufficiently intrusive to induce the patient to move and re-start their breathing, but not so intrusive as to cause the patient to wake up. Initial indications showed vibration strength to be too high, and further work is ongoing.

DISCUSSION & CONCLUSION

The system can pick up breathing signals clearly and easily. Work is ongoing in testing performance with different mattress thicknesses and when a patient is not lying directly above the mat. Further improvements could be made by using more than one mat at different locations under the mattress, and by measuring and combining different measured variables, e.g. the audio signal of a person's breathing/snoring noises from a microphone, to allow highly reliable detection of sleep apnea episodes.

Further work on the vibrating device to re-start breathing is ongoing. Although intervention by a vibrating device may not be equally successful for all patients, for some patients, this type of system could have the potential to non-invasively reduce the number of nightly awakenings, significantly improving sleep, health and quality of life.

REFERENCES

PATIENT SPECIFIC MODELLING OF THE HYBRID PROCEDURE: THE CLINICAL NEED & CHALLENGES IN USING PATIENT SPECIFIC DATA

Andrew Young\textsuperscript{1}, Mark Danton\textsuperscript{2}, Sean McKee\textsuperscript{3} & Terry Gourlay\textsuperscript{1}

\textsuperscript{1} Department of Bioengineering, University of Strathclyde, Wolfson Centre, Glasgow
\textsuperscript{2} Cardiothoracic Surgery Department, Royal Hospital for Sick Children, Yorkhill, Glasgow
\textsuperscript{3} Department of Mathematics & Statistics, University of Strathclyde, Livingstone Tower, Glasgow
andrew.g.young@strath.ac.uk

Abstract – The Hybrid Procedure is a palliative treatment used in treatment of Hypoplastic Left Heart Syndrome and related anomalies. By banding the pulmonary arteries and stenting the Patent Ductus Arteriosus flow to the pulmonary and systemic circulations can be controlled. This research aims to allow testing of different configurations of banding and stenting to optimise the circulation for an individual patient. A summary of the research and obstacles overcome and still being addressed are presented.

INTRODUCTION
Hypoplastic Left Heart Syndrome (HLHS) is a rare congenital heart disease which is characterised by an underdevelopment of the left-sided structures of the heart. It results in a lack of oxygenated blood reaching the systemic organs. The body naturally tries to compensate with the right ventricle supplying the systemic circulation ($Q_s$), as well as the pulmonary circulation ($Q_p$), via the Patent Ductus Arteriosus (PDA). The Hybrid Procedure utilises this natural response by stenting open the PDA (which would otherwise close) and surgically banding the branch pulmonary arteries. This is necessary as the resistance to flow is much lower in the pulmonary circuit and so to control the ratio of $Q_p:Q_s$ the bands must be tightened sufficiently. Figure 1 adapted from Galantowicz et al. illustrates the Procedure [1].

METHODS
Using a multi-scale approach we intend to couple Computational Fluid Dynamics, based on 3D geometry of the surgical region from clinical scans, with a zero-dimensional Lumped Parameter Model (LPM) with all patient-specific parameters to be derived directly from clinical data [2, 3]. The patient-specific geometry will be generated using the commercial software Mimics (Materialise, Leuven, Belgium). The initial LPM has been designed to be as simple as possible, yet detailed enough to fully characterise the remainder of the cardiovascular system, excluding the surgical region modelled by 3D CFD. Quantification of some data has proven problematic.

REMARKS
One of the major difficulties in generating the parameters needed is the quality and consistency of the raw clinical data. When accessing the historical data it is not always possible to have a complete set of data required for parameter identification. It is essential that the data comes from as consistent physiological conditions as possible to avoid using mismatched parameters. Even when a full set of consistent data is available, it is necessary to employ averaging techniques. This overcomes potential errors in digitizing the data, originally of visual graphical form, and discrepancies in its interpretation. It also accounts for variation over different heart cycles with the data collected over multiple heart beats. The current research has identified previously unconsidered factors that are potentially important to the clinician in banding applications, through interpretation of available clinical data.

REFERENCES