SYMPOSIUM BM01

TUTORIAL: 3D Printing of Passive and Active Medical Devices
November 25 - November 25, 2018

* Invited Paper

TUTORIAL
3D Printing Methods for Medical Applications

Sunday Morning, November 25, 2018
Hynes, Level 2, Room 200

3D printing methods enables distributed manufacturing, mass customization, and rapid prototyping of medical devices. The tutorial "3D Printing Methods for Medical Applications" seeks to impart information to the audience on the use of 3D printing methods to process polymer, metal, ceramic, and biological materials. This course includes coverage of 3D printing principles, advantages of 3D printing over traditional subtractive manufacturing processes, materials for 3D printing, 3D printing methods, and applications of 3D printing.

8:30 AM
3D Printing Technologies for Healthcare Roger Narayan; University of North Carolina at Chapel Hill and North Carolina State University

Laser-based processes may be used for additive manufacturing and bioprinting of structures with unique microscale and nanoscale structures. We have demonstrated use of matrix assisted pulsed laser evaporation- direct write for layer-by-layer processing of cells and scaffold materials. Three-dimensional patterning of cells and cell-scaffold composites have been demonstrated using this approach. We have also recently examined additive manufacturing of three-dimensional structures using two photon polymerization. In two photon polymerization, ultrashort laser pulses are used to selectively polymerize photosensitive resins and form complex microscale and/or nanoscale structures. The nonlinear nature of two photon absorption enables polymerization of structures with features below the diffraction limit. Recent medical applications of two photon polymerization have involved fabrication of microneedle arrays and scaffolds for tissue engineering. Our results indicate that matrix assisted pulsed laser evaporation- direct write and two photon polymerization are attractive techniques for additive manufacturing and bioprinting, respectively.

9:30 AM BREAK

10:00 AM
Printing Cells: Process Challenges and Application Wei Sun; Drexel University and Tsinghua University

3D Bio-Printing uses cells and biomaterials as building blocks to fabricate personalized 3D structures or functional in vitro biological models. The technology has been widely applied to regenerative medicine, disease study and drug discovery. This presentation will report our recent research on printing cells for construction of micro-organ chips and for building in vitro 3D tumor models. An overview of advances of 3D Bio-Printing will be given. Enabling methods for cell printing will be described. Examples for 3D Printing of tissue engineering model, drug metabolism model and disease model will be reported, along with results of printing parameters on cell viability and 3D tumor structural formation, characterization of cell morphologies, proliferations, protein expressions and chemoresistances. Comparison of biological data derived from 3D printed models with 2D planar petri-dishes models will be conducted. Discussions on challenges and opportunities of 3D Bio-Printing will also be presented.

11:00 AM
3D Printing of Hard Biomaterials Amit Bandyopadhyay; Washington State University

3D Printing (3DP) or Additive manufacturing (AM) is an approach to process parts directly from its computer aided design (CAD) file. AM is changing the landscapes of current industrial practices. On-demand manufacturing using 3DP technologies is a new trend that will significantly influence many industries and product design protocols. Since there is no need for any part specific tooling, different parts can be built using the same machine. Most of these parts are near net-shape and require only small finishing operation. Unlike even 10 years back, when most of these 3DP produced parts were used for touch and feel, and design optimization, functional parts via additive manufacturing is becoming common in most industrial sectors.

We have worked on additive manufacturing of hard materials, primarily metals and ceramics, over the last two decades. We have used fused deposition modeling, laser engineered net shaping and powder bed based 3D printing processes. Using these 3DP approaches, we have manufactured parts with compositional, functional and structural gradation mostly for space and biomedical applications. I will focus on some of the key success stories from our research, as well as current challenges in the field.

SYMPOSIUM BM01

3D Printing of Passive and Active Medical Devices
November 26 - November 27, 2018

Symposium Organizers
Susmita Bose, Washington State University
Richard Hague, University of Nottingham
Roger Narayan, North Carolina State University
Wei Sun, Drexel University and Tsinghua University

* Invited Paper

SESSION BM01.01: 3D Printing of Passive and Active Medical Devices I
Session Chairs: Douglas Chrisey and Yong Huang
Monday Morning, November 26, 2018
Sheraton, 2nd Floor, Liberty B

8:00 AM *BM01.01.01
Emerging Organ Models and Organ Printing for Regenerative Medicine Ali Khademhosseini; Department of Bioengineering, Chemical Engineering, Radiology, University of California, Los Angeles, Los Angeles, California, United States.

Engineered materials that integrate advances in polymer chemistry, nanotechnology, and biological sciences have the potential to create powerful medical therapies. Our group aims to engineer tissue regenerative therapeutics using water-containing polymer networks called hydrogels that can regulate cell behavior. Specifically, we have developed photo-crosslinkable hybrid hydrogels that combine natural biomolecules with nanoparticles to regulate the chemical, biological, mechanical and electrical properties of gels. These functional scaffolds induce the differentiation of stem cells to desired cell types and direct the formation of vascularized heart or bone tissues. Since tissue function is highly dependent on architecture, we have also used microfabrication methods, such as microfluidics, photolithography, bioprinting, and molding, to regulate the architecture of these materials. We have employed these strategies to generate miniaturized tissues. To create tissue complexity, we have also developed directed assembly techniques to compile small tissue modules into larger constructs. It is anticipated that such approaches will lead to the development of next-generation regenerative therapeutics and biomedical devices.

8:30 AM *BM01.01.02
Laser Based Direct Write Techniques for Studying Cellular Interactions Douglas B. Chrisey and Jayant Saksena; Tulane University, New Orleans, Louisiana, United States.

Due to their ability to carry out both additive and subtractive processing of a wide range of materials in a non-contact manner with superior precision and speed, lasers are a promising tool to create reproducible constructs for cell based assays. Laser direct write technologies – such as our custom-designed matrix assisted pulsed laser evaporation (MAPLE) bioprinting system – combine the power of laser processing with computer aided design to allow us to print as well as ablate cells, cell aggregates and biomaterials with high resolution. Here, we present some interesting applications of the excimer laser driven MAPLE platform for cell printing and ablation, tissue dissection, biomaterial micromachining and 3D microbead fabrication for studying interactions between cells and their microenvironmental cues in vitro. We have printed breast and colon cancer cells, fibroblasts and macrophages in spatially defined patterns on hydrogel substrates and live rat mesenteric tissue to develop physiologically relevant models for cancer cell migration and invasion. We have micromachined spoke and channel patterns into PDMS substrates to analyze competitive cell migration in context of cancer and atherosclerosis. We have also developed a reproducible and customizable wound healing assay using laser ablation of adherent cells. We have fabricated and patterned 3D microbeads encapsulating heterogeneous cell types to elucidate cancer-adipose interactions. Finally, we have dissected user-specified regions of excised mouse colonic tissue to create testable sections. Our work demonstrates the immense versatility of laser based direct write technologies in biology and medicine.

9:00 AM *BM01.01.03
3D Printing of Passive and Active Medical Devices—A Clinician-Scientist's Perspective Shervanthi Homer-Vanniasinkam[1, 2, 3]; [1]Division of Surgery & Department of Mechanical Engineering, University College London, London, United Kingdom; [2]Vascular Surgery, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; [3]Division of Surgery, University Hospitals Coventry & Warwickshire/University of Warwick, Coventry/Warwick, United Kingdom.

The burgeoning field of 3D printing is rapidly invading the medical sphere with an ever-expanding portfolio of applications in healthcare. Since Charles Hull invented stereolithography in the early 1980s, this printing technology has evolved greatly, and to an exponential degree, in the last decade.
The applications of 3D printing in medicine are many, and growing. In this talk, some important uses of the technology will be presented, and, as time permits, discussed from a clinician-scientist's perspective.
In surgery, 3D printing is being increasingly utilised in patient-specific surgical planning to aid intraoperative navigation in complex operative procedures, using precise personalized anatomical information; in producing implants and prostheses; and in educating and training young surgeons.
Other applications include 3D bio- and molecular printing of functional living constructs and organs, in drug delivery, and for custom-made medical equipment and products eg surgical tools and instruments.
Several groups of researchers, including clinician-scientists, are working on exciting developments in areas embracing all aspects of patient care from

surgical procedure planning to printing scaffolds and tissues for clinical implantation. Whilst currently there is widespread interest in harnessing this technology in all fields of medicine, in order to realize the full potential of 3D printing, it is perhaps important to prioritize areas in which to focus our research and development endeavours. Clinician involvement in this process is vital, so that minds can be focused on unmet clinical needs.
Currently, despite the huge strides made by 3D printing in recent years, there remain challenges for the routine implementation of this technology in the clinical sphere; these include the time taken to prepare the object or device ie long processing times (and hence, limited applicability in the urgent and emergency settings), the accuracy of the devices or models produced, the expense of doing so (despite the decreasing costs of the printers) and importantly, the associated regulatory aspects.
The clinical community is both excited by the promise of what 3D printing can deliver in terms of patient care, and wary of some of the potential dangers of wholly embracing this new field. Thus, it is important for clinicians, scientists and industry to develop a scientifically and socially conscious platform from which to foster the further development of this technology within clearly defined and ethically responsible boundaries. We should jointly strive to achieve this goal so that the promise that 3D printing holds for improved healthcare, is realized.

9:30 AM BM01.01.04
Towards the Development of Performant Silicone Elastomeric Compositions for 3D Printing of Customizable Parts Remi Thiria[1], Karsten Schlichter[2], Jean-Marc Frances[2] and Damien Djian[2]; [1]R&D, Elkem Silicones NA, York, South Carolina, United States; [2]Elkem Silicones France, Lyon, France.

Due to their outstanding properties like biocompatibility, hypoallergenicity, chemical inertness, thermo-stability resistance and flexibility at low temperatures, soft silicone elastomers are the material of choice in many healthcare applications such as prosthesis, drug delivery, implantable devices, comfort care, audiology and implantable devices.
Traditional manufacturing processes such as casting and injection molding, are currently used for the preparation of biocompatible materials or medical devices however there is a strong need for customized silicone parts.
Additive manufacturing (AM) and especially 3D printing is a tool that offers increased design freedom and enable users to redesign existing parts but also create unique parts that can not be manufactured with any of the current traditional manufacturing processes.
This technical lecture will introduce the new challenges and benefits of AM to make personalized silicone elastomers against the traditional ways of conception/processing. Due to its low elastic modulus and poor shape retaining ability during the layer-by-layer process, silicone elastomer AM could be technically challenging. A good understanding of the relationship between input and output parameters during the AM is key. Mastering such parameters along with the 3D printer machine and the silicone chemistry have allowed us to predict both the aspect and performances of the 3D printed part.

9:45 AM BM01.01.05
Patient-Specific Printing of Bioresorbable and Biocompatible Ceramics by Lithography-Based Ceramic Manufacturing Shawn M. Allan[1], Martin Schwentenwein[2], Daniel Bomze[2] and Johannes Homa[2]; [1]Lithoz America, LLC, Troy, New York, United States; [2]Lithoz GmbH, Vienna, Austria.

Lithography-based Ceramic Manufacturing (LCM) has emerged as a state-of-the-art technology for the production of dense high-performance ceramics in field of additive manufacturing (AM). LCM polymerizes ceramic slurries, which consist of ceramic particles dispersed in a photocurable binder matrix, in a layer-by-layer manner using light. The green-body is durable enough for handling and mechanical post-processing. After the AM process, the green-body is thermally processed to remove the polymer binder and densify the ceramic. Tremendously diverse and complex parts can be fabricated directly from CAD files. Parts formed by LCM exhibit the same mechanical properties as parts formed by conventional manufacturing processes.
LCM allows fabrication of bio-inert zirconia, an exceptionally tough ceramic, for permanent bone replacements and dental implants, crowns, bridges and orthodontic products. LCM also enables the structuring of bioresorbable ceramics like tricalcium phosphate (TCP) or hydroxyapatite (HA). These bioceramics are used in the biomedical field for patient-tailored implants, derived from CT scans. This provides the best compatibility for the patient and easy-to-use handling for the surgeon. The freedom of design facilitates cell scaffolds with defined macroporosity (e.g. cancellous bone shape) for the ingrowth of cells and vascularisation, allowing the delivery of nutrients and the removal of metabolic waste.
This contribution gives an overview about the capabilities of the LCM process, potential applications as well as current challenges. Resolution, reproducibility, surface roughness of the different materials and economic feasibility will also be topic of this presentation.

10:00 AM BREAK

10:30 AM *BM01.01.06
Framed Biopapers—Degradable Substrates for Printing, Handling, Stacking and Device Integration of 3D Printed Tissue Constructs Russell K. Pirlo[1, 2]; [1]Chemistry, U.S. Naval Research Laboratory, Washington, District of Columbia, United States; [2]Radiological Sciences, Uniformed Services University of Health Sciences, Bethesda, Maryland, United States.

Despite the expanding use of 3D bioprinting and a growing number of commercially available 3D bioprinters, there has been limited effort to develop a universal cell and tissue culture platform that enables the plethora of new approaches made possible with 3D printing. Traditional cell culture formats like the well-plate and transwell insert are routinely employed as the receiving container for bioprinted tissues but they present challenges when it comes to perfusion, harvesting, transfer of the printed tissues and accessibly to other tools and instruments. The ability to fabricate tissues in “freeform” is one of the advantages of 3D bioprinting, yet tissues remain confined to the receiving substrate, or lack a method of registration with other devices. The U.S. Naval Research Laboratory has developed “framed biopapers” as a novel and potentially universal format for 3D printing, handling, stacking and transferring tissues with registration between layers and devices.
In its most basic application, a single framed biopaper may be used as the base substrate for freeform 3D bioprinting. In this way, the framed biopaper provides a method to handle the 3D printed construct and easily releases the tissue construct through dematerialization of the biodegradable biopaper. Additionally, the frames of the biopaper provide for a registration mechanism for transfer from one bioprinting or biofabrication tool to another, as well as to bioreactors and analytical instruments, such as a microscope or plate reader. Furthermore, framed biopapers enable an asynchronous layer-by-layer fabrication approach whereby sheet-like layers are printed to individual biopapers and allowed to mature independently before stacking. This allows for specific application of growth factors or stimulus and the construction of complex heterotypic tissues, especially those with a laminar architecture. Finally, we envision that the frame of the biopaper may even be used as a surgical guide for implantation of tissue constructs, precision engineered to fit into a defect/void with alignment of implant and native vasculature and other tissue architecture for more rapid suture, anastomosis and integration into the body.

11:00 AM *BM01.01.07
Bioprinting—Implementation, Process Dynamics and Process Induced Cell Injury Yong Huang; University of Florida, Gainesville, Florida, United States.

Various manufacturing innovations have been adopted to facilitate tissue engineering practices for better biomedical applications. Among them, maskless

(including extrusion-, laser- and inkjet-based) three-dimensional (3D) cell bioprinting is a revolutionary advance for printing arbitrary cellular patterns as well as creating heterogeneous living constructs. Thus far, effective printing of cell-laden viscoelastic fluids and printing-induced injury to living cells still pose a significant challenge to ensuring the scale-up of robust bioprinting. Using laser bioprinting (laser-induced forward transfer) and inkjet bioprinting as two jet-based model printing systems, we have been studying the bioink jettability and printability as well as printing-induced cell injury problems, aiming to achieve robotic bioprinting. The jettability and printability of cell-laden viscoelastic bioinks are defined and characterized using material properties- and printing conditions-related non-dimensional numbers. The printing-induced cell injury and post-transfer cell viability are estimated based on the process-induced cell thermomechanical loading during the cell droplet formation and landing processes.

In this talk, the perspective of ongoing bioprinting research and various bioprinting technologies are first introduced. Then the jettability and printability of cell-laden viscoelastic bioinks are discussed using the dimensionless Ohnesorge and elasto-capillary numbers to capture the influence of material properties along with the Weber number to capture the influence of printing conditions. Furthermore, the modeling of laser-induced cellular droplet formation and landing processes is presented, and the relationship between the mechanical loading information and post-transfer cell injury/viability is established using an apoptosis signaling pathway-based modeling approach. Finally, this talk shares some thoughts regarding basic scientific challenges related to bioprinting.

11:30 AM BM01.01.08
Photocurable Thiol/Yne Resins for the Manufacturing of Functional Biocompatible Structures Thomas Griesser; Institute of Chemistry of Polymeric Materials & Christian Doppler Laboratory for Functional and Polymer Based Ink-Jet Inks, University of Leoben, Leoben, Austria.

The last years have seen an increasing interest in the development of photo-polymerizable monomers providing low cytotoxicity and high thermo-mechanical properties in their cured state.[1] This fact can mainly be explained by the rapid progress in UV based additive manufacturing technologies such as stereolithography, digital light processing or 3D ink-jet printing, which enables the fast, accurate and individual fabrication of biocompatible structures. In this context also the tissue compatibility of photopolymers has to be considered in particular for medical devices that are in direct contact with blood or bone.
In this contribution, the versatility of the thiol-yne photo-click reaction[2] for the fabrication of biocompatible photopolymers is shown at the example of tailor-made alkyne and thiol monomers. For that purpose, commercially available acrylate monomers were modified using the carbon and oxa michael addition reaction to obtain multifunctional alkyne building blocks.
It turned out that these synthesized monomers offer curing rates similar to the acrylates, while providing much higher conversion and lower monomer cytotoxicity. This reaction leads to highly uniform polymeric networks exhibiting a sharp and defined thermal glass transition together with outstanding impact resistance, which makes these polymers interesting for challenging applications such as medical implants.[3] Not only non-degradable, but also degradable monomers were designed, enabling the selective adjustment of the resorption behavior of the resulting polymers.[4]
The herein described monomer systems pave the way towards the individual fabrication of tissue compatible photopolymers with tunable thermo-mechanical properties and resorption behavior.

(1) Mautner, A.; Steinbauer, B.; Russmüller, G.; Lieber, R.; Koch, T.; Stampfl, J.; Liska, R. *Designed Monomers and Polymers* **2016**, *19*, 437.
(2) Lowe, A. B.; Hoyle, C. E.; Bowman, C. N. J. *Mater. Chem.* **2010**, *20*, 4745.
(3) Oesterreicher, A.; Gorsche, C.; Ayalur Karunakaran, S.; Moser, A.; Edler, M.; Pinter, G.; Schlögl, S.; Liska, R.; Griesser, T. *Macromolecular Rapid Communications* **2016**, *37*, 1701.
(4) Oesterreicher, A.; Wiener, J.; Roth, M.; Moser, A.; Gmeiner, R.; Edler, M.; Pinter, G.; Griesser, T. *Polym. Chem.* **2016**, *7*, 5169.

11:45 AM BM01.01.09
Manufacturing Microstructured Medical Devices Using Multi-Step 3D Printing Technologies Roger Narayan; North Carolina State University, Raleigh, North Carolina, United States.

In this presentation, the use of multi-step 3D printing technologies, which incorporate digital micromirror device-based stereolithography, two photon polymerization, pulsed laser deposition, matrix assisted pulsed laser evaporation, piezoelectric inkjet printing, and/or micromolding, to create small-scale medical devices for transdermal drug delivery will be considered. Microneedles are small-scale lancet-shaped devices that may be used for delivery of pharmacologic agents into the skin. We have use 3D printing techniques to microneedles such as digital micromirror device-based stereolithography and two photon polymerization to create microneedles with well-defined tips and complex shapes directly from computer models. Printing techniques including pulsed laser deposition, matrix assisted pulsed laser evaporation, and piezoelectric inkjet printing have been used to decorate the 3D printing microneedles with medically active agents. For example, visible light dynamic mask microstereolithography and micromolding have been used to prepare microneedles out of poly(methyl vinyl ether – co – maleic anhydride) (PMVE/MA); coatings containing agents such as amphotericin B and miconazole have deposited on the microneedles using piezoelectric inkjet printing. Disk-diffusion studies demonstrated the antifungal activity of the inkjet printing-modified microneedle arrays. Examples involving the use of multi-step 3D printed microneedles for various medical applications will be considered.

SESSION BM01.02: 3D Printing of Passive and Active Medical Devices II
Session Chairs: Rigoberto Advincula and Reginald Hamilton
Monday Afternoon, November 26, 2018
Sheraton, 2nd Floor, Liberty B

1:30 PM *BM01.02.01
Laser Direct Energy Deposition Additive Manufacturing of NiTi Shape Memory Alloys Reginald F. Hamilton, Beth Last, Emily Jenkins and Todd Palmer; Engineering Science and Mechanics, The Pennsylvania State University, University Park, Pennsylvania, United States.

Additive Manufacturing (AM) has gained significant attention for processing shape memory alloys because they have circumvented many of the challenges associated with the conventional methods. Shape memory alloys are a class of multifunctional materials that undergo large shape changes, and upon heating or removing external stimuli “remember” their original shape and form. Underlying reversible solid-state atomic and microstructure length scale phase transitions beget the bulk scale memory. Consequently the shape memory alloy behavior can be tailored using manufacturing techniques that provide freedom to design the microstructure. The AM techniques for NiTi are either powder-bed based technologies such as Selective Laser Melting, or flow-based methods such as Laser Directed Energy Deposition (LDED). LDED deposits powder through nozzles directly into the laser focus melt pool. LDED AM is a potential tool for *in-situ,* i.e. during fabrication, microstructure design. The laser-based layer-by-layer AM techniques can result in microstructural

anisotropy, which is characterized in terms of the grain and microconstituent morphologies. During the additive manufacturing (AM) process, individual passes and layers are deposited. The deposition of passes and layers creates overlapping regions between adjacent passes and interfacial zones between successive layers. Within the overlapping and interfacial regions, previously deposited material is remelted is also reheated as heat is conducted away from the solidifying material. The remelting and reheating in these local regions will bring about microstructure anisotropy. Multi-scale deformation measurements correlate microstructure to underlying physical mechanisms in order to establish the interrelationships between novel fabrication technologies and shape memory functionality. The purpose of this work is to correlate the layerwise built-up microstructures to the shape memory behavior of LDED AM NiTi shape memory alloys.

2:00 PM *BM01.02.02
Hydrogel Bioinks for 3D Printing Applications Jason Burdick; University of Pennsylvania, Philadelphia, Pennsylvania, United States.

Hydrogels represent a class of biomaterials that have great promise for the repair of tissues, particularly due to our ability to engineer their biophysical and biochemical properties. 3D printing approaches are now being developed to process hydrogels into structures with the appropriate shapes and patterns for tissue repair; however, printing processes are often not compatible with hydrogels optimized for a desired cell response. Thus, we have developed techniques to both screen hydrogels for a desired cell response and to process these materials into printable bioinks.
Towards MSC chondrogenesis, we have developed a screening platform using the patterning of photocrosslinkable norbornene-modified hyaluronic acid hydrogels with biochemical signals. These include peptides that mediate cell-matrix adhesion (i.e., RGD) or cell-cell adhesion (i.e., HAVDI). When cells are encapsulated within the hydrogels incorporating orthogonal gradients, optimal formulations can be identified through imaging of MSC differentiation markers (e.g., Sox9, aggrecan). As these are non-viscous precursor solutions, they are difficult to 3D print using traditional printing approaches, such as extrusion-based printing. With extrusion-based printing, a bioink must flow during extrusion, but then be rapidly stabilized post-extrusion to maintain the desired printed structure. To address this, we have developed two approaches to 3D print non-viscous bioinks: (i) curing the material with light through a transparent conduit immediately prior to extrusion, and (ii) processing the materials into microgels using microfluidics that can be jammed and printed as solids. Both of these approaches have been successful in the processing of non-viscous hydrogel precursors into stable structures and have been used to encapsulate cells with high cell viability. Ultimately, the design of new bioinks and printing processes will lead to successful applications of 3D printing in the repair of tissues.

2:30 PM BREAK

3:00 PM *BM01.02.03
3D Printed Ceramic-Metal Composites to Minimize Metal Ion Release from Articulating Surfaces of Load-Bearing Implants Amit Bandyopadhyay, Anish Shivaram, Murat Isik, Jose Avila and Susmita Bose; School of Mechanical and Materials Engineering, Washington State University, Pullman, Washington, United States.

Cobalt-chromium-molybdenum (CoCrMo) alloys are widely used in load-bearing implants, specifically in hip, knee, and spinal applications, due to their excellent wear resistance and their being economic compared to titanium-based alloys. However, due to wear induced metal ion release from the implants and poor biocompatibility at implant-tissue interface, there is a significant interest to find an alternative to CoCrMo alloy. We hypothesize that adding calcium phosphate (CaP) based ceramic in the form of hydorxyapatite can minimize metal ion release concerns in CoCrMo alloy.
CoCrMo-CaP composite coatings were processed using a commercial laser-engineered net shaping (LENS™) system. After LENS™ processing, CoCrMo alloy was subjected to laser surface melting (LSM). Samples were investigated for microstructure, phase stability, and wear induced damage. It was found that wear resistance of CoCrMo was enhanced by ~ 5 times due to the formation of an *in situ* tribofilm of CaPs, and achievement of a fine dendritic microstructure in the case of LSM treated CoCrMo. *In vitro* cell material interactions study using human osteoblasts cell line was performed. For *in vivo*, rat and rabbit distal femur models were used for a period of 5 and 12 weeks. *In vitro* and *in vivo* study showed improved biological response for surface modified CoCrMo compared to untreated CoCrMo approximately a 5-fold increase in osteoid formation. Our results show that careful surface modification treatments can simultaneously improve wear resistance and *in vivo* biocompatibility.
The presentation will focus on processing as well as physical, mechanical and biological characterization of 3D printed CaP-CoCrMo composites with a focus on minimizing metal ion release.

3:30 PM *BM01.02.04
3D Printing of Multifunctional Tissue Engineering Scaffolds Min Wang; Department of Mechanical Engineering, The University of Hong Kong, Hong Kong, Hong Kong.

Tissue engineering has advanced significantly over the past three decades and many human body tissues may be regenerated successfully, providing desired functions in the human body. A few approaches are used for human tissue regeneration, which include cell-, factor- or scaffold-based tissue engineering. Using scaffolds to assist tissue regeneration has been the dominant approach. In scaffold-based tissue engineering, it is important to develop suitable scaffold materials and employ appropriate scaffold manufacturing technologies to make desirable scaffolds, which will lead to successful tissue regeneration. Many materials have been investigated for different scaffolds and scaffold fabrication techniques have been studied by numerous researchers. Materials for tissue engineering are generally biodegradable polymers and scaffolds are produced by either non-designed manufacturing techniques (e.g., solvent casting/porogen leaching) or designed manufacturing techniques. Using designed manufacturing, which includes a host of additive manufacturing technologies (the so-called “3D printing”), for scaffold fabrication has distinctive advantages and has therefore attracted great attention in the tissue engineering field. However, some 3D printing technologies impose stringent requirements for stock materials and studies have been conducted on preparing stock materials and on evaluating the physical and mechanical properties of scaffolds made of these stock materials. Furthermore, existing, general 3D printing technologies may not be suitable for constructing multifunctional tissue engineering scaffolds in which biological molecules or even live cells need to be incorporated. Hence, new 3D printing technologies specifically for handling delicate biomolecules and/or cells are urgently needed. Our group has investigated selective laser sintering (SLS), a well-established 3D printing technology, for making osteoconductive and osteoinductive scaffolds for bone tissue engineering. In this process, we developed nanocomposite materials as scaffold materials which provided osteoconductivity. For the novel scaffolds, we also incorporated a growth factor which provided osteoincuctivity. Our studies showed that bone tissue regeneration was greatly promoted with the SLS-formed multifunctional scaffolds. We have also developed a low-temperature, extrusion-based 3D printing technique for constructing relatively strong scaffolds with the incorporation of biomolecules or cells. Very promising results were obtained using this new 3D printing technology. This talk will give an overview of 3D printing and its application in tissue engineering. It will introduce our work in this area and discuss issues in scaffold design and 3D printing.

4:00 PM BM01.02.05
Inkjet Printing of Melanin as a Biocompatible Functional Electronic Material Ashkan Shafiee[1], Elham Ghadiri[2], Warren Warren[3] and Anthony

Atala[1]; [1]Institute for Regenerative Medicine, Wake Forest School of Medicine, Winston-Salem, North Carolina, United States; [2]Chemistry, Wake Forest University, Winston-Salem, North Carolina, United States; [3]Chemistry, Duke University, Durham, North Carolina, United States.

Biocompatible electronic has become a focus of attention owing to the need in biomedical applications. Smart electronic devices capable of communicating with biological structures such as human tissues and organs are the requirement for many sophisticated purposes in medicine. Melanin is one of the most stable biopolymer, found in almost every live organism, versatile for application in the emerging field of bioelectronic devices. Melanin pigments are found in human skin, hair, eyes and the brain in different forms. For many years, it was viewed simply as a coloring agent with some photoprotective properties, but that view always ignored some obvious features. The functionality of melanin as a natural pigment is defined (although not fully understood) by its physical and chemical properties, such as its featureless broad UV-NIR optical absorption, antioxidant properties, and temperature/water dependent photoconductivity. Melanin also shows in vivo and in-vitro biocompatibility. All these properties identify melanin as a unique alternative for using as the functional material in the bioelectronic devices.

This paper report the inkjet printing of synthetic melanin nanoparticles with different size for electronic applications. Inkjet printing deposition with computer-assisted abilities can pattern different types of materials on various flexible or rigid substrates. Inkjet printing deposits patterns with Pico-liter size droplets of the functional materials with micrometer resolution. This economic consumption makes this technique much more affordable compared to other deposition techniques such as spin coating and dip coating.

Through solution-based chemical synthesis, we have prepared melanin nanoparticles with controlled size and chemical structures of melanin-like nanoparticles, pheomelanin and eumelanin. The active layer of the electronic device consists of melanin nanoparticles based film prepared with inkjet printing technique. Nanoparticles solutions with different sizes of 70 nm, 100 nm, and 250 nm were printed on transparent conductive electrode using Jetlab II Microfab, piezoelectric printer. The optoelectronic and photophysical processes in the films are studied using steady-state UV-NIR diffuse reflectance spectroscopy and ultrafast time-resolved broadband pump-probe spectroscopy technique. Using ultrafast broadband spectroscopy measurements, we identified the spectral signature of excited state formation and compared excited state relaxation in melanin nanoparticles with different sizes. This research can open up the new avenue of research toward biocompatible electronic manufacturing.

4:15 PM BM01.02.06
Rheology and Direct Ink Writing of Strong Cellulose Reinforced Composites Michael Hausmann[1, 2], Gilberto Siqueira[1], Rafael Libanori[2], Patrick Rühs[2], Dimitri Kokkinis[2], Tanja Zimmermann[1] and André Studart[2]; [1]Empa, Swiss Federal Laboratories for Materials Science and Technology, Dubendorf, Switzerland; [2]ETH Zürich, Dubendorf, Switzerland.

Cellulose nanocrystal (CNC) is a bio-based and renewable material extracted from wood and algae or produced by bacteria. The alignment of CNCs is crucial for direction specific enhanced mechanical properties in composite applications. We utilize direct-ink writing (DWI) to assemble complex cellulose-based geometries with controlled orientation and spatial distribution of nanocrystals within the printed structure. Using polarized imaging rheology we correlate the dynamic flow behavior of CNC-based inks with the quality of nanocrystal alignment occurring during 3D printing. In order to control the quality of alignment during the 3D printing process, the printing pressure and the viscoelastic properties of the material have to be well characterized. After printing, the resulting part and its mechanical properties are determined in order to create composites with well-defined properties. By understanding the effect of the concentration of reinforcing nanocrystals on the rheological properties of the ink during the printing process, 3D objects with improved printability and mechanical properties were obtained. Our findings pave the way towards the fabrication of high-performance materials with renewable resources using a cost-effective additive manufacturing technique.

4:30 PM BM01.02.07
Structure-Function Relationships of Varying Microarchitecture and Surface Topography of 3D Printed Ti-6Al-4V Fabricated by Selective Laser Melting Cambre N. Kelly[1], Nathan T. Evans[2], Cameron W. Irvin[2], Savita Chapman[2], Ken Gall[1] and David L. Safranski[3]; [1]Duke University, Durham, North Carolina, United States; [2]Georgia Institute of Technology, Atlanta, Georgia, United States; [3]Medshape, Atlanta, Georgia, United States.

As the manufacturing of medical devices via additive manufacturing (3D Printing) continues to increase, better understanding of structure-function relationships of microarchitecture and surface topography are needed. Selective laser melting (SLM) of Ti-6Al-4V of implants with interconnected porosity have become widespread in orthopedic and other load bearing applications where porous structures encourage bony ingrowth and the stiffness of the implant can be tuned to reduce stress shielding. SLM allows high resolution control over design, including the ability to introduce porous surfaces or regions with spatial variations in pore size, shape, and connectivity. Investigation of the effect of construct microarchitectural design and surface topography on mechanical behavior of 3D printed Ti-6Al-4V showed a dominating effect of porosity on monotonic and fatigue behavior as compared to solid samples. Irrespective of surface treatment and resulting surface roughness, the fatigue strength of 3D printed samples containing bulk or surface porosity was approximately 20% to 25% of the ultimate tensile strength of identical printed porous material. For the vast range of microarchitectures which can be fabricated to tune construct porosity and resulting stiffness, creation of predictive models of fatigue behavior based on monotonic properties would allow for rapid iteration of design for devices with microarchitecture specified not only to patient anatomy, but also bone quality and loading profiles for tailored reduction of stress shielding.

4:45 PM BM01.02.08
3D Printed Functional and Biological Materials on Moving Freeform Surfaces Zhijie Zhu, Shuang-Zhuang Guo, Tessa Hirdler, Cindy Eide, Xiaoxiao Fan, Jakub Tolar and Michael McAlpine; University of Minnesota, Minneapolis, Minnesota, United States.

Conventional 3D printing technologies typically rely on open-loop, calibrate-then-print operation procedures. An alternative approach is adaptive 3D printing, which is a closed-loop method that combines real-time feedback control and direct ink writing of functional materials in order to fabricate devices on moving freeform surfaces. Here we demonstrate that the changes of states in the 3D printing workspace in terms of the geometries and motions of target surfaces can be perceived by an integrated robotic system aided by computer vision. A hybrid fabrication procedure combining 3D printing of electrical connects with automatic pick-and-placing of surface-mounted electronic components yielded functional electronic devices on a free-moving human hand. Using this same approach, cell-laden hydrogels were also printed on live mice, creating a model for future studies of wound-healing diseases. This adaptive 3D printing method may lead to new forms of smart manufacturing technologies for directly printed wearable devices on the body and for advanced medical treatments.

Monday Afternoon, November 26, 2018
8:00 PM - 10:00 PM
Hynes, Level 1, Hall B

BM01.03.01
Vascularized Heterogeneous Cardiac Tissue Network by a Direct Patterning with a 3D Bioprinter Jooran Kim and Jin Seok Lee; Sookmyung Women's University, Ithaca, New York, United States.

3D bioprinting is a widely used technology to dispense cell-laden biomaterials for rapid fabrication of complex 3D tissue constructs or artificial organs. To date, many studies have been investigated the deposition and patterning of cell-laden bioinks with a 3D bioprinter. However, the precise positioning, reasonable mechanical properties, and controlled cell distributions of constructs in 3D bioprinting system still remains technical challenges.
In this study, we developed heterogeneous cell-laden microchannel network using human umbilical vein endothelial cell-cardiomyocytes by a direct patterning with a 3D bioprinter. We fabricated 3D tissue constructs consisting of the core (human umbilical vein endothelial cell -laden collagen) and the sheath (cardiomyocytes-laden gelatin methacrylate). We could achieve a stable 3D multilayered core-sheath structure with the reasonable elastic modulus. This system also facilitated cell alignment and migration within each constructs and promoted vascular network with high cell viability. *Calcium imaging* was used to optically probe intracellular *calcium ion* signals during excitation-contraction coupling in *cardiomyocytes within 3D vascular network.*
This paper presents the new approach for fabricating vascularized heterogeneous 3D scaffolds and highly controlled deposition technique of bioinks. The cell-laden 3D constructs could be extended to serve as *in vitro* models for clinical cardiovascular disease researches and cardiovascular tissue regenerations.

BM01.03.02
Microarchitecture Developments for Periodontal Regeneration Using Periodontal Ligament Stem Cells Chan Ho Park; Department of Dental Biomaterials, Kyungpook National University, Daegu, Korea (the Republic of).

Periodontal ligament (PDL) with structural connectivity between cementum and alveolar bone tissues has key functions to optimize positional stabilities of teeth, transmit and absorb various stresses under masticatory/occlusal loading conditions, or promote tissue remodeling by mechanical stimulations. The oriented PDL formations with micron-scaled dimensions and calcified interfacial tissue formation with fibrous tissue anchorages are challenging in bone-ligament complex neogeneses. We investigated the 3-D microarchitectures, which can spatiotemporally organize PDL for fibrous connetive tissue formations.

The periodontal regeneration scaffolds had three compartmentalized microarchitectures; cementogenesis platform (~200um), PDL-guiding architectures, and bone scaffolds. After computer designs, 3-D printing system manufactured micron-scaled wax molds and biodegradable material (poly-ε-caprolactone; PCL) was casted into wax molds. The architectures were characterized with micro-CT, SEM, and confocal microscope for topographies. In in-vitro human PDL cell cultures and in-vivo subcutaneous model system, cell orientations or angulations were analyzed with nuclear morphologies and deformations.

In in-vitro experiments, microgrooves on scaffold architectures can angularly organize and geometrically control cell orientations for 7-day and 21-day cultivations. In particular, micro-patterns on microarchitectures can predictably and accurately control PDL cell orientations with high proliferations. Moreover, microgroove-patterned scaffolds promisingly provided more predictable cell alignments and cell orientations were significantly angular-controllable with statistical difference in in-vivo.

The additive manufacturing system can fundamentally manufacture various microarchitectures with micron-scaled patterns, which are designed in CAD. Based on topographical cues, PDL stem cells can be spatiotemporally regulated for fibrous connective tissue and mineralized tissue formations as well as scaffolds can control specific orientations of ligament cells and tissues. Therefore, the investigation demonstrates the compartmentalized microarchitectures facilitate to regenerate periodontal complexes which have structural similarities to natural periodontia.

BM01.03.03
3D Printing of Antimicrobial PLA/GO Nanocomposite Implants Vijayvedhan Jayanthiharikrishnan[2], Digvijay Shinde[1], Prabir Patra[1], Tae Won B. Kim[3], Sarosh Patel[4] and Tarek Sobh[4]; [1]Biomedical Engineering, University of Bridgeport, Bridgeport, Connecticut, United States; [2]Mechanical Engineering, University of Bridgeport, Bridgeport, Connecticut, United States; [3]Orthopaedic Oncology, Cooper University Health Care, Camden, New Jersey, United States; [4]Computer Science and Engineering, University of Bridgeport, Bridgeport, Connecticut, United States.

Graphene based medical implants have sparked widespread interests in the field of 3 D bioprinting due to its anti-microbial nature, very large aspect ratio associated with its 2D structures, and its ability to form functionally graded printable structures with polymers. Here we explore the 3 D printing of Poly L-lactic acid/Graphene oxide (PLA/GO) nano-composite for its anti-microbial property as bone implant and scaffold for bone cell proliferation. The nanocomposites were prepared through FDM (Fused deposition modelling) and our laboratory built LDM (Liquid deposition modelling) 3D printing. GO was dispersed in 1,4 dioxane using ultrasonication followed by dissolving PLA in the GO dispersions. LDM utilized the viscosity driven controlled stretching of the PLA/GO solution to print the solid structural form onto a heated bed that vaporizes the solvent and leaves behind the required structure. For the FDM process, the nano-composite was fed in the form of a filament. We utilized the dried and powdered form of the nano-composites to form the essential PLA/GO filaments structures using the filament extruder. We plan to integrate electrostatic jetting of PLA/GO nanocomposites through the micro nozzle using FDM system for attaining controlled porosity and microstructure, thereby closely mimicking the bone microenvironment. Anti-microbial activity of GO was measured with staphylococcus aureus, 60% reduction of bacterial growth was achieved.

BM01.03.04
A Multi-Structured 4D Stent with Large Deformation and Faster Temperature Response Je Hoon Oh[1], Wonjin Jo[2], Jongbeom Ghim[1], Myoung-Woon Moon[2] and Kyu Hwan Oh[1]; [1]Department of Materials Science and Engineering, Seoul National University, Seoul, Korea (the Republic of); [2]3D Printing Group, Computational Science Research Center, Korea Institute of Science and Technology, Seoul, Korea (the Republic of).

4D printing is a technology that makes the 3D printed structure deformed by responding the environmental stimuli such as water, temperature or UV. Especially, 4D printing has been actively studied for applications in medical devices such as a stent or a scaffold, which can be deformed under body fluid conditions to the intended shape. Even though the 4D structures transform properly under temperature or water, one may wait for longer duration to achieve its final configuration, which is not desired in medical level application.
In this presentation, we introduce a multi-structured 4D stent with large deformation and faster response to the small temperature change. A multi-structure

3D printing scheme is presented by printing a raster line in curved or coiled configuration by using a fused deposition modeling (FDM) type 3D printer with a shape memory polymer (SMP). The printed configurations in several curved shapes such as wavy or coiling shape were achieved by setting two main parameters of the interval between the printer bed and the nozzle as well as the filament flow rate. As increased the interval from 0.2~0.3 mm to 1~2 mm and the flow speed of 3 times faster than the normal printing conditions, the extruded raster line patterns were changed from straight to wavy or coiled. Since the thermoplastic SMP has a viscoelastic property, the configuration of the printed patterns was formed by a liquid rope-coiling effect that is a phenomenon based on buckling instability of viscoelastic material. It was also found that by tuning the deformation temperature below or above the glassy temperature, Tg, of the SMP, the curved line was deformed 1.5 times more than the straight line with much faster recovery rate. By alternating stacking layers printed with the curved line pattern over the straight line pattern, we fabricated a 4D stent structure with larger and faster response to warm temperature of our body fluid. It is expected that this 4D stent can alleviate the problem of blood vessel scarring during the insertion of the stent.

BM01.03.05
Three-Dimensional Printing of Magnetic Data Storage Structures Corey Breznak and Paris von Lockette; The Pennsylvania State University, University Park, Pennsylvania, United States.

Traditionally, barcodes encode data in a binary format by using groups of parallel lines with varying distance between them. Although a barcode is simple to fabricate, the complexity of the data that can be stored is limited. This research aims to design a method to encode more complex forms of data with higher information densities using 3-d printed magnetic structures. The work presented investigates the basic principles for 3-d magnetic patterning as a means of information storage, tagging, and/or part identification.
In this work, a structure is fabricated using proscribed patterns of magnetic and nonmagnetic regions. These structures are similar to present day barcodes, where the magnetic regions generate an external magnetic field, the *stray* field, that can be interrogated with a Hall effect or similar magnetic probe. The regions of magnetic and nonmagnetic field can be spaced apart at varying distance, or the thickness of each region can be varied, both of which affect the resolution of the magnetic *signature* of the stray field generated by the pattern. The patterns yield a magnetic equivalent to the binary optical nature of bar codes. However, unlike with the fabrication of barcodes, other processing variables influencing the stray field of the structure can be altered to add complexity to the data encoding. For example, by using hard magnetic powders such as barium hexaferrite, which consists of magnetically anisotropic plate-like particles, the magnetic regions can be oriented in arbitrary directions yielding more intricate stray fields, and consequently more complex magnetic signatures and higher information density.
This work first provides a proof of concept using neodymium magnetics inserted into a 3-d printed patterned structure to produce the stray field, which is characterized using a gaussmeter. The creation of this structure is the simplest proof of concept of a magnetic bar code. A second proof of concept 3-d prints both the nonmagnetic and magnetic parts of the structure using Protopasta magnetic filament (consisting of PLA with 45 wt.% iron particles) and standard ABS filament in a dual material FDM printer. Printing alternating regions of magnetic and nonmagnetic material form the now passive magnetic structure. A force gauge with a magnetic tip is used to determine the signature of the stray field resulting from the magnetic pattern. Finally, a computational model is developed to simulate stray field and resulting signature of the printed magnetic structures for comparison with experiments. Future work includes using magnetic filament consisting of hard magnetic particles such as barium hexaferrite, whose magnetic anisotropy facilitates complex magnetic alignments within the magnetic regions of the printed structure. Complex alignments allow increasingly sophisticated magnetic signatures, permitting an increase in the complexity of stored data, as well as an increase in information density.

BM01.03.06
3D Printing of Multifunctional Hydrogel Actuators for Biomedical Application Youzhou Yang, Jianfeng Zang, Hanchuan Tang and Yueying Yang; School of Optical and Electronic Information and Wuhan National Laboratory for Optoelectronics, Huazhong University of Science & Technology, Wuhan, China.

Hydrogels are wet and biocompatible and are used as scaffolds for tissue engineering, vehicles for drug delivery, actuators for optics and fluidics, and model extracellular matrices for biological studies. Three-dimensional (3D) printing methods, especially direct ink writing, have been wildly used, allowing the rapid and complex design and fabrication of hydrogels. Taking advantages of 3D printing, hydrogels with different properties can be easily manipulated. Lots of existing works have reported 3D printing of tough hydrogels for biomedical application. We employed responsive particles embedded in hydrogel precursor as the ink for the direct ink writing process. Subjected to the in situ external fields, the as-prepared precursor was printed in well-designed paths with on-demand properties. In this way, we prepared hydrogel actuators not only with notable mechanical property, but also with large deformation and programmable deformation mode. Moreover, using our strategy we demonstrate a soft active bandage that can rub the ointment on affected areas with a controllable manner, and an untethered gripper for medicine.

BM01.03.07
3D Printed Tissue Engineering Constructs Embedded with Electrospun Nanofiber Mats Using Various Biomaterials Suk-Hee Park, Young Won Kim, Han Bit Lee, Ye Ji Yoon and Yong Son; Korea Institute of Industrial Technology, Ansan-si, Korea (the Republic of).

Recently, the most important issues in the tissue engineering field are to mimic the natural extracellular matrix (ECM) and to manufacture the customized structures with patient-specific morphology. These are the critical factors for regulating functions of cultured cells and being used as the clinical-level applications. In these respects, nanoscale fabrication and 3D printing technologies have attracted much attention from the scientists and engineers in the relevant fields. In this presentation, we are going to introduce new hybrid bio-printed constructs, which consist of 3D printed parts and electrospun nanofiber mats. When it comes to electrospinning process, it could formulate not only randomly-network fibrous mat of it natural processed form but also highly-oriented fiber arrays. Depending on the fiber orientation, the cultured cells on the scaffolds could be modulated in terms of their biological functions and behaviors. The biomaterials for 3D printing could be classified to two groups; i) thermoplastic rigid polymers and ii) hydrogel-based bio-ink. When the thermoplastic biomaterials, for which polycaprolactone (PCL) was used in our studies, were combined with the electrospun mats, they were effectively supportive to sustain the morphologies of nanofiber mats. Since the supportive constructs were fabricated in the way of CAD/CAM-fashioned process, they were expected to overcome various obstacles in practical uses of the fragile nanofiber scaffold and meet the needs for clinical applications in specific surgeries. As for the hydrogel-based materials, which physically involved biologically-living cells, they were 3D-printed in the layer-by-layer manner. When the layering of bio-inks were processed with insertion of nanofiber mats between the hydrogel layers, the integrated constructs had enhanced properties in terms of structural resolution as well as mechanical toughness and stiffness. The improved performances of fiber-reinforced hydrogel constructs were expected to achieve the morphological and biophysical mimicry of native soft tissues. Taken together, the combinatory fabrication techniques involving 3D printing and electrospinning would allow for a wide range of feasible applications in the scaffold-based tissue engineering.

BM01.03.08
3D Printing and Post-Processing of PEEK Structures and Their Potential Applications to Bone Tissue Engineering Suk-Hee Park, Seong Je Park, Ji Eun Lee, Han Bit Lee, Jae Won Choi and Yong Son; Korea Institute of Industrial Technology, Ansan-si, Korea (the Republic of).

3D printing, CAD/CAM-based processing approach, has been considered as an effective tool to satisfy the many requirements in the trends of

manufacturing industry changing rapidly from mass production to mass customization. Fused deposition modeling (FDM), or material extrusion (ME) in ASTM terminology, has been one of the most commonly and widely used processes owing to its various advantages, such as low-cost material and hardware, simple processing mechanism, and wide material usage. Recently in the industry of 3D printing manufacturing fields, high-strength polymers with reliable performances have attracted much attention from the relevant researchers and engineers. In this presentation, we introduce the FDM-based 3D printing and the post-processing of polyetheretherketone (PEEK), which is one of the representative super engineering polymers. PEEK is the material as difficult to be processed as its high mechanical performance. We first developed custom-made 3D printing system, which was able to deal with the engineering plastic materials. Specifically, the 3D printer included several thermostatic control systems to modulate the environmental conditions of printing, such as the temperature of the surrounding air in the printing chamber. The use of temperature-controlled conditions in not only the nozzle but also in the chamber instead of room temperature was necessary in order to stably print the engineering polymers without defects or delamination in the final product. We studied the optimized parameters for the stable printing process, such as nozzle/chamber temperature, nozzle speed, printing tool-path, and extruding rate. With these process parameters, the maximum tensile strength of the resulting PEEK parts was achieved at approximately 80% of the bulk material property. In addition, we studied the effects of heat treatment on the mechanical property and crystallinity. The heat-based post-processing could improve the tensile strength up to 90% of the bulk material property, which was comparable to mechanical properties of bone. Based on the optimized conditions from process design to post-process, we tested the feasibility of manufacturing of orthopedic products and bone implants.

BM01.03.09

Thiol-Yne Photo-Click Chemistry—Towards Biocompatible and Tough Photopolymers for 3D Printing Delara Hartmann, Andreas Oesterreicher and Thomas Griesser; Institute of Chemistry of Polymeric Materials & Christian Doppler Laboratory for Functional and Polymer Based Ink-Jet Inks, Montanuniversität Leoben, Leoben, Austria.

Recent years have seen an increasing interest in the development of photo-polymerizable monomers providing low cytotoxicity and high impact resistance in their cured state. This fact can mainly be explained by the rapid progress in UV based additive manufacturing technologies such as stereolithography, digital light processing or 3D ink-jet printing which enables the fast, accurate and individual fabrication of biocompatible structures for hard tissue engineering. In this contribution, the versatility of the thiol-yne photo-click reaction for the fabrication of biocompatible photopolymers is shown at the example of tailor-made bi- and multifunctional alkyne and thiol monomers. This reaction leads to highly uniform polymeric networks exhibiting a sharp and defined thermal glass transition together with outstanding impact resistance [1] making these polymers interesting for challenging applications such as medical implants. A particular focus was set on the development of low odour thiols as promising alternatives to commercially available mercapto propionic acid derivates. Thiol-yne resins based on these monomers provide both, high reactivities comparable to those of acrylates and mechanical properties appropriate for the fabrication of medical devices in their cured state. The herein described monomers pave the way towards the fabrication of tailor-made photopolymers suitable for hard tissue engineering.

[1] Thiol-X Chemistries in Polymer and Materials Science Andrew B. Lowe and Christopher N. Bowman Editors, Royal Society of Chemistry, Cambridge 2013.

BM01.03.11

***In Vitro* Perforation of the Round Window Membrane via Direct 3D Printed Microneedles** Aykut Aksit[1], Wenbin Wang[1], Daniel N. Arteaga[2], Miguel Arriaga[1], Xun Wang[1], Hirobumi Watanabe[1], Karen Kasza[1], Anil K. Lalwani[2, 1] and Jeffrey W. Kysar[1, 2]; [1]Mechanical Engineering, Columbia University, New York, New York, United States; [2]Otolaryngology, Columbia University, New York, New York, United States.

We report the use of Two-Photon-Polymerization (2PP) lithography to manufacture precision microneedles for the purpose of intracochlear drug delivery.

The cochlea, or inner ear, is a space fully enclosed within the temporal bone of the skull, except for two membrane-covered portals connecting it to the middle ear space. One of these portals is the round window, which is covered by the Round Window Membrane (RWM). A longstanding clinical goal is to deliver therapeutics into the cochlea to treat a plethora of auditory and vestibular disorders. Standard of care for several difficult to treat diseases calls for injection of a therapeutic substance through the tympanic membrane into the middle ear space, after which a portion of the substance diffuses across the RWM into the cochlea. The efficacy of this technique is limited by an inconsistent rate of molecular transport across the RWM.

A solution to this problem involves the introduction of one or more microscopic perforations through the RWM to enhance the rate and reliability of diffusive transport. Hence, ultra-sharp polymer microneedles specifically designed to perforate the RWM are made using direct 3D printing via 2PP lithography.

The needles are 3D printed, developed and mounted on sterile 23 Gauge blunt syringe tips for practical use. The needles are then used to perforate freshly excised guinea pig membranes. The perforation force is collected, and the resulting holes are analyzed via confocal microscopy, which has the benefit of visualizing the fibers that give the RWM its mechanical properties.

The microneedle has tip radius of curvature of 500 nm and shank radius of 50 μm. It perforates the RWM with a mean force of 1.19 mN. The resulting perforations performed in-vitro are lens-shaped with major axis equal to the microneedle shank diameter and minor axis about 25% of the major axis, with mean area 1670 μm^2. The major axis is aligned with the direction of the connective fibers within the RWM. The fibers were separated along their axes without ripping or tearing of the RWM suggesting the main failure mechanism to be fiber-to-fiber decohesion.

The needles are imaged using a Scanning Electron Microscope (SEM) after use, and it is seen that the tips of these microneedles are bent to some extent, limiting their reusability. Therefore, radii of curvature of the tips are systematically changed in order to find an optimal shape for the needles with the purpose of enhancing the mechanical strength and preventing blunting.

These results establish a foundation for the use of 2PP as a means to fabricate microneedles to perforate the RWM and other similar membranes requiring precision manufacturing of complex geometries. The small perforation area along with fiber-to-fiber decohesion are promising indicators that the perforations would heal readily following in-vivo experiments. An optimal needle geometry is currently being researched for the purpose of RWM perforation.

BM01.03.12

Study of Fusion in 3D Printing of PLA/Graphene Composites Yuval Shmueli[1], Xiaoxin Wang[2], Steven Wu[3], Derek Zheng[4], Lan Jiang[5], Caroline Zeng[6], Dilip Gersappe[1], Miriam Rafailovich[1], Matthew York[7] and Zhuolin Xia[1]; [1]Stony Brook University, Stony Brook, New York, United States; [2]Padua Franciscan High School, Parma, Ohio, United States; [3]Clear Lake High School, Houston, Texas, United States; [4]Monta Vista High School, Cupertino, California, United States; [5]University High School, Irvine, California, United States; [6]Wayzata High School, Plymouth, Minnesota, United States; [7]Case Western Reserve University, Cleveland, Ohio, United States.

Fused deposition modeling (FDM) printing is an emerging 3D printing technology in which thermoplastic filaments are extruded and deposited in certain manner according to computer input design. Polylactic acid (PLA) is a common biodegradable polymer being used in FDM printing and has great potential to be the main component in future biomedical devices. However, since it has poor thermal conductivity properties it is often leads to failing interfilaments fusion and hence reduces the overall product mechanical and functional properties.
In this work we incorporate graphene nano platelets (GNPs) to examine their effect on the thermal profiles during printing and the resulted mechanical properties. We studied the conditions of different nozzle temperatures and varied the distance between adjacent filaments and between deposited layers by adjusting the Gcode input to the printer. We used high resolution infra-red thermal camera to monitor the temperatures at the printing process. Then we correlated these profiles with (scanning electron microscopy) SEM analysis and dynamic mechanical analysis (DMA) properties of the printed structure. We also used microbeam small angle X-ray scattering (SAXS) measurements to study the macrostructure of the printed filaments as function of the radial position from the interfilaments interface to the filaments core. In addition, we modeled the temperature profiles and the flow mechanics of GNPs flow in the polymer matrix using Lattice Boltzmann Modeling (LBM).
We show the great effect of GNPs inclusion on the fusion process while printing and how it affects the resulted properties and can be used in future potential applications. The experimental results combined with the modeling results enable us to present the optimal conditions and composition to improve the fusion and hence the strength of the printed structures.
We Acknowledge support from the National Science Foundation (Inspire Award No. 1344267) and The Morin Foundation Trust.

BM01.03.13
Self-Folding of 3D Printed Shape Memory Polymers with High Degree of Shrinkage Akihiro Nojiri[1,3], Eiji Iwase[3] and Michinao Hashimoto[1,2]; [1]Digital Manufacturing and Design Centre, Singapore University of Technology and Design, Singapore, Singapore; [2]Pillar of Engineering Product Development, Singapore University of Technology and Design, Singapore, Singapore; [3]Department of Applied Mechanics, Waseda University, Tokyo, Japan.

Self-folding is a strategy to fabricate 3D shapes from planar sheets. 3D printed planar structures have been demonstrated to form 3D shapes via self-folding due to shrinkage of polymers. The degree of polymer shrinkage due to heat is typically low, and achievable 3D shapes have been limited in size and complexity. In this work, we demonstrated self-folding of a polyurethane-based shape memory polymer (SMP) printed by a fused deposition modeling (FDM) 3D printer. SMP transfers from rubber states to glass states by the change of temperature, and this phase transition is typically used to memorize specific shapes. We used this characteristic not for shape memory but for self-folding. When SMP is printed in rubber states by FDM, internal stress is introduced to the printed SMP structures on the build plate. Above its glass transition temperature (T_g), the SMP structure releases internal stress and shrinks. This shrinking is due to the phase transition and the release of internal stress. We demonstrated that the 2D structures consisting of 3D printed SMP were readily transformed to the 3D structures through this mechanism. We achieved to control the degree of shrinking by varying (1) printing temperature, (2) FDM nozzle speed and (3) multilayer design of the planar sheet. These parameters allowed defining bending angles and directions of resulting 3D structures (such as valley folds, mountain folds and their combinations) due to the difference in the internal stress between adjacent layers of SMP printed under different conditions. The folding angle of 3D printed SMP sheets was precisely controlled between -180° to 180° by changing the printing parameters. The developed principles allowed fabricating complex 3D shapes ranging from a dice to a crane.

We highlight that the polyurethane-based SMP patterned by 3D FDM printer exhibits high degree of shrinking. In our demonstration, the radius of curvature of the resulting structures was as small as 1.8 mm, which was one order smaller than the corresponding structures consisting of 3D printed polylactic acid (PLA). As the result, fabrication of complex 3D structures on the order of millimeters was readily achieved. The use of SMP added an advantage; the 3D structures after shrinking were memorized. The obtained structures were recovered above glass transition temperature (T_g) multiple times after manually deformed. Overall, we demonstrated fabrication of the 3D structures with shape memory via programmed shrinkage of 2D structures printed by FDM. Unlike previous demonstrations, our design principle relied on the phase transition of SMP that offered high degree of shrinkage, which permitted fabrication of complex structures with the combination of anisotropic folds and convex/concave features.

BM01.03.14
The Effect of Surface Roughness of 3D-Printed PLA Scaffolds on the Cell Attachment, Proliferation and Differentiation of Dental Pulp Stem Cells Kuan-Che Feng[1], Wenqi Zhao[2], Benjamin Chang[4], Bhuvna Murthy[7], Ethan Ho[5], Rushi Patel[3], Antony Deluxe[6], Marcia Simon[1] and Miriam Rafailovich[1]; [1]Stony Brook University, Stony Brook, New York, United States; [2]Milton Academy, Milton, Massachusetts, United States; [3]Herricks High School, New Hyde Park, New York, United States; [4]Woodbridge High School, Irvine, California, United States; [5]Northfield Mount Hermon School, Gill, Massachusetts, United States; [6]Wheatley High School, Old Westbury, New York, United States; [7]Huron High School, Ann Arbor, Michigan, United States.

Three-dimensional (3D) printed scaffolds provide a promising approach in the field of tissue-engineering for its ability to precisely control scaffold architecture at the micron-scale. Previous studies have shown that topographical features on the surface of scaffolds can determine the efficiency of cell attachment and proliferation; yet, little is known about their effect on cellular differentiation. Here, we aimed at investigating the influence of the surface roughness of 3D-printed polylactic acid (PLA) scaffolds on cellular response.
Sub-micron scale roughness on 3D FDM printed structures can result from “shark skin” formation, which were shown to be a result of slip-stick instabilities during fiber extrusion when attractive forces were present between the polymer and the extrusion nozzle. Here we first present a quantitative analysis of shark skin formation in PLA filaments as a function of the printing speed and nozzle temperature, where the roughness was characterized using atomic force microscopy. We then plated dental pulp stem cells on scaffolds printed at different speeds and with different roughness amplitude. Control samples were produced by molding PLA between Kapton sheets, minimizing the surface roughness. In all cases the extend of biomineralization in the absence of dexamethasone, was higher on the printed substrates, than equivalent PLA substrates produced via molding. qRT-PCR of marker genes (ALP, OCN, DSPP) demonstrated significant differences in the cell response and differentiation lineage between molded and printed substrates. Differences were also observed between samples with different sharkskin amplitude and underscoring the influence of surface morphology on differentiation outcome. These results illustrate the the challenges in production of reproducible materials for tissue culture when 3D printing technologies are employed.

BM01.03.15
Study of Hexagonal Boron Nitride (hBN) in Fused Deposition Modelling (FDM) 3D Printing Won Il Lee[1], Yuval Shmueli[2], Young-Soo Seo[1] and Miriam Rafailovich[2]; [1]Nanotechnology and Advanced Materials Engineering, Sejong University, Seoul, Korea (the Republic of); [2]Materials science and chemical engineering, Stony Brook University, The State University of New York, Stony Brook, New York, United States.

Hexagonal boron nitride (hBN) is two dimensional ceramic material with excellent chemical, physical and mechanical properties. Although it is an electrical insulator, it has high thermal conductivity, thermal stability and also it is not toxic and biocompatible. Therefore, this innovative material has the potential of being used in variety of applications.
We incorporated hBN in a polylactic acid (PLA) and polypropylene (PP) matrix in 5 and 10 wt% to study the effect in the 3D printing process and for potential thermal management applications. Dynamic mechanical analysis measurements showed improvement in the mechanical properties and enhance

ductility of the printed structure. The presence of the nanoparticles leads to better printing resolution and filaments fusion due to the confinement in the extrusion in the printing process. The hBN did not prevent and interfere with the polymer chains diffusion and affect the filaments fusion process. We measured thermal conductivity properties using infrared thermal camera and compared different printing orientations and molded samples. We saw that addition of hBN improve the thermal conductivity by approximately 10 % comparing to the pure polymer and that the heat conductance is enhanced with the filament orientation relatively to the molded structure with no orientation. We conducted in-situ WAXS measurements simultaneously with high resolution infrared thermal imaging to study the crystallization forming in the matrix. The results showed that addition of hBN did not cause and effect in the crystalline formation comparing to the pure polymer. In the future we will introduce boron nitride nanotubes (BNNTs) into the polymeric matrix to examine their effect on the printed matrix. We will also perform chemical surface modification of both types of the nanoparticles to examine if it will improve the compatibility between the particles and the polymer matrix and by that improving even more the mechanical and conductance properties.

BM01.03.16
Characterization of Antibiofilm Activity of Silver Nanoparticles Synthesized *In Situ* on 3D Printed Polylactic Acid Scaffolds Michael Cuiffo[1], Stephen Walker[1], Yuval Shmueli[1], Fan Yang[1], Anastasia Popova[2], Isha Brahmbhatt[3], Kuan-Che Feng[1], Adriana Pinkas-Sarafova[1] and Miriam Rafailovich[1]; [1]Stony Brook University, Stony Brook, New York, United States; [2]Hackley School, Terrytown, New York, United States; [3]Ardsley High School, Ardsley, New York, United States.

Biofilms are bacterial communities highly resistant to antibiotics, biocidal agents, and human immune system. Microorganisms that grow on medical devices form biofilms, and once formed they cannot be completely removed. The need for prevention of biofilm formation and growth leads to different approaches for the modification of materials used for medical devices. Silver nanoparticles, with known antimicrobial properties, have been used to modify polymers. Since silver nanoparticles express their antimicrobial properties by releasing silver ions, when mixed with a polymer before device preparation, the ion release level will be limited by the degradation of the polymer. Polylactic acid (PLA) is a biodegradable and FDA-approved polymer for use in numerous resorbable surgical devices. The Brunst method has recently been patented as an accessible and inexpensive method for in situ synthesis of silver nanoparticles as a coating on PLA. This coating can promote a rapid and prolonged release of silver ions able to inhibit biofilm formation. PLA scaffolds were printed using two 3D printers, a Makerbot Replicator 2X and Ultimaker 2 Extended+, with corresponding filaments, and characterized with a laser microscope and FTIR. The Brunst method was used with two concentrations of AgNO3 (0.1M and 0.01M) and 0.001M NaBH4 for the in situ deposition of silver nanoparticles. We tested the ability of the PLA-AgNO3 scaffolds to inhibit biofilm formation and growth against two strains of bacteria, Staphylococcus aureus (gram-positive) and Escherichia coli (gram-negative). The PLA-AgNO3 scaffolds were also evaluated for the interaction of the modified surfaces with Dental Pulp Stem cells (DPSCs).
We found significant differences in surface chemistry and roughness of scaffolds produced by different printers. PLA scaffolds coated with 0.1 M nanoparticle showed significantly smaller size of the biofilms for both microorganisms than the one with 0.01 M nanoparticles. Bacterial adhesion and biofilm formation was higher on Ultimaker 2 Extended+ printed scaffolds for both strains. The DPSCs had a similar correlation and attached better to the Ultimaker samples in comparison to the Makerbot samples.

SESSION BM01.04: 3D Printing of Passive and Active Medical Devices III
Session Chairs: James Friend and Ken Gall
Tuesday Morning, November 27, 2018
Sheraton, 2nd Floor, Liberty B

8:00 AM *BM01.04.01
3D Printing of Synthetic Materials for Structural Implants Ken Gall; Duke University, Durham, North Carolina, United States.

In this talk I will overview the 3D printing of biomedical implants from synthetic materials, including soft polymers (PCU), hard polymers (PEEK), and metals (Titanium). We will focus on basic materials science regarding the mechanical properties of the printed structures and relationships between structural porosity and resulting mechanical properties. Examples of how the basic science research has supported translation into various implants will be provided. Discussion will also center on regulatory paths for various printed implants, and the opportunities new materials and new printign methods could play in the future of medicine.

8:30 AM BM01.04.02
Multifunctional 3D Printed Implant/Biomaterial Surfaces Richard Jackson[1], Stephen Patrick[1] and Joe Bear[2, 1]; [1]University College London, London, United Kingdom; [2]Kingston University, London, United Kingdom.

Stem cell proliferation, adhesion and differentiation on implants and biomaterial substrates are affected by the three dimensional morphology, topology, and interconnectivity of their immediate environment. This in turn means that the chemistry of, and the biochemistry at the material surface is of paramount importance. For example, the hydrophobicity of polymer objects means initial cell adhesion is insufficient in many cases which is of critical importance in bone implants. In this paper we show that by 3D printing polymers using Selective Laser Sintering (SLS) it possible to control porosity and use that porosity to chemically modify the materials properties of the implant.

We present results on the synthesis of nylon-12 scaffolds by 3D printing and demonstrate their versatility as matrices for cell growth, differentiation, and biomineral formation. We demonstrate that the porous nature of the printed parts makes them ideal for the direct incorporation of preformed nanomaterials or material precursors, leading to nanocomposites with very different
properties, such as tunable hydrophobicity, enabling conducive or non-conducive environments for cell growth.

Additives such as those derived from sources such as tetraethyl orthosilicate applied at a low temperature promote successful cell growth, due partly to the high surface area of the porous matrix. The incorporation of pre-synthesized nanomaterials such as iron oxide nanoparticles
led to a material that showed rapid heating in response to an applied ac magnetic field, showing promise for the control of gene expression and chemical-free sterilization. These methods also avoid using altered polymer feedstocks and contaminating or even damaging commonly used selective laser sintering printers, as well as being compatible with each other and interchangeable with each other in the modification process.

We believe this technique for chemically treating 3D printed matrices has great potential for use in addressing current issues surrounding bone grafting, implants, and skeletal repair, and a wide variety of possible incorporated material combinations could impact many other areas.

8:45 AM BM01.04.03
3D Printing of Silk Fibroin/Calcium Phosphate for Bone Regeneration Vincent Fitzpatrick[1], Jin Guo[1], Chunmei Li[1], Sagvan Balata[2], Alekya Karpurapu[2], Michael Strunk[2] and David Kaplan[1]; [1]Tufts University, Medford, Massachusetts, United States; [2]Zimmer ETEX, Cambridge, Massachusetts, United States.

Non-union bone fractures are a major issue in orthopedic surgery, from diagnosis to healthcare costs, and more importantly regarding treatment-related complications (Nandra et al. 2016). While autografts are the gold standard for non-union fracture repair, they can be associated to pathological symptoms at the donor site, including pain, risk of infection, blood loss, and increased operative time (Silber et al., 2003; Sasso et al., 2005). These fractures are also limited by the amount of donor material available, which is usually harvested on the iliac crest. Allografts, on the other hand, alleviate donor site issues and are available in larger quantities, but do not provide the same quality of patient outcomes as autografts, especially in terms of osteoinductivity (Lohmann et al., 2000; Bostrom et al., 2005). Therefore, there is a need to find alternative solutions to both techniques, using new biomaterials and a tissue engineering approach. This includes the use of synthetic bone fillers such as calcium phosphate (CP)-based materials and biological factors like growth factors or miRNAs to improve bone regeneration. However, these bone fillers do not allow refined control of the geometry of the graft, and seldom offer adequate porosity for rapid colonization of the implant by cells, efficient exchange of nutrients and timing of implant degradation with replacement by newly synthesized bone. Additive manufacturing techniques like 3D printing provide tight control of geometry and porosity, and are therefore of interest for non-union bone fracture repair. These techniques include pre-fabricated and fully set CP scaffolds, which reduce operative time and prevent the risk of setting failures.
In this study we developed a slow setting reactive CP-based bioink, using silk fibroin as a binder, and used this bioink to generate porous 3D constructs for bone regeneration. These structures were biocompatible and presented adequate mechanical properties in physiological conditions, and their shape was well-controlled even for complex geometries. Finally, their porosity could be precisely tuned to be within a range compatible with efficient osteogenesis (Karageorgiou & Kaplan, 2005).
From a biological perspective, our 3D constructs induced osteoblastic differentiation in vitro, and we observed a rapid cell response and efficient neo-osteogenesis when combined with biological factors, namely bone morphogenetic protein 2 (BMP-2) and miRNA-214 inhibitor. Furthermore, the materials could be loaded with antibiotics, providing an encouraging solution to prevent infection of non-union fractures, which has been associated with a myriad of symptoms in patients, including deformities and limb-length inequalities (Jain & Sinha, 2005).
Overall, our 3D-printed CP/silk fibroin constructs offer an exciting research avenue in patient-specific treatment of non-union bone fractures, while reducing the risk of negative side effects and eliminating the need for donor site surgery.

9:00 AM BM01.04.04
3D Printing of Spatially Patterned Magnetically Responsive Hydrogels Patricia Monks[1, 2], Robert Murphy[1], Shane Clerkin[3], John Crean[3], Dermot F. Brougham[2] and Andreas Heise[1]; [1]Department of Chemistry, Royal College of Surgeons in Ireland, Dublin, Ireland; [2]School of Chemistry, University College Dublin, Dublin, Ireland; [3]School of Biomolecular and Biomedical Science, University College Dublin, Dublin, Ireland.

Hydrogels, baring similarities to the extracellular matrix and having excellent water retention capabilities, have emerged as a biocompatible material for applications in tissue engineering and as drug delivery devices. Next generation gel applications include as “bio-inks” for 3D printed bio-materials for cell scaffolding and ultimately organ printing[1]. To realise this potential, it is critical to finely control the deposition of the hydrogel in the printing process to produce high fidelity structures[2].

Due to their small size, superparamagnetic iron oxide nanoparticles offer distinguishable advantages from bulk, arising from rapid reorientation of their moments. This results in rapid heating in AC magnetic fields and in attractive forces in permanent magnetic fields irrespective of initial moment orientation. The integration of magnetic nanoparticles into hydrogels has the potential to alter the properties of the original material and create a hydrogel matrix that can be manipulated in situ using magnetic fields.

We are working towards the incorporation of magnetic nanoparticles in the fabrication of novel 3D printable architectures which allows for unique applications as stimulus responsive materials. Specifically, high resolution printing (~100 μm) of these structures, will facilitate control over magnetic response with cellular resolution. The potential for high through-put with printed gel bed arrays also opens up new screening possibilities[3].

An open-source 3D printer was successfully built and modified to allow extrusion of hydrogels with parameters of moderate temperature and pressure that will support cell viability. Magnetic nanoparticles were synthesised, stabilised and incorporated homogenously into a printable hydrogel network with concentrations of up to 120 mM Fe which yields a temperature rise of 15°C in bulk.

A star copolypeptide based ink, which spontaneously forms hydrogels through hydrophobic interactions, allows for rapid prototyping enabling the fabrication of defined intricate microstructures[4]. The chemical design allows the bulk phase of the hydrogel to remain intact after application of shear (during extrusion) due to its self-recovery behaviour. Here we demonstrate; (i) reproducible and robust extrusion of a polypeptide hydrogel network; (ii) spatial patterning of thermally active components and drug loading, and; (iii) in situ manipulation using applied magnetic fields with high resolution thermal mapping. The technical development of the responsive nanocomposite gels and preliminary results showing cell specification will also be described.

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9:15 AM BM01.04.05
A 3D Microdevice for the Isolation of Cancer-Associated Circulating Cells Within the Bloodstream Elise Bou[1], Kayum Jiménez Zenteno[1], Aurore Estève[1], David Bourrier[1], Christophe Vieu[1], Bernard Malavaud[2] and Aline Cerf[1]; [1]LAAS-CNRS, Toulouse, France; [2]Department of Urology, Toulouse Cancer Institute, Toulouse, France.

This work introduces an engineered 3D microdevice for the capture of circulating tumor cells (CTCs) directly from the bloodstream. Our innovation relies on an intravascular label-free device enabling the trapping of CTCs based solely on their physical characteristics [1].

CTCs are tumor cells detaching from a primary tumor to reach the bloodstream. They represent a reliable tool for diagnostic and prognostic purposes as an alternative to solid biopsies [2]. Therefore, many technologies have been developed to isolate CTCs from blood. *In vitro* systems are limited by the volume

of blood that can be analyzed, manipulation factors including blood sampling and preprocessing, as well as cellular exposure to high pressure levels [3]. *In vivo* approaches could offer the advantages of probing higher volumes of blood, increasing the interrogation frequency, and preserving the viability of collected cells. Thus, our approach combines both the advantages of a label-free and an *in vivo* isolation of CTCs.

Our capture devices are designed to be inserted into the human forearm vein through a conventional medical catheter. They are composed of a microfilter and a guiding strip. Both parts are fabricated in Nickel through a two-step process using photolithography and electrodeposition. The first step consists in the fabrication of the filtering membrane containing uniformly distributed micrometric pores. In a second step, the walls of the microfilter and the guiding strip are produced. After fabrication, microfilter are mounted onto the guiding strips in order to obtain 3D-like devices perpendicular to the incoming flow.

The prototype has been validated *in vitro* using a fluidic platform mimicking *in vivo* conditions of blood pressure and flow velocity. We succeeded in capturing human prostate cancer cells (PC3) spiked into whole blood in a few minutes, with no blood preprocessing required and with extremely low contamination levels. We also succeeded in capturing cells injected into the bloodstream of a rat model confirming its robustness to withstand *in vivo* conditions as a further step towards its application in clinical routine. Captured cells can be easily characterized and collected for further functional and downstream analysis. This minimally invasive technology could offer high-quality information to physicians and serve as a tool for personalized therapeutic follow-up in clinical routine.

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9:30 AM BREAK

10:00 AM BM01.04.06
3D Printing Scaffolds Based on Calcium Phosphate and Glass Slurries Optimized Using Statistical Experimental Design Carlos Paucar[1], Natalia Jaramillo[1], Claudia P. Garcia[1], Alejandro Pelaez[2], Sebastian Restrepo[1], Niza Otero[1] and Ana Moreno[1]; [1]National University of Colombia, Medellín, Colombia; [2]Universidad Cooperativa, Medellin, Colombia.

Wound healing in oral tissues (i.e: gingiva and bone) exhibit a complex equilibrium between eukaryotic and prokaryotic cells. Ceramic 3D printing allows rapid prototyping of scaffold with controlled features as shapes, porosity, size, connectivity and differential density layers to mimic bone structure. However, bulk are strong related with chemical composition and thermal processing to obtain degradability and bioactivity. The slurry plasticity affects the size layer and mechanical properties during “green” state. Experimental design approach implies the use of statistical tools that allow the multivariate analysis with the minimum number of experiments to mixtures.

The aim was to optimize a ceramic paste based on calcium phosphate and bioglass to produce 3D printing scaffolds for dentistry. A full factorial statistical design was conducted to optimize the plasticity of calcium phosphate and bioglass slurry. Plasticity ad-hoc model included variables defined as particle size and ratio calcium phosphate/bioglass. Sintering was conducted at 950°C/3h. Scaffold characterization was conducted using XRD, FTIR and SEM. Biological characterization includes bacterial adhesion of S. mutans as oral bacterial model.
Optimized Surface response of plasticity was found using 70 wt% calcium phosphates, 30wt% bioglass. Successful scaffolds were produced by 3D printing- They shown a Schwarz Diamond shape, interconnected pores, wide size pore distribution and minimum thickness layer (~200 µm). XRD diffractogram shows presence of β-TCP and amorphous glass. S. mutans shown a reduced adherence to 3D printing scaffold compared to control. Synergy between 3D printing, material processing and Statistical Experimental Design can be considered as robust methodology to develop new scaffolds with potential use in dental applications.

10:15 AM BM01.04.07
Preparation and Application of Functional Polymeric Nanoparticles Based on Poly(methacrylate)s Stephanie Schubert, Turgay Yildirim and Paul Klemm; Friedrich-Schiller-University Jena, Jena, Germany.

The development of functional polymeric nanoparticles is essential for breakthroughs in nanomedicine. By tuning the polymer characteristics and subsequently applying optimized formulations for the procedure of nanoparticles, tailored nanoparticles with varying release properties, degradation behavior, targeting groups and size distributions can be developed. For the preparation of polymeric nanoparticles, nanoprecipitation is a good choice since it is a facile, mild, and low energy input process. In combination with high-throughput devices such as microfluidics, pipetting robots, inkjet printers, and automated analytical instrumentation, the abilities of nanoprecipitation can broaden tremendously with significant effects on new applications. Selected examples in the field of gene- and drug delivery vehicles will be presented, *e.g.*dual pH-value and redox responsive nanoparticles and polymersomes based on a methacrylate copolymer library [1,2,3]. The functionalization of the polymers with Raman active targeting structures enables the label-free visualization of cell uptake processes [4].

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10:30 AM BM01.04.08
3D Printed Ultra-High Density, High Aspect Ratio Microelectrode Arrays for Next-Generation Neural Probes and Drug Delivery Applications Mohammad S. Saleh, Mark Nicholas, Rriddhiman Bezbaruah, Jay Reddy, Maysam Chamanzar, Eric Yttri and Rahul Panat; Carnegie Mellon University, Pittsburgh, Pennsylvania, United States.

In this research, we will demonstrate for the first time the use of 3D printing to realize customizable high-throughput ultra-high density arrays of 3D microelectrode probes for biological applications. The electrode density in the probe is several thousand per square centimeter; an order of magnitude improvement over the current state of the art. The proposed probes are critical in achieving a better understanding of biological systems such as the dense

neural networks in a brain or enabling the next-generation neural interface for neural prosthetics. The electrodes of the probes are fabricated in a layer by layer fashion from a dense aerosol stream of silver nanoparticle ink from an aerosol-jet 3D printer. Probes with extremely high aspect ratios (up to 30:1 height to diameter ratio or more) are achieved with heights exceeding 2 mm. Flexibility and versatility of this technique are demonstrated by the realization of a variety of microelectrodes and tip geometries. Further, we have studied and optimized the electrode metallurgy; mechanical properties; electrical isolation and response; adhesion to soft and hard substrates; and biocompatibility. As a result of this investigations, a complete process parameter control was developed to adjust the mechanical properties of the electrode arrays over a wide range of strong-brittle and ductile-tough behavior. Further, we also report the buckling behavior of high aspect ratio electrodes under compression and their correlation with materials grain size have been reported.

10:45 AM BM01.04.09
Robust Hydrogel-Solid Hybrids in Biomedical Applications Hyunwoo Yuk and Xuanhe Zhao; Department of Mechanical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts, United States.

Taking advantage of superior biocompatibility and tissue-like physical and mechanical properties, hydrogels have found a widespread usage in various sectors of biomedicine. Despite their unique advantages, integration of hydrogels in biomedical applications typically suffers from several technical challenges. Particularly, weak and unstable assembly between hydrogels and other solids (e.g., inorganic materials, polymers, and tissues) significantly limits the realization of functional hydrogel-based biomedical applications. Recently, we have developed a range of technologies to achieve robust interfacial bonding between hydrogels and other solids, enabling the new class of robust hydrogel-solid hybrids. In this talk, taking advantage of this new developments, we will discuss various examples of applicational translation of robust hydrogel-solid hybrids in biomedicine. We will first cover general mechanisms for robust wet adhesion of hydrogels followed by specific example applications, including hydrogel hybrid neural probes for long-term neural sensing and modulation, hydrogel skins for diverse polymers with arbitrary shapes, and tissue adhesives for flexible devices.

11:00 AM BM01.04.10
pH-Switched Rapid Shape Morphing of 3D Printed Polyrotaxane Monoliths Qianming Lin, Longyu Li, Miao Tang, Xisen Hou and Chenfeng Ke; Department of Chemistry, Dartmouth College, Hanover, New Hampshire, United States.

Designing shape morphing[1] materials featuring dynamic molecular motions in response to external stimuli will enable the development of next generation smart materials. Traditional shape morphing design relies on (1) engineering the (de)hydration process and (2) programming the heat-induced shape changing polymers. Incorporating smart molecular systems and controlling their dynamic features across the nano-to-macroscale, in combination with the state-of-the-art 3D printing technology could enable the development of fast-responsive 3D printing materials.[2-3] In this presentation, we report the synthesis of a polypseudorotaxane-based 3D printing inks that consists of α-cyclodextrins and dimethacrylamide polyethylene glycols. After 3D printing and photo-crosslinking, the mechanically interlocked rings in the polyrotaxane network can be switched between stationary and randomly shuttling states through the (de)protonation their hydroxyl groups. This nanoscale ring motion is amplified in a synchronized manner, resulting in fast shape morphing macroscopically. Copolymerizing acrylate monomers with the polypseudorotaxanes affords a copolymer network, which respond to pH and ionic strength.[4] We also performed dual-material 3D printing using two hydrogel inks mentioned above, and fabricated a hybrid monolith with multiple shapes macroscopically. Our work demonstrates that, by switching the ring motions in a molecular interlocked architecture in combination with pH/ionic-responsive moieties, a fine spatiotemporal control of the hybrid 3D printed object's shape morphing process has been achieved.
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11:15 AM BM01.04.11
Development of a Ceramic—Polymer Biofilament to Obtain Scaffolds Using Additive Manufacture Claudia P. Garcia[1], Paula A. Nevado[1], Alex Lopera[1, 2], Marlon Rincon Fulla[1, 2], Juan Luis Palacio[2, 1], Maria A. Zaghete[3], Glenda Biasotto[3], Juan Rivera[2], Hugo Estupiñan[4] and Carlos Paucar[5]; [1]Física, Universidad Nacional de Colombia sede Medellin, Medellin, Colombia; [2]Ciencias, Institucion Universitaria Pascual Bravo, Medellín, Colombia; [3]Universidade Estadual Paulista Júlio de Mesquita Filho – Unesp, Araraquara, Brazil; [4]Materiales, Universidad Nacional de Colombia, Medellín, Colombia; [5]Quimica, Universidad Nacional de Colombia, Medellín, Colombia.

One of the most common materials to be used in scaffolds for osseous regeneration applications are calcium phosphates (CaPs) and more specifically bicalcic phosphates (BCPs) because to their properties of osteoconductivity, bioreabsorbability, biocompatibility and composition similar to the mineral phase of the bones. In the manufacture of scaffolds it is important to consider not only the biocompatibility but also the porosity, topography, morphology and mechanical behavior that are adequate to promote osteogenesis and angiogenesis. The additive manufacturing (AM) offers many possibilities to control these characteristics entering in the field of personalized medicine satisfying the particular needs of each patient. Currently research in the manufacture of scaffolds for bone regeneration from CaP are focused on obtaining formulations of ceramic pastes with the appropriate rheological and mechanical characteristics to be used in 3D printing on bioploters with ceramic paste printing kits. Many of these formulations are expensive due to the conditions of obtaining, storing, handling and the difficulty to guarantee repeatability of the appropriate conditions of each print in time as well as the high cost of the bioploter or appropriate printing kit for each paste. In this work a biofilament to be used in any low cost commercial 3D printer was developed. The biofilament is a ceramic / polymer composite based on calcium phosphates (CPs) and polylactic acid (PLA). The chemical route used to obtain the particles of CPs was the combustion method in solution. This method allowed to obtain in a simple way nanoparticles with a good price / quantity ratio. X-ray diffraction showed that the particles without thermal treatment consisted of the mixture of hydroxyapatite (HAP), and tricalcium phosphate (both alpha and beta phases), while the heat treatment of the CPs at 800°C for 2 hours enhanced the crystallization of HAP and B-TCP. Field Emission Electron Microscopy showed that the powders obtained with and without thermal treatment consisted of porous aggregates of micrometric size conformed by 100 nm nanoparticles. These powders were used to obtain biofilaments by hot extrusion in a Wellzoomextrude equipment with a Ceramic-Polymer ratio of 15%-75% weight respectively. The biofilaments obtained were characterized by scanning electron microscopy, EDS, FTIR, biodegradability and cytotoxicity. The filaments were tested in a low cost cast filament printer (Micromake 3D-Delta printer) obtaining different pieces with appropriate geometries to be used as scaffold.

11:30 AM BM01.04.12
Cell Proliferation Assessment of PLA and Alumina Scaffolds Fabricated by Additive Manufacturing Jhon A. Ramirez, Valentina Ospina, Angie Alejandra Rozo, Maria Isabel Viana, Sebastian Ocampo, Sebastian Restrepo, Neil Aldrin Vasquez, Carlos Paucar and Claudia P. Garcia; Universidad Nacional de Colombia sede Medellin, Medellin, Colombia.

Every day around the world people are being diagnosed with some kind of disease where the only solution is to replace the damage tissue or organ. Tissue Engineering is an alternative and promising approach that pretends to replace the damage tissues or organs by using structures known as scaffolds which

mimic the extra cellular characteristics of the specific tissue what is desired to replace where later healthy cells obtained from the patient will be harvested in an appropriated media to guarantee *in vitro* proliferation, compatibility and normal tissue growing at the moment of the implantation. The scaffolds could be biodegradable and be completely replaced with new tissue which is the case of the poly-lactic acid (PLA) that degrades to form lactic acid, nevertheless, there are also biocompatible scaffolds that do not degrade and are also bioinert which is the case of the scaffolds made with alumina which, despite not interacting with the surrounding tissue, are being studied thanks to their excellent mechanical properties. The triply periodic minimal surfaces (TPMS) are mathematically defined so that they occupy a minimum area given a boundary in R^3 presenting crystallographic groups symmetry that repeat three-dimensionally guaranteeing an interconnected porosity. The porosity percentage and pore size can be controlled from the design, being this a great advantage for scaffolds design for the use in regenerative medicine. In this work scaffolds based on two different geometries were fabricated by additive manufacturing (AM): one based on a TPMS, the Schwarz D surface, and another one based on a rectangular geometry with orthogonal through-holes. For the scaffolds fabrication two different materials were used: PLA in filament form, and alumina in printable paste form. The obtained scaffolds structure was characterized by X-ray diffraction and scanning electron microscopy and the cell proliferation was assessed for each geometry and material using fluorescence microscopy and DNA quantification by nanodrop. The additive manufacturing allowed to obtain scaffolds with the assessed materials guaranteeing the pores interconnectivity in each one of them. Curve surfaces fabricated with PLA were more favorable for cell attachment and proliferation of the CHO K1 cell line.

SESSION BM01.05: 3D Printing of Passive and Active Medical Devices IV
Session Chairs: Rigoberto Advincula and Michael McAlpine
Tuesday Afternoon, November 27, 2018
Sheraton, 2nd Floor, Liberty B

1:30 PM BM01.05.01
***In Situ* X-Ray and Thermal Characterization of FDM 3D Printing** Yuval Shmueli[3], Jiaolong Jiang[3], Thomas Howell[3], Ellen Wachtel[1], Gad Marom[2], Dilip Gersappe[3] and Miriam Rafailovich[3]; [1]Weizmann Institute of Science, Rehovot, Israel; [2]The Hebrew University of Jerusalem, Jerusalem, Israel; [3]Stony Brook University, The State University of New York, Stony Brook, New York, United States.

Fused deposition modeling (FDM) printing is an emerging 3D printing technology in which thermoplastic filaments are extruded and deposited in certain manner according to computer input design. FDM is a rapidly developing new area where new methodology is required to explore phenomena far from equilibrium. In this study, we use *in-situ* synchrotron X-ray scattering and high resolution infra-red imaging to study in-situ the relationship between the extrusion parameters, the filaments deposition directionality and the internal structure of the nanocomposite. In two steps study we place first “home-made” extrusion setup and then open-walls 3D printer in the beamline.
The results are then compared with Lattice Boltzmann Modeling which simulates the welding between filaments as a function of nozzle parameters, printing protocols, and the system thermodynamical response function. In filled systems, using in-situ X-rays scattering, we observed the effect of extrusion shear forces on the orientation of the nanoparticles and the influence of the particle/polymer interactions on the polymer crystallization. This phenomenon (“Transcrystallization”) leads to templating of the polymer crystalline structures by the fillers which, we show, can enhance the thermal, mechanical and electrical properties of the printed nanocomposite structures, under directional control by the printing algorithm. The results of in-situ printing measurements show how the parameters of sample temperature, printing orientation and materials composition affect the internal structure and crystalline structure formation.
We Acknowledge support from the National Science Foundation (Inspire Award No. 1344267) and The Morin Foundation Trust.

1:45 PM BM01.05.02
3D Printed Functionalized Organic Electrochemical Transistors for Glucose Sensing Jiaxin Fan, Darren Majak and Manisha Gupta; Electrical and Computer Engineering, University of Alberta, Edmonton, Alberta, Canada.

The invention of organic semiconductors unravels new possibilities for fabricating electronic devices specially with 3D printing techniques. The development of flexible and wearable biosensing devices, based on organic electronics, has received a great amount of attention due to demands for affordable, non-invasive, and continuous monitoring of physiological parameters for healthcare and medical diagnostics. PEDOT:PSS based organic electrochemical transistors (OECTs) are ideal candidates for flexible and customizable biosensors which, due to the simple device structure and material stability, can be fabricated with 3D printing techniques.
In this study, we have 3D printed functional OECTs, using an Optomec Aerosol Jet 5X 3D printer with commercially available materials. These devices were assembled as follows: first, a Parylene C substrate was thermally deposited, then a gate electrode as well as the source and drain electrodes were printed with commercially available platinum and silver nanoparticle ink respectively, the channel was then printed using PEDOT:PSS ink, and finally the passivation layer was printed with commercially available UV-curable polymer that was cured in-situ. The printed OECTs with similar channel dimensions (W= 95 mm, W/L = 4, d=374 nm) have shown high peak transconductance (g_m= 998.3 mS), low threshold voltage (0.51 V) and high current ON/OFF ratio ($I_{D,ON}/I_{D,OFF}$= $3.3x10^3$).
Functionalization improves the capability of detecting a particular analyte. OECTs have been demonstrated as glucose sensors, which show electrical response to changes in glucose concentration levels. Expanding on this work, we have also conducted studies of surface immobilization of glucose oxidase (GOx), which is commonly used for glucose detection. We have conducted the functionalization by the standard technique of dip-coating and also implemented 3D printing of the GOx. Results from glucose measurement with no functionalization and with the dip-coated and 3D functionalized will be presented here.

2:00 PM BM01.05.03
3D Printing of Hexagonal Boron Nitride Nanocomposites for Biomedical and Electronic Applications Linda M. Guiney, Nikhita D. Mansukhani, Adam E. Jakus, Shay G. Wallace, Ramille N. Shah and Mark C. Hersam; Northwestern University, Evanston, Illinois, United States.

Two-dimensional (2D) materials possess a broad range of interesting properties enabling applications in energy, electronics, and biomedicine. Additionally, the field of three-dimensional (3D) printing has become increasingly attractive for both biomedical applications as well as printed electronics. By incorporating 2D materials into 3D printable inks, their properties can be harnessed for functional and customizable biological constructs, specifically in

bioelectronics. For example, as implantable electronics are developed, thermal management will be a major challenge, where even small changes in temperature can result in deleterious perturbations to the surrounding tissue. Thus, there is a need for thermally conductive but electrically insulating flexible materials that can be incorporated into novel electronic implants. Hexagonal boron nitride (hBN) nanocomposites offer one potential solution due to their thermally conductive yet electrically insulating nature in addition to the high biocompatibility of hBN. Here, a high-content hBN-polymer nanocomposite ink is reported, which can be 3D printed to form mechanically robust, self-supporting constructs. To achieve these 3D printable nanocomposites, hBN is dispersed in poly(lactic-*co*-glycolic acid) and extruded at room temperature to form complex architectures that maintain their shape upon extrusion and can span large gaps without sagging or deformation. These constructs possess high mechanical flexibility and stretchability following 3D printing at compositions of up to 60% vol. hBN (solids content). The enhanced thermal conductivity, up to 2.1 $W K^{-1} m^{-1}$, due to the presence of hBN within the matrix suggests utility in thermal management applications. Furthermore, the constructs show high levels of cytocompatibility with human mesenchymal stem cells for up to one month, suggesting their utility for printed bioelectronics.

2:15 PM BM01.05.04
3D and 4D Printing of Biomedical Grade Thermoplastic Polyurethanes (TPU)s and Nanocomposites Rigoberto C. Advincula; Case Western Reserve University, Cleveland, Ohio, United States.

The use of 3D printing to create prototypes and devices from biocompatible polymeric materials has appended the design functionality of polymeric materials for biomedical devices enabling rapid development for new applications. Biomedical grade polymers can be further classified into thermoplastics, thermosets, and elastomers based on their thermo-mechanical properties. However, it is not as simple as the classification into these groups when it comes to their intending in-vivo or in-vitro applications. The transition to a final phase or cross-linked structure results in new properties. This is more evident with the choices of 3D printing methodologies (FDM, SLA, SLS, VSP) which can make use of blended or formulated compositions. We have demonstrated the 3D printing of biomedical grade thermoplastic polyurethanes (TPU) with compatibility to mammalian NIH 3T3 cells. However, 4D printing allows the design of new materials and applications based on integrating the chemistry of conversion with the printing mode. In this talk, we demonstrate the fabrication of concept objects and elastomeric actuators based on the use of biomedical grade TPU melts and extruded viscous solutions. The result is an extrudable precursor nanocomposite elastomer which can be printed via viscous extrusion printing (VEP) or VSP and then converted to an elastomeric actuating material with very high cyclic compressibility. Other work based on the use of SLA, SLS, FDM, towards high strength nanocomposite and biomaterials will be discussed.

2:30 PM BREAK

3:00 PM *BM01.05.05
3D Printing Functional Materials and Devices Michael C. McAlpine; University of Minnesota, Minneapolis, Minnesota, United States.

The ability to three-dimensionally interweave biological and functional materials could enable the creation of devices possessing unique and compelling geometries, properties, and functionalities. Indeed, interfacing active devices with biology in 3D could impact a variety of fields, including regenerative bioelectronics, smart prosthetics, biomedical devices, and human-machine interfaces. Biology, from the molecular scale of DNA and proteins, to the macroscopic scale of tissues and organs, is three-dimensional, often soft and stretchable, and temperature sensitive. This renders most biological platforms incompatible with the fabrication and materials processing methods that have been developed and optimized for functional electronics, which are typically planar, rigid and brittle. A number of strategies have been developed to overcome these dichotomies. Our approach is to use extrusion-based multi-material 3D printing, which is an additive manufacturing technology that offers freeform, autonomous fabrication. This approach addresses the dichotomies presented above by (1) using 3D printing and imaging for personalized, multifunctional device architectures; (2) employing ‘nano-inks’ as an enabling route for introducing diverse material functionality; and (3) 3D printing a range of functional inks to enable the interweaving of a diverse palette of materials, from biological to electronic. 3D printing is a multiscale platform, allowing for the incorporation of functional nanoscale inks, the printing of microscale features, and ultimately the creation of macroscale devices. This blending of 3D printing, functional materials, and ‘living’ platforms may enable next-generation 3D printed devices, from a one-pot printer.

3:30 PM BM01.05.06
Hydrophobic Coatings Increase the Contact Angle and Improve the Printability of Collagen Bioinks Louis X. Wang[1], Nicole Diamantides[2] and Lawrence Bonassar[2]; [1]Materials Science and Engineering, Cornell University, Ithaca, New York, United States; [2]Biomedical Engineering, Cornell University, Ithaca, New York, United States.

Collagen hydrogels show promise for use as bioinks in extrusion-based 3D bioprinting[1]. However, compared to some other natural and most synthetic hydrogels, collagen displays slow gelation times and poor mechanical stability, resulting in inferior printing characteristics[2]. Recent efforts to improve the printability of collagen have shown that the rheological properties of collagen bioinks are a good indication of their printing accuracy[3]. However, little is known about the effect of surface tension of bioinks and its effect on printability. In this study, we examine how hydrophobic surface coatings affect the contact angle of collagen bioinks and how this relates to printing accuracy. Type I collagen hydrogels were either fabricated to form a final collagen concentration of 4, 8, or 12 mg/mL, and riboflavin crosslinked gels were fabricated by adding 0.5 mM riboflavin and photocrosslinking with blue light for 10 seconds at the beginning of bioink dispensing for both contact angle and printability testing. Contact angle measurements were taken on glass coverslips either cleaned with 70% ethanol or coated with a polysiloxane solution (Rain-X™) and printability was assessed by printing lines (50 x 0.8 mm) on cleaned or coated glass coverslips using a Fab@Home 3D printer.[3]
Collagen drops printed on coated glass had dramatically higher contact angles than those printed on uncoated glass. On uncoated glass, collagen concentration had a more modest effect on contact angle than that of the coating. The addition of riboflavin did not have a significant impact on contact angle. The accuracy of printed lines increased with both collagen concentration of the bioink and the use of coated glass. Similar to the contact angle measurements, the effect of the coating decreased as collagen concentration increased. For printability testing, this is likely related to the fact that 12 mg/mL bioinks on uncoated glass were already approaching the 0.8 mm intended line width imposed by the diameter of the printing nozzle. These results will be used to change printing accuracy without changing bioink formulation and allow for a wider range of printabilities with finer resolution

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3:45 PM BM01.05.07
Characterization and Validation of 3D Printed Polycarbonate Urethane for Biomedical Applications Andrew T. Miller[2, 1], Natalia von Windheim[1, 2] and Ken Gall[1, 2]; [1]Mechanical Engineering and Materials Science, Duke University, Durham, North Carolina, United States; [2]restor3d, Durham, North Carolina, United States.

Polycarbonate urethanes (PCUs) are gaining in popularity in many biomedical applications due to their low stiffness, biocompatibility, and high strength. As a thermoplastic, PCUs can be 3D printed through a process known as fused deposition modeling (FDM). FDM offers many benefits such as: cheaper, faster, and easier prototyping, custom or complex geometries and architectures, and potentially even final component or device manufacturing. However, such processing will have implications on the material microstructure and ultimately the mechanical properties, particularly fatigue performance. The purpose of this study was to assess the effects and viability of FDM with PCU in an effort to realize new opportunities in the biomedical field for this promising soft material.

PCUs of three different hardnesses (75A, 85A, and 95A) were obtained in pellet form. Test samples were formed through either injection molding (IM) of pellets or extrusion into filament and then processing via FDM. Material structures were characterized through DSC, DMA, ^{1}H NMR, and FTIR. Mechanical tests included monotonic tension, compression, shear, and tensile fatigue. In addition, monotonic tension and tensile fatigue tests were performed on printed crosshatch scaffolds, which are fundamental to the biomedical field, to probe the effects of architecture.

FDM parameters were identified that resulted in samples consistently >99% solid. Monotonic tests indicated FDM samples matched IM in terms of tensile failure stress, while exhibiting significantly larger failure strain. Shear tests demonstrated no significant difference in shear strength between FDM and IM samples, which indicates strong layer bonding for FDM samples. Fatigue tests show an apparent improvement in strain-based fatigue for FDM samples. When plotted against stress amplitude, fatigue data indicates that solid FDM samples successfully matched IM samples in tensile fatigue despite the small percentage of voids. The crosshatch architecture resulted in a minor detriment to fatigue performance, even after adjusting for porosity. However, the effects were small relative to stiffer materials such as PEEK and titanium. Overall, the results show great promise for printed specimens of PCU, both solid and with architecture.

This study demonstrated the effectiveness of FDM as a processing method for PCU based on the performance of FDM samples. The results are both unexpected and significant, as they indicate potential for printing soft devices while maintaining a high level of performance, including in fatigue. This is promising for biomedical applications where custom geometries or complex architectures utilizing a soft, biocompatible material are desired. Potential applications are numerous, ranging from transvaginal meshes to custom, composite osteochondral devices.

4:00 PM BM01.05.08
Hierarchical Co-Assembly Enhanced Direct Ink Writing Longyu Li, Qianming Lin and Chenfeng Ke; Chemistry, Dartmouth College, Hanover, New Hampshire, United States.

The development of smart materials and devices has attracted increasing attention owing to their capability of altering the macroscale properties in a controlled manner.[1] Integrating these synthetic functional materials with 3D printing technology, *i.e.* the extrusion-based direct ink writing[2-4] (DIW) enables the amplification of their nanoscale properties into the macroscale by taking advantage of the controlled hierarchical assembly and pre-designed macroscale 3D geometry. Currently, small-molecule-based 3D printing materials are very rare owing to the difficulties of facilitating 3D printability as well as preserving their molecular functions macroscopically. In this presentation[5], we report a general approach of integrating functional small molecules into 3D printing materials and transferring their molecular features to the macroscale through supramolecular templation, post-printing hierarchical co-assembly, and covalent crosslinking. A variety of inorganic and organic inks were 3D-printed, and their superstructures were refined by post-printing hierarchical co-assembly. Our method not only enhances the printing resolution by up to one order of magnitude, but also enables precise spatial control over nanoscale features such as molecular assembly over a large scale. Fluorescence tracking experiments provided a molecular understanding of the dynamic co-assembly process at the macroscale and enabled the development of simultaneous color- and shape-changing 4D printable materials in response to the external stimuli. Furthermore, we showcased a benzene-1,3,5-tricarboxamide-based monolith capable of expanding and contracting through the insertion and removal of the correspondent supramolecular pillars. We believe that this new approach will initiate the development of small-molecule-based 3D printing materials and greatly accelerate the development of smart materials and devices that are capable of accomplishing complex tasks in response to environmental stimuli.

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4:15 PM BM01.05.09
3D Printing of Shape-Memory Thermoplastic Polyurethane for Biomedical Applications David Safranski[1], Natalia von Windheim[2] and Ken Gall[2]; [1]MedShape, Inc., Atlanta, Georgia, United States; [2]Duke University, Durham, North Carolina, United States.

Thermoplastic polyurethanes are used in a variety of biomedical devices, such as catheters, implantable defibrillators, wound care dressings, and orthopaedic implants. Due to their easy melt processing, these polymers are ideal for 3D-printing via fused deposition modeling. Prior studies of the shape-memory behavior of thermoplastic polyurethanes has been limited to either cast, pressed, or injection molded parts. The overall goal of this work is to

determine the effect of build orientation on thermo-mechanical properties, mechanical behavior, and shape-memory performance of a 3D-printed shape-memory thermoplastic polyurethane. A biomedical grade shape-memory thermoplastic polyurethane was extruded into 3.0 mm filament for 3D-printing via a LulzBot TAZ5. ASTM D638 Type V dogbones and rectangular samples were printed in each of three build orientations (flat, on-side, and vertical). The print speed was set to 500 mm/min and the nozzle temperature was 215°C. Dynamic mechanical analysis (TA Q800) was used to determine the glass transition temperature and rubbery modulus. Tensile behavior was determined using an MTS Insight 2 with a laser extensometer according to ASTM D638. Toughness was calculated as the area under the stress-strain curve. Unconstrained recovery for each build orientation was assessed with a 180° bend recovery test.
The glass transition temperature as determined from the peak of the tan delta curve was nearly equivalent for all three build orientations at 78°C. However, the storage modulus was increased for the flat orientation at 1515 MPa, compared to 1042 MPa and 1122 MPa for the on-side and vertical orientations, respectively. Rubbery modulus above the glass transition temperature was nearly equivalent amongst the build orientations at 29 MPa. All tensile samples displayed linear elastic behavior, followed by yielding and plastic deformation. The on-side and flat orientations displayed strain-hardening; however, the vertical build orientation did not experience hardening at higher strains. The failure strain was 70, 152, and 212% for the vertical, on-side, and flat orientations, respectively. The ultimate stress was 19.8, 30.8, and 44.4 MPa for the vertical, on-side, and flat orientations, respectively. The toughness was 13.1, 37.3, and 63.5 MJ/m^3 for the vertical, on-side, and flat orientations, respectively. Shape-recovery was near 97% for each build orientation for the bend recovery test. Unconstrained shape-recovery was not dependent upon build orientation; however, tensile properties improved when the flat build orientation was used. However, a 70% failure strain in the vertical build orientation is still 10x greater than other common FDM thermoplastics, such as ABS or nylon. These superior mechanical properties will allow for the design and manufacture of complex biomedical devices.

4:30 PM BM01.05.10
3D Patterned Hydrogels for Controlled Growth Factor Release Pengrui Wang; University of California, San Diego, La Jolla, California, United States.

3D printed hydrogels can provide dimensional control over the release of molecules enveloped in them. Owing to their controllable degradability, capability to protect enveloped molecules from degradation, hydrogels provided physiochemical interactions with agents such as growth factors to regulate their release kinetics. Amongst the commonly used hydrogels, heparin have shown prolonged release due to its high negative charge density. Researches have shown heparin gels can trap positively charged molecules such as growth factors by electrostatic forces to delay their delivery. Another negatively charged hydrogel, hyaluronic acid, has been widely engineered for applications such as would healing and cosmetic surgeries due to its role in granulation and cell migration. Recent development in 3D printing of modified hyaluronic acid has inspired its application in controlled drug release. Engineered release of growth factors are potent strategies for regulating cell regeneration in tissue engineering, but spatially patterning them in a facile manner to achieve releasing of multiple factors in a controlled manner is still challenging. Additionally, mathematical modeling of the drug release from engineered structure is also lacking. In this work, we presented a heparin and hyaluronic acid-based hydrogel system that was 3D printed to allocated multiple growth factors at different locations within the same construct to achieve sequential release over weeks. Mathematical models of release kinetics were developed and verified. Furthermore, we have observed the stimulus effect on angiogenesis *in vitro* and tissue regeneration *in vivo* from engineered sequential release. We hope that our findings could provide a more comprehensive understanding of release kinetic of hydrogels for the community.

4:45 PM BM01.05.11
3D/4D Printed MicroRobotic Machines for Biomedical Applications Hen-Wei Huang; ETH Zurich, Zurich, Switzerland.

In the past decade, the development of microelectromechanical system (MEMS) and smart nanocomposite materials has enabled roboticists to construct miniature three-dimensional (3D) mobile machines with programmable morphology and motility from two-dimensional (2D) materials through self-folding *(1, 2)*. These self-folded micromachines wirelessly driven by electromagnetic fields exhibit great potentials in revolutionizing current procedures in minimally invasive medicines by means of targeted drug delivery, micro-tissue transplantation, and robotic cell scaffolds *(3, 4)*. However, self-folded functional micromachines are mostly limited to their monotonous cylindrical structures, such as tubular, helical, and spiral shapes, which in turn constrains the possibility of integrating multiple functionalities into a single machine.
Owing to the progress in 3D printing techniques with the resolution at micro/nano scales, robotic micromachines with sophisticated 3D shapes and spatially controlled mechanical properties can be engineered via direct-laser-writing (DLW) on polymers capable of spatiotemporally modulating the cross-linking degree *(5)*. Extra functionalities can be extended on the printed structures simply by incorporating other functional materials. In this work, 3D printed compound microstructures, which is impossible to be implemented through folding 2D materials, are devised to be a robotic microtransporter composed of a helical propeller for wirelessly controlled propulsion and an Archimedes screw for delivering therapeutic micro-agents. We demonstrate such compound machines can implement on-demand loading, encapsulation, and transport of multiple, various therapeutic micro-agents, ex. different sizes of cells and various kinds of drugs.
Furthermore, using environmentally stimuli-responsive hydrogels as the printing materials endow the micromachines with sensing and shape morphing capabilities, also known as 4D printing. By coordinating the sensory input with shape morphing output, the control loop can be closed without external imaging feedback and intricate integrations of sensors and actuators, paving the way of autonomous targeted delivery inside the human body.
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