The background of the entire page is a microscopic image of green, spherical cells, likely bacteria or yeast, arranged in various patterns and clusters. The cells are illuminated from the side, creating a sense of depth and highlighting their individual structures. The overall color palette is a range of green tones, from light lime to dark forest green.

Fourth Annual Biomaterials Discovery Workshop

15th and 16th January 2020
Jubilee Conference Centre
Nottingham, UK

Conference
Pack

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Programme

Wednesday 15th January 2020

Registration open from 9:00

09:30 - Welcome

09:40 - **Prof. Omid Veischi** (Rice University Texas)
Immune Modulatory Biomaterials for Cell-Based Therapies

10:40 - Dr. Laurence Burroughs (University of Nottingham)
The ChemoTopoChip: Combinatorial Material-Topography Screening

11:00 - Dr. Graziela Figuerdo (University of Nottingham)
Data Handling: Intelligent Analysis and Management

11:20 - *Morning Break*

11:40 - Rowan Earlam (University of Nottingham)
Recombinant spider silk protein hydrogels for tissue engineering

12:20 - Aysegul Dede-Eren (Eindhoven University of Technology)
Highway to Tenogenesis: From in vivo to in vitro approach to engineer a culture microenvironment for tendon fibroblasts

12:40 - *Lunch and posters*

13:40 - Joris Meurs (University of Nottingham)
High throughput surface proteomics for examining cellular response on biomaterial surfaces

14:00 - Dr. Amanda Wright (University of Nottingham)
Imaging and sensing the micro-environment of cells in 4D

14:20 - **Prof. Sarah Cartmell** (University of Manchester)
Innovation in Orthopaedic Tissue Repair

15:20 - *Afternoon Break*

15:40 - **Prof. Jennifer Elisseeff** (Johns Hopkins)
The immunology system in tissue repair and biomaterial response

16:40 - Closure

18:30 - Optional dinner at Baresca for those who have pre-registered

Thursday 16th January 2020

Registration open from 9:00

09:30 - Welcome

09:40 - **Prof. Alvaro Mata** (University of Nottingham)

Turning molecules into functional biomaterials through supramolecular engineering

10:40 - Prof. Patricia Dankers (Eindhoven University of Technology)

Supramolecular polymeric materials as synthetic extracellular matrices: from design to high throughput screening

11:40 - Dr. Andrew Hook (University of Nottingham)

Surface analysis and biomaterial development

12:00 - *Lunch and posters*

13:00 - **Prof. Tim Tolker-Nielsen** (University of Copenhagen)

Mechanisms of biofilm-associated antimicrobial tolerance

14:00 - Dr Olutoba Sanni (University of Nottingham)

Discovery of a polymer using a predictive structure relationship model capable of reducing biofilm formation

14:20 - Dr. Nicola Farthing (University of Nottingham)

Holographic microscopy as a tool to understand the interaction of swimming cells with biomaterials

14:40 - Kiril Kalenderski (University of Nottingham)

A new bacterial resistant polymer catheter coating to reduced catheter associated urinary tract infection - a first-in-man pilot study

15:00 - *Afternoon break*

15:30 - **Ann Kramer** (Electrospinning Company)

The next step: Translating electrospinning biomaterials research into a medical device

16:30 - Poster award presentation and closure

16:45 - Drinks reception

Wednesday 15th January 2020

Speakers

Prof. Omid Veisheh (Rice University Texas)

Immune Modulatory Biomaterials for Cell-Based Therapies

Immune cell recognition of implanted biomedical devices initiate a cascade of inflammatory events that result in collagenous encapsulation of implanted materials which leads to device failure. These adverse outcomes emphasize the critical need for biomaterials that do not elicit foreign body responses. One prime example for the use of this technology is with the development of a bioartificial pancreas for the treatment of patients suffering from diabetes. Immunoisolation of insulin producing cells with porous biomaterials provide an immune barrier that is a potentially viable treatment strategy for Type1 diabetic patients. However, clinical implementation has been challenging due to host immune responses to implanted materials. To address this challenge, we have focused our efforts on the development of improved biomaterials for the use in pancreatic islet cell transplantation.

To enable the discovery of novel superbiocompatible biomaterials we have developed a high throughput pipeline for the synthesis and evaluation of >1000 material formulations and prototype devices. Here, we describe combinatorial methods we have developed for covalent chemical modification and in vivo evaluation of alginate-based hydrogels. Using these methods, we have created and screened the first large library of hydrogels and identified leads that are able to resist foreign body reactions in both rodents and nonhuman primates. These formulations have been used to generate optimized porous alginate hydrogels fabricated with tuned geometries to enhance biocompatibility. Significantly, our lead formulation has enabled us to achieve the first long-term glycaemic correction of diabetic animals without immunosuppression using stem-cell derived human islets.

Dr. Laurence Burroughs (University of Nottingham)

The ChemoTopoChip: Combinatorial Material-Topography Screening

The use of biomaterial surface topography as a tool for influencing cell fate and attachment is an emerging field gaining a large amount of attention from the scientific community. However, very little is understood about the underlying mechanisms controlling cell behaviour; even less is known about synergistic effects between the chemistry of the substrate and surface topography influencing biological response.

High-throughput screening systems such as polymer microarrays have been developed as key tools for material screening, but are limited to an essentially planar, non-native cell environment.¹ The TopoChip, an analogous system develop by de Boer *et al*, has been used to assess the impact of micro-topographies on cell attachment and fate.² However, to date

no biological studies have been carried out into the synergistic effects of chemistry and topography.

In an attempt to better understand the impact of both chemistry and topography on cell response, we have developed a high-throughput screening platform dubbed the ChemoTopoChip. This novel system allows for the simultaneous screening of 28 polymer chemistries in combination with 35 randomly-generated micro-topographies, providing a total of 980 chemistry-topography combinations on one chip. We have employed the ChemoTopoChip to identify bioactive chemistry-topography combinations capable of directing macrophage polarisation and human mesenchymal stem cell differentiation, confirming this platform as a next-generation biomaterials screening tool.

1. A. L. Hook *et al*, *Biomaterials*, **2010**, *2*, 187-198; Y. Mei *et al*, *Nat. Mater.*, **2010**, *9*, 768-778
2. F. F. B. Hulshof *et al*, *Biomaterials*, **2017**, *137*, 49-60; H. V. Unadkat *et al*, *Proc. Natl. Acad. Sci.*, **2011**, *108*, 16565-16570

Dr. Graziela Figuerdo (University of Nottingham)

Data Handling: Intelligent Analysis and Management

High throughput synthesis and characterisation technologies generate high volumes of data for large numbers of biomaterials, with diverse chemical and topographical properties. Quantitative structure-property relationship methods are machine learning (ML)-based methods that have been highly successful in making predictions of useful properties driving the biological phenomena within complex materials. We present the overall analysis pipeline employed to achieve our predictive models. We discuss the process of data collection, storage and pre-processing. Subsequently, we introduce the ML methodology used for the selection of the materials descriptors with high correlation with the biological activity, followed by the approaches to determine existing correlations. We conclude our talk by showing the platform developed for data and code storage to allow for experiments reproducibility within the Programme Grant.

Rowan Earlam (University of Nottingham)

Recombinant spider silk protein hydrogels for tissue engineering

Recombinant spider silk protein hydrogels combine the excellent biomaterial properties of silk such as strength, elasticity and biocompatibility with the tunability of hydrogels. The recently described and highly expressing spider silk protein NT2RepCT has been used to form physical and chemically cross-linked hydrogels. At 37 °C and above, NT2RepCT undergoes conformational changes from α helices to β pleated sheets leading to hydrogel formation. The effect of pH and salt were investigated to create a range of hydrogels. Glutaraldehyde was used to stabilize the hydrogels, significantly increasing the Young's modulus of the biomaterial.

Aysegül Dede-Eren (Eindhoven University of Technology)

Highway to Tenogenesis: From *in vivo* to *in vitro* approach to engineer a culture microenvironment for tendon fibroblasts

Tendon fibroblasts lose their phenotype during *in vitro* subculture due to the lack of mechanical stimulation, ECM composition and structure. To date, different microenvironments such as micro patterned surfaces have been used as a culturing substrate to induce re-differentiation of late passage tenocytes. However, this approach does not preserve native tendon cell morphology which is essential for tenogenic phenotype. Therefore, we engineered an *in vitro* environment by imprinting native tendon to polystyrene which bears the native tendon structure (Figure 1). We used PDMS negative imprint as the intermediate step.

SEM and AFM analysis show that imprinted tendon has the micro-structures of the native tendon. We have demonstrated that tendon imprints can induce an upregulation on tenogenic markers in the late passage tendon fibroblasts. In future studies, we will focus on the synergistic effect of ECM proteins such as collagen type I, polymers that have been used in tendon tissue engineering (e.g. silk). Our results applicable not only for prolong *in vitro*

expansion of tendon fibroblasts, but also can be used in cell therapies for tendon regeneration.

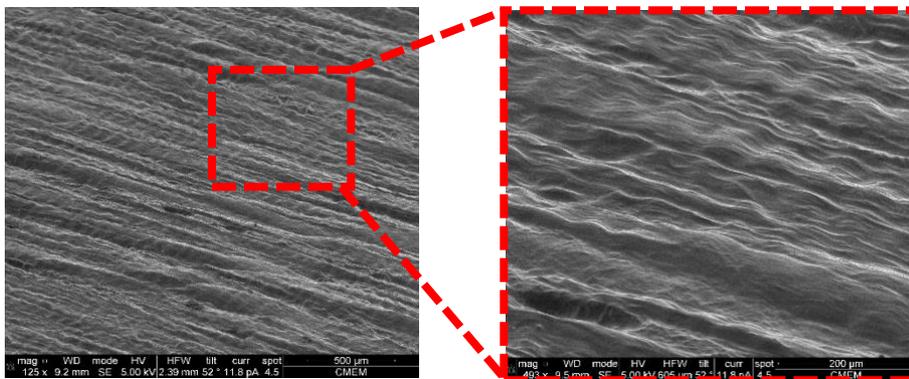


Figure 1. SEM image of tendon imprint of polystyrene

Joris Meurs (University of Nottingham)

High throughput surface proteomics for examining cellular response on biomaterial surfaces

Pluripotent stem cells are a valuable source for cell production and have a huge potential to serve a multitude of applications in regenerative medicine. Biomaterials have been discovered that assist as synthetic substrates for pluripotency maintenance during expansion, but the mechanism by which they achieve this is not well understood because of poor characterisation of the biointerface. The pre-adsorption of proteins from the culture medium is believed to be a crucial element in this process. Here, we investigate the adsorption of Essential 8™ proteins in relation to cellular response quantitatively. To investigate the role of protein adsorption in cell-material response, Essential 8™ cell culture medium is used here as a model. A range of homopolymers is selected from previously acquired data of human induced pluripotent stem cells (hiPSC) screening experiments and incubated with medium. After medium removal and surface wash, adsorbed proteins are digested *in situ* and subsequently analysed with liquid extraction surface analysis-tandem mass spectrometry (LESA-MS/MS). Label-free protein quantification is done by summing peptide intensities per protein. The protein quantity is then correlated against the OCT4+ cell count to determine the relation between protein adsorption and cellular response.

Dr. Amanda Wright (University of Nottingham)

Imaging and sensing the micro-environment of cells in 4D

In order to generate more realistic representations of the *in vivo* microenvironment many scientists are switching from 2D cell cultures to 3D culture environments. This change is having unprecedented impact in the life sciences, including the growth and assay development of 3D cancer cells and organoid spheroids. Standard microscopy technologies are not well-suited to imaging in 3D. Hence, there is a real need for technology to catch-up, to allow scientists to study 3D cultures in real-time at length-scales comparable to, and smaller than, individual cells. Heterogeneities of the extracellular matrix on the micron and sub-micron length-scale are known to influence cell behaviour and fate, but at present the interplay between the matrix and the cells is very poorly understood. To meet this challenge, we are developing a new instrumentation and methodology to not only image live cells in real-time in 3D culture, but to map to these images the physical properties of the extracellular matrix local to the cells (i.e. the micro-rheology of the matrix). I will discuss the optical technologies that we are combining to achieve our goal - *light sheet microscopy, optical trapping, multiplane imaging and adaptive optics*. Presenting data that demonstrates our ability to produce 3D images of living cells deep into a 3D cell culture and to use an optically trapped micron-sized bead as a local probe to perform high sensitive micro-rheology measurements for gathering new information on the local mechanical properties of the extracellular matrix.

Prof. Sarah Cartmell (University of Manchester)

Innovation in Orthopaedic Tissue Repair

The growth of new bone tissue *in vitro* requires a variety of different factors that need to be controlled and optimised. One of these factors that has previously not been considered for bone tissue engineering is electrical stimuli. Given that bone is piezoelectric in nature, it is feasible to assume that local electrical regimes have an effect on osteogenesis. There are clinical products currently on the market that deliver electrical currents locally via a cathode to fracture sites. These products demonstrate significant clinical improvements in bone repair.

We have recently designed a variety of different bioreactors to both house the developing tissue and also control the applied electrical stimuli in either capacitive or direct contact methods to *in vitro* cultures. These bioreactors have enabled us to assess the potential use of this stimuli for *in vitro* bone tissue engineering purposes. It has also allowed us to further study the mechanism by which the activity of primary human mesenchymal stem cells are altered both in terms of cell proliferation and differentiation. A novel finding of the importance of the faradic by product of H₂O₂ proximal to the cathode as result of the direct electrical stimulus will be presented and its subsequent role in influencing primary mesenchymal stem cell proliferation. The morphology of primary cilia on these cells after electrical stimulation has been applied will also be discussed, in addition to the effect of varying electrical regime on cell response. The use of conducting polymers and piezoelectric materials to apply electrical regimes to the cells will be discussed.

In addition, data relating to a new product to assist the repair of tendons will be presented. The UK incidence of flexor tendon injuries necessitate >18,000 repairs per annum (30-42 per 100,000 worldwide) (de Jong et al 2014), many of whom have multiple tendon injuries, and their repair remains an unmet clinical need as only 75% achieve a satisfactory functional result (Su et al, 2005). Currently, inadequate tendon repair surgery results in the formation of scar tissue which is structurally and biomechanically inferior to natural tendon tissue. Tendon injuries can be severely disabling, with significant rehabilitation time and high healthcare costs. Our approach utilises a novel PCL electrospun device in augmentation with current suturing to enable improved healing and restore natural tissue architecture and biomechanical properties. This device is used to augment current tendon suturing techniques allowing topographical guidance for successful bridging of tendon repair (which currently is not met as 5% of tendon repairs rerupture) - thus eliminating the need for secondary surgery. Data gathered from our research indicates that its presence in the tendon significantly increases the production of important extracellular matrix proteins and reduces the production of inflammatory cells in comparison to current suturing techniques alone. This demonstrates that patients have the potential to receive much faster and stronger tendon healing with this product in place which could reduce physiotherapy session need by 50%. Our large data sets all indicate biological safety and will be presented.

Prof. Jennifer Elisseeff (Johns Hopkins)

The immunology system in tissue repair and biomaterial response

There are profound deficits in how humans, and adults in particular, heal and recover from tissue damage. The alternative to productive tissue healing is the formation of dysfunctional scarring, which underlies chronic degenerative arthritic conditions, autoimmune diseases and fibrosis. The immune system is a first responder to trauma and depending on phenotype can orchestrate downstream processes including stem cell activation, vasculogenesis and new matrix production. The immune system can also act as powerful “brakes” to tissue repair as in the case of aging and infection that occurs in parallel with tissue trauma. We will discuss immune profiles associated with functional and dysfunctional tissue repair and how this can be modeled with biomaterials and leveraged in therapeutic development for tissue regeneration.

15th January Poster Presentations

<u>Name</u>	<u>Title</u>	<u>Institution</u>
Adja Toure	High Throughput Screening of Polymeric Biomaterials for Personalised 3D Printed Treatments	University of Nottingham
Alessandro Carabelli	Prevention is the best cure – identifying the key properties of polymers that reduce dangerous biofilm formation	University of Nottingham
Ami Nash	The development of novel formulations for the spray delivery of therapeutic cells for traumatic brain injury	University of Nottingham
Lisa Kämerling	New immune instructive polymeric microparticles to direct the adaptive immune system via dendritic cell activation	University of Nottingham
Andrea Alice Konta	Two – Photon Polymerization (2pp) 3d Printing Of New Biodegradable Polymers For Ocular Therapy	University of Nottingham
Bunty Sharma	Synthesis and characterizations of metallosurfactant based self-assembled structure for encapsulations of photosensitizer and their use in Photodynamic Therapy	University of Nottingham
Catherine Vasey	Nanotherapeutics for neurosurgically-applied drug delivery in the treatment of Glioblastoma Multiforme	University of Nottingham
Charlotte Henshaw	Micropipette Manipulation Techniques to Inform Microparticle Design and Production	University of Nottingham
Dara O'Brien	Epoxy-Amine Resins from Terpenes with Applications in Synergistic Antifungal Treatments	University of Nottingham
Eduardo Pernaut-Leza	Screening Combinatorial Material Microarrays to identify inducers of Epithelial to Mesenchymal Transition	University of Nottingham
Fatma Nabil Elshishiny	Fabrication of Layer-by-Layer Biocomposite Scaffold for Skin Regeneration:In-vitro Study	The American University in Cairo
Francesco Pappalardo	Co-flow Microfluidic System For The Production Of Tuneable Elastic Gelatin Methacryloyl Microparticles	University of Nottingham
Ilona Sica	T cell activation and function investigated using fully-defined 3D culture	University of Nottingham
Jamie Thompson	Investigating glycosaminoglycans in development and disease using fully defined 3D cell culture environments and human pluripotent stem cells	University of Nottingham

Speakers

Prof. Alvaro Mata (University of Nottingham)

Turning molecules into functional biomaterials through supramolecular engineering

There is great interest to develop new materials with properties that resemble those of biological systems such as hierarchical organization, the capacity to grow or self-heal, and the ability to guide complex biological processes. Supramolecular chemistry offers an exciting opportunity to grow such materials from the bottom-up but the ability to transform nano-scale design into devices with practical utility at the macroscale remains a challenge. The talk will present new supramolecular fabrication tools that combine self-assembly with engineering principles to build with molecules. These approaches take advantage of phenomena such as multicomponent self-assembly, protein order-disorder synergies, and diffusion-reaction processes to guide assembly of multiple types of building blocks hierarchically. The resulting materials exhibit properties such as hierarchical organization¹⁻³, the capacity to grow^{2,3}, tuneable mechanical properties^{2,4}, and anisotropic bioactivity⁵. These materials are being used for the regeneration of tissues such as enamel, bone, and blood vessels as well as the development of more biologically relevant in vitro models.

- 1) Hedegaard et al (2018). *Advanced Functional Materials* 10.1002/adfm.201703716.
- 2) Elsharkawy et al (2018). *Nature Communications* 10.1038/s41467-018-04319-0.
- 3) Inostroza-Brito et al (2015). *Nature Chemistry* 7(11), 897-904. 10.1038/nchem.2349.
- 4) Redondo et al (2019). *Biomacromolecules*. 10.1021/acs.biomac.9b00224.
- 5) Aguilar et al (2017). *Advanced Functional Materials* 10.1002/adfm.201703014.

Prof. Patricia Dankers (Eindhoven University of Technology)

Supramolecular polymeric materials as synthetic extracellular matrices: from design to high throughput screening

The extracellular matrix is a complex assembly of various molecules held together via both covalent and noncovalent interactions. In order to make materials with comparable properties it is proposed that supramolecular materials based on hydrogen bonding units are eminently suitable. Synthetic supramolecular materials can be made that are composed of supramolecular monomers polymerized via similar interactions. This results in dynamic materials. An important challenge in the synthesis and formulation of synthetic extracellular matrices, is besides the balance between dynamics and robustness, the introduction of complexity. This complexity can exist of bioactive molecules that are either supramolecularly or covalently attached to the materials, or might originate from the assembly of the supramolecular monomers into various (hierarchical) structures. Both parameters will heavily influence the function of the materials synthesized when brought into contact with cells and tissues.

We have shown that the assembly and the respective dynamics in the supramolecular structure of supramolecular hydrogels is of eminent importance in steering cell adhesion and differentiation. The ability to tune the on-off rate of bioactive peptide ligands is shown. On the contrary, the incorporation of bioactive peptide additives on solid supramolecular materials is much more robust. Here, various methods of bioactivity introduction have been investigated, varying from heparin peptide binding peptides to immobilize heparin binding growth factors, supramolecular cucubituril host-guest chemistries to bio-orthogonal post-modifications based on inverse electron-demand Diels-Alder reactions.

Importantly, the modular nature of supramolecular polymeric materials and the ability to apply various supramolecular additives for bioactivation or non-fouling activity introduction make these systems interesting targets to study in a high throughput screening fashion. We have recently synthesized a library of extracellular matrix derived peptides which have been screened via a design of experiments set-up, in comparison with full length extracellular matrix proteins. Interestingly, we showed that simple active molecules as additives in supramolecular polymeric elastomers can outperform protein coatings.

Dr. Andrew Hook (University of Nottingham) Surface analysis and biomaterial development

The materials typically used for medical devices have been selected based upon mechanical properties and, consequently, their surface properties often induce an unfavourable biological response. For example, silicone, used to create catheters, support bacterial biofilm formation. There is a need to develop new materials that can be applied to biomedical applications, but this is hampered by the complexity of the biological-material interactions.

Surface analysis of materials, using time-of-flight secondary ion mass spectrometry (ToF-SIMS), combined with high throughput screening can aid in the development of biomaterials by enabling the creation of structure-function relationships that aid with the design of novel biomaterials. ToF-SIMS is of particular interest as the resultant spectra contain sufficient chemical detail to discern subtle differences between different materials. This approach has been successfully used to develop novel materials that prevent bacterial biofilm formation.

Here we describe the use of ToF-SIMS to analyse libraries of materials displayed as material microarrays for the development of novel biomaterials. This approach has been used to assess the functionalisation of materials with different polysaccharides. Using multivariate analysis, ToF-SIMS was able to successfully differentiate between different materials. This will be useful for optimising the use of polysaccharides in biomaterial systems.

Prof. Tim Tolker-Nielsen (University of Copenhagen)
Mechanisms of biofilm-associated antimicrobial tolerance

Microbial biofilms are causing a variety of tissue-associated and implant-associated persistent infections [1]. The ability of biofilms to tolerate antibiotics and components of the host immune system is at the root of the problematic infections they are causing [2]. Although antibiotics may decrease the number of bacteria in biofilms, they cannot completely eradicate the bacteria, and hence relapses of biofilm-based infections often occur. Therefore, common regimes for treating biofilm-based infections involve removal of infected tissues or implanted devices, followed by long-term antimicrobial therapy. Knowledge about the molecular mechanisms which are involved in biofilm-associated antimicrobial tolerance may form a basis for the development of drugs and treatment scenarios that can eradicate medically relevant biofilms. In this talk I present our work on identifying molecular mechanisms involved in the tolerance of biofilms to antimicrobial agents. This includes components of the biofilm matrix that sequester antibiotics [3,4], enzymatic systems that block entry of antibiotics by addition of specific molecules to cell surface components [5,6], as well as oxidative stress responses [7].

[1] Costerton JW, Stewart PS, and Greenberg EP (1999) Bacterial biofilms: a common cause of persistent infections. *Science* 284,1318-1322.

[2] Ciofu O, Tolker-Nielsen T (2019) Tolerance and resistance of *Pseudomonas aeruginosa* biofilms to antimicrobial agents - How *P. aeruginosa* can escape antibiotics. *Front Microbiol.* 3;10:913.

[3] Goltermann L, Tolker-Nielsen T (2017) Importance of the exopolysaccharide matrix in antimicrobial tolerance of *Pseudomonas aeruginosa* aggregates. *Antimicrob. Agents Chemother.* 61(4). pii: e02696-16.

[4] Chiang WC, Nilsson M, Jensen PO, Hoiby N, Nielsen TE, Givskov M, Tolker-Nielsen T (2013) Extracellular DNA shields against aminoglycosides in *Pseudomonas aeruginosa* biofilms. *Antimicrob. Agents Chemother.* 57, 2352-2361.

[5] Pamp SJ, Gjermansen M, Johansen HK, Tolker-Nielsen T (2008) Tolerance to the antimicrobial peptide colistin in *Pseudomonas aeruginosa* biofilms is linked to metabolically active cells, and depends on the *pmr* and *mexAB-oprM* genes. *Mol Microbiol* 68, 223-240.

[6] Nilsson M, Rybtke M, Givskov M, Høiby N, Twetman S, Tolker-Nielsen T. (2016) The *dlt* genes play a role in antimicrobial tolerance of *Streptococcus mutans* biofilms. *Int J Antimicrob Agents.* 48:298-304.

[7] Nilsson M, Jakobsen TH, Givskov M, Twetman S, Tolker-Nielsen T. (2019) Oxidative stress response plays a role in antibiotic tolerance of *Streptococcus mutans* biofilms. *Microbiology.* 165:334-342.

Dr Adam Dundas (University of Nottingham)
(Presented by Dr Olutoba Sanni)

Discovery of a polymer using a predictive structure relationship model capable of reducing biofilm formation

Synthetic materials are an everyday component of modern healthcare yet often fail routinely as a consequence of medical device centred infections. The incidence rate for catheter-associated urinary tract infections is between 3 and 7 % for each day of use, meaning over a prolonged period of time infection is inevitable. Development of biomaterials resistant to bacterial colonization can play an important role in reducing device-associated infections. This work focuses on the development and validation of a quantitative structure-activity relationship which was used to predict a material that can prevent biofilm formation. Monomers were identified using a QSAR, *alpha*, which correlates the calculated partition coefficient (cLogP) and number of rotatable bonds to biofilm adhesion. Identified monomers

were synthesised using a transesterification method, which a microwave-method has also been investigated by designing and building a bespoke microwave reactor. These monomers were, when polymerised, shown to be able to successfully resist biofilm formation from six different pathogens: *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Escherichia coli* and *Staphylococcus aureus*. This has shown how computational models can help to build upon current understanding of surface-bacteria interactions to help develop improved biomaterials that can be used to improve on current healthcare devices, which have shown to be ineffective at stopping biofilm formation on surfaces.

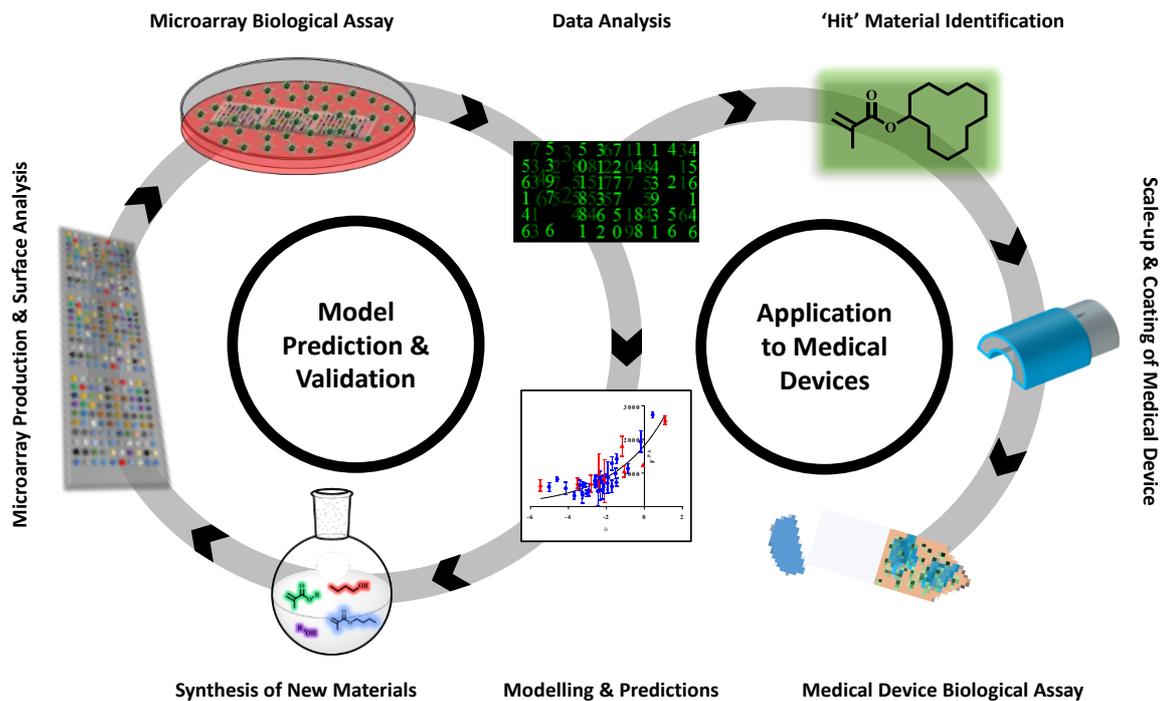


Figure 1: Biomaterial feedback-loop showing the use of computational models to develop new biomaterials for the prevention of medical device related infections. This works by building upon knowledge to help identify new materials in an iterative screening and testing process which creates better computational models that can predict new biomaterials.

Dr. Nicola Farthing (University of Nottingham)

Holographic microscopy as a tool to understand the interaction of swimming cells with biomaterials

Every year 700,000 people die from drug resistant infections [1]. With this figure predicted to rise to a staggering 10 million, costing 100 trillion USD by the year 2050, there is a pressing need to develop new ways of treating resistant infections and to limit the use of antibiotics to prevent further resistance developing. Many resistant infections are associated with biofilms and this has driven an interest in developing methods to prevent or limit biofilm growth without antibiotics. A key area of investigation is the treatment/ coating of surfaces to either prevent the initial attachment stage of biofilm formation or discourage attached cells progressing into a full biofilm.

Polymers that either promote or prevent biofilm formation, with no effect on bacterial growth, have been identified using high-throughput polymer arrays and monomer libraries

[2]. Here we investigate the interaction of planktonic cells with the polymers to elucidate the mechanisms driving the biofilm resistance/ promotion of the polymers. Multiple individual bacteria are observed and tracked over time near the surface as well as in the bulk of the media using a novel multimode microscope, capable of employing the complementary imaging techniques of digital holographic microscopy (DHM), differential interference contrast (DIC) and total internal reflectance microscopy (TIRM) [3]. This allows the influence of the polymers on bacterial behaviour to be investigated.

In this work, the role of flagellar location, glycosylation and motors on how cells approach, and attach to either biofilm-promoting or biofilm-inhibiting polymer surfaces was investigated. The interaction with the surfaces of *Pseudomonas aeruginosa* mutants was compared to the wild-type to elucidate the key aspects of motility. The aims are to identify the key bacterial regulatory pathways and surface components responsible for the observed differences in polymer interactions. This information will inform the further development of surfaces that resist bacterial biofilm formation.

[1] Tackling Drug-Resistant Infections Globally: Final Report and Recommendations – The Review on antimicrobial resistance – chaired by Jim O’Neill (2016).

[2] Antifouling and antimicrobial biomaterials: an overview. APMIS (2017). I. Fancolini, C. Vuotto, A. Piozzi, G. Donelli.

[3] Simultaneous tracking of *Pseudomonas aeruginosa* motility in liquid and at the solid-liquid interface reveals differential roles for the flagellar stators. A L. Hook, J L. Flewellen, J-F. Dubern, A M. Carabelli, I M. Zaid, R M. Berry, R D. Wildman, N. Russell, P. Williams, M R. Alexander. (2019). mSystems 4:e00390-19

Kiril Kalenderski (University of Nottingham)

A new bacterial resistant polymer catheter coating to reduced catheter associated urinary tract infection – a first-in-man pilot study

Bacterial biofilms and their associated crystalline deposits are frequently described as causes of long-term indwelling urinary catheter failure. Following bacterial attachment to the catheter surface, biofilms and mineralization develop, which can result in complications associated with catheter associated urinary tract infections (CAUTIs), such as catheter blockage and incontinence. We describe a novel antibacterial coating for urinary catheters, comprised of a polyacrylate copolymer of ethylene glycol dicyclopentenyl ether acrylate (EGDPEA) and di(ethyleneglycol) methyl ether methacrylate (DEGMA), enabling the medical devices to resist bacterial biofilm formation, and urinary tract infection within a clinical environment. We demonstrate the improved resistance of the coated catheters to biofilm biomass accumulation, in comparison with uncoated devices, in patients undergone urinary tract surgery. We also investigate the origin of mineral biomass accumulation on the two different types of catheter. In addition, we provide an insight in to the composition of the bacterial communities on two different uncoated clinical catheter sample biofilms, as well as from urine. This is the first-in-man clinical study which investigates biofilm formation and mineralization on the new polymer coated (Camstent) silicone catheters in comparison with uncoated catheters.

Ann Kramer (Electrospinning Company)

The next step: Translating electrospinning biomaterials research into a medical device

Electrospinning has received an ever-increasing amount of attention academically, as judged by the rise in the number of publications over the last three decades. It has been established as a fast, facile and versatile low-cost fabrication technique for micro- and nanofibrous materials. A significant amount of that scientific effort is focussed on the use of electrospun biomaterials for the intended use in novel, implantable biomedical devices. Nevertheless, there is significant discrepancy between the academic effort undertaken so far, the generation of intellectual property coming out of that effort and the relatively low number of actual devices utilising electrospun materials available. This presentation aims to shine light on the difficulties and pitfalls associated with taking promising electrospinning research out of the lab and into phase I clinical trials with a focus on materials, manufacturing and regulatory challenges. It will include case studies and observations from a variety of biomaterial translation projects, including the production of synthetic corneal implants for Phase I clinical trials in India translating from research undertaken at The University of Sheffield and the development of a membrane that is incorporated into an orthopaedic medical device, now FDA 510K approved and sold in the USA.

16th January Poster Presentations

<u>Name</u>	<u>Title</u>	<u>Institution</u>
Jeni Lockett	Multiplexing infection, immune response and biomaterials using multimodality imaging approaches	University of Nottingham
Jennifer Ashworth	Peptide gel tissue models of fully-defined composition and mechanics for probing cell-matrix interactions in breast cancer	University of Nottingham
Joris Meurs	High throughput surface proteomics for examining cellular response on biomaterial surfaces	University of Nottingham
Kiril Kalenderski	A New Bacterial Resistant Polymer Catheter Coating to Reduce Catheter Associated Urinary Tract Infection (CAUTI) – A First-in-man Pilot Study	University of Nottingham
Leonardo Contreas	Evaluation Of Classification Models To Predict Bacterial Attachment To Polymers	University of Nottingham
Lorena Lizarraga	Polyhydroxyalkanoates-Based Materials for Peripheral Nerve Regeneration	University of Nottingham
Marica Malenica	Towards continuous production of sintrable core-shell particles for biomedical application	University of Nottingham
Matt Vassey and Le Ma	3D ArchiChip - Exploring the relationship between material geometry and chemistry on immune cell responses using two-photon printing	University of Nottingham
Moniek Schmitz	From design to high through-put screening of multifunctional antimicrobial supramolecular biomaterials	Eindhoven University of Technology
Nazia Mehrban	Designing Chemically and Physically Tunable Materials for Clinical Applications	UCL
Phanikrishna Sudarsanam	High throughput screening of topographies to mitigate fibrosis in glaucoma drainage devices	Eindhoven University of Technology
Qin Hu	A new platform for high-throughput design complex 3D architectures for two-photon lithography based micro 3D printing for biological study	University of Nottingham
Sarah Mcginlay	A Three-Dimensional Model of Adipogenesis Using Alginate Fibres	University of Nottingham
Valentina Cuzzucoli Crucitti	Microparticles With Defined Surface Chemistry Enabling The Control Of Bacteria Biofilm Formation	University of Nottingham

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