PhD PROJECT PROPOSAL

PhD PROJECT TITLE

"Hierarchical Topological Tailoring of Alloys for Biological Functionality"

PhD SUPERVISORY TEAM

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PROJECT ABSTRACT

Alloy selection for metal implants has traditionally focussed on homogenous bulk properties to tackle aseptic loosening and infection, however, there is a growing body of research recognising the importance of topological features in biological functionality. Advanced processing techniques (additive manufacturing/3D printing, surface modification and solidification/solid-state reactions) can control topological features on a range of length scales (i.e. from nano- up to milli- meter. The proposed project aims to explore topological hierarchy in new alloy systems such as Ti-Ag & Ti-Cu to demonstrate how topology can be used to design for improved biological response, namely bone integration and anti-microbial response.

APPLICATION OF TOPOLOGY

Three advanced metal processing techniques will be used to hierarchically control topological features across length-scales to selectively modify biological response.

(1) Additively manufacturing (Metal 3D Printing): metallic lattices with varied topology in the mm range, to promote bone ingrowth, and limit stress shielding enhancing implant osteointegration.

(2) Laser surface texturing: 2D/3D micro and nano patterns can be matched to conform with bacteria to optimise antimicrobial efficacy of Cu/Ag alloy systems.

(3) Solidification & solid-state reactions: bulk and surface structures of dendrites/blended powders/eutectics ~1-100µm, to morphologically complex intermetallic solid-state precipitation ~10nm-1µm, tailored to optimise antimicrobial resistance to bacteria and viruses.

DETAILED PROJECT DESCRIPTION

The short and long term stability of metallic implantable devices are regularly at risk from poor bone implant integration. Limited biocompatibility of the native material or aseptic loosening and bacterial colonisation will result in implant failure with revisions requiring partly or complete removal of the device. The social and economic costs coupled with bacteria developing resistance to common therapeutics, are critically calling for novel strategies to optimise cell-surface interactions [1]. In this regard, transition metals of the d-block, (i.e. Cu, Zn, Ag, Cd) and other metals and metalloids from groups 13–16 (i.e. Al, Ga, Ge, As) are capable of displaying antimicrobial effectiveness pushing forward the development of novel alloy systems [2]. Nevertheless, alloy selection for metal implant manufacture has traditionally focussed on bulk properties with limited regard to surface topology in the mechanical and biocompatibility requirements of the device.

Bacterial and mammalian cells have been shown to be heavily affected by the physicochemical properties of the colonised material [3,4], enabling biological control through topological and chemical modifications. Advanced manufacturing techniques can influence and control topological features on a range of length scales: from nano-, through micro-, and up to milli- meter. For example, additively manufactured metallic lattices with unit cells in the mm range can promote bone ingrowth to improve implant anchoring, however, the characteristic powder-adhered surface roughness makes an ideal site for bacterial colonisation [5,6]. Likewise, laser surface texturing of a surface can potentially be matched to the size of cells to provide suitable adhesion sites on the micro scale whereas specific nano-precipitate morphology may be necessary to realise the optimum antimicrobial efficacy of copper or silver alloy systems. On the other hand, solidification & solid-state reactions and precipitation provide means by which topological microstructures can be tailored both in the bulk and surface of the material (from dendrites/blended powders/eutectics with 1-100µm scale, to morphologically complex intermetallic precipitation with 10nm-1µm scale). The union of these processes allows the development of a hierarchical structure where biological behaviour of eukaryotic and prokaryotic cells may be independently controlled (Figure 1). Herein, the student will develop these three processes and, taking advantage of structural differences between bacteria, ~0.5-2 µm, and mammalian cells, 50-100 µm, fine tune mineralisation (scaffold and laser texturing) and infection (patterning and solid-state reactions) of the orthopaedic implant. The proposed CDT project aims to explore this hierarchy of topological control in alloy systems not currently used within mainstream implant manufacture (e.g. Ti-Ag, Ti-Cu, Zr-X etc.) to demonstrate how careful application of material processing techniques may ultimately alter the biological response of the device. Consequently, further insight into the relationship between topography and biological response will be obtained while providing a novel toolkit for the optimization of implantable devices processes and bespoke implants, critical for the biomedical field.

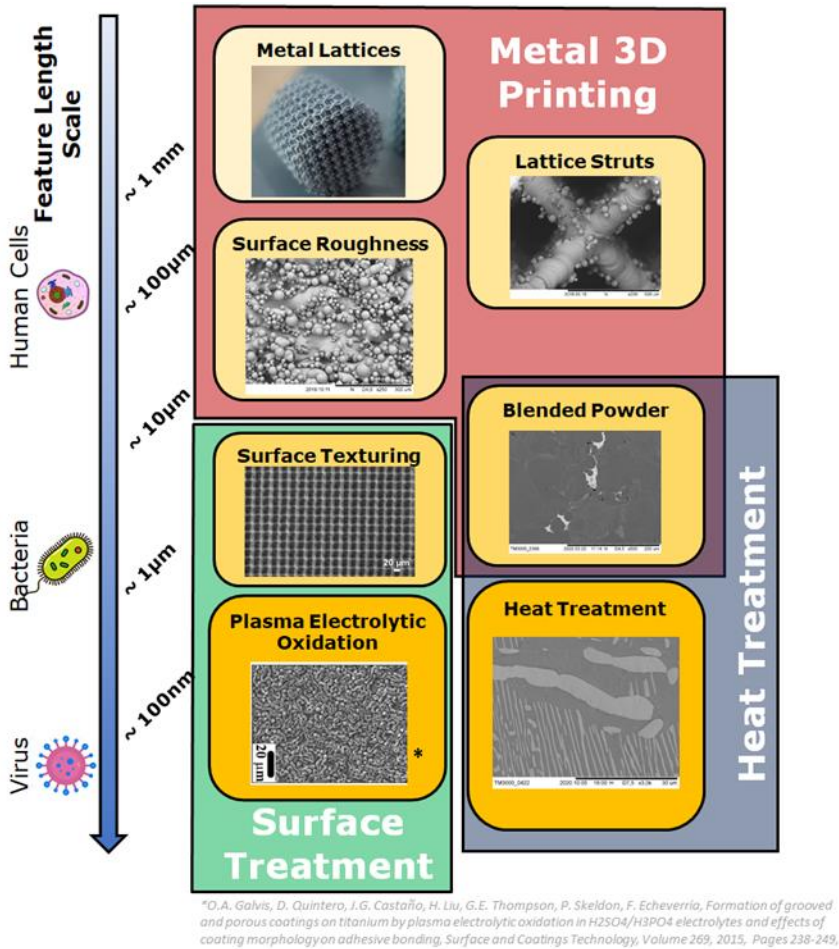

Figure 1. Diagram showing the different range of topological features, their potential biological significance, and examples of processing techniques able to control them.

Over the duration of the project, the student will be trained to gain skills in alloy development and material characterisation. Experimental techniques will comprise of alloy preparation through conventional casting and selective laser melting, including thermal, chemical and physical post processing. These will include but not be limited to homogenisation, ageing, etching, blended powder processing, etc. Initial characterisation techniques will cover general physicochemical analysis of the developed topologies through SEM-EDS, XRD, DSC, profilometry, wettability and ion release studies. Further assessment will include bacterial and mammalian cell interactions through confocal imaging and standardised recovery tests. In addition, the student will be required to disseminate their work in the form of publications and presentations in relevant congresses.

Both principal and co-investigators have a profound background in the development and assessment of metallic alloys for healthcare applications through numerous on-going collaborations with industrial partners. Dr. Cox is a Lecturer in the School of Chemical Engineering and the Healthcare Technologies Institute (HTI) at the University of Birmingham (UoB) with over 30 peer reviewed articles (h-index 10), industrial white papers, and filed five patent applications in healthcare technologies. She is part of the AMPLab and the centre for Custom Medical devices, EPRC funded and in partnership with the largest UK engineering company, Renishaw Ltd. It has two RenAM 500M powder bed fusion systems for bespoke implant research and access to structural and chemical analysis techniques for biomaterials including wet chemistry preparation areas and cell culture facilities. Dr. Knowles is a Lecturer in Nuclear Materials, Royal Academy of Engineering Research Fellow & UKRI Future Leaders Fellow in the School of Metallurgy & Materials. His area of expertise lies on the development of bcc superalloys, Ti-based alloys and High entropy alloys with collaborations with CCFE, TIMET and Rolls Royce. The union of both academics provides an ideal combination of alloy development, implant manufacturing and biological assessment which coupled with their industrial partners provides the perfect environment for the translation of medical devices.

The candidate will have a 1st class Undergraduate or Masters degree (or equivalent) in Materials Science, Mechanical Engineering, Physics or related discipline. A background in microstructural characterisation, mechanical and/or biological evaluation of material testing would be advantageous.

[1] Hall, T.J. et al. A call for action to the biomaterial community to tackle antimicrobial resistance. Biomaterials Science 8, 4951-4974 (2020).
[2] Glenske, K. et al.. Applications of metals for bone regeneration. International journal of molecular sciences, 19(3), 826 (2018).
[3] Ting, M. et al. Classification and Effects of Implant Surface Modification on the Bone: Human Cell–Based In Vitro Studies. Journal of Oral Implantology 43, 58-83 (2017).
[4] Bohinc, K. et al. Metal surface characteristics dictate bacterial adhesion capacity. International Journal of Adhesion and Adhesives 68, 39-46 (2016).
[5] Damiati, L. et al. Impact of surface topography and coating on osteogenesis and bacterial attachment on titanium implants. Journal of tissue engineering 9, 2041731418790694 (2018).
[6] Villapún, V.M. et al. A design approach to facilitate selective attachment of bacteria and mammalian cells to additively manufactured implants. Additive Manufacturing 36, 101528 (2020).