Abstracts

Keynote and Invited Speakers

KEYNOTE SPEAKERS

Prof. Justin Cobb

Imperial College London, United Kingdom

Surgical interfaces: why current technology fails

Joint Replacement surgery today is a mature but segmented industry, with the same technology and materials delivering successful outcomes in the hip, with many patients having a single operation that will last lifelong. More expensive and rather less effective outcome is obtained by total knee joint replacement, with the risks of surgery being finely balanced with the benefits in many people. In the spine, disc replacement has been around for years. But it has been stopped in several developed countries because of problems.

The burden of disease in society is almost the opposite of this: far more people suffer from degenerative spinal pain than from any other joint. Next most common is knee pain. Damage to the medial compartment is very much more prevalent than in the hip in every country in the world. The societal burden of wearing out is large and increasing, for the obvious reason that we are all living longer and putting more ‘ miles on the clock’ that any generation before. The technology solutions we can offer today are well short of delivering the ‘lifetime guarantee’ that could reasonably be expected by a patient with a worn joint. Superior Interface technologies are needed, as part of the revolution in joint surgery, minimising the size of the device, while maximising its effectiveness. To meet the growing demand for comfort in older age, it is essential that we optimise the benefit and reduce the risks of surgery.

Three examples will be given of practical problems with huge societal consequence, where our current technologies are barely fit for purpose: much is needed from biomaterial research.

Hip resurfacing is a more conservative, safer and more effective intervention that hip replacement. However until now this device type has required a hard-on-hard metal

articulation. Problems of wear, resulting in wear debris causing local and systemic issues. The next generation of resurfacings are in the very early stages of clinical trial, using either hard-on-hard ceramic bearings, or a hard-on soft metal on plastic alternative. These will be described and the issues of their interfaces discussed.

In the knee, the mechanical environment is more complex. The three separate compartments have very different loading patterns: the medial compartment is almost a ball and socket joint, while both the lateral and patella-femoral joints have combination rolling and sliding articulations , so a monolithic replacement of stiff metal has interfaces that are far from ideal: the medial side may have a loading pattern of pure compression, while the lateral side may actually experience tension at the time of peak loading. The implications for device design, both monolithic and multicompartmental, and the opportunities for invention will be explored.

In the spine, a much more limited range of motion is required of a disc arthroplasty, but access remains hard, and the requirement for a stable interface with bone is paramount, as displacement may cause paralysis or death or both. With ageing, the spine commonly loses bone mass. When this natural process is combined with stress shielding owing to a stiff device, collapse of the bone is a common consequence. The opportunities for novel devices and interfaces here will also be explored.

Finally the hard/soft tissue frontier will be explored: the interface between soft tissue and bone is a natural fatigue point, leading to painful avulsions. Fatigue failure may result in extrusion of a meniscus or disc, and secondary problems both up and downstream. The problems and opportunities that this soft tissue failure brings will be discussed, with examples of opportunities.

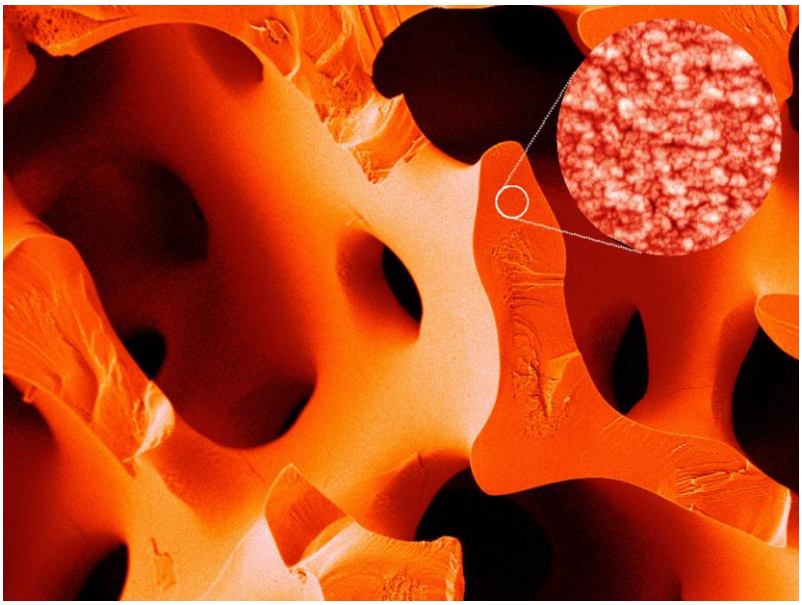
Prof. Helmut Cölfen

Department of Physical Chemistry, Universität Konstanz, Germany

Bio- and bioinspired mineralisation

Biomineralisation is the process by which living organisms form highly sophisticated organic - inorganic hybrid materials. Characteristic for these materials is their outstanding materials performance, their complex morphology and often hierarchical structure (see figure). In addition, they are formed in aqueous environment and ambient conditions which makes them attractive archetypes for advanced materials synthesis.

In this presentation, some typical Biominerals and their properties will be introduced. It will be shown that their advantageous properties are a result of their hierarchical composite structure. It will be also demonstrated that some of these mineral structures are not built according to the classical textbook knowledge of crystallization. Such non-classical mechanisms bear great potential for the design of new crystalline (hybrid)materials. Therefore, it is highly attractive to mimic Biominerals in an attempt to synthesize advanced materials. This will be demonstrated for Nacre and sea urchin spines. For Nacre, a material very close in the advantageous properties to the natural archetype can be synthesized just using the natural components. Taking inspiration from the mesocrystalline sea urchin spine structure, the performance of calciumsilicatehydrate – the binder of cement can be tremendously improved. It will be highlighted that a fracture resistant mesocrystalline cement can be produced, which outperforms the mechanical properties of cement or concrete by factors. This demonstrates the huge potential of Bio-inspired mineralization.



Microstructure of a sea urchin spine (Scanning electron micrograph) – a biological mesocrystal. Although the spine has the properties of a single crystal, its morphology exhibits no crystal faces, which are typical for single crystals.

Prof. Peter Fratzl

Max Planck Institute of Colloids and Interfaces, Potsdam, Germany

Tesselation – a natural strategy for improving fracture resistance

Surface tiling or three-dimensional tessellation are well-known ways of filling surfaces or volumes, respectively, for example in brick-and-mortar arrangements. Similar strategies are used by Nature at the microscopic level and even at the nano-scale to assemble materials with excellent fracture resistance, based on comparably weak components[1]. Best known is the widely studied nacre found in some sea shells, but the principle is much more general and nearly omnipresent in skeletons of vertebrates, in insect cuticles or tough protein-based fibers. Tesselated materials often result from a step-wise assembly and – in addition to improved fracture properties as compared to a homogenenous bulk-like material – they may have a range of interesting mechanical behaviors including actuation[2] and mechanosensing with extreme sensitivity[3]. For periodic multilayers, the simplest version of a tessellation, one can define a criterium according to which strength and damage tolerance are considerably improved with respect to the homogenous bulk[4]. Rotational plywood structures that are found in many biological materials, such as bones or insect carapaces, follow similar rules[5] and are critical for reducing fracture resistance in bone[6]. Since the fabrication of graded materials is becoming more economical with advances in 3d-fabrication, one can foresee that tessellated materials may become an interesting direction for materials development.

1. THE MECHANICS OF TESSELLATIONS - BIOINSPIRED STRATEGIES FOR FRACTURE RESISTANCE. P. Fratzl, O. Kolednik, F. D. Fischer, M. N. Dean, Chem. Soc. Rev. 45, 252 - 267 (2016)
2. BIOMATERIAL SYSTEMS FOR MECHANOSENSING AND ACTUATION. P. Fratzl, F. G. Barth, Nature 462, 442 - 448 (2009)
3. THE VIRTUES OF TILING: P. Fratzl, Nature 516, 178 - 179 (2014)
4. IMPROVEMENTS OF STRENGTH AND FRACTURE RESISTANCE BY SPATIAL MATERIAL PROPERTY VARIATIONS. O. Kolednik, J. Predan, F. D. Fischer, P. Fratzl, Acta Materialia 68, 279 - 294 (2014)
5. CRACK DRIVING FORCE IN TWISTED PLYWOOD STRUCTURES. F.D. Fischer, O. Kolednik, J. Predan, H. Razi, P. Fratzl, Acta Biomaterialia 55, 349-359 (2017).
6. FRAGILITY OF BONE MATERIAL CONTROLLED BY INTERNAL INTERFACES. W. Wagermaier, K. Klaushofer, P. Fratzl, Calcified Tissue International 97, 201 - 212 (2015)

Prof. André R. Studart

Complex Materials, Department of Materials, ETH Zurich, Switzerland

3D Printing of Hierarchical Porous Materials

Porosity is extensively exploited in natural materials as an effective means to reduce weight, minimize resources or enable the transport and storage of fluids and nutrients. Because porosity inevitably reduces the strength of materials, the incorporation of pores should occur with minimum impact on the mechanical performance of the structure. To this end, porous biological materials like plant leaves, animal skulls and bird beaks often exploit porosity gradients at multiple length scales to generate mechanically efficient structures. In this talk, I will present a new processing route for the 3D printing of foams and emulsions into hierarchical and graded porous structures of high mechanical efficiency. The multiscale spatial control over porosity and pore sizes achieved with this method provides a rich design space for the digital manufacturing of porous materials for engineering, catalytic and biomedical applications.

INVITED SPEAKERS

Prof. Mauro Alini

AO Research Institute, Davos, Switzerland

MSC and Complex Loading Pattern for Cartilage Repair

Research in the use of mesenchymal stem cells (MSCs) to enhance orthopaedic repair has dramatically increased over the last 20 years. The unique properties of MSCs and their natural presence within the bone marrow make them an attractive source of cells for novel therapeutics. When considering the natural repair environment, it is clear that the microenvironment the cells experience plays a major role in the repair response. Within the musculoskeletal system, one of the major drivers of repair is the mechanical load applied to the cells within the defect.

When developing new therapies *in vitro*, static culture is the most commonly used method. However, it is clear that due to the critical role mechanics plays *in vivo*, a more physiological loading regime in vitro would be most appropriate and this can be achieved by the use of bioreactors. Using a multiaxial load bioreactor system, we have been investigating the effect of mechanical stimulation on human stem cell differentiation. Performing studies in the absence of growth factors, specifically Transforming growth factor β (TGF β), allows the direct effect of the mechanical strain applied to be elucidated. Our bioreactor system allows for the application of shear, compression or a combination of both stimuli to establish the phenotypic changes induced within MSCs. In particular, the effect of the various mechanical stimuli on chondrogenic differentiation will be discussed and compared to responses seen in chondrocytes.

As a model system, human bone marrow derived MSCs are embedded in a fibrin gel, which is then retained in a macroporous biodegradable polyurethane (PU) scaffold. This system provides a naturally occurring support matrix (fibrin), while allowing for cyclical load to be applied due to the resilience of the PU scaffold. Neither compression alone, nor shear alone can induce a change in MSC phenotype within this system. However, we have

demonstrated that a combination of compression and shear is able to induce chondrogenic differentiation and this is due to increased endogenous expression of TGF β from the loaded cells. Finite Element modelling of the bioreactor system demonstrated that the degree of principle component strain was the main driving force in this system.

Using this multiaxial load bioreactor system we are able to investigate novel treatments and therapies in vitro, under physiologically relevant kinematic load. In addition, potential rehabilitation protocols to be used after cell therapy in cartilage repair can also be investigated.

Prof. Marc Bohner

RMS Foundation, Switzerland

Calcium phosphate surfaces and bone regeneration

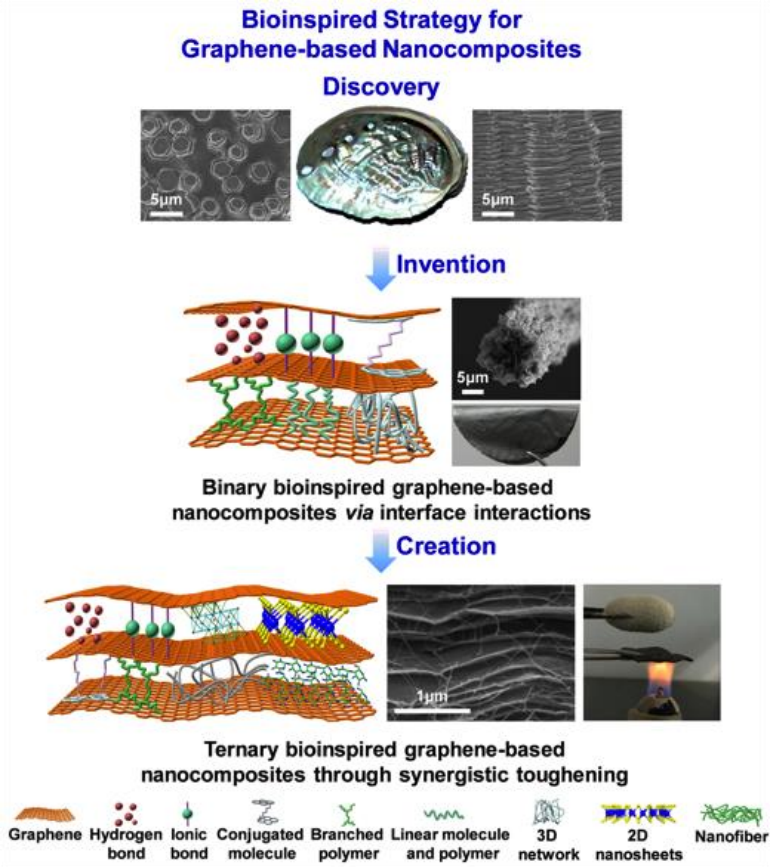
Interfaces between biomaterials and biological tissues have been extensively studied over the past 50 years. Aspects of interest have been numerous, such as the effect of surface topography, hydrophilicity, or composition on the biological response. Calcium phosphate materials have been used as bone graft substitutes since the 1970's. These materials are often considered to be the best biomaterials for such applications. Surprisingly, very little is known on the link between calcium phosphate properties and their biological response. At the "8th International Workshop on Interfaces" in 2011, I reported that calcination at ≈500°C modifies the chemical and biological response of β-tricalcium phosphate, α-tricalcium phosphate, and hydroxyapatite. At that time, these effects were attributed to physical changes. Most recent investigations with XPS suggest that these changes are more likely due to chemical changes at the surface, such as phosphate depletion. The aim of my talk will be to review past and present activities of my group in trying to understand and control the link between calcium phosphate surface chemistry and reactivity. Topics such as thermal treatments and impurity levels will be addressed.

Prof. Qunfeng Cheng

School of Chemistry, Beihang University, Beijing, China

Email: cheng@buaa.edu.cn

Bioinspired graphene-based nanocomposites



With its extraordinary properties as the strongest and stiffest material ever measured and the best-known electrical conductor, graphene could have promising applications in many fields, especially in the area of nanocomposites. However, processing graphene-based nanocomposites is very difficult. So far, graphene-based nanocomposites exhibit rather poor properties. Nacre, the gold standard for biomimicry, provides an excellent example and guidelines for assembling two-dimensional nanosheets into high performance nanocomposites. The inspiration from nacre overcomes the bottleneck of traditional approaches for constructing nanocomposites, such as poor dispersion, low loading, and weak interface interactions. Herein, we summarizes recent research on graphene-based artificial nacre nanocomposites,[1-6] and focuses on the design of interface interactions and synergistic effects for constructing high performance nanocomposites.

References

1. J. Peng, **Q. Cheng***, Adv. Mater. 2017, 1702959.
2. **Q. Cheng**; C. Huang, A. P. Tomsia.* Adv. Mater. 2017, 27, 1703155.
3. **Q. Cheng**, L. Jiang*, Angew. Chem., Int. Ed. 2017, 56, 934.
4. S. Gong, H. Ni, L. Jiang, **Q. Cheng***, Materials Today 2017, 20, 210.
5. Y. Zhang, S. Gong, Q. Zhang, P. Ming, S. Wan, J. Peng, L. Jiang, **Q. Cheng***, Chem. Soc. Rev. 2016, 45, 2378-2395.
6. Y. Zhang, Y. Li, P. Ming, Q. Zhang, T. Liu, L. Jiang, **Q. Cheng*,** Adv. Mater. 2016, 28, 2834.
7. S. Wan, J. Peng, L. Jiang, **Q. Cheng*,** Adv. Mater. 2016, 28, 7862.

Prof. Jérôme Chevalier

Materials Science Department (MATEIS), INSA Lyon, France

Towards ductile bio-ceramics: Zirconia-based composites with transformation-induced plasticity

40 years ago, Garvie and co-workers reported that the transformation of metastable tetragonal zirconia grains towards the monoclinic symmetry could give rise to a powerful strengthening mechanism. Their results even led them to consider zirconia systems as analogues of certain steels. This seminal paper created an extraordinary excitement in the ceramic community and is still the subject of extensive research, debates and controversies. It has to be admitted that transformation toughening is widely used in a series of zirconia materials and leads to an increase in strength when compared to non-transformable ceramics (zirconia exhibits the highest strength of oxide ceramics), but the translation into tough, strong and sufficiently stable materials is not fully addressed. For most industrial applications, indeed, zirconia ceramics fail by cracking at low strains and with a much larger scatter in the strength values than metals and statistical approaches of failure are required. Also, the common yttria stabilized zirconia ceramic may suffer aging in some particular conditions. In our latest research, conducted in the framework of two European projects (FP7 - LONGLIFE and H2020 – FTI -SISCERA), we have developed a new class of ceria doped zirconia-based composites that can reach high biaxial strength and high toughness associated with a significant strain to failure, and do not exhibit aging. Moreover, the mechanical behaviour law is, in some extent, analogue to a metal with a significant amount of transformation-induced plasticity, high strain (for a ceramic) and almost no dispersion in strength data. Such zirconia composites could open new avenues in applications where the advantages of ceramics were dampened by their failure properties. They are currently under industrial development for dental implant applications.

Prof. Brian Derby

School of Materials, University of Manchester, UK

Bio-Inks for 3D Inkjet Printing of Vasculature: Feature Resolution and Interfacial Energy

Inkjet printing is a versatile tool used in additive manufacturing/3D printing with the benefit of multi-material deposition of picolitre volumes of material. A number of previous studies have demonstrated the utility of inkjet printing in producing vascularized structures and depositing cells for applications in tissue engineering and regenerative medicine. Despite the small droplet size delivered by inkjet printing (a 1 pL drop has a diameter of approximately 12.5 μm), state-of-the-art bioprinted structures have minimum features in the range 100 – 200 μm and have shown little improvement in resolution over the last 10 years. In order to print vascularised structures to allow transport of oxygen and nutrients to prototissues in culture, this current resolution may not be adequate.

In order to print vascular structures a sacrificial temporary support material is used to define the vasculature around which a hydrogel matrix is deposited. The sacrificial material is removed and replaced with culture media or a similar fluid once the construct is built. The width of a printed line is the resolution limiting lateral dimension for 3D printing and hence the minimum dimension of the vascular channels. Currently 3D printed vascular structures, using both inkjet and extruded filament methods, have been fabricated from gelatin methacrylate (GelMA) using a poloxamer fugitive hydrogel (Pluronic F127) for the vasculature. The minimum feature size is ≈ 200 μm in the x-y plane, the limiting factor is the high degree of wettability of the inks on the gelled deposit from their low contact angle; low contact angles lead to poor lateral resolution. Here we present results using a new approach and material formulation for the vascular material using formulated and modified gelatine based bioinks for both the vasculature and the hydrogel matrix. This allows better control of interfacial energies and leads to improved printed feature resolution. The approach also simplifies the design of the printer by allowing similar temperature control for both inks, unlike the case with poloxamer/GelMA inks where the two printed components must be delivered at different temperatures.

Prof. Horst Fischer

Dental Materials and Biomaterials Research, RWTH Aachen University Hospital, Germany

Latest achievements in 3D bioprinting

Recent years have revealed a remarkably increase in research activities in the field of 3D bioprinting worldwide. The motivation for research and development on this topic is to treat in the future tissue defects by personalized three-dimensional tissue substitutes made of the patients' own cells and manufactured by hydrogel-based 3D printing techniques. Apart from possible in vivo applications, bioprinting techniques can be used to realize novel in vitro tissue models. Such so called 'organ-on-a-chip' models can be used to investigate fundamental scientific questions or are applied as screening platforms for novel drugs. In the talk latest achievements in the field of 3D bioprinting are presented which include innovative printing techniques as well as novel insights regarding the biochemical and mechanobiological interaction between the printed hydrogels and the embedded living cells.

Prof. Maria-Pau Ginebra

Department of Materials Science and Metallurgy, Universitat Politècnica de Catalunya, Barcelona, Spain

The impact of biomimetism in synthetic bone grafts: from the lab to the market

The design of bone substitutes that can enter the physiological bone turnover cycle, i.e., that can be resorbed and replaced with new bone the same way that impaired bone is replaced in the bone turnover process, is a great challenge. But how can this be achieved? New approaches, based on the combination of advanced fabrication technologies with the biomimetic processing of self-setting calcium phosphates, will be presented. These methods allow obtaining biomimetic hydroxyapatite via precipitation reactions at body temperature, in conditions that are very close to the ones leading to biomineralization phenomena. The impact of different properties, like stoichiometry, crystallinity, nanostructure and pore architecture, in the biological performance of calcium phosphate bone substitutes, and specifically on the osteoinduction and osteogenic potential, will be described.

In the second part of the talk, I will introduce some issues related to the translation of these scientific developments to the market, based on my experience as founder of the spin-off company Mimetis Biomaterials, which develops biomimetic bone substitute materials.

Prof. Liam M. Grover

School of Chemical Engineering, University of Birmingham, UK

Structuring soft materials to inhibit scarring

The translation of medical technologies into the clinic can be hindered by an onerous regulatory framework. Demonstrating the safety of novel materials compositions can represent a major cost that ultimately prevents medical companies from investing in product development. We are developing new methods that allow for the structuring of already approved materials compositions so that they exhibit physical properties that are suitable in a range of different applications. By taking this approach, we hope that we will derisk the development of medical technologies for early investment, allowing them to be taken to the point of clinical trial. In this talk, I will discuss how we have used shear processing to develop a material that is shear thinning, but rapidly thickens when applied to a surface. This material has demonstrated utility as an eyedrop to prevent scarring following microbial keratitis and has also been used as a support matrix in the bioprinting of complex tissues.

Prof. Paul V. Hatton

School of Clinical Dentistry, The University of Sheffield, UK

Biofunctional Modifications to Bioactive Glasses for the Manufacture of Innovative Medical Devices

Introduction: Bioactive glasses have been employed in a variety of medical applications for over 30 years, with two compositions (45S5 and 53P4) dominating the market throughout this period. While there is good evidence for stimulation of bone tissue regeneration by these established materials, new clinical demands including compromised bone tissue healing and increased risks of deep bone infection have stimulated recent research into modified bioactive glasses. The aim of this research is to review progress in the design and manufacture of truly multi-functional bioactive glasses that combine stimulation of enhanced bone tissue regeneration with potent antimicrobial properties.

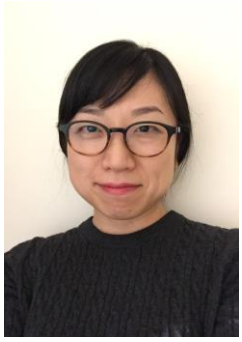
Methods: All glasses used in this research were fabricated via the melt route using reagent grade chemicals and a platinum crucible at temperatures between 1350 and 1450 °C. Characterisation included x-ray fluorescence (XRF), differential thermal analysis (DTA), x-ray diffraction (XRD), and was followed by in vitro testing of biocompatibility or antimicrobial activity using established models. The potential enhancement of osteoconduction by strontium was investigated by substituting CaO with SrO in the 45S5 composition (Santocildes-Romero 2015), whereas the introduction of antimicrobial activity was further demonstrated using a bioactive borosilicate glass (Fernandes et al. 2016).

Results: Substitution of calcium with strontium in all of the bioactive glass compositions investigated resulted in enhanced osteogenic differentiation in vitro. These data, combined with the results of published studies, suggested that Sr-containing bioactive glasses are consistently superior to the existing commercial compositions, and it would be advisable to accelerate the translation of these novel compositions for clinical use. Moreover, Sr-substitution also enhanced the antimicrobial activity of novel bioactive borosilicate glasses, and it appears that there are a number of candidate ions that are associated with this valuable new property (Fernandes et al. 2017).

Discussion & Conclusions: This research demonstrated that existing bioactive glass compositions may be further modified to both enhance their osteoconductive properties and/or introduce enhanced antimicrobial activity. While these enhanced, multi-functional properties were related to the specific metal oxides introduced to the glass, it was also noted that these substitutions also altered the physical properties of the glass. These physical changes also influenced interaction with the biological environment, and therefore most likely contributed to the enhanced properties.

References: (1) Santocildes-Romero, M. E. et al. 2015 J. Tissue Eng. Regen. Med. 9 619-31 (2) Fernandes, J. S. et al. 2016 ACS Biomater. Sci. Eng. 2 1143-1150 (3) Fernandes, J. S., et al 2017 Acta Biomater 59 2-11.

Acknowledgements: Collaborators are gratefully acknowledged for their contributions to this work including Martin Santocildes-Romero, João S. Fernandes*, Cheryl Miller, Aileen Crawford, and Ian M. Reaney from the University of Sheffield, and Ricardo A. Pires and Rui L. Reis from the 3B's Research Group, University of Minho, Portugal. This research was funded in part by the UK EPSRC Centre for Innovative Manufacture in Medical Devices (MeDe Innovation, EP/K029592/1) and a PhD student placement supported by the Portuguese Foundation for Science and Technology (PhD Grant BD/73162/2010).



Prof. Akiko Obata

Division of Advanced Ceramics, Nagoya Institute of Technology, Japan

Osteoblast-like Cell Reactions to Ions Released from Bioceramics

Akiko OBATA, Toshihiro KASUGA

Several inorganic ions released from bioceramics have been reported to stimulate osteogenic cell functions and to promote bone formation in body [1]. In particular, trace amounts of silicate and calcium ions released from 45S5-type bioactive glass (BG) were reported to enhance several functions of human osteoblasts. Our group has developed siloxane-doped vaterite (SiV) with using aminopropyltriethoxysilane (APTES) as the siloxane source and found upregulations of the proliferation and differentiation of osteoblaste-like cells by the extract of SiV [2]. Such cell reactions to silicate and calcium ions are expected to depend on types of bioceramics, which provide the ions, based by thorough assessment of previous studies. Most of bioceramics release several inorganic ions simultaneously through their dissolution. We believe that there are combined effects of multiple stimulations for cells by several types of ions and ionic state of released ions may influence the expression of the ion effects on cell functions. In the present work, osteoblast-like cell functions were examined when they were cultured in media containing silicate ions with two different ion structures or three different ions, Si, Ca and Mg.

The proliferation and mineralization of human osteoblast-like cells (SaOS-2) were promoted in the Si-conditioned media in ion-concentration-dependent manner. For example, the proliferation was up-regulated in BG and SiV-conditioned media with 10 ~ 20 ppm and 30 ~ 50 ppm, respectively. Thus, the stimulatory effects by silicate ions on the cell functions was varied by material components and/or the ionic state of the ions. The two materials release silicate ions with different ionic state because of the different silicon source used; BG and SiV release ions with Q^n species and T^n species including aminopropyl groups, respectively.

Mouse osteoblast-like cells (MC3T3-E1 cells) were cultured in single-, dual- or tri-ion-conditioned media with Si-Ca-Mg system. The proliferation ability of the cells was different

between the single- and dual-ion-conditioned media. This indicates that there are synergistic and antagonistic effects of ion mixtures on up/down regulation of the cell functions.

References

[1] Hoppe A., Güldal N. S. & Boccaccini A. R. (2011), A review of the biological response to ionic dissolution products from bioactive glasses and glass-ceramics. *Biomaterials*. *32*, 2757-2774.

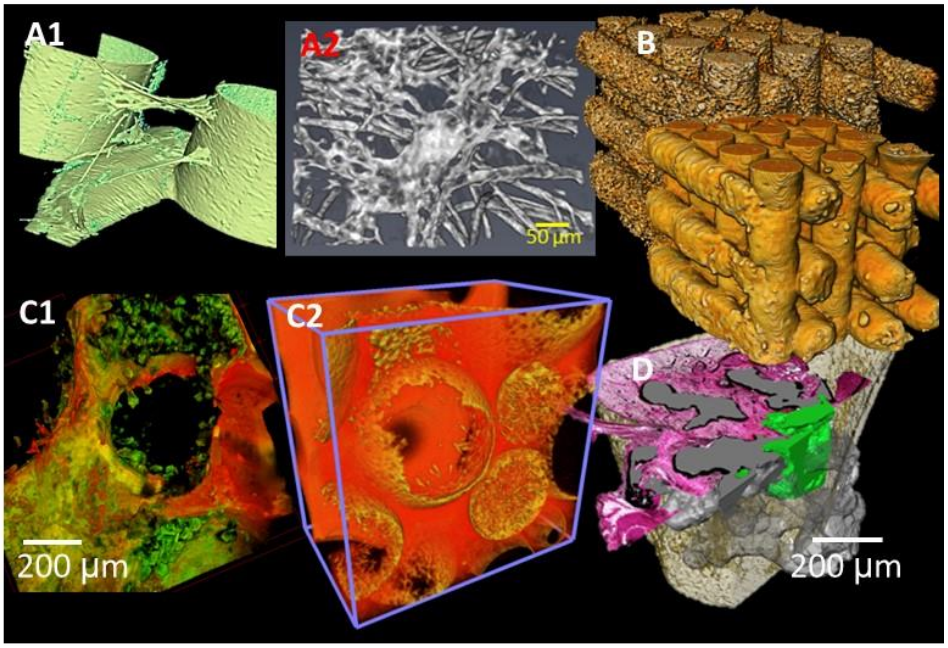
[2] Obata A., Tokuda S. & Kasuga T. (2009), Enhanced in vitro cell activity on silicon-doped vaterite/poly(lactic acid) composites. *Acta Biomaterialia*. *5*, 57-62.

Dr. Gowsihan Poologasundarampillai

School of Dentistry, University of Birmingham, UK

Biomedical materials and their multiscale characterisation

Combination of bottom-up ‘soft-chemistry’ sol-gel processing and top-down manufacturing processes have allowed the synthesis of porous hierarchical structures for biomedical applications. This talk will focus on the development of 3D porous scaffolds and their multiscale characterization. Techniques employing light, x-rays and electrons to probe materials and their interactions with biological tissues will be presented. The talk will highlight the power of multimodal correlative imaging approaches in providing unique insights into structure and function of biomedical materials with a specific focus on bioactive glasses and organic-inorganic hybrids.



3D images of scaffolds with cells/tissues. A-Cells on 3D printed (A1) and electrospun (A2) scaffolds, B-sintering of bioactive glasses, C-protein adsorption (C1) and mineralisation (C2), D correlative imaging of bone-Ti-implants.

Prof. Alexandra E. Porter

Department of Materials, Imperial College London, UK

Correlative Microscopy of the Biology-Materials Interface for Development of Nanomedicines

Multimodal materials combine materials with complementary imaging and therapeutic capabilities into one platform and are receiving increasing interest in the field of cancer theranostics. These surface modified nanomaterials carriers offer several advantages, such as high drug loading capacity, ability to evade efflux pump action at the brain microvessels, and size-tunability. By integrating different component modules into these platforms, it should be possible to combine the qualities of each module to modulate their properties for flexible treatment of a range of diseases. We are developing multifunctional luminescent nanomaterials for delivery of chemotherapeutic drugs to treat breast cancers and for delivery of therapeutics across biological barriers, such as the lung epithelium and blood brain barrier. Before these materials can be used commercially, it is vital to assess their safety to human health and the environment. Thus, we are also adapting these materials to assess the potential health and ecological consequences of the increasing prevalence of new classes of nanoparticulate material in the environment.

The talk will describe our understanding of the fundamental properties of current and new generation multimodal bionanomaterials and how their physicochemical properties might relate to their bioreactivity, translocation and ultimate fate, weighed against the advantages such materials offer in nanomedicines. In this paper, I will discuss our work on application correlative, multiscale spectro microscopy techniques to characterise the nanomaterials-biology interface. Key challenges include the need for high spatial and energy resolution allowing discrimination of subtle chemical signatures. Information about dynamic processes is also required to track how these nanomaterials degrade and transform in different environments in situ, since alterations to their physicochemistry will alter their ultimate bioreactivity. The talk will highlight new insights that are gained by using advanced characterisation techniques, and discuss the benefits of correlative approaches between in situ X-ray and electron spectroscopies.

Prof. Fabrice Rossignol

French National Center for Scientific Research (CNRS), Institute of Research on Ceramics (IRCER), Limoges, France

Re-shaping ceramic industry through additive manufacturing: dream or reality, that is the question.

Although there is today a hype on Additive Manufacturing (AM), it cannot be considered as an industrial revolution. Indeed, 3D numerical manufacturing from a CAD file, initially called rapid prototyping, has already been studied for more than 20 years in the case of ceramics with significant achievements. The present industrial revolution is actually linked to the massive exploitation of the so-called « internet of things » which connects in a global value chain, AM, augmented reality, big data, autonomous robots, simulation, system integration, cybersecurity, cloud computing to name a few. But, does this new paradigm will really re-shape in the short term the ceramic industry which is sometimes a bit conservative? We will discuss this important question through some examples of achievements in laser stereolithography and inkjet printing for applications in Information and Communication Technologies (ICTs) and Biomaterials, sharing on this basis our vision of the future strategic research lines necessary to boost the AM of ceramics.

Prof. Chiara Vitale-Brovarone

Politecnico di Torino, Turin, Italy

3D bone-like scaffolds containing smart nanomaterials to treat osteoporotic fractures

Chiara Vitale-Brovarone[a], Giorgia Montalbano[a], Giulia Molino[a], Giorgia Novajra[a], Daniele Pasciuto[a,c], Sonia Fiorilli[a], Gabriela Ciapetti[e], Monica Mattioli-Belmonte[d], Patrizia D'Amelio[f], Giovanni Vozzi[b,c]

[a]Dipartimento di Scienza Applicata e Tecnologia, Politecnico di Torino, Torino, Italy
[b]Dipartimento di Ingegneria dell'Informazione, University of Pisa, Pisa, Italy
[c]Research Center "E. Piaggio", University of Pisa, Pisa, Italy
[d]DISCLIMO, Università Politecnica delle Marche, Ancona, Italy
[e]Laboratorio di Fisiopatologia Ortopedica e Medicina Rigenerativa, Istituto Ortopedico Rizzoli, Bologna, Italy
[f] Università di Torino, Geriatric and Bone Unit Department of Medical Science, Torino, Italy

*e-mail: chiara.vitale@polito.it

Osteoporosis is a worldwide spread disease and its incidence is continuously growing as the population ages; it results in bone loss and decreased bone strength that lead to an increase in the risk of low-energy fractures. Antiresorptive agents such as bisphosphonates are mainstays of the therapy for osteoporosis but some concerns on their possible adverse effects were raised.

From an overall perspective, the ultimate solution is still to be found and thus, in the frame of the ERC BOOST, we are working on the development of a biomimetic scaffold engineered to be used in case ofosteoporotic fractures.

Healthy and osteoporotic bone geometries are obtained from tomographic scans of human bone tissues discarded during surgical interventions (following ethical approval by Istituto Ortopedico Rizzoli-Italy). A multi-material platform able to combine different rapid prototyping techniques has been developed in order to meet all the constraints related to the features of the materials to be processed and the degree of versatility and resolution needed. To this aim, the STL file derived by the tomographic analysis of bone samples is used to process the optimised biomaterials in order to fabricate the smart scaffolds, reproducing as close as possible the 3D architecture and chemistry of healthy human bone

tissue. Type I collagen, at different concentrations, was used as a matrix to mimic bone chemistry whereas mesoporous bioactive glass/nano-hydroxyapatite were embedded within the collagen fibers. Growth factors (IGF and β-TGF) were encased in the scaffold struts using several approaches in order to simulate the growth factors stored in the extracellular matrix, and their retained activity was assessed.

The fabricated scaffolds will be tested into bioreactors by means of a co-culture of osteoblasts and osteoclasts in order to define the influence of both chemical and topographical stimuli on the osteoblast-osteoclast coupling. The proposed approach will allow us to decode how biomaterial chemistry and topography at any scale (macro-, micro- and nano) influence the multifaceted coupling process of bone resorption and formation, with particular focus on the cell cross-talk between osteoclasts and osteoblasts.

Acknowledgements

The authors acknowledge the financial funding from European Union (ERC – BOOST, GA 681798), by the Italian Minister of Research, Progetto FARE Ricerca in Italia (GRACE) and by Fondazione CRT under the initiative La Ricerca dei Talenti.