INTRODUCTION

We extend a warm welcome to this very different event! It combines two significant meetings. The first is the biennial Polymer Process Engineering meeting (actually the 13th time this conference has run - these began in 1985 in Bradford, with one gap). This highly-regarded meeting covers a range of polymer-related interests, and enjoys a strong industrial support and wide-ranging academic inputs. Its themes are (i) Resource Efficiency, which covers energy/ carbon footprint issues as well as recycling/reuse of materials; (ii) Polymer Micro & Nanotechnology, reflecting the growing interest in micromoulding and associated technologies, including a feature on the successful Nanofactory venture; (iii) Healthcare technologies, a major and strategic theme reflecting a wide range of healthcare needs including materials and processing developments, pharmaceuticals processing and delivery technologies, and implants and keyhole surgery approaches. The exciting new EPSRC Centre of Innovative Manufacturing in Medical Devices ('MeDe Innovation' - Leeds, Bradford, Newcastle, Nottingham and Sheffield Universities) is also introduced, and the UKIERI programme (Bradford – Institute of Chemical Technology Mumbai) is represented.

PPE-13 will run in conjunction with the fifth RCUK Bradford Science Bridges China/ EPSRC Global Engagements Research Workshop on Advanced Materials for Healthcare and beyond. This follows our extremely successful first four workshops held in Beijing, November 2011, Chengdu, April 2012, Bradford, September 2012 and Chengdu, March 2013. This Research Workshop, '*International Co-operation*' again brings together a strong and growing community of UK and Chinese academic experts and industrial participants, together with government representatives, in the exploitation of advanced materials, mainly polymer-related materials, with particular interest for application in healthcare technologies, but now also looking beyond this area. The Workshop will explore research interests and identify potential co-operations, including researcher exchanges, joint research student supervision, joint international laboratories and industrial collaborations. Features of this workshop include the involvement of industry, and a focus on our Research Exchanges, which have been important part of our capacity building in research.

There will again be a strong emphasis on posters, here reflecting the Researcher Exchanges under our Science Bridges China programme. We will build on our funding success, including the Joint RCUK-MOST call (Dec 2012), and the Program of introducing foreign talents from the world leading academic institutions to Chinese universities (111 Scheme), Sep 2012, and MeDe Innovation. The Workshop will continue to encourage strategic UK-China collaborations, and develop high quality projects for the RCUK, EPSRC, MOST and NSFC International Collaboration programmes. These activities form a continuing expression of the UK-China Advanced Materials Research Institute (AMRI), which we launched at the Chengdu Workshop in April 2012.

The RCUK Bradford Science Bridges China/ EPSRC Global Engagements programme focuses on healthcare technologies, which is one of three strategic areas identified for co-operation between China and the UK. Fuller details on the Science Bridges China platform, the Global Engagements programme and current projects, are provided in a later section of this booklet. Our Advanced Materials emphasis means that we also naturally address other industry sectors, and new applications of advanced materials:

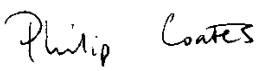
'Advanced Materials' includes:

- *nanomaterials/ nano-biomaterials*
- *biological scaffolds*
- *bone fixation*
- *dental materials*
- *drug delivery*
- *engineered surfaces/ interfaces*
- *medical devices (including surgical technologies, instruments, assistive technologies)*
- *medical packaging*
- *precision processing*
- *prostheses*
- *regenerative therapies*
- *soft tissue fixation*
- *smart (stimuli responsive) materials*
- *stents*
- *wound care*

Outlines of research interests for participants are available on our UK-China AMRI web site, www.ukchina-amri.com. Many of the participants have experience of working together with other groups, and across discipline boundaries. We believe that building such skills, trust and friendship between collaborators is of great value and importance for our groups and for our nations.

We look forward to working together with you, and to a very fruitful Workshop!

with warm regards



Professor Phil Coates FREng Conference Chairman

PPE'13 – UK China AMRI

Norcroft Conference Centre, University of Bradford
26-28 November, 2013

PROGRAMME

Tuesday 26 November

8.45 Welcome;
Prof Mike Bevis tribute
P D Coates on behalf of R Crawford, P Hornsby, P Allan

Resource Efficiency

9.00 *Investigation of thermal efficiency in single screw extrusion*
J Verra-Sorroche, C Abeykoon, A Kelly, E C Brown, P D Coates, Polymer IRC, University of Bradford;
J Deng, K Li, E Harkin-Jones, M Price Queen's University Belfast

9.25 *Liquid Milk Packaging Sustainability*
A Moorthy, Nampak Plastics & D Mato, Closed Loop Recycling

9.50 *Carbon footprints in polymer processing*
R Kent, Tangram Technology Ltd

10.15 *Polymeric Pharmaceutical Formulations: Towards Green Processing*
AL Kelly, T Gough, C Kulkarni, S Korde, S Deshmukh, A Paradkar, P D Coates, Polymer IRC, University of Bradford; S A Halsey, Thermo Fisher Scientific

10.40 Coffee, Exhibition & Posters

Micro & Nano Technology

11.10 *Processing of Composites and blends containing carbon nanotubes*
T McNally, International Institute for Nanocomposites Manufacturing, WMG, University of Warwick

11.35 *Carbon nanotube composites – electrical and shape memory effects*
D Li, G Fei, H Xia, Sichuan University,
P D Coates, B R Whiteside, P Spencer, Polymer IRC, University of Bradford

12.00 *Micro Injection Moulds - Design and Manufacture*
G Clark, Microsystems Ltd

12.25 *Simulation of two-component micromoulding*
G. Tosello, Technical University of Denmark; F. Costa, S. Ray, and R. Speight, Autodesk Moldflow Inc

12.50 Lunch, Exhibition & Posters

13.50 *Demoulding of microfluidic parts*
C Griffiths, Manchester University

14.15 *Temperature measurements at the polymer melt and mould cavity wall interface using a high speed thermal camera*
M Babenko, B R Whiteside, K Norris, G Gonzalez Castro, J Sweeney, Polymer IRC, University of Bradford,
S Bigot, Cardiff University

14.40 *Tensile deformation of oriented poly(ε-caprolactone) and its miscible blends with poly(vinyl methyl ether)*
Z. Jiang, Y Men, Changchun CIACCAS, B R Whiteside, P D Coates, Polymer IRC, University of Bradford

15.05 Tea, Exhibition & Posters

15.35 *The application of micro molding in fabrication of polymer sheet with micro structures*
Daming Wu, Yajun Zhang, Beijing University of Chemical Technology

16.00 *Nanofactory – Strategy and Case Studies*
S Rainton, S Kelly, Nanofactory;
Cases: *SofMat anti-counterfeiting*, P Harrison, Sofmat Ltd;
Organ viability assays, B Thomson; Aedstem Ltd
Recycling laminate layer from architectural glass - polyvinyl butyral polymer (PVBp); Gary Hopkins, GB Cullet Ltd

16.50 demonstrations

18.00

18.30 Conference Banquet

Wednesday 27 November

8.40 ***Formal welcome and updates: UK-China AMRI***
P D Coates, G Li (Sichuan University) co-chairs of AMRI;
J Du UKTI;
University of Bradford Senior Management Team/ Director of International Strategy;
tbc: Chinese Embassy; Leeds City Region LEP

Healthcare Technologies

9.25 *Investigation of plasma treatment on polymeric micro-injection moulded microneedle for protein drug delivery.*
K J Nair, B R Whiteside, C A Grant, R Patel, K Norris, A R Paradkar, Polymer IRC, University of Bradford

9.50 *Micro-processing of Polymer Blends and Composites*
L Li, H Xia, J Zhang, N Chen, Y Chen, Q Wang, Sichuan University,
B R Whiteside, M T Martyn, T D Gough, P D Coates, Polymer IRC, University of Bradford

10.15 *Extrusion: scaling up from lab to production*
R Bottom, Thermo Fisher Scientific

10.40 Coffee, Exhibition & Posters – Group Photograph

11.10 *Super Toughening of Brittle Polylactide with Novel Slide Graft Copolymer via in-Situ Reactive Compatibilization, Crosslinking and Chain Extension*
L Zhang, X Li, H Kang, J Shen, Beijing University of Chemical Technology; T Nishi, C Zhao, K Ito, University of Tokyo; P Coates, University of Bradford

11.35 *Polymer colloids for controlled delivery of growth factors of importance in the development of blood vessels*
S Rimmer, Polymer IRC, Sheffield University

12.00 *Drug delivery – quantitative structure studies*
X Yin, H Li, Q Shao, Z Guo, C Liu, T Xiao, J Zhang, Shanghai Institute Materia Medica
CAS; Y He, Shanghai Synchrotron Radiation Facility; P York, University of Bradford; MD Matas, AstraZeneca

12.25 *Pharmaceutical processing for enhanced bioavailability*
A Paradkar, A L Kelly, T Gough, J Kendrick, Pharmaceutical Engineering Science, Polymer IRC, University of Bradford; Y Chen, Q Wang, Sichuan University; A Nangia, University of Hyderabad; G Yadav, ICT Mumbai

12.50 Lunch, Exhibition & Posters *[+ UK-China AMRI Board meeting]*

13.50 *Shape memory polymers for biomedical applications*
D Farrar, Smith & Nephew Ltd; P Caton-Rose, G Thompson, I M Ward, P D Coates, Polymer IRC, University of Bradford

14.15 *Thinking big in minimally invasive surgery*
G Proffitt, Surgical Innovations Ltd

14.40 *Property gradient materials for tissue repair*
P Twigg, Polymer IRC, University of Bradford

15.05 Tea, Exhibition & Posters

15.35 *Large Diameter Ceramic-on-CFR-PEEK Hip Joint Replacements*
J Wu, Durham University

16.00 *MeDe Innovation – a new EPSRC Centre for Innovative Manufacturing of Medical Devices*
K Dalgarno, Newcastle University; P Hatton, Sheffield University, I Ahmed, D Grant, Nottingham University, P D Coates, University of Bradford

16.45 *Cationic heterolipid based nanocarriers for anticancer therapeutics,*
Vandana B. Patravale, Institute Of Chemical Technology, Mumbai, India [Bradford-ICT Mumbai UKIERI Programme]

17.05 demonstrations

18.00

18.30 Banquet

Thursday 28 November

Advanced Materials for Healthcare Technologies

8.30 *Bioactive nanoparticles with well controlled structure*, Dong Qiu, ICCAS Beijing

8.50 *Cell-biomaterial interactions,* Aileen Crawford, University of Sheffield

9.10 *Poly(vinyl alcohol) based composites for joint soft tissue repair,* Chuhong Zhang, Sichuan University

9.30 *New PLA based polymers,* Kamyar Afarinkia, Martin Royappa, Institute of Cancer Therapeutics, University of Bradford

9.50 *Meeting Future Healthcare Needs with Innovation & Technology – An Orthopaedic industry perspective* - Alan Ashby, DePuy Synthes

10.10 Coffee & Posters

10.40 *Clinician's viewpoint – NIHR Healthcare Technology Co-operative for Wound Prevention and Treatment* Peter Vowden, Bradford Teaching Hospitals NHS Foundation Trust

11.05 *Solid phase processing of PLA based blends and composites for blood-contacting medical devices*, Zhengqiu Li, Xiaowen Zhao, Lin Ye, Sichuan University

11.30 *Modulation of Surface Properties with Polyelectrolyte Multilayers* Zhaohui Su, Zhigang Xie, Yubin Huang, Changchun CIACCAS

11.50 *Regulation of Polymer Blend Morphology using Nanoparticles,* G Li, Yajiang Huang, Qi Yang, Tian Xia, Miqiu Kong, Yuan Mei, Sichuan University; Phil Coates, Fin Caton-Rose & Mike Martyn, University of Bradford

12.10 *AFM nano-mechanics: from collagen fibrils to collagenous tissue,* Colin Grant, Pete Twigg, Advanced Materials Engineering, Polymer IRC; Desmond Tobin, Centre for Skin Science, University of Bradford

12.30 *Haemodynamic studies,* Clive Beggs, University of Bradford

12.50 Lunch & Posters

14.00 ***Workshop session*** (Polymer IRC WB19)

17.30

18.30 Banquet

PPE'13 / UK-China AMRI: ABSTRACTS

T1 Appreciation: Michael John Bevis BSc PhD FIMMM FInstP FREng, 1940 -2012

The research undertaken by Michael (Mike) Bevis covered many aspects of materials science and engineering, including the crystallography of deformation twinning and martensitic transformation in metals, transmission electron microscopy of dislocations and interfaces in metals and crystalline polymers, recycling of plastic waste and the moulding technology of polymers and ceramics. His work in moulding technology was particularly successful and occupied a major part of his academic career. This was brought about by his energy and vision in establishing the Wolfson Centre for Materials Processing at Brunel University in 1987. Under his direction. the Centre received strong support from collaborating companies and pioneered research and development on new moulding and extrusion technologies. Many of which became licensed worldwide. When he stepped down as Director of the Centre in 1994, owing to the advancing symptoms of multiple sclerosis, he remained active as Consultant Director for another 13 years.

Mike was born on 25 April 1940 on Jersey in the Channel Islands. He studied at Battersea College of Technology for a BSc in Physics from the University of London, graduating in 1962. He undertook theoretical research for his PhD on twinning in metals and related topics under the supervision of Alan Crocker at Battersea before being appointed to a lectureship in the Department of Metallurgy at the University of Liverpool in 1965, where initially he continued his research on metals. However, Derek Hull, Head of Department, had started to apply his expertise on deformation and fracture of metals to the mechanical properties of polymers, and Mike joined him and a colleague to form the Polymer Research Group. It soon became a leading group in the UK, and over the next seven years Mike led projects on the properties of amorphous and crystalline polymers, the recycling of plastic waste and moulding of thermoplastics. His research and accomplished teaching led to early promotion to Senior lecturer and then Reader, before he left in 1977 for a Professorial Chair and Headship of the Department of Non-Metallic Materials at Brunel University. When the department merged with Metallurgy in 1984 he became the first head of the new Department of Materials Technology. Mike's door was always open, and he inspired his research students and staff to realise their true potential with his enthusiasm and dedication. Although his desk, and any table-top in sight, often appeared to be laden with piles of paperwork, seemingly random to the casual observer, Mike treated the apparent chaos without concern and always seemed to be able to put hands on any document he sought.

He met Diana Holloway in 1962 and they married in 1964. Colleagues. students, international visitors and their many other friends experienced warm hospitality in Liverpool, Uxbridge and later Kendal, to where he and Di retired in 2002. Di's unstinting care and positive attitude after Mike was diagnosed with multiple sclerosis in 1980 enabled him to remain active in research at a high level for another two decades. Although confined to a wheelchair from 1987, he did not let difficulties stand in his way and was able to travel widely in the UK and abroad with Diana's support. He bore the problems they encountered with fortitude and rarely alluded to his condition unless it was touched by his keen sense of humour. He was delighted to be taken along the Great Wall of China in his wheelchair when appointed to a visiting professorship in Beijing, and was amused that French police took his inability to stand to be due to drunkenness when, on the way to a conference in Nice, his caravanette overturned into a ditch. He hadn't touched a drop at the time.
He published more than 200 research papers and received recognition and honours from many quarters. He was elected Fellow of the Royal Academy of Engineering in 1986, was awarded the A A Griffith Medal of the Institute of Materials in 1987 and the Swinburne Medal of the Plastics and Rubber Institute in 1990, was a vice-president of the Institute of Materials from 1992-1995 and, in 2000, was made a Freeman of the Worshipful Company of Horners, a livery Company of the City of London with strong links to the plastics industry. He was UK Editor of International Materials Reviews from 1999-2007 and was presented with an Innovation Award by Lady Thatcher in 1994. In recognition of his role as founding Director of the Wolfson Centre and his lasting contribution to Brunel University, a new hall of residence named the Michael Bevis Hall was opened by the University Chancellor, Lord Wakeham, in 2009. He died peacefully on 28 April 2012 after suffering a stroke and is survived by Diana, their three children Katie, Andrew and Sarah, and three grandchildren.

David Bacon FREng
University of Liverpool

Addendum:
Mike Bevis was a major force in the significant upsurge of polymer engineering research in the UK. I was privileged to work with Mike and, together with Professor Roy Crawford of Queens Belfast, we co-operated to

develop large scale programmes and a research strength in UK polymer processing which is maintained to this day. This had spin-off effects in helping to promote the underpinning areas such as fundamentals of polymer rheology (led by Professor Tom McLeish FRS). He also contributed greatly to the success of this journal both as contributor and long-standing member of our Editorial Board. The warm collaborations in the polymer engineering community (across Bradford, Brunel, Queen's, Warwick and Loughborough Universities in particular, but with many others involved) reflect the spirit and drive, and we are privileged to acknowledge Mike as one of the leaders. His personal touch, insight and energy will be much missed.

Phil Coates FREng

T2 Investigation of thermal efficiency in single screw extrusion

J. Vera-Sorroche[1], C.Abeykoon[1], A.L.Kelly[1], E.C.Brown[1], P.D.Coates[1], J.Deng[2], K.Li[2], E. Harkin-Jones[3] and M.Price[3]*

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In this work, in-process monitoring techniques have been used to examine the thermal dynamics in single screw extrusion. Thermocouple grid sensors in conjunction with infrared thermometry have been employed to provide detailed information of the thermal homogeneity of the melt. In addition, energy consumption was monitored to quantify the process energy demand. A wide range of polymers were extruded using three extruder screw geometries at several set temperatures and screw rotation speeds. Results showed that processing conditions and polymer rheology had a significant effect on bulk temperature and the magnitude of temperature fluctuations. Specific energy consumption was found to be predominantly dependent upon extruder screw type and polymer type.

T3 Liquid Milk Packaging Sustainability

Ashwin Moorthy, Nampak Plastics & Dharminder Mato, Closed Loop Recycling

Sustainability of HDPE plastic milk bottles is significantly improved through its ability to be lightweighted and recycled back into milk bottles. Production with HDPE and recycled HDPE (rHDPE) blends have established no adverse effect on processability and mechanical performance of the product at current inclusion rates. The joint presentation details the findings of the investigation and trials carried out with higher inclusion rates of rHDPE and on the effects of the decontamination process in the production of rHDPE.

T4 Carbon Footprinting in Plastics Processing

Dr Robin Kent
Tangram Technology Ltd.

Energy management focuses on reducing the use and cost of energy but an inevitable result of this will be a reduction in the carbon footprint. Whilst reducing the use and cost of energy is often the main objective, reducing the carbon footprint of a site can have significant benefits both in terms of public relations but also in terms of conforming to the range of government regulations that are appearing around the world. Establishing a site carbon footprint is not difficult. Gathering the information necessary for good energy management will result in gathering much of the information necessary to produce a carbon footprint. There is also a need for some additional information but this is generally easily obtained and only needs to be formatted correctly to produce a site carbon footprint.

A site carbon footprint can be used to communicate progress in energy management, to set and meet external targets from customers and to set and meet external targets from government regulators. It is also a useful tool to concentrate minds on one of the reasons for reducing energy use.

At present, calculating a site carbon footprint is optional in most parts of the world but this may not remain so for much longer. Initiatives such as 'carbon trading' and 'carbon taxes' are being discussed in most countries and these discussions will inevitably mean that site carbon footprinting will be necessary. In addition, many

large customers, particularly retailers such as Walmart™, are encouraging suppliers to calculate their carbon footprint. This will cascade down the supply chain to the plastics processors who supply these retailers directly or indirectly.

At the consumer level there is also interest in carbon footprints but at this level the interest is more on the product carbon footprint. This is a much more difficult proposition than a site carbon footprint. Most plastics processors produce a component and do not produce a complete product. Therefore, they cannot produce a complete product carbon footprint. Despite this, they do need to know how these are calculated so that they can take part in the information gathering that is necessary for a product carbon footprint.

T5 Polymeric Pharmaceutical Formulations: Towards Green Processing

AL Kelly, T Gough, C Kulkarni, S Korde, S Deshmukh, A Paradkar, PD Coates, Centre for Pharmaceutical Engineering, Polymer IRC, University of Bradford; SA Halsey, Thermo Fisher Scientific

The pharmaceutical industry has conventionally relied on large scale use of solvent-based batch processes. These typically require multiple process steps such as crystallisation, grinding, blending, drying, tablet compaction and coating to be performed before a final dosage form is produced. The use of large amounts of solvents may be harmful to the environment and the batch nature of such processes leads to large amounts of waste being produced. Recently there has been an increased drive within the pharmaceutical industry to adopt 'Green' processes to improve efficiency and reduce waste. Pharmaceutical manufacturing plants typically generate 25 to 100 kilograms of waste per kilogram of product, a ratio known as the environmental or 'E-factor'. The drive towards adopting greener processes has led to significant reductions in waste and improvements in efficiency. Green chemistry practices such as the use of aqueous solvents, ambient temperature processes and sustainable feedstock materials have been widely adopted, together with more efficient high throughput screening techniques. Another route to improve process efficiency is the use of polymeric matrices as carriers of amorphous drug forms. Polymers are used primarily to improve the solubility of poorly soluble drugs by melt mixing in twin screw extruders, but extrusion is a continuous, solvent free, highly efficient single step process. Extrusion is readily controlled and lends itself well to real-time quality control, or process analytical testing (PAT). Here, the use of polymer processing techniques in pharmaceutical manufacturing is illustrated by a number of case studies. Several matrix polymers have been used including PVP-VA, HPMCAS and Soluplus, a graft copolymer. The application of injection moulding to achieve a final dosage form has also been investigated using a model system of HPMCAS and ibuprofen. In-process measurement techniques have been used to improve process understanding and quality control; in particular a novel transmission spectroscopy technique has recently been applied to a transparent formulation of carbemazepine and PVP-VA.

T6 Processing of composites and blends containing carbon nanotubes

Tony McNally
International Institute for Nanocomposites Manufacturing, WMG, University of Warwick, CV4 7AL, UK

Background

Despite almost two decades of research effort with regard composites of carbon nanoparticles and polymers, their widespread commercial exploitation has yet to be fully realised. This in the main is a consequence of the combined challenges of achieving effective dispersion and distribution of nanoparticles in polymer melts and of fully characterizing and modelling the interface between particle and polymer across the length scales. An appreciation of the parameters which govern nanoparticle dispersion during melt mixing has been studied intensively for only a small number of polymer/CNT systems and much less so for composites of polymers and graphene(GO). It has been proposed that CNT dispersion in polymer melts follows three distinct mechanisms; infiltration of the polymer melt into CNT primary agglomerates, agglomerate rupture and erosion of CNTs from agglomerate surfaces [1], all of which are governed by the melt temperature and the forces acting on the melt during mixing. Typically, the relationship between varying processing parameters, including screw speed, residence time, melt temperature, screw configuration, and nanoparticle dispersion is investigated using a combination of microscopic techniques and the extent of nanoparticle dispersion interpreted by assessing nanoparticle network formation studied using electrical and rheological techniques [1-5]. Processing variables as well as thermodynamic considerations also play a role in the localization of CNTs in immiscible polymer blends [6]. The majority of the published literature has focused on understanding the

factors which effect nanoparticle dispersion during mixing. However, the as-extruded polymer/CNT composite can then experience a second thermo-mechanical cycle as in injection moulding. Furthermore, secondary processing in the solid state and quasi-solid state, as in thermoforming and blow moulding, of composites of polymers and CNTs has largely been ignored to date [7]. Indeed, irrespective of the level of nanoparticle dispersion achieved during initial melt mixing, the final properties of the composite material are determined by the extent of deformation and any subsequent strain induced crystallization and re-localisation of nanoparticles (Figure 1). Efforts are also on-going to improve nanoparticle dispersion by using a combination of processing techniques, including using a three roll mill after melt mixing in a twin screw extruder [8].

The presentation will provide an overview of melt processing of composites and blends of polymers and carbon based nanoparticles, with a focus on carbon nanotubes.

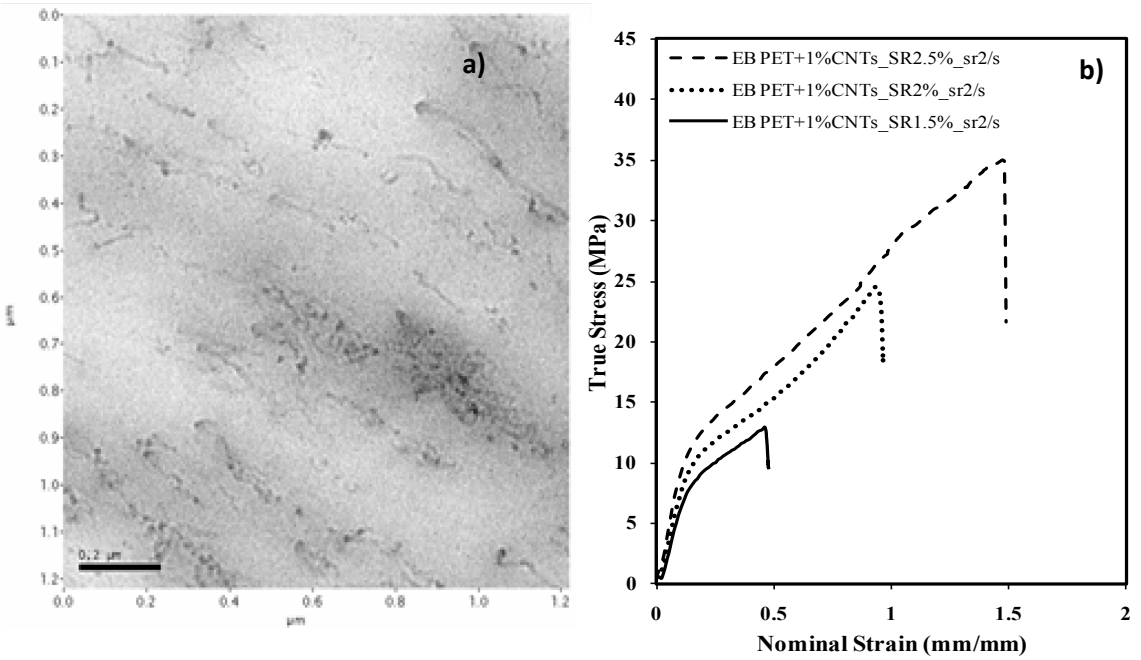

Fig. 1: *a) HR-TEM image showing alignment of MWCNTs in a PET matrix and b) true stress versus nominal strain curves for composites of MWCNTs and PET showing significant strain hardening on equi-biaxial deformation.[7]*

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3. McClory, C., Pötschke, P., McNally, T., "Influence of screw speed on electrical and rheological percolation of melt mixed high impact polystyrene/MWCNT nanocomposites", *Macromol. Mater. Eng.*, 296, 59-69, **2011**.
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8. Pötschke, P., et al., "Improvement of carbon nanotube dispersion in thermoplastic composites using a three roll mill at elevated temperatures", *Compos. Sci. Technol*., 74, 78-84, **2013**.

T7 Carbon nanotube composites – electrical and shape memory effects

D Li, G Fei, H Xia, Sichuan University,
P D Coates, B R Whiteside, P Spencer, Polymer IRC, University of Bradford

Shape memory polyurethane-carbon nanotube composites were prepared by twin-screw melt extrusion and subsequently processed using microinjection molding to obtain components with surface micropatterns. Then an electro-activated surface micropattern tuning system was developed which could recover the original micropatterned surface of the components after a thermal deformation by applying a current which heats the component using resistive heating. In order to optimize the technique, three key areas were investigated in this work: conductivity of the microinjection molded microparts, the retention of shape memory micropatterns on the surface of microparts during annealing treatment, and the macroscopic area shrinkage of microparts after thermal treatment. It has been found that the electrical conductivity of microinjection molded parts is relatively low due to the high shear rates prevalent in the process. An annealing treatment improves the electrical conductivity by several orders of magnitude, but can be detrimental to the dimensional stability of the micropatterns, which depends significantly on the micro-injection molding parameters, especially the mold temperature. Increasing the mold temperature, melt temperature, injection speed and injection pressure result in better retention of the micropattern and improved dimension stability during annealing treatment.

The new method of analysing in-situ TEM images obtained from different temperatures is further investigated. Meanwhile, computer modelling of Carbon nanotube filled polymer composite is employed in order to better understand the electrical conductive behaviour of the composite. Random dispersion of CNTs is employed in our Monte Carlo simulations. CNTs network recognition that employs periodic boundary conditions is developed. Different dispersion states of CNTs including fully dispersed, aligned and agglomerated are simulated. The probability of percolation is also predicted by measuring the faction of realisations that percolate.

T8 Micro Injection Moulds - Design and Manufacture

Gary Clark, Microsystems Ltd

An example of the challenging precision moulds and inserts required for micromoulding is shown here – the challenges and successes will be discussed.

T9 Simulation of two-component micromoulding

G. Tosello[1], F. Costa[2], S. Ray[2], and R. Speight[2]*
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[2] Moldflow R&D Center, Autodesk Australia Pty. Ltd., 259-261 Colchester Road. Kilsyth, Australia.
[*] Corresponding author: shishir.ray@autodesk.com

In this paper, Three Dimensional (3D) simulations of filling phases for a two-component micro injection moulding are presented. A Technology Preview version of Autodesk Simulation Moldflow Insight software was used to accurately predict filling patterns at component-level and micro surface feature-level in a polymer-polymer two-component micro injection moulding process. Flow front predictions for the first and second components are compared against the short shots of the part over the whole miniaturized component and within the surface micro structures.

Introduction

Multi-component micro injection moulding is one of the key replication technologies for high precision manufacturing of multi-material micro products. One of the key challenges in multi-component micro injection moulding technology is the achievement of a full surface replication of the first component when moulding the second component. This aspect is particularly critical when dealing with increasingly small shot sizes (typical mass of micro moulded components is in the range of 10^1-10^2 mg) as well as surface micro structures (typically with features in the range of 10^0-10^2 µm). Producing good quality micro injection moulded parts is generally achieved through trial and error. Numerical simulation of the micro moulding process will avoid costly tooling modifications and reduce the number of mould trials.
Previous software validation studies of the micro injection moulding process have demonstrated the simulation of single-component sub-100 mg miniaturized parts. High accuracy predictions of flow-pattern, injection cavity pressure, and part dimensions were achieved through the use of appropriate mesh densities and accurate representations of the process and boundary conditions [1]. In the present study, two-component micro injection moulding experiments and corresponding 3D finite element simulations were carried out. This gave insight into the polymer flow characteristics when injecting polymer melt over miniaturized polymer components with surface micro structures. For the two-component micro injection moulding experiments, a high accuracy injection machine with an optimized moulding process as well as high precision micro tools, specifically developed for micro multi-material applications, was used.

Experiment

Sequential two-component micro injection mouldings were conducted to gather experimental data. These data were used to establish a reliable simulation method suitable for the two-component micro injection moulded parts. Parts were moulded on an injection moulding machine (Engel ES 80/25 HL-Victory) equipped with an 18 mm diameter reciprocating screw adapted to micro injection moulding applications. The material for the first component was polyoxymethylene (POM BASF Ultraform H2320 004, melt-temperature = 200 °C), and the material for second component was acrylonitrile butadiene styrene (ABS Dow Magnum 3416 SC, melt-temperature = 260 °C). The illustrations of these components are given in figure 1.

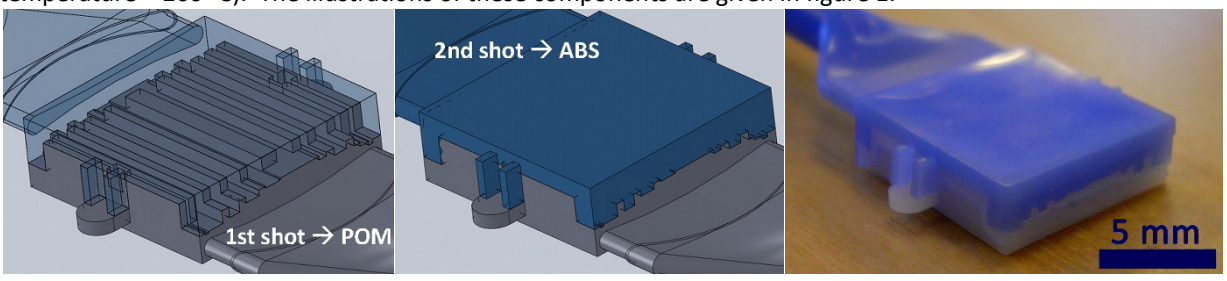
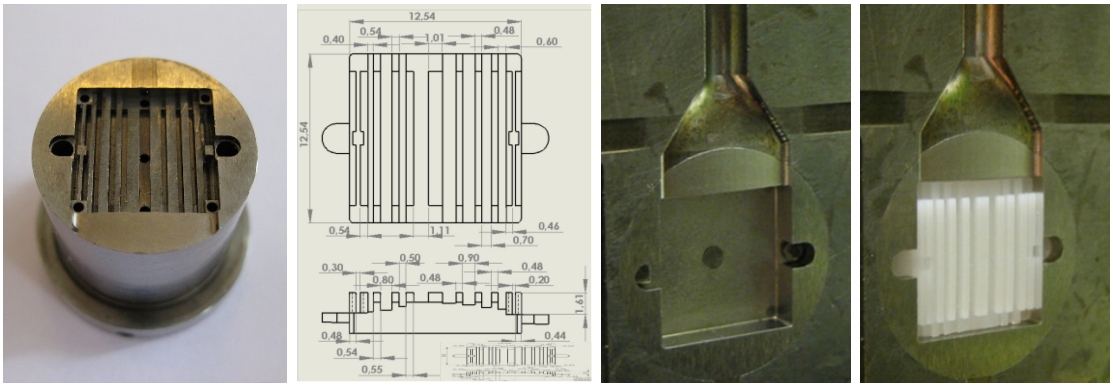


Figure 1: Two-component injection moulding of micro structured component.
A mould with interchangeable micro cavity inserts was used to mould the first component, a 12.5 mm by 12.5 mm part, and then to over mould the entire part by injecting the second component. The interchangeable micro cavity is depicted in figure 2.



(a) (b) (c) (d)

Figure 2: First shot: (a) micro structured tool, (b) part design; second shot: (c) tool cavity, (d) first moulded component inserted prior the second component moulding cycle.

Short shots of the first component (POM) and second components (ABS) were moulded by increasing Velocity to Pressure switch-over point for the same charge stroke. The corresponding injection speed profiles used in the injection moulding machine control unit were recorded to be later used in the numerical simulation software.

Simulation

Numerical simulations were performed using a Technology Preview version of the Autodesk Moldflow Insight software which included an optional feature to simulate a slip boundary condition at the cavity wall [2, 3, and 4]. When wall-slip was modelled in the simulation, a free slip condition was used for polymer-mould contact wherever the local pressure was below 1 MPa. 3D meshes for both first and second components were prepared from 3D CAD models of the full geometries, i.e., including runners, sprues, gates, components, and their micro structured surfaces; see figure 3. A coarse yet precise mesh was used for the feeding system (element edge length in the order of 500-1000 µm). A finer mesh (element edge length of 100-200 µm) was used for the gate and the micro features, where high resolution analysis of shear rate and thermo-mechanical conditions of the polymer flow are required.

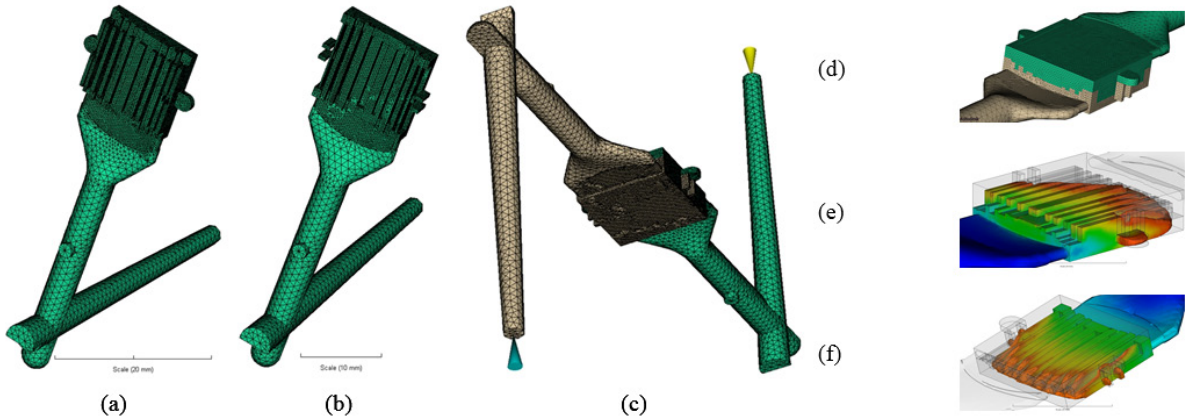


Figure 3: Meshes: (a) first component, (b) second component, and (c) and (d) combined two-components; Filling pattern: (e) first componet (POM), and (f) second component (ABS).

Process settings in the simulation were implemented taking into account actual processing conditions for both first and second moulding components. A particular aspect to consider is the implementation of the injection speed in the simulation filling control settings, as it is defined in the injection moulding machine. An “Absolute ram speed vs. time” setting was employed with a maximum injection speed of 45 mm/s.

Comparisons of numerical simulations against short-shots of the first component are given in figure 4.

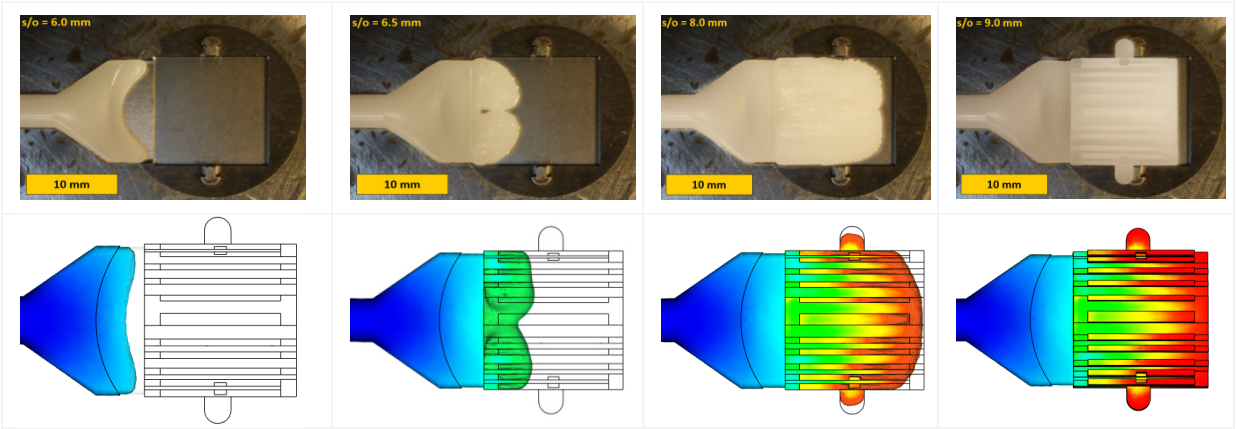


Figure 4: First component comparison of flow front positions between experiment and simulation.

From the above filling pattern comparisons, it is clear that with wall slip, the predicted filling patterns are much closer to the moulded short shots.
Comparisons of numerical simulations against short-shots of the second component are shown in figure 5. The simulations were performed without the wall slip condition.

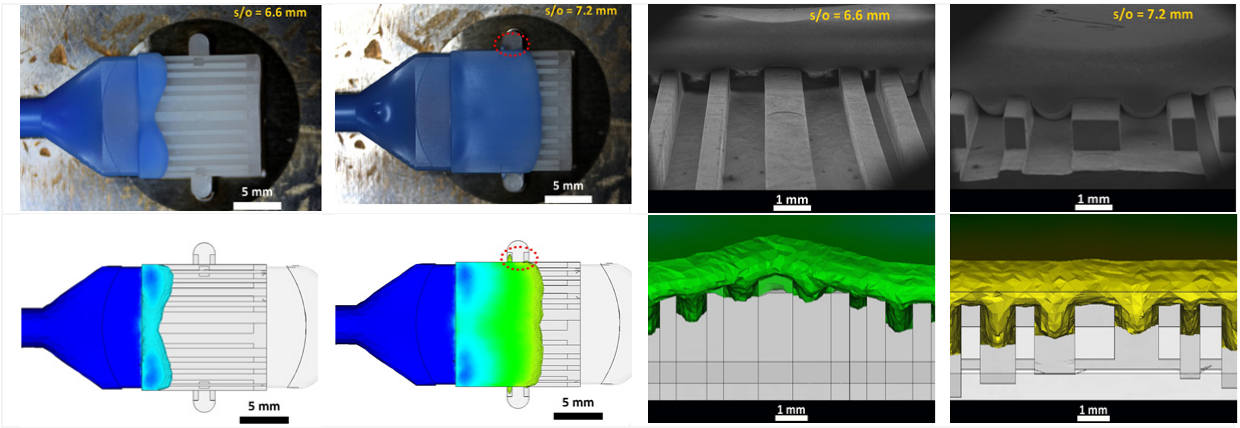


Figure 5: Second component comparison of flow front positions between experiments (top) and simulations (bottom): on the component (left), and on the surface micro features (right).

Conclusion

Autodesk Simulation Moldflow Insight software predicts flow patterns reasonably well for micro injection moulding process. Key features fundamental to obtaining high quality results are high accuracy cavity modelling and meshing, accurate processing conditions implementation, and suitable boundary conditions. In particular, a newly developed wall slip boundary condition was applied, resulting in a more accurate flow pattern prediction of the overall part and of miniaturized flow markers.

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T10 Demoulding of microfluidic parts

C Griffiths, University of Manchester, UK

Micro injection moulding (μ-IM) as a replication method is one of the key technologies for micro manufacture. An important stage in μ-IM which can affect the accuracy and mechanical properties of the produced components is part demoulding. With a focus on condition monitoring of the process, this paper reports the findings of several experimental studies on part demoulding behaviour. In addition to process factors, the demoulding was studied as a function of diamond like carbon (DLC) and a nano scale texturing of amorphous hydrogenated carbon (aC:H) coating applied to the replication tools. Using a representative microfluidics part, the results obtained from each of the studies can be used to identify the best processing conditions in regards to demoulding behaviour of micro parts.
Keywords: Micro injection moulding; Demoulding; Condition monitoring; Diamond like Carbon; Surface structuring; Microfluidics

T11 Temperature measurements at the polymer melt and mould cavity wall interface using a high speed thermal camera

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The thermal behaviour at the interface between polymer melt and mould cavity is an important phenomena for microinjection moulding. The small component masses and high surface area to volume ratios can be significantly influenced by the thermal behaviour of the polymer, affecting internal morphologies and therefore the mechanical properties of the final product. In this work we focus on the characterisation of the cooling behaviour of the polymer melt using a high speed infrared camera directly in microinjection moulding process. The visualisation system consists of a high speed infrared camera (IRCAM Equus 81k), a 45° first surface mirror and sapphire windows, which represent one half of the mould cavity. The thermal properties of the sapphire are very similar to those of P20 mould steel, which means that heat flux through the sapphire will be similar to that of the steel mould. The infrared camera has a spectral range of 1.5 to 5 μm, a sensitivity (NETD) of 20 mK and can capture data at speeds up to 30 000 fps.

T12 Tensile deformation of oriented poly(ε-caprolactone) and its miscible blends with poly(vinyl methyl ether)

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The structural evolution of micro-molded poly(ε-caprolactone) (PCL) and its miscible blends with noncrystallizable poly(vinyl methyl ether) (PVME) at the nanoscale was investigated as a function of deformation ratio and blend composition using in situ synchrotron small-angle X-ray scattering (SAXS) and scanning SAXS techniques. It was found that the deformation mechanism of the oriented samples shows a general scheme for the process of tensile deformation: crystal block slips within the lamellae occur at small deformations followed by a stress-induced fragmentation and recrystallization process along the drawing direction at a critical strain where the average thickness of the crystalline lamellae remains essentially constant during stretching. The value of the critical strain depends on the amount of the amorphous component incorporated in the blends, which could be traced back to the lower modulus of the entangled amorphous phase and, therefore, the reduced network stress acting on the crystallites upon addition of PVME. When stretching beyond the critical strain the slippage of the fibrils (stacks of newly formed lamellae) past each

other takes place resulting in a relaxation of stretched interlamellar amorphous chains. Because of deformation-induced introduction of the amorphous PVME into the interfibrillar regions in the highly oriented blends, the interactions between fibrils becomes stronger upon further deformation and thus impeding sliding of the fibrils to some extent leading finally to less contraction of the interlamellar amorphous layers compared to the pure PCL.

T13 The application of micro molding in fabrication of polymer sheet with micro structures

Daming Wu, Yajun Zhang
Beijing University of Chemical Technology, Beijing, 100029, China)

The rheological behaviour of polymers in micro channels were tested on a self-built device. In our experiment the solution of sodium carboxymethylcellulose(CMC) which exhibits pseudoplastic behavior when the concentration of the solution exceeds 3% was used as a substitution of polymer. By means of rolling-rolling method and injection molding method we have prepared series polymer sheets with micro semi sphere array, micro V-cut array and micro needles. The sheets with micro semi sphere array and micro V-cut array have found application in high performance diffusion materials for LED lighting system.

T14 Nanofactory

Sue Rainton, Nanofactory

The nature and extent of the ERDF supported Nanofactory programme, across 6 universities in the Yorkshire and Humber Region will be covered, followed by some specific case studies.
To help overcome the decline in research and development of small and medium-size companies (SME) six universities in the UK's Yorkshire and Humber region formed Nanofactory (www.nanofactory.org.uk). The region supports a large SME base, but historically, a low number of these (approximately 7%) have undertaken R&D with a university, and investment in R&D by these companies has been below the national average. Nanofactory's university partners of Bradford, Huddersfield, Leeds, Sheffield, Sheffield Hallam and York have secured funding from the European Regional Development Fund to help influence innovation by regional SMEs and to grow the region's economy.
SMEs often face a number of barriers that prevent them from investing in, or undertaking, R&D into areas of emerging technologies. These include a lack of knowledge of how these advances can be exploited; a lack of knowledge of the market opportunity that new technology offers; and a fear of innovating in isolation. Nanofactory's three main goals are to bring together a network of the established regional expertise in nanotechnology and other emerging technologies, to increase regional R&D spend through supporting SMEs, and to deliver new technologies through to the market as new products and processes.

T14a SofMat anti-counterfeiting

P Harrison, SofMat Ltd

SofMat Ltd is a company that has utilised the technology base in Bradford to produce discrete features that are intended for use in the brand protection and anti-counterfeit sectors. The Nanofactory project has assisted the company to win a TSB grant which has funded an in-depth market survey, to define potential markets and clients, in addition to funding overseas visits. These visits have resulted in high-level discussions with pharmaceutical companies that may result in significant amounts of investment to fund product commercialisation.
We will present an overview of the counterfeit issue, a review of the technology and marketplace, and the lessons learned when dealing with the representatives of large corporations.

T14b Organ viability assays

Brian Thomson, Aedstem Ltd

An example of a current project between the Polymer MNT RKT Centre, University of Bradford, and a local company is the development of a novel organ viability assay. The Centre was approached by AedStem Ltd through the Nanofactory scheme to assist with the design, optimisation and production methods for the islet viability assay kit so that it is ready for regulatory submission.

This project aims to improve the availability and utilisation of donated tissues in transplantation procedures. The project addresses an unmet clinical need for functional viability assays that could verify donated organs from 'marginal' donors that retain sufficient activity to be used in transplant procedures. The initial assay was designed for use with pancreatic islet transplantation, but subsequent 'proof-of-concept' work has shown that an analogous approaches can be used to produce solid organ viability assays (e.g. for liver and pancreas transplants) as well as cell suspensions (e.g. marrow-derived MSC).
The initial design concept consisted of two main components – an assay cassette which houses islets taken from the donor organ and a reagent tray. AedStem Ltd needed the Centre's help to design the mould to produce the two components of the kit: the assay cassette containing the islets and the reagent tray. The initial prototype design was refined to optimise it for high volume manufacturing processes without adversely affecting functionality. The support of University of Bradford Nanofactory team is acknowledged.

T14c Recycling laminate layer from architectural glass - polyvinyl butyral polymer (PVBp)

Gary Hopkins, GB Cullet Ltd

GB Cullet Ltd is a 2004 established Glass Re-cycling company based in Wombwell, Barnsley. Being environmentally friendly is the main focus of the company.
One of the recycled materials by the company is laminate layer from architectural glass - polyvinyl butyral polymer (PVBp). The company contacted the Nanofactory team at University of Bradford to assist with analysis aiming to determine the average flake size, moisture content, presence of any minor contamination in these materials and possible applications for the recycled material.
The analysis was performed in the case of the flake size measurement with software developed at University of Bradford. The Thermal Gravimetric Analysis (TGA) was performed on the sample to measure the moisture content. Raman Spectroscopy was used to identify the minor contaminants type.

W1 Formal Welcome and Updates

University of Bradford Senior Management Team -
Deputy Vice Chancellor, Prof Barry Winn; Director of International Strategy, Billy Mitchell;
Dr Jiansheng Du, UKTI;
Chinese Embassy (tbc),
Prof Guangxian Li, Prof Phil Coates UK China AMRI

In this session, we formally welcome all delegates and officials, and provide brief updates from the UKTI (Dr Jiansheng Du) and UK-China AMRI. We reflect that our international activities follow strategic themes, in particular advanced materials for healthcare technologies, and involve many different institutions, increasing research capacity and capability, with associated high quality outputs, and developing strong industry collaborations for the outworking of our research, and its increased impact.

W2 Investigation of plasma treatment on polymeric micro-injection moulded microneedle for protein drug delivery.

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The emergence of microneedle (MN) technologies offers a route for pain free, easy to administer drug delivery, but technological barriers still remain which pose significant challenges for manufacture of microneedle systems with high volume outputs at low cost. Our approach is to develop new routes for MN manufacture primarily using micro-injection moulding (µIM) processes with high performance engineering thermoplastics.
Despite the extraordinary versatility of these materials, there is one property that markedly reduces the ability to coat these devices with APIs, namely a highly hydrophobic surface. These problems arise because the plastics surfaces have relatively poor wetting and adhesion properties, which are due to the low surface energy and absence of polar surface groups. A well-documented solution for this problem is the use of plasma treatment of polymer surfaces to increase surface energy, so here we have developed techniques to assess the surface energy and BSA adsorption before and after plasma treatment. A range of candidate materials were selected on the basis of processing characteristics, mechanical properties and regulatory requirements. Moulded specimens of each material have been manufactured using µIM and samples from each production batch have been subsequently subjected to a range of plasma treatment methods. These samples were coated with BSA (bovine serum albumin) to study the protein adsorption on polymer surfaces. Sample surfaces structures before and after plasma treatment were studied using AFM and surface energies have been obtained using contact angle measurement and calculated using Owens-Wendt theory. Finally adsorption performance and BSA release kinetics for each sample set was assessed using a Franz diffusion cell. Initial results indicate that plasma treatment significantly increases the surface energy and roughness resulting in better adsorption and release of BSA.

Keywords: Microneedle, Micro-injection moulding, Plasma treatment and Bovine serum albumin.

W3 Micro-Processing of Polymer Blends and Composites

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B. R. Whiteside, M. T. Martyn, T. D. Gough, P. D. Coates, Polymer IRC, University of Bradford, Bradford, BD7 1DP, UK

There are increasing requirements for the miniaturized polymer parts in many high-tech fields such as photoelectric communication, biochemistry, medical care, information storage, precision machinery, etc [1-4]. However, the micro devices mainly based on single-component polymer material [2, 4] can hardly meet the demands of multi-functions. In addition, the confined space, high surface-interface interaction, difficult filler dispersion and the high stress, flow rate and temperature gradient in polymer micro processing are also challenges [2]. This paper reported the following strategies: organic/inorganic hybrid method to realize the functionalization of micro devices; solid state shearing milling (S^3M) to solve the dispersion and compatibility problems in highly filled polymer micro devices; molecular complexation technique to improve the processability of polymers such as PVA. Several polymer blend and composite systems, including poly(vinyl alcohol)/hydroxyapatite (PVA/HA), polyamide 11/barium titanate (PA11/BT), thermoplastic polyurethane/carbon nanotubes (TPU/CNTs), natural rubber/graphene (NR/GE) and polyoxymethylene/ poly(ethylene oxide) (POM/PEO) systems, were studied. S^3M method combined with molecular complexation greatly improved the filler dispersion, compatibility and processability of PVA/HA and PA11/BT composites, making them suitable for micro processing, even at high loading of fillers (Fig. 1 and Fig. 2). The prepared TPU/CNTs nanocomposite suitable for flexible medical micro electrode showed a good conductivity and mechanical property. The increases in both injection temperature and mold temperature and also the annealing treatment were advantageous to enhancement in the conductivity of the micropart (Fig. 3). For POM/PEO blend system, the typical hierarchical skin-core structures were identified in the micropart and there were shish-kebab orientation structures observed in the shear layers (Fig. 4).

Keywords: micro processing, micro device, multi-function, polymer blend and composite

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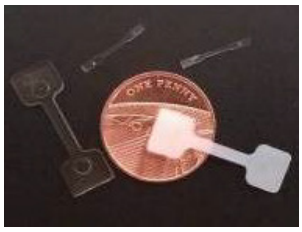

Fig. 1 The micro-injection moulded samples of PVA/n-HA composites (30 wt%)

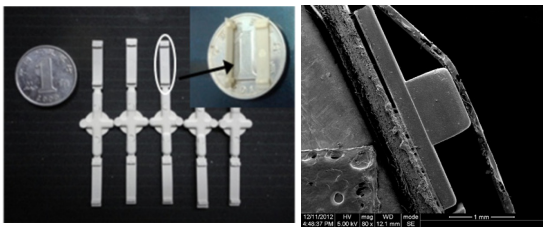

Fig. 2 The micro-injection moulded samples of PA11/BT (80 wt%) composite

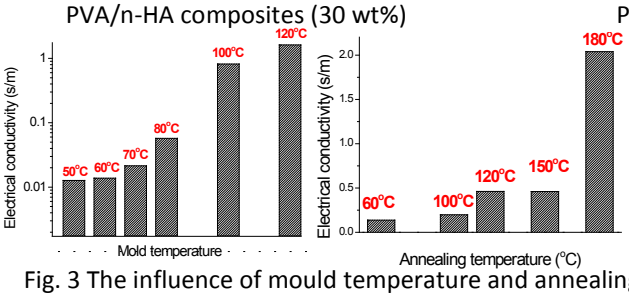

Fig. 3 The influence of mould temperature and annealing on the conductivity of TPU/CNTs micro-injection moulded nanocomposite

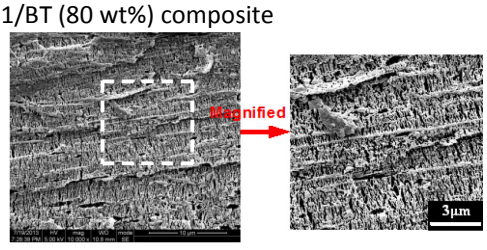

Fig. 4 The SEM photo of the shear layer in POM/PEO micropart

W4 Extrusion: scaling up from lab to production

Rod Bottom
Sales Account Manager
Thermo Fisher Scientific

Preamble
Especially, but not exclusively, the pharmaceutical industry is often material limited in the early stages of formulation development. To accommodate this, a number of new small-scale laboratory extruders have appeared on the market enabling scientists to explore initial feasibility studies and early stage product development of "interesting" candidates. At the same time it can quite quickly become vital that materials developed at this early stage can also be produced at the larger (production) scales to exactly the same quality and performance. In order to achieve this, the processing conditions used in the early stage must be "scalable".

Details
Parallel twin-screw extruders (PTW's) are widely used for continuous mixing and dispersing tasks in a number if industries. They are capable of being adapted to allow varying levels of shear intensity, dispersion and residence time as well as processing temperature. Each of the setup "variables", for example screw configuration and barrel length, can have a significant effect on the eventual product quality/performance and understanding these effects forms an important part of any future scale-up exercise.
Certain variables are mechanically scalable by the machinery manufacturers, for example screw/barrel length to diameter ratio (L/D) and screw element geometries. However for each product the effect of other process variables needs to be understood. This will include the effects of steel temperatures and material feed rates on critical parameters such as residence time and melt temperature.
Given that the desired outcome of scale-up is to produce material identical in all ways to the material produced during development, the processing "experience" felt by the product should be independent of the scale of machine. If this is achieved then identical product will be made.
Quality by Design (QBD) principles can be applied to extrusion processes to explore the available knowledge and design space and to specify the desired control space.

W5 Super Toughening of Brittle Polylactide with Novel Slide Graft Copolymer via in-Situ Reactive Compatibilization, Crosslinking and Chain Extension

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The novel ''sliding graft copolymer'' (SGC), in which many linear poly-ε-caprolactone (PCL) side chains are bound to cyclodextrin rings of a polyrotaxane (PR), can be used to toughen brittle polylactide (PLA) effectively with the reactive processing agent methylenediphenyl diisocyanate (MDI). It is shown that the interfacial reaction between the hydroxy groups (-OH) of PLA and SGC and the isocyanate group (-NCO) groups of MDI resulted in copolymers containing urethane linkages, and thus that can act as effective compatibilizers between two immiscible polymers. Secondly, the sliding graft copolymer was in-situ cross-linked with MDI (c-SGC) during melt processing. The formation of new cross-linked elastomeric particle in the PLA matrix was confirmed with the help of Fourier transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC) and x-ray diffractograms (XRD). In this new industrially approach, the elongation at break and the notched Izod impact strength of PLA/SGC/MDI (40/10/2) blend were improved to 235.7 % and 48.6 KJ/m2, respectively, due to the presence of c-SGC particles. Transmission electron microscopy (TEM) images showed sea-island morphology of PLA/c-SGC particles. Scanning electron microscopy (SEM) micrographs proved not only the formation of c-SGC particles but also compatibilizer between the PLA and SGC phases, signifying the enhancement of compatibility between PLA and SGC. Upon compatibilization, a brittle-to-ductile transition occured in the presence of c-SGC particles, effected by the debonding between the two phases. Moreover, the

gel permeation chromatography (GPC) and FT-IR results indicated that MDI also performed as the chain extender to increase the molecular weight of PLA. This is the first report on employing novel slide graft copolymer to toughen PLA.
Key words: PLA, Sliding Ring Materials, Toughening, Crosslinking

W6 Polymer colloids for controlled delivery of growth factors of importance in the development of blood vessels

Stephen Rimmer, University of Sheffield

The delivery of growth factors is important in regenerative therapies. In natural wound healing, these medium molar mass proteins are the key signalling molecules that initiate and control the production of viable tissue. However, all previous attempts to administer theses cytokines have failed because they are rather unstable (half lives are typically less than 1 hour at 37 □C) and both temporal and spatial control is required. Now in vivo many growth factors bind to the negatively charged glycosaminoglycan heparin. This binding interaction is vital in developing the function and stability of the growth factors and we consider that other charged polymers, which might be more easily processed into devices, could perform the same function. Another approach is to produce devices that can bind endogenous heparin this we have achieved by preparing biocompatible hydrogels that are functionalised with triargine peptides; arg-arg-arg is a simplified model of the heparin binding domains of growth factors.
A useful format for a growth factor-binding additive would be a sub-micron or nano-particle, which could be formulated into a range of materials. With this in mind, core-shell particles have been prepared by surfactant-free emulsion polymerisations of butyl methacrylate in the presence of either linear or highly branched poly(acrylamidomethylpropane sulphonate)s (L-PAMPS or HB-PAMPS) with dithioate end groups: using a "shell-first" approach. The particles were loaded with vascular endothelial growth factor (VEGF) or platelet derived growth factor (PDGF). The release of the growth factors was shown to be controlled by the architecture of the shell and we proposed a mechanism that involves both ionic interaction of the PAMPS with the heparin-binding domains of the growth factors and size exclusion mediated diffusion. In a second system we produced another type of core-shell particle with a phosphate shell. Release of VEGF was shown to be controlled by the structure and swelling of the shell and by combining the two classes of particles it is possible to control the availability of these important growth factors over many weeks in a manner that has not previously been achieved.

W7 Drug delivery – quantitative structure studies

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A deliverable drug must be in a suitable form for administration. In most cases, drugs are given in solid dosage forms as well as non-solution suspensions, which are all structured dosage forms. Attentions have been paid to the two extremes of the structure, namely, molecular level structures in size of nanometer or less than nanometer, and macro-level structures in size of millimeters or larger. While the macro-level structures are identical to the structure of the conventional dosage forms as tablets or capsules, the molecular level structures of micelle, liposome, and cyclodextrin inclusions are well investigated with either molecular simulation or experiments. Yet the microstructure of dosage forms sized between hundreds nanometers to millimeters has been almost an ignored area due to the lack of sensitive in situ imaging method and difficulties to quantify the three dimension features. As the primary element of innovation for the drug delivery system, the architecture of the solid pharmaceutical dosage forms is the ground work to have an optimized drug delivery. With the high resolution of micron and submicron, the synchrotron radiation X-ray microtomography (SR-μCT) technique can show the static three dimensional morphology and the structural characteristics of the solid dosage forms, such as powders, particulate drug delivery systems and tablets. Furthermore, the SR-μCT in situ determination correlates the dynamic structure transformation of the pharmaceutical dosage forms with

the drug release kinetics during the drug release phase. Therefore, it's possible to identify the significant structural factors governing the drug release rate of the controlled/sustained release systems, which provide new measure and novel methodologies for the design and quality control of drug delivery systems. A China-UK team has commenced the SR-μCT researches in structural characterization of powders, internal and microstructure of pharmaceutical preparations and structure based drug release kinetics, e.g., the identification of crystal polymorphs, quantitative profiling of mixing and segregation of granules, fractal analysis of complicated structure, the hydration dynamic characteristics of poorly water-soluble drugs in gel forming matrix tablets and the three dimensional release kinetics of monolith osmotic pump tablets. An N-in-One structure analysis of crystals, powders, sub-structure units is extremely of interest for characterization particulate systems like sustained release pellets as well as the shape transformation of crystal or particles in tablets under pressure.

Key words: architecture of pharmaceutical dosage forms; drug release mechanism; synchrotron radiation X-ray microtomography; n-in-one structure analysis; fractal dimension

W8 Pharmaceutical Processing for Improving Bioavailability

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Active pharmaceutical ingredients (APIs) are most conveniently developed and delivered as solid dosage forms due to their ease of administration, high patient compliance and cost-effectiveness. It has been estimated that more than 40% of APIs suffer from a bioavailability issue because of their low water solubility. For APIs with solubility-limited bioavailability, a challenge in the product development is to improve their solubility without compromising the stability and other performance characteristics. One of the effective ways to tailor the properties of an API is through 'crystal engineering'. An API can exist in a number of solid forms such as amorphous, polymorphs, solvates, salts and co-crystals. Each form may display its own unique physicochemical properties of pharmaceutical importance. Such diversity offers the opportunity of tuning key physiochemical properties of the pharmaceutical product without compromising the physiological activity of the API as the molecular structure is preserved.

The interdisciplinary team at CPES in association with the collaborators has developed a range of technologies for engineering of crystalline drug materials. The technologies explored for crystal engineering include hot melt extrusion, spray drying, microwave assisted synthesis and continuous milling. Apart from developing some new co-crystals, efforts have been made to probe mechanistic understanding.

The key technologies using hot melt extruder are Solvent Free Continuous Co-crystallisation (SFCC) and High Temperature Extrusion (HTE). These solvent free, scalable thermo-mechanical technologies provide green approach to achieve commercialisation. We are also exploring continuous milling as another green approach.

Dielectric heating by microwaves accelerate and maintain the saturated solution state of reacting components at the crystal interface leading to fast co-crystallisation. Co-crystallisation under microwave irradiation is shown to be controlled by the saturation of solvent at the reacting interface between the co-crystal components as well as the solvent dielectric properties.

Spray drying provides the rapid super saturation of the solution and change in temperature are considered to be critical factors in the generation of polymorphs or metastable or multicomponent crystalline forms. We are focusing on understanding the role of thermodynamic and kinetic factors in the formation of co-crystals by this technique.

W9 Shape memory polymers for biomedical applications

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Shape memory polymers are stimuli-responsive materials that are capable of undergoing a shape change in response to an external stimulus such as heat, light, pH, magnetic field etc. We discuss here the ability to impart shape-memory properties to a range of medical grade polymers, particularly bioresorbable copolymers of polylactide and polyglycolide. The key to this technology lies in orientation of the polymer molecules using solid phase deformation processes such as die-drawing.

The shape-memory effect can be exploited in a wide range of medical devices. In particular the use of the effect to create implantable devices with enhanced fixation in bone has been investigated, with examples including screws, suture anchors, IM nails and joint replacements. In such applications, control of activation temperatures within a range acceptable in the body is critical, and this can be achieved by appropriate choice and control of polymer composition.

W10 Thinking big in Minimally Invasive Surgery

Giles Proffitt, Surgical Innovations Ltd

Working within the constraints of small business, an SME perspective on successful innovation in MIS. Highlighting how SI seek to address the clinical, technical and market challenges in developing devices for existing and emerging surgery.

W11 Property gradient materials for tissue repair

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Chuhong Zhang, Qi Wang, State Key Laboratory of Polymer Materials Engineering, Sichuan University
Aileen Crawford, University of Sheffield
Dujin Wang, Dong Qiu, Dr Yulan Su, Institute of Chemistry, Chinese Academy of Sciences. Beijing
Jun Jie Wu, University of Durham

Osteoarthritis is a currently incurable condition and a leading cause of functional disability and loss of independence in older adults globally, causing significant economic impact (1-2% GDP). This project proposes a novel cell-conducting osteochondral implant for the treatment of osteoarthritis and traumatic lesions of articular cartilage, which have a similar prevalence in Chinese and Caucasian populations. The implant is a polyvinyl alcohol-based hydrogel nanocomposite, which exhibits compositional/structural regions that mimic the appropriate biomechanical properties of the different regions of native tissue (i.e. subchondral bone, mineralised cartilage and cartilage) and support regeneration of cartilage tissue in situ. This implant should extend the pain-free function of osteoarthritic joints, thereby enhancing patient quality of life and mobility while reducing patient demands on health and social support services. In addition, the need for total joint replacement, with its potential problems of prosthesis loosening and limited lifespan, would be delayed.
This collaboration brings together the requisite multidisciplinary and complementary strands of research, and essential scientific expertise, from the partner institutions into a world class team to conduct the project. The proposal builds on links made through the RCUK Science Bridges China programme and the RCUK Global Exchanges programme and is funded through the RCUK-MoST Cooperation Programme in Global Priorities.
Building on existing expertise and experience, we will develop water-containing poly-vinyl alcohol materials with inclusions of bioceramics (bony attachment), hyaluronic acid (viscosupplementation), and biological actives. By controlling the structure-properties relationship of our materials, through use of polymer chemistry and processing, we will also control the mechanical and gelation behaviour of these materials. In addition, this polymer system is highly biocompatible and is also known to have properties suitable for controlled release of biologically active compounds.

W12 Large Diameter Ceramic-on-CFR-PEEK Hip Joint Replacements

Jun Jie Wu, Centre for Biomedical Engineering, University of Durham

A novel material combination of a large diameter Zirconia-toughened-alumina (ZTA) head and a pitch-based carbon fibre reinforced poly ether–ether-ketone (CFR-PEEK) MOTIS cup has been studied using Durham Hip Simulators and Friction Simulator. The temperature change of the lubricant caused by the frictionalheat was measured in situ. Friction factors measured using the Durham Friction Simulator were lower for the worn CFR-PEEK cups compared with unworn. This correlated with the decreased surface roughness.

W13 MeDe Innovation – a new EPSRC Centre for Innovative Manufacturing of Medical Devices

Kenny Dalgarno, David Grant, Ifty Ahmed, Paul Hatton, Phil Coates

MeDe Innovation
EPSRC Centre for Innovative Manufacturing In Medical Devices

MeDe Innovation (The EPSRC Centre for Innovative Manufacturing in Medical Devices) researches and develops advanced design and manufacturing methods for the medical device sector.
Our innovative design and manufacturing advances focus on class 3 medical devices for musculoskeletal disease, where the cost of device failure and need for throughout life reliability are high.
Growth of the sector looks set to remain at 10% worldwide for the foreseeable future – with Asia offering a significant opportunity with 30% predicted growth - and this is driving an increased demand for better reliability and lifetime performance of medical devices. Our research aims to answer this demand, underpinning the development of musculoskeletal medical device manufacture to provide methods of producing reliable, effective devices.
It will also support the development of the sector and satisfy the health service's requirement for new, innovative and cost effective treatment options. These devices – and manufacturing processes – will ensure that the patients of the future are provided with devices that offer enhanced standards of reliability and performance.
The Centre is a collaborative research project which brings together expertise from the universities of Leeds, Newcastle, Nottingham, Bradford and Sheffield as well as a range of expert clinicians from across the UK. Our 12 founding industry members are embedded within our research projects, with many more forming an industry-wide network.
MeDe Innovation (The EPSRC Centre for Innovative Manufacturing in Medical Devices) is part of a wider initiative funded by the UKs Engineering and Physical Sciences Research Council (EPSRC) aimed at maximising the impact of innovative research for the UK.
Each Centre has been set up to respond to a specific business need and will support existing industries as well as opening up new industries and markets in growth areas. Funded support from the EPSRC will be used as a platform from which the Centres can secure further investment from industry and other funders.
As well as working extensively with academic, clinical and industry partners, MeDe Innovation will maintain a close contact with the other Centres for Innovative Manufacturing which provides further opportunities for our research.
MeDe Innovation is a collaboration of five of the UKs leading universities, each with its own research strengths, which in combination provide a powerful platform upon which to build robust solutions to the challenges faced by medical device manufacturers.
The partner universities are:
University of Bradford
University of Leeds
University of Nottingham
Newcastle University
University of Sheffield
MeDe Innovation has been formed to support the medical devices sector in addressing some of its major challenges. This rapidly growing sector is experiencing strong demand for innovation in manufacturing processes, evolving environmental and regulatory requirements and calls for greater personalisation and increased reliability of medical devices.
Our research will focus on the development of advanced methods of functionally stratified design and near-patient manufacture, to deliver cost-effective processes to ensure that patients receive the right product – featuring an enhanced standard of reliability and performance - at the right time.

W14 Cationic heterolipid based nanocarriers for anticancer therapeutics

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Bradford- ICT Mumbai UKIERI Programme

Cancer treatment has been a crucial need of current time. Almost all anticancer drugs and therapeutic genes (DNA, siRNA, shRNA etc.) have intracellular components of the cells like cytoplasm and nucleus as one of their

pharmacological sites for exhibiting therapeutic activity. Despite their promising efficacy, their intracellular availability has been critically hampered due to lack of self ability to transfect the cell membrane. Further, endosomal escape proves to be a rate limiting step as the bioactive needs to get released into the cytosolic space prior to its degradation in the lysosomal compartment. This necessitates the need for effective strategies which facilitate superior transfection and endosomal escaping ability and enhance the intracellular availability of therapeutics. Taking this into consideration, we have designed and synthesized a novel amphiphilic, cationic heterolipid in our lab. This cationic heterolipid was employed in fabricating cationic self-microemulsifying drug delivery system (C-SMEDDS) using etoposide (Etp) as a model drugfor intratumoral (IT) delivery and further examined for its ability to deliver Etp in the intracellular space. The developed Etoposide loaded C-SMEDDS (ECS) exhibited an average globule size < 50 nm and zeta potential + 32 mV without any phase separation or drug precipitation even after 24 h. ECS were screened for series of cell biological experiments and compared with plain Etp and Etp SMEDDS devoid of cationic heterolipid (ENCS) to elucidate its transfection ability. In vitro anti-proliferative activity against B16F10 melanoma cells demonstrated superior efficacy of ECS ($p < 0.05$) compared to ENCS. Clonogenic assay showed prolonged retention ability of ECS followed by sustained cytosolic release of Etp in cancer cells, evident as lack of complete cell colonies growth post treatment ($p < 0.01$) compared to ENCS. Cell cycle analysis indicated highest cell arrest (83.92%) by ECS in G2-M phase ($p < 0.05$) compared to (64.35%) by plain Etp and (66.96%) by ENCS, suggesting highest transfection efficiency of ECS which resulted in enhanced intracellular bioavailability of Etp. Post-transfection ECS were able to majorly get co-localized in cytoplasmic, perinuclear and nuclear space of cancer cells as evident by confocal images and flow cytometry histograms. Intracellular trafficking results elucidated that ECS could have followed multiple pathways viz clathrin coated pits, cytoskeletal reorganization and/or energy dependent uptake pathway to translocate in the intracellular space and could have bypassed the endosomal barrier either by proton sponge effect or flip flop mechanism. Further, in vivo antitumor efficacy study was conducted in B16F10 inoculated C57BL/6 mice. ECS exhibited superior tumor regression activity both at therapeutic (12 mg/kg) and sub-therapeutic (6 mg/kg) dosewith 100% survival compared to plain Etp suspension (IT route), ENCS (IT route) and Etp solution (IV route). Localized delivery of ECS at tumor site with excellent ability to deliver the therapeutic moiety in cytoplasmic space might help in circumventing the life threatening side effects associated with Etp (IV route).

Th1 Bioactive nanoparticles with well controlled structure

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Bioactive nanoparticles are commonly used fillers for biomedical polymers, in order to improve their bioactivity and mechanical performances. Particles below 100 nm showed better performances in compositing with polymer matrix. However, the synthesis of bioactive glass nanoparticle is not straightforward as they are usually made by milling, where heavy aggregation is hardly avoidable. We have developed a method to make bioactive nanoparticles with good colloidal stability by post modification of well defined colloidal silica and found these particles can be used to improve bioactivity and mechanical performance of polymer scaffold.

Th 2 Cell-biomaterial interactions

Aileen Crawford, Centre for Biomaterials & Tissue Engineering, School of Clinical Dentistry, University of Sheffield

Regenerative medicine technologies offer potential in the restoration of damaged musculoskeletal tissues and biomaterials have a central role to play in these technologies. To date, a variety of biomaterials and fabrication processes have been used to produce scaffolds for tissue engineering of cartilage and bone. However, appropriate interaction between cells and a biomaterial is vital to the quality and function of the resultant tissue formed. Apart from a physical support for cells, many biomaterials have the potential to be custom-designed to provide relevant physical and biochemical cues to help regulate cell function and behaviour. This 'instructive' role of biomaterials could facilitate tissue regeneration whether delivered to a tissue defect as a biomaterial-based cell therapy to or as a cell-free medical device to promote tissue regeneration *in situ*. In the body, the extracellular matrix (ECM) of a tissue is the 'natural' biomaterial scaffold which provides the structural support and microenvironment for the body cells and also the bulk, shape, and strength of many tissues such as tendon, cartilage and bone. In addition, natural ECMs can modulate cell function and migration through their various cell adhesion sites and ability to locally bind, store and release bioactive factors. Further

understanding of cell-ECM interactions could give valuable clues which can be used to create synthetic biomaterials with similar biological function.

Th3 Poly(vinyl alcohol) based composites for joint soft tissue repair

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With the development of society and economy, population aging has become a serious global social problem. The osteoarthritis caused by the articular cartilage degeneration is one of the most common health problems of aging population and has seriously affected the elderly and their families. Repairing of the degraded parts is a conservative treatment to delay or replace the joint replacement with low cost and can effectively reduce the suffering of patients.

Gradient materials, which can effectively linking the bone and cartilages, have potential applications in repairing of the articular cartilage defects. Poly(vinyl alcohol) (PVA), a polymer materials with multi-hydroxyl groups, strong polarity, stable chemical properties, high mechanical properties, excellent bio-compatibility with human body and excellent compatibility with medical bioceramics, bioactive glass and natural fibers, is a good candidate to prepare gradient materials used for joint soft tissue repair. The key is realizing the thermal processing of PVA and preparing the three-dimensional materials with various modulus, shapes as well as the gradient structure which can well connect to bone and cartilage.

In this paper, based on our novel technology for thermal processing of PVA and by adopting the nontoxic modifiers suitable for medical applications, three kinds of PVA based nano-composites including PVA/hydroxyapatite (HA), PVA/gel/HA and PVA/β-Tricalcium phosphate (β-TCP) were successfully prepared through thermal processing. The thermal processing windows for these composites were above 130^{o}C, which were wide enough for hot pressing, extruding and injection molding. And further based on the solid state shear milling (S^3M) technology for nano-composite developed in our SKLPME, the well dispersion of nano-particles in PVA matrix was achieved under the strong shear force of pan-mill mechnochemical reactor. The particles content could be up to 40wt%, without using any coupling agent or compatibilizer. The thermal plasticizing mechanism including the interactions and the water states in systems, the mechanical properties, the swelling behaviors as well as the bioactivities of the composites were studied. By using water as physical foaming agent and the nano-particles as nucleating agent, PVA foams with uniform cell structure were also obtained. The studies in this paper provided the good bases for preparing gradient PVA based nano-composites used for joint soft tissue repair.

Keywords: PVA based composites, thermal processing, solid state shear milling, joint soft tissue repair

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Th4 New PLA based polymers

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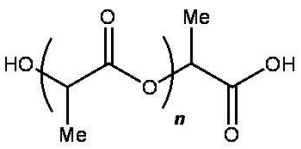
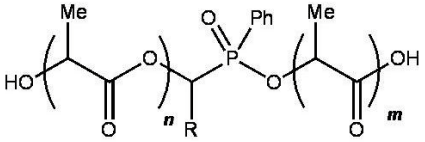
The increased awareness of the impact of man-made materials on the environment, coupled with the growing concern over depletion of petroleum resources over the next decades, has prompted an urgent need for research into non-petroleum based, environmentally-benign, new materials. Poly(lactic acid) (PLA), a linear polymeric ester made up of lactic acid monomer building blocks (Figure 1), has been a particularly attractive starting point in these efforts. PLA is derived from renewable plant sources, for example starch and sugar, and is biodegradable due to facile cleavage of the ester linkage in the polymer's backbone under both chemical and enzyme-mediated conditions. However, in spite of its desirable features, expanding the use of PLA in consumer products has some significant obstacles which necessitate improving its performance and characteristics.



Poly(lactic acid) PLA



An example of a PLA-PPA polymer

Our research aims to improve the properties of PLA through co-polymerisation of lactic acid with a corresponding phenylphosphinic acid (Figure 1). We have developed a method of the preparation of this novel class of polymers and have carried out investigation on their physiochemical properties.

Th5 Meeting future healthcare needs with innovation & technology – an orthopaedic industry perspective

Alan Ashby
DePuy Synthes

This presentation will focus on future healthcare needs in chronic musculo-skeletal diseases and the challenges that face stakeholders in meeting expectations.
Example technology and service development directions to address these requirements will be explored and challenged.

Th6 Clinician's viewpoint – NIHR healthcare technology co-operative for wound prevention and treatment

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Honorary Visiting Professor Wound Healing Research, University of Bradford

Bradford is home to one of England's only dedicated Wound Healing Research Units and now hosts the NIHR Healthcare Technology Co-operative (HTC) in Wound Prevention and Treatment. This organisation, which is a strategic partnership between academics and clinicians from several university hospitals across England, acts as a platform for innovation, identifying and developing promising concepts for medical devices derived from an established network of patients, clinicians, academics and industry. It provide theoretical, methodological and design expertise and a clinical base to develop these concepts into testable interventions and devices, testing the feasibility, effectiveness, cost effectiveness and acceptability of proposed innovations in NHS settings and various care pathways and promotes their adoption and the spread of best practice.

The management and prevention of skin breakdown is a major area of unmet clinical need and unregulated clinical practice yet is a key area for the UK medical devices industry and a major quality indicator for NHS care provision. Under the umbrella term skin breakdown a variety of distinct wound types are recognised ranging from acute surgical and traumatic wounds, through a range of inherited skin conditions such as Epidermolysis Bullosa to chronic wounds that include diabetic foot ulceration, pressure ulceration and venous ulcers. Currently a wide range of "wound dressing" products and devices are employed to achieve moist wound healing including hydrogels, hydrocolloids, alginates, foams and transparent films some of which incorporate antimicrobial agents. In addition devices offering topical negative pressure therapy, electrical stimulation, oxygen therapy, laser therapy, ultrasound and cold plasma treatment have been developed. Frequently substantive clinical trial evidence for treatment effectiveness and indications for use are lacking and therefore the adoption of innovation is thwarted. Improving understanding of the mechanism of causation and the cellular and biochemical processes of healing offer the opportunity for targeted device development in the future both as a supportive diagnostic tool and a therapeutic strategy.

Wounds are a major clinical problem; audit has confirmed a point prevalence of 3.55 wounds per 1000 population, the prevalence rising for all wound types with age (1). With an increasing incidence of obesity and diabetes skin breakdown and secondary complications such as amputation are predicted to get worse. The cost implications of a single category IV pressure ulcer has been estimated at £14k (2) while the overall cost to the NHS of caring for patients with skin breakdown is conservatively estimated to be £2.3bn-3.1bn per year (at

2005-2006 costs), around 3% of the total estimated out-turn expenditure on health (£89.4bn) for the same period (3).

Th7 Modulation of surface properties with polyelectrolyte multilayers

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The layer-by-layer (LbL) electrostatic assembly technique has become a relatively mature and effective method for fabrication of functional thin films and surface modification. By direct assembly of biomacromolecules into multilayers via charge interactions, we can tune the surface properties of the substrates. Generally for as-assembled polyelectrolyte multilayers, charges on the polycation and the polyanion balance each other, and the salt ions only reside at the surface as the counterions for the excess charges on the polyelectrolyte last deposited. By taking advantage of the counterions at the surface of the LbL assemblies, we apply the ion exchange chemistry to multilayers to modulate the surface wetting properties. We show that the surface wettability can be tuned rapidly and reversibly from superhydrophilic to superhydrophobic, and completely erasable and rewritable gradient wettability can be achieved using this approach.

Th8 Solid phase processing of PLA based blends and composites for blood-contacting medical devices

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Solid phase processing of PLA based blends and nanocomposites was explored in an effort to improve the mechanical properties and blood compatibility of PLA as blood-contacting medical devices. Through solid hot stretching technology, highly-oriented PLA/MWNTs composites and PLA/TPU blend were fabricated. The mechanical properties of the composites and blends can be improved dramatically by stretching. Stress-induced crystallization and orientation of PLA matrix as well as alignment of filler occurred during drawing. And the key finding was the fact that the oriented samples showed obviously enhanced in vitro blood compatibility. In order to further improve the properties of PLA as biomaterials, PLA with enhanced melt strength was prepared and the draw ratio as high as 900% can be reached for modified PLA. The samples at high draw ratio showed highly molecular orientation and promising blood compatibility. The bionic character of oriented PLA and its anti-coagulation mechanism were explored.

Th9 Regulation of polymer blend morphology using nanoparticles

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With the increasingly wide utilization of various nanoparticles in polymer industry, the role of nanoparticles in polymer processing has far exceeded that they are usually recognized. In this study, we demonstrated that nanoparticles can control the morphology and dynamics of polymer blends in a versatile way. First, the morphology change and the corresponding molecular mechanism of polystyrene (PS)/poly (vinyl methyl ether) (PVME) blends induced by hydrophilic or hydrophobic silica nanoparticles were studied. It was found that silica nanoparticles can change the miscibility and phase separation mechanism of PS/PVME blends via alternating the component dynamics, where the chemical nature of nanoparticles plays a vital role. Second, nanoparticles were found to improve the morphological stability of immiscible polymer blends by accelerating the crystallization of crystallizable polymeric component. The addition of silica nanoparticles was also found to suppress the development of nodular morphology on crystalline fibrils under shear flow by heterogeneous crystallization. It has been suggested that the loading of a relative high content of silica nanoparticles, the

application of a rapid quenching and low rate shear flow are in favor of the shape stability of PBT fibrils under shear flow.

Keywords: nanoparticles, polymer blends, morphology, rheology, crystallization

Th10 AFM nano-mechanics: from collagen fibrils to collagenous tissue

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Collagen is the most abundant protein in the human body and it is one of the most important due to its role in the strength of biomechanical tissues. Here we utilise the AFM's capabilities to test the mechanical properties of both collagen fibrils and collagenous tissue at the nanometre level. We find that the properties of reconstituted bovine Achilles tendon collagen fibrils have the capacity to be fine-tuned in their aqueous media, with potential applications in tissue engineering of scaffolds [1]. The properties are also shown to be reversible.

The collagenous tissue of porcine sclera (white of the eye) has a multi-layer structure, with the episclera outermost and the stroma being the bulk of the tissue. Imaging fresh unfixed tissue from the stroma reveals collagen fibrils within an extra cellular matrix under physiological conditions. The nano-mechanics of the episclera are shown to have a bimodal distribution, whereas the stroma has a skewed distribution between the two components of the biphasic tissue [2].

Skin is the largest organ of the human body and can be considered a multi-layer bio-material that is often called upon to protect against mechanical, chemical and bacterial attack. Damage to the skin due to wounding (e.g. accidental graze or surgical intervention) can result in scar formation as part of the healing process. Histological studies have shown that collagen fibrils in scar tissues are highly aligned, rather than adopting the random orientation seen in the healthy tissue. This change of orientation, together with other structural changes, causes a change to the biomechanical properties of the tissue at the nano-level [3].

The biomechanical properties of arteries are an important factor in the overall function of the circulatory system. However, our understanding of how the structure and composition of arteries controls the biomechanics is poor and little is known about the properties of the discrete layers within these blood vessels. The tunica adventitia provides an outer covering of the arteries and veins. It is made of fibrous connective tissue (collagen and elastin), adipose tissue, nerve endings and cells (macrophages, mast and fibroblasts). This outer layer of collagenous fibres allows the blood vessels to stretch, preventing overexpansion due to the pressure exerted on the endothelial walls by pulsatile blood flow. We have examined the nano-mechanical and visco-elastic properties of the tunica adventitia of porcine "elastic" (aorta and pulmonary) arteries under physiological conditions. Distinctive mechanical behaviour is found between the tunica adventitia of the two artery sections in their static moduli and creep. AFM dynamic nanoindentation is used to examine the viscous dissipation of the tissue [4].

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Th11 Constricted venous outflow: Does it alter cerebrospinal fluid dynamics?

Clive Beggs, School of Engineering & Informatics, University of Bradford

Few topics in medicine have in recent years produced such controversy as chronic cerebrospinal venous insufficiency (CCSVI). Since this vascular syndrome was first identified in 2009 1, it has divided opinion. On one extreme, are those who advocate that CCSVI causes multiple sclerosis (MS), while at the other end of the spectrum are those who deny that the syndrome exists at all. Consequently, the debate on CCSVI has become polarized – a situation, which all too easily, can result in a loss of objectivity.

So what is one to make of CCSVI? Are there any grounds for believing that it might be associated with neurological disease, or is the syndrome a complete irrelevance? Perhaps some insights can be gained from the world of fluid dynamics and biomechanics. Because there are no obvious moving parts, it is all too easy to ignore the biomechanics of the brain. Yet the intracranial space is a finely tuned dynamic mechanism, involving three fluids (blood, cerebrospinal fluid (CSF) and interstitial fluid), all of which interact with each other in a precise and orderly manner. Traditionally, the cerebral venous system has been viewed simply as a series of collecting vessels channelling blood back to the heart. However, recent research is revealing that the cerebral venous system plays an important role in regulating the intracranial fluid system 2, 3 - a role that appears to influence both perfusion of the brain parenchyma 4 and the dynamics of the CSF system 5.

Recently a new cervical plethysmography technique has been developed 6, which revealed the hydraulic resistance of the cerebral venous drainage system to be on average 63.5% greater in MS patients diagnosed with CCSVI compared with CCSVI negative healthy controls 7. This suggests that CCSVI is associated with mild venous hypertension (<5 mmHg) in the dural sinuses; something that would tend to inhibit the bulk flow of CSF, as some have observed in MS patients 8-10. Venous hypertension of this magnitude would also tend to reduce intracranial compliance 2, thus altering the dynamics of the CSF in the aqueduct of Sylvius (AoS). Indeed, a number of studies have revealed increased aqueductal CSF pulsatility in MS patients 8-10 and CCSVI positive healthy controls 11; something which suggests that CCSVI is associated with altered CSF dynamics, irrespective of whether or not MS is present.

While there is evidence linking mild venous hypertension with changes in CSF dynamics, the clinical implications of these changes are unclear. It may be that increased CSF pulsatility in the AoS induces ventricular reflux and edema formation in the periventricular white matter, as has been observed in patients with normal pressure hydrocephalus 12. Given, that ventricular reflux has also been implicated with periventricular lesion formation in MS 13, 14, there is need for further research to assess whether or not CCSVI is associated with CSF reflux from the lateral ventricles into the brain parenchyma.

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