FAMU-FSU Engineering

Department of Chemical and Biomedical Engineering

RESEARCH DAY

April 2, 2021

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Keynote Presentation

Advanced Manufacturing of (Bio)pharmaceutical Products

Richard D. Braatz, Ph.D.

Chemical Engineering Department, Massachusetts Institute of Technology

Abstract

This presentation describes technologies for the advanced manufacturing of (bio)pharmaceutical products. The specific strategies that are described are: (1) optimization of each unit operation by exploiting process intensification, (2) automated high-throughput microscale technology for fast continuous process research and development, (3) plug-and-play modules with integrated control and monitoring to facilitate deployment, (4) dynamic models for unit operations for automated plant-wide simulation and control design, and (5) autonomous/smart data analytics and machine learning. These strategies are demonstrated in applications including in continuous viral vaccine production, monoclonal antibody manufacturing via batch processing, and fully automated end-to-end (semi-)continuous manufacturing.

Biography of Dr. Richard Braatz

Dr. Richard D. Braatz is the Edwin R. Gilliland Professor at the Massachusetts Institute of Technology (MIT) where he does research in advanced manufacturing systems. He received an MS and PhD from the California Institute of Technology and was the Millennium Chair and Professor at the University of Illinois at Urbana-Champaign and a Visiting Scholar at Harvard University before moving to MIT. He has consulted or collaborated with more than 25 companies including Novartis, Merck, Pfizer, Bristol-Myers Squibb, Biogen, Amgen, Sanofi, and Abbott Laboratories. He has been recognized by a number of honors and awards, and is a member of the U.S. National Academy of Engineering.

List of Student 30-minute Presentations

1. "Transient Evolution of Shear-Banding Flow Formation in Wormlike Micellar Fluids" by Peter Rassolov
2. "In Vitro Culture Expansion Shifts the Immune Phenotype of Human Adipose-derived Mesenchymal Stem Cells" by Richard Jeske
3. "Structure-Performance Relationships of Polymer-Based Composites Used in Extrusion Printing" by Roneisha Haney

Student 30-minute Presentation #1

Transient Evolution of Shear-Banding Flow Formation in Wormlike Micellar Fluids

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Shear-banding flows of wormlike micellar solutions exhibit complex transient features that are still not well understood. One such feature, and the main focus of our work, is transient flow reversal, or a temporary and localized flow opposite to the direction of applied motion. In ongoing work, we study this phenomenon by using rheometry in combination with particle tracking velocimetry (rheo-PTV) to obtain spatially and temporally resolved flow fields for shear banding micellar solutions. We found that there are several parameters that affect the transient evolution of flow in shear banding wormlike micelles: fluid elasticity, E = Wi / Re, where Wi and Re denote the Weissenberg number and Reynolds number respectively; micellar entanglement, Z; flow ramp up rate, a; and the viscosity ratio, $\beta = \eta_s / (\eta_0 - \eta_s)$ where η_0 and η_s denote the zero shear viscosity and solvent viscosity respectively. In the first part of this talk, I will focus on the effects of E and a at nearly fixed Z and β. Following initial application of shear flow, transient flow reversal is observed beyond critical thresholds of E and a, while in some cases, the transient flow reversal disappears beyond a second critical threshold of E. We further observed that, depending on E and a, the quasi-steady state flow may feature multiple shear bands instead of the classically observed two-band profile. Additionally, transient and in some cases quasi-steady wall slip is reported for these experiments. In the second part of this talk, I will discuss the effects of micellar entanglement, Z, on the evolution of flow at fixed E and β. Our results indicate that high Z is necessary but not sufficient for transient flow reversal.

Student 30-minute Presentation #2

In Vitro Culture Expansion Shifts the Immune Phenotype of Human Adipose-derived Mesenchymal Stem Cells

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Human mesenchymal stem or stromal cells (hMSCs) are known for their potential in regenerative medicine due to their differentiation abilities, secretion of trophic factors, and regulation of immune responses in damaged tissues. Due to the limited quantity of hMSCs typically isolated from bone marrow, other tissue sources, such as adipose tissue-derived mesenchymal stem cells (hASCs), are considered a promising alternative. However, differences have been observed for hASCs in the context of metabolic characteristics and response to *in vitro* culture stress compared to bone marrow derived hMSCs (BM-hMSCs). In particular, the relationship between metabolic homeostasis and stem cell functions, especially the immune phenotype and immunomodulation of hASCs, remains unknown. This study thoroughly assessed the changes in metabolism, redox cycles, and immune phenotype of hASCs during *in vitro* expansion. In contrast to BM-hMSCs, hASCs did not respond to culture stress significantly during expansion as limited cellular senescence was observed. Notably, hASCs exhibited the increased secretion of pro-inflammatory cytokines and the decreased secretion of anti-inflammatory cytokines after extended culture expansion. The NAD+/NADH redox cycle and other metabolic characteristics associated with aging were relatively stable, indicating that hASC functional decline may be regulated through an alternative mechanism rather than NAD+/Sirtuin aging pathways as observed in BM-hMSCs. Furthermore, transcriptome analysis by mRNA-sequencing revealed the upregulation of genes for pro-inflammatory cytokines/chemokines and the downregulation of genes for anti-inflammatory cytokines for hASCs at high passage. Proteomics analysis indicated key pathways (e.g., tRNA charging, EIF2 signaling, and protein ubiquitination pathway) that may be associated with the immune phenotype shift of hASCs. Together, this study advances our understanding of the metabolism and senescence of hASCs and may offer vital insights for the biomanufacturing of hASCs for clinical use.

Student 30-minute Presentation #3

Structure-Performance Relationships of Polymer-Based Composites Used in Extrusion Printing

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Development of composite based materials with controlled and enhanced properties is key in a number of applications such as thermal interface materials, sensors and light weight aircraft wings to name a few. The wide range of matrix-filler combinations allows for versatility in their properties, enabling them to be applied in many fields. Composite materials are often matched to a particular application. By carefully choosing the reinforcement, the composite can be tailored to meet the specific requirements (electrically conducting, mechanically robust, or thermally conducting).

Direct ink writing (DIW) of graphite-epoxy composites has gained significant importance in several applications in fabricating highly conductive free-standing 3D structures. Processing the composite inks, consisting of highly loaded graphene nanoplatelets, first involves a detailed understanding of the underlying rheological properties. However, little is known about the effect of processing/print parameters, e.g., print speed has on the orientation of such 2D particles during the printing process and how this subsequently influences the final cured composite's macroscopic properties. In this work, inks with solid loadings of 7-18 wt% were dispersed into a low viscosity epoxy resin (EPON 862) to form a shear thinning, viscoelastic material. The optimal GNP loading for printing is determined through rheological measurements, and the electrical and thermal properties are measured as a function of particle concentration and print speed. The results show a sharp increase in electrical conductivity by a factor of ten as the print speed is increased from 5 to 40 mm/s, and all printed samples had conductivities higher than 10^{-3} S/cm.

Additionally, thermal conductivity results show a similar trend, where through-thickness conductivity increases from 1.01 to 9.75 W/m-K. We attribute this change in conductivity to the shear stresses generated during the deposition of the ink, resulting in a shift in the orientation of the 2D platelet-like fillers. Such results showcase the ability to tune the macroscopic properties of a printed structure with a constant loading of filler. The present work helps develop design rules for the processing of graphene-based 3D structures with enhanced properties using additive manufacturing. We envision using such structures in applications such as heat sinks, thermal interface materials, shielding materials for electronic devices, and light-emitting devices, to name a few.

List of Student 3-minute Presentations

1. “Modeling Dynamic Swelling of Polymer-Based Artificial Muscles” by Shefik Bowen
2. “Reductive Species in A Nanosecond Pulse Plasma Discharge Gas-Liquid Reactor” by Radha Krishna Murthy Bulusu
3. “Engineering Auxetic Scaffolds for Human Stem Cell Differentiation” by Xingchi Chen
4. “Tracking Phagosome-Derived Vesicles with Microfabricated Microparticles Loaded with DiI” by Wenhao Cheng
5. “Perfluorinated Carbon Degradation Using A Nanosecond-Pulsed Plasma Gas–Liquid Flowing Film Reactor” by Rachel Gallan
6. “Elucidating Mechanism of Recovery in Cerebral Ischemia Via Stem Cell Derived Extracellular Vesicles Using MRI” by Shannon Helsper
7. “Structural and Functional Network Alterations in a Rodent Stroke Model” by David Hike
8. “Metabolic Impact of Spontaneous Trigeminal Allodynia in Sprague-Dawley Rats: Implications for Migraine & other Neurological Disorders” by Samuel W. Holder
9. “Lithium Salt Transport in Diblock Copolymer Electrolyte” by Kyoungmin Kim
10. “Lignin-Based Polyesters: Synthesis and Characterizations of Lignin-graft-poly(ethylene brassylate) with high mechanical properties” by Sundol Kim
11. “The Influence of The Octanol-Water Partition Coefficient on The Drug Loading of Block Polymer Nanoparticles” by Guanrui Li
12. “Unlayered Crystalline Structure from Rapid Cooling of Long-Spaced Aliphatic Polyesters” by Stephanie F. Marxsen
13. “Magnetite-core/gold-shell Nanoparticles for the Detection and Quantification of Trace Contaminants in Food Products” by Anna Mills
14. “Use of Fast Scanning Calorimetry to Obtain Crystallization Rates from The Melt of Polyethylene-Like Materials at Industrial Processing Conditions” by Carlos Germosen Polanco
15. “Propulsion Kinematics and Magnetic Manipulation of Achiral Swimmers in Viscous Media” by David Quashie Jr.
16. “Towards Co-Culture Cancer Tissue Models: Rheological Characterization of Alginate-Gelatin Hydrogels” by Tyler Gregory
17. “Engineering Brain-Specific Pericyte and Endothelial Cell Co-culture from Human Stem Cells for Studying Immune Response” by Mark Marzano
18. “Mesenchymal Stem Cell Impacts on Cerebral Microstructural Diffusion Recovery After Ischemic Attack” by Ande Bagdasarian
19. “Controlling Nanostructure of Block Copolymer Membranes” by Omar Taleb
20. “Comparing the Bone Regeneration Capacity of Extracellular Vesicles Isolated from Bone Marrow-Derived and Adipose-Derived Mesenchymal Stem Cells” by Yuan Liu

Student 3-minute Presentation #1

Modeling Dynamic Swelling of Polymer-Based Artificial Muscles

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Recent global conflict and wars have highlighted the need for a decisive advantage on the battlefield where the human military service member is the most important factor in any war. Until now, the service member has not been muscularly and practically enhanced. Mimicking nature, artificial muscles not only provide a customizable strength increase, but with design of select materials, could lead the next generation of robotics as well with low profile undetectable polymer materials. Modeling the actuation of advanced polymers is essential for developing materials that meet design metrics. Using first principles of thermodynamics and transport phenomena, numerical solution methods were employed to model polymeric swelling, diffusion, and migration. Volumetric swelling of polymer fibers can be modeled using the code developed, while maintaining full customizability for parametric studies or analysis of experimental data. This study will aid efforts to identify the best material candidates for practical use as artificial muscle fibers.

Student 3-minute Presentation #2

Reductive Species in A Nanosecond Pulse Plasma Discharge Gas-Liquid Reactor

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Interaction of water with plasma results in dissociation of water molecules (H_2O), which leads to the formation of oxidative species i.e. hydroxyl radicals (OH), hydrogen peroxide (H_2O_2), atomic oxygen (O), and reductive species like atomic hydrogen (H), molecular hydrogen (H_2), and aqueous electrons. The main objective of this work is to utilize an Ar carrier gas combined with water solutions of either chloroacetate ($Cl\text{-}CH_2COONa$) and potassium ferricyanide ($K_3[Fe(CN)_6]$) to determine the production rate and energy yield of e^-_{aq} produced in our gas-liquid reactor. Chloroacetate ($Cl\text{-}CH_2COONa$) and potassium ferricyanide ($K_3[Fe(CN)_6]$) react with e^-_{aq} to form Cl^- and Fe (II), respectively, which are measured using ion chromatography and UV-vis spectroscopy, respectively. A nanosecond power supply is used at 16 kV (input voltage), 40 ns (pulse width) and 5 kHz (pulse frequency).

Student 3-minute Presentation #3

Engineering Auxetic Scaffolds for Human Stem Cell Differentiation

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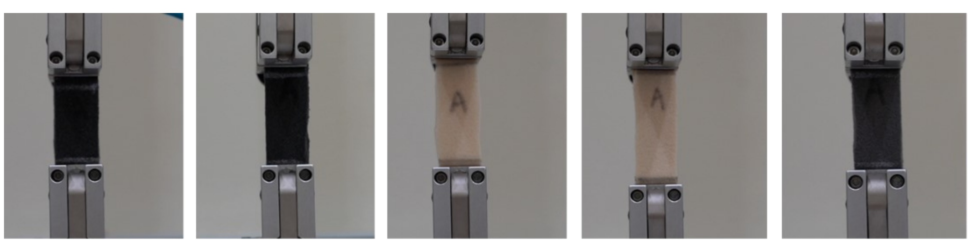
Negative Poisson Ratio (NPR) materials are one of the meta materials and attract high attention in biomedical applications. The auxetic materials (i.e. scaffolds that can display negative Poisson's ratio) have high porosity, intendent resistance, shear resistance which are interesting properties in tissue engineering especially the vascular tissue regeneration. Polyurethane (PU) materials have been used recently as tissue engineering scaffolds. Due to the different ratios and categories of the components of di- or triisocyanate and polyol in PU, they have wide use for different tissue culture systems. Stem cells mechanosense the stiffness of their microenvironment, which impacts lineage commitment and differentiation. In addition, the high porosity can offer good transport of biomolecules for nutrient delivery and growth factor induction. In our experiments, five different auxetic PU foams were characterized as the scaffolds to investigate the behavior of human induced pluripotent stem cells (hiPSCs) on the materials. This scaffolds can be used with locally tunable force-displacement properties at length scales appropriate for tissue interaction. The surfaces of the foams were modified with chitosan, dopamine, heparin to enhance the adherence and proliferation of hiPSCs. Then, we investigate the vascular and neural differentiation of hiPSCs on different foams with distinct elastic modulus and Poisson's ratio, which describes the degree of a material that contracts (or expands) transversally when axially strained. With different modulus of the foam, the cell shows different adherent density and different differentiation capacity. This approach represents a versatile and multifunctional scaffold fabrication and could lead to a suitable system for establishing hiPSCs culture models in the applications of disease modeling and drug screening.



110 115 210 215 315

Table 1. Elastic modulus and Poisson's ratio of different auxetic scaffolds

Sample ID	110	115	210	215	315
E (Pa)	1400	700	2700	700	1800
Poisson's ratio	-0.297	-0.508	-0.347	-0.322	-0.348
Applied Strain(%)	25	42	4	44	18

Student 3-minute Presentation #4

Tracking Phagosome-Derived Vesicles with Microfabricated Microparticles Loaded with DiI

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Phagocytosis is a process by which a cell such as macrophage internalizes a micrometer-sized particle. It plays a critical role in immunity, and tissue remodeling and repair. Phagocytosis is characterized by the internalization of the particle in a vacuole called phagosome inside the cell. Formation, maturation and resolution of the phagosome is a complex process and is not well understood. Among this process is the appearance and trafficking of intracellular vesicles that are apparently derived from the phagosome and named phagosome-derived vesicles (PDVs). Existing techniques for tracking PDVs reply on using particles that can be enzymatically degraded into soluble fluorescent fragments inside the phagosome. These techniques are incapable of detecting whether components of the phagosome membrane are in the PDVs. We are seeking to develop a novel method for tracking PDVs by using microparticles loaded with DiI, which is a widely used carbocyanine membrane dye. The microparticles are produced using a microfabrication technique called microcontact printing, which allows a tight, versatile control on the size and composition of the microparticles. In this presentation, we report the following findings. (1) The microparticles were readily phagocytosed by RAW264.7 macrophages. (2) DiI-stained puncta outside the phagosomes were found in cells that contained the microparticle-laden phagosomes. (3) Several lines of evidence indicated that the puncta were PDVs. (4) The PDVs were acidic and were used by the cells to phagocytose zymosan bioparticles. This technique promises to be useful for deepening our understanding of phagocytosis and developing new therapy for treating diseases via manipulating phagocytosis.

Student 3-minute Presentation #5

Perfluorinated Carbon Degradation Using A Nanosecond-Pulsed Plasma Gas–Liquid Flowing Film Reactor

Rachel Gallan, Radha Krishna Bulusu, Dr. Robert Wandell, Dr. Bruce Locke
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A common environmental stressor in ground and drinking water is the presence of compounds with carbon-fluorine bonds or perfluorinated carbons. These compounds have been used in a wide range of applications because of their durability, amphiphilic properties and high surface activity. New methods to degrade perfluorinated compounds are needed due to their resistance to natural biodegradation processes. Perfluorinated compounds also tend to bioaccumulate, which is an issue due to their effects on human health. We have investigated the degradation of perfluorinated compounds using a nanosecond-pulsed plasma gas-liquid flowing film reactor. A ground water surrogates with 5000 ng/L of two major perfluorinated carbon contaminants, perfluorooctanoic acid PFOA and perfluorooctanesulfonic acid PFOS, were treated by the plasma reactor with a nanosecond pulsed power supply with settings of 16 kV applied voltage, 40 ns pulse width, and 5 kHz frequency, and with the liquid phase flowing at 2 ml/min and argon carrier gas. The parent compounds degradation and their reaction products are used to determine degradation efficiency and possible degradation pathways and mechanisms.

Student 3-minute Presentation #6

Elucidating mechanism of recovery in cerebral ischemia via stem cell derived extracellular vesicles using MRI

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Trophic and immunomodulatory effects render human mesenchymal stem cells (hMSC) promising candidates for cell therapy in stroke treatment. We have demonstrated MRI to be a sensitive metric to assess therapy efficacy in an ischemic stroke model via biochemical markers measured longitudinally using sodium (^{23}Na) chemical shift imaging (CSI) and relaxation enhanced MR spectroscopy (RE-MRS). Ultra-high field at 21.1 T provides increased sensitivy, enabling insight into ionic and metabolic homeostasis while assessing therapeutic efficacy. This approach may yield a particularly advantageous method to investigate hMSC derivatives such as extracellular vesicles (EV), which are endosomally-produced vesicles that carry immunomodulatory and regulatory secretions.[1-2] EV should target neurodegeneration,[3] and appear to aid in tissue recovery following ischemic stroke in rat models.[3-5]

Similar to cellular therapy, *in vivo* tracking of EV is imperative to determining bio-distribution, which has remained limited in MRI applications. Labeling of EV with superparamagnetic iron oxides (SPIO) contrast agents via sonication has been pursued. *In vitro* MRI of EV suspended in 1% agarose gel following labeling demonstrates robust uptake of SPIO. Varying methods of purification of labeled EV from excess SPIO following sonication are compared. *In vivo* MRI demonstrates sufficient contrast for visualization of EV localized to the ischemic hemisphere. Therapeutic analysis of ischemic lesion volumetric, sodium signal changes, and metabolite levels in subjects administered EV in parallel to cell administered subjects is underway.

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Student 3-minute Presentation #7

Structural and Functional Network Alterations in a Rodent Stroke Model

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Stroke is the fifth cause of death and a leading cause of disability in the United States[1]. It is characterized by a sudden onset of numbness or weakness, especially on one side of the body, confusion or trouble speaking and understanding speech, dizziness, or sudden headache[2]. This study utilizes a middle cerebral arterial occlusion (MCAO) to induce an ischemic stroke, which has been instituted in rats as a reliable model of large artery occlusion in humans[3]. This work focuses on utilizing graph theory applied to functional Magnetic Resonance Imaging (fMRI) assessed in the resting state and Diffusion Tensor Imaging (DTI) at 21.1 T to provide a method for monitoring the progression of structural and functional recovery following ischemia. Current data shows functional recovery in multiple areas of the brain indicating that neural plasticity plays a roll in allowing for the restructuring of the brain to maintain functional ability. However, graph metrics do not return to the same level as naïve animals by Day 30. Structural recovery shows alterations taking place outside the ischemic area, indicating more neural plasticity acting to mitigate damage caused by the infarction. The continuous degradation that occurs for multiple days post ischemia can be seen in the structural data and limits the ability for tractography to be used for any meaningful connectivity analysis before day 5. This research has potential to be used to monitor the progression of stroke. Such classifications may assist in defining treatment regiments (another branch of active study) earlier in disease progression, possibly before irreversible damage is done. Furthermore, this work will help to expand the application of DTI, fMRI and network theory to identification and assessment of recovery progression of other neurodegenerative diseases.

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Student 3-minute Presentation #8

Metabolic Impact of Spontaneous Trigeminal Allodynia in Sprague-Dawley Rats: Implications for Migraine & other Neurological Disorders

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Approximately 50% of male Sprague-Dawley rats have been reported to develop spontaneous trigeminal allodynia (STA)[1]. Examined behaviorally, STA presents similarly to migraine, and can be alleviated through triptans, a class of migraine treatment. These similarities raise questions about the implications of an unevaluated factor within the commonly used Sprague-Dawley rat model. To evaluate STA, an established model for migraine, nitroglycerin (NTG)-induced central sensitization, was chosen. *In vivo* relaxation-enhanced MR spectroscopy (RE-MRS) was performed at 21.1 T within the female Sprague-Dawley rat thalamus. STA was determined behaviorally through application of Von Frey filaments to the periorbital region. Filaments ranged from 0.008-26 g, and were increased sequentially until an aversive withdrawal occurred in 2 of 3 or 3 of 5 applications. The trial was repeated four times, 1 h apart, on alternating sides. Animals were separated into two behavioral groups, naturally resilient (NR) and STA. Prior to scanning, animals were anesthetized with 5% isoflurane in oxygen for surgery implantation of an intraperitoneal line to deliver nitroglycerin (NTG) *in situ*. Post-surgery, rodents were maintained at 2-3% isoflurane in oxygen for scanning, then promptly sacrificed. Groups examined were NR animals dosed with saline (N=8), 2-mg/kg NTG (N=6) or 10-mg/kg NTG (N=6), and STA animals at identical dosages (N=7, N=3, and N=4, respectively). Spectra were acquired using a relaxation-enhanced (RE) spin-echo sequence localized to a 4x3x3-mm^3 voxel via Localization by Adiabatic SElective Refocusing (LASER). The voxel was centered between thalamic lobes. With an effective TE=54 ms and TR=2.5 s, spectra were averaged eight times per repetition, with 32 repetitions performed. Scans repeated every 20 min out to 2 h post-injection. Spectral data was normalized to the NAA signal; ratios are presented as a percentage change from baseline values. Statistical analysis was performed in JMP Pro 15 (SAS, Inc). The Von Frey examination denoted a clear difference between NR and STA animals. While STA animals may appear resilient during individual trials, their variance between trials is large, reaching mechanical sensitivity thresholds as low as 1.4 g. However, NR animals never drop below a threshold of 10 g and experience much less variance. Thalamic spectra show the clearest distinction between STA and NR groups with saline injection. At later times, saline STA glutamate/glutamine (Glx) is significantly and progressively elevated from baseline levels, unlike saline NR. Notably, despite being spontaneous, STA saline appears to display a Glx buildup over time, with larger variations at later times. With NTG injection to induce central sensitization, NR and STA Glx signal changes are consistent; only one time point shows a significant difference (t=55 min). NTG appears to overwhelm the spontaneous buildup of Glx, with STA showing possible increases in variance. With lactate (Lac), NR and STA cohorts are remarkably similar over time with NTG injection. As glycolysis increases to meet rising cellular energy demands, these Lac trends are consistent with previous examinations of the NTG model in male Sprague-Dawley rats, albeit occurring earlier in females[2]. The earlier Lac significance might be a sex-specific dose response, which is under evaluation.

References:

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Student 3-minute Presentation #9

Lithium Salt Transport in Diblock Copolymer Electrolyte

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Polymer electrolytes can contribute to development of safe and clean energy systems by replacing flammable liquid electrolytes in lithium-ion batteries if poor ion transport properties are addressed. Moreover, battery energy density can be dramatically improved if lithium dendrite formation is prevented. A rigid non-conducting block can be introduced to form a diblock copolymer electrolyte providing high mechanical strength that can resist dendrite growth, but ionic conductivity is simultaneously decreased by reducing the volume fraction and connectivity of the conductive phase. The ionic conductivity can be improved by increasing salt concentration, but high salt concentration can increase the local concentration gradient, the number of ion clusters, and the strength of interaction between ions and polymer moieties. Therefore, it is important to understand the influence of salt concentration and ion interaction on transport behavior in such electrolyte systems. In this study, the transport properties of diblock copolymer/lithium salt electrolyte were measured by electrochemical and spectroscopic techniques. Fourier transform infrared spectroscopy (FTIR) was used to investigate the interaction between lithium bis-trifluoromethanesulfonylimide (LiTFSI) salt and a polystyrene-poly(ethylene oxide) block copolymer. A systematic and quantitative analysis was achieved with a combination of peak deconvolution and consideration of polymer swelling. Salt diffusion in the block copolymer matrix was measured using time-resolved FTIR. Electrochemical impedance spectroscopy was used to ionic conductivity. Cation transference number was measured by Bruce-Vincent method. The dissociation of salt molecules was studied by Raman spectroscopy. Strong correlation between the transport properties and the degree of dissociation was observed.

Student 3-minute Presentation #10

Lignin-Based Polyesters: Synthesis and Characterizations of Lignin-graft-poly(ethylene brassylate) with high mechanical properties

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Non-degradable petroleum-based plastics waste issue is a global challenge that requires urgent attention due to its harmful impact on humans and the environment. This prospectus reports preliminary results and research plans of biomass lignin-based biodegradable polymers. Lignin is an important biomass that can be a raw material to produce functional polymers due to its abundance, low price, sustainability, and high concentration of aromaticity. However, not thoroughly understood lignin modifications and characterizations limit the potential as a new sustainable raw material. The biomass lignin can be integrated with the concept of aliphatic polyesters to produce biomass-based biodegradable polymers. Among various biodegradable polylactides poly(ethylene brassylate) (PEB) is a relatively unexplored polymer with advantages of low cost and sustainable resource, castor oil. In preliminary results, we have synthesized a new lignin-containing copolymer, lignin-graft-poly (ethylene brassylate). First, the lignin was chemically modified by sebacic acid to introduce a carboxylic acid functionality onto lignin. Herein, the abundant hydroxyl groups were used for the modification of lignin. Another precursor of the copolymer, poly (ethylene brassylate) was prepared by ring-opening polymerization of ethylene brassylate in the presence of a catalyst, 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD). The condensation polymerization of modified lignin and poly (ethylene brassylate) was occurred by the reaction between 1,5,7-triazabicyclo[4.4.0]dec-5-ene terminus of the poly (ethylene brassylate) and carboxylic acid of modified lignin. A low melting temperature (78 ℃) of the new polymer enables an easy thermal process. Mechanical properties of the new lignin-graft-poly (ethylene brassylate) can be conveniently controlled by changing mass ratios of lignin and poly (ethylene brassylate). The highest modulus is 471.99 MPa, which is 3-fold higher than homo poly (ethylene brassylate).

Student 3-minute Presentation #11

The Influence of The Octanol-Water Partition Coefficient on The Drug Loading of Block Polymer Nanoparticles

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Amphiphilic block polymer nanoparticles (PNPs) are a potential drug carrier for poorly water-soluble drugs, such as paclitaxel. The hydrophilic block acts as the PNP corona, while the hydrophobic block forms the core. Polymerization induced self-assembly (PISA) is an emerging method for the synthesis of PNPs. Compared with the conventional methods, the polymerization, self-assembly of nanoparticles, and encapsulation of drug can be conducted simultaneously during PISA, which simplifies preparation steps and avoids the use of toxic organic solvents. However, the influence of the core block hydrophobicity on the PISA process is not well understood. In my project, I will study the influence of the octanol-water partition coefficient (log P) of the core block on the drug loading ability of the PNPs. I hypothesize that if the log P values of the drug and hydrophobic core are similar, the drug loading efficiency will be maximized. Currently, I have successfully synthesized poly(glycerol monomethacrylate)$_{47}$-poly(2-hydroxypropyl methacrylate)$_x$ (PGMA$_{47}$-PHPMA$_x$) PNPs with three different lengths of the hydrophobic PHPMA block. NMR diffusometry and dynamic light scattering are used to measure the diffusion coefficient and hydrodynamic radius of the PNPs . We anticipate that as the PHPMA block increases in length, the PNP morphology will transition from spherical micelles, to worms, and to vesicles.

Student 3-minute Presentation #12

Unlayered Crystalline Structure from Rapid Cooling of Long-Spaced Aliphatic Polyesters

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We report the first known instance where formation of layered crystals in long-spaced polyesters is bypassed on rapid quenching from the melt. Aliphatic polyesters spaced by 18 to 48 carbons in both the diol and diacid components of the repeating unit form orthorhombic, highly symmetric layered crystals on relatively slow or isothermal crystallization. Though the unit cell is maintained on rapid quenching to 0 °C and lamellar crystals still form, the X-ray reflection of the ester layer disappears in PE-48,48 and weakens substantially in the shorter-spaced polyesters. Since all crystal thicknesses are larger than the distance between consecutive ester groups, the esters must be inside the crystals in a random distribution. On heating, such unlayered crystals transform to the layered type at temperatures between 45 and 60 °C, which further melt at temperatures ranging from 98 to 110 °C with increasing methylene spacer length. Rapidly quenched PE-48,48 develops only the unlayered structure, while shorter-spaced polyesters form a mixture of unlayered and layered crystals, indicating a larger depth of quenching is required for the development of the unlayered form with decreasing methylene spacer length. We posit that on fast crystallization, lamellar crystals form via random chain folding and fast staggering of polyester segments, while on slower crystallization, ester layering is facilitated by maximizing packing of the full length of methylene units via van der Waals interactions and intermolecular dipole-dipole interactions of ester groups.

Student 3-minute Presentation #13

Magnetite-core/gold-shell Nanoparticles for the Detection and Quantification of Trace Contaminants in Food Products

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Magnetic-core/gold-shell nanoparticles (MAuNPs) are of interest for enabling rapid and portable detection of low-level adulterants in complex media, such as food. Gold coating provides biocompatibility as well as facile functionalization with antibodies and poly(ethylene glycol) (PEG). Antibodies enable specific detection of the antigen of interest. PEG mitigates non-specific adsorption. After incubating the particles in a complex mixture so that antibodies and antigens bind, the particles can be removed with a magnetic field that acts on the magnetic iron oxide cores (MNPs). The particles can then be deposited as a film for surface-enhanced Raman spectroscopy (SERS). SERS can detect trace amounts of compounds due to enhancement afforded by surface plasmons of metallic nanoparticles. MNPs were synthesized using a simple co-precipitation method, then subsequently stabilized using ethylenediaminetetraacetic acid (EDTA). The gold coating was applied through the reduction of chloroauric acid by hydroxylamine at room temperature in aqueous solution onto the MNPs to form MAuNPs. The presence of the gold coating was confirmed by energy dispersive x-ray spectroscopy (EDS) and selected area electron diffraction (SAED) of micrographs obtained via high-angle annular dark-field scanning transmission electron microscopy (HAADF-STEM). The addition of EDTA to the MNPs resulted in enhanced reversible agglomeration but decreased irreversible aggregation of the MNP cores, as ascertained by dynamic light scattering (DLS). MNPs were determined to be 11 ± 2 nm in diameter. After gold coating, MAuNPs were found to be 27 ± 11 nm, yielding a gold layer thickness of approximately 8 ± 6 nm, as determined by transmission electron microscopy (TEM) and confirmed by grazing-incidence small-angle x-ray scattering (GISAXS). The MAuNPs functionalized with a reporter molecule showed appreciable Raman signal enhancement when compared with blank substrates coated with the same concentration of the reporter molecule. This enhancement proves their functionality as a label-free, reliable, and sensitive sensing technique for detection and quantification of trace contaminants, such as canola oil in olive oils in the commercial food industry or virus particles in saliva or mucus in a clinical setting.

Student 3-minute Presentation #14

Use of Fast Scanning Calorimetry to Obtain Crystallization Rates from The Melt of Polyethylene-Like Materials at Industrial Processing Conditions

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Polyethylene-like materials with in-chain acetal units (-O-CH_2-O-), precisely spaced by long methylene runs (between 12 and 26 CH_2), crystallize from the melt in four different crystallographic forms (polymorphs) depending on the depth of undercooling. The polymorphs were characterized via wide angle X-ray diffraction as disordered, hexagonal, Form I, and Form II phases with increasing crystallization temperature. Classical differential scanning calorimetry (DSC) demonstrated that the transition from Form I to Form II occurs in a narrow temperature range (< 1°C). At the transition, there is a minimum in the crystallization rate and extremely low levels of crystallinity. The latter recovers at temperatures above the transition. Because the disordered and hexagonal phases of these long-spaced polyacetals develop at large undercooling, not accessible by DSC, in the present work we have used fast scanning calorimetry (FSC) to obtain isothermal crystallization rates and heats of fusion of these samples. All polyacetals display inversions in the crystallization rate and low heat of fusion at the transition temperature between the disordered and hexagonal form, as well as in the transition between hexagonal and Form I polymorphs. These results, which indicate a general behavior of precision polyethylene-like materials reveal critical structure-property relationships needed for tuning industrial melt processing conditions of these and similar sustainable polymers.

Student 3-minute Presentation #15

Propulsion Kinematics and Magnetic Manipulation of Achiral Swimmers in Viscous Media

David Quashie Jr,[1,*] Hassana O'Conner,[1] Sophie Jermyn,[1] Paige Nielson,[1] Shannon Kelly,[1] David Gordon,[1] Camilo Ramirez,[1] Prateek Benhal,[1] Jamel Ali[1]
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Wireless control of small scale actuators using magnetic fields will play vital roles in future biomedical applications, including the targeted delivery of therapeutics. The Scallop theorem has long governed the fabrication, design, and control of micro and nano robotic swimmers at extremely low Reynold's number. As opposed to the more common flexible and chiral swimmers, geometrically simpler achiral structures have often relied on nearby solid boundaries to break the symmetry of cyclic swimming strokes. However, achiral swimmers with greater than two planes of geometric symmetry have been found capable of propulsion in the absence of confining walls. To magnetically control swimming of achiral structures in bulk fluids, the direction of magnetization must not lie on the dominant geometric axes; else kinematic time-reversal is maintained. Here the use of uniform rotational magnetic fields is used to induce achiral translation. We characterize the swimming of rigid linked, three and four bead structures in dilute polymer solutions of methylcellulose, demonstrating the effect of polymer concentration on velocity. Methylcellulose was chosen as its concentration can be tuned to represent the body's fluidic microenvironment. We further show effect of varying magnetic rotational frequency on precession angle and translation. Finally, by incrementally increasing the external magnetic field we determine the step-out frequency for these microrobots.

Student 3-minute Presentation #16

Towards Co-Culture Cancer Tissue Models: Rheological Characterization of Alginate-Gelatin Hydrogels

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Tissue models that closely mimic the tumor microenvironment are necessary for rapid high throughput screening of anticancer drugs. Currently, major bottlenecks in drug development are associated with limitations in our ability to manufacture heterogeneous cell-laden gels that mimic human tissues both physiochemically and structurally. The ability to control the viscoelastic properties of these gels and their micro-structure is critical to cell growth and tissue formation. In our current work, we investigate the optimization of the rheological parameters of a gelatin-alginate (Gel-Alg) hydrogel for eventual printing of co-culture of breast cancer tissues. By tuning the concentration of gelatin and alginate, we show that we can change/control the elastic modulus of the gels from 92.6 Pa to 395.6 Pa after ionic crosslinking with a 5% (w/v) CaCl2- solution for three minutes and 648.3 Pa after crosslinking for four minutes, thus making them ideal candidates for fabricating tissue models. Incubation of gels in a cell culture medium decreases the modulus. The most dramatic drop in moduli occurs in the first 3 days of incubation, from 648.3-245.0 Pa (at 3 min crosslinking) and 395.6-167.0 (at 4 min crosslinking). Less dramatic changes in moduli occur in the following days. In addition to the viscoelastic properties, the hydrogel system exhibits shear-thinning characteristics with viscosities of 153.0-3.6 Pa s at a shear rate of 1-50 s-1, which makes them ideal candidates/inks for 3D printing. Among the various Gel-Alg hydrogel compositions tested, 3%Alg-4%Gel (w/v) hydrogels were determined to have the optimal combination of moduli and viscosity, which resulted in the least post-print spread (line width 0.83 mm) and the best line uniformity (1.04). Future experiments are being carried out to incorporate breast cancer cells in the developed ink to print a 3D tissue scaffold and to investigate organoid formation.

Student 3-minute Presentation #17

Engineering Brain-Specific Pericyte and Endothelial Cell Co-culture from Human Stem Cells for Studying Immune Response

Mark Marzano[1]*, Zizheng Wang[2], Timothy Hua[4], Qing-Xiang Sang[4,5], Xueju Wang[2], Yan Li[1,5]
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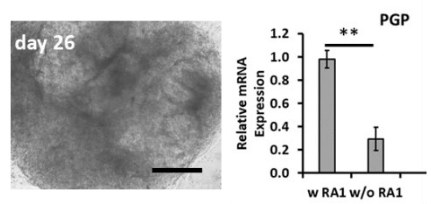
Background: Recently, the in vitro blood brain barrier (BBB) models derived from human pluripotent stem cells have been given extensive attention in therapeutics due to the implications it has with the health of the central nervous system (CNS). It is essential to create an accurate model of the BBB in vitro in order to better understand the properties of the BBB and how it can respond to immune stimulation and be passed by targeted or non-targeted cell therapeutics, more specifically extracellular vesicles.

Methods: Brain-specific pericytes (iPCs) were differentiated from iPSK3 cells using dual SMAD signaling inhibitors and Wnt activation plus fibroblast growth factor 2 (FGF-2). The derived cells were characterized by immunostaining, flow cytometry and RT-PCR. In parallel, blood vessels organoids were derived using Wnt activation, BMP4, FGF2, VEGF and SB431542. The organoids were replated and treated with retinoic acid to enhance the blood brain barrier (BBB) features in the differentiated brain endothelial cells (iECs). Co-culture was performed for the iPCs and iECs in transwell system and 3D microfluidics channels.

Results: The derived iPCs expressed common markers PDGFRb and NG2, as well as brain-specific genes FOXF2, ABCC9, KCNJ8, and ZIC1. The derived iECs expressed common endothelial cell markers CD31, VE-cadherin, as well as BBB-associated genes BRCP, GLUT-1, PGP, ABCC1, OCLN, SLC2A1. Both cells responded to the stimulation of amyloid beta 42 oligomers. The co-culture in transwell system showed the property of trans-endothelial electrical resistance (TEER). The co-culture was also demonstrated in 3D microfluidics channels, which can be used to study immune response.

Conclusion: The derived iPCs and iECs have brain-specific properties and the co-culture of iPCs and iECs provides an in vitro BBB model. This study has significance in establishing micro-physiological systems for neurological disease modeling and drug screening.



Left: Day 26 blood vessel organoids. Scale bar: 200 μm. Right: PGP (multidrug resistance protein) was promoted with Retinoic Acid. ** indicates significant difference.

Student 3-minute Presentation #18

Mesenchymal Stem Cell Impacts on Cerebral Microstructural Diffusion Recovery After Ischemic Attack

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Stroke occurrence is a widely researched topic in the context of diffusion MRI. Diffusion tensor imaging (DTI) quantifications of mean, axial and radial diffusivity (MD, RD and AD), and fractional anisotropy provide insights into hindered diffusion. As DTI protocols do not probe structures characterized by non-Gaussian water displacement associated with restricted diffusion, other probes of tissue microstructure like Diffusion Kurtosis Imaging (DKI) can evaluate intra-voxel diffusion tortuosity. Further, Neurite Orientation Dispersion and Density Imaging (NODDI) provides insight into intra-, extra-cellular and CSF structural compartments, as well as neuronal orientation. Though initially utilized to quantify neurite density, the intracellular volume fraction (ICVF) should provide an indicator of neurite swelling in the context of stroke pathology. Studies have shown the therapeutic efficacy of adult human mesenchymal stem cells (hMSC) in treating ischemic stroke, but none have compared the aforementioned advanced diffusion MRI techniques in characterizing them. This study aims to assess DTI, NODDI and DKI metrics comparatively to evaluate ischemic recovery following hMSC treatment.

This work utilizes DTI, NODDI and DKI processing techniques on diffusion data acquired at 21.1 T to identify specific microtissue changes in ischemic brain tissue following adult human mesenchymal stem cell (hMSC) treatment compared to controls. All scanning was conducted on days 1, 3, 7 and 21 post-MCAO and stem cell administration. Results show 2D hMSC significantly reduced cell swelling (via ICVF) at nearly every time point in white matter while preserving orientation integrity (ODI) and normal levels of restriction (DTI metrics), while also maintaining lower directional tortuosity (kurtosis) in the early phase. In grey matter, 2D hMSC restored DTI metrics to naïve levels quicker than control treatments, with reduced cell swelling, and faster return to naïve-like ODI. Grey matter kurtosis had high variability, but trends in the axial direction appear to be most consistent regardless of treatment.

Student 3-minute Presentation #19

Controlling Nanostructure of Block Copolymer Membranes

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Nanostructured materials, such as block copolymers, make it possible to combine disparate properties in a single material. It is difficult to design a homogeneous material that exhibits rapid, selective transport and mechanical strength. And yet, such properties are required in battery electrolytes and membrane separations. In our previous study, block copolymer structure was determined a function of salt concentration and temperature. [1] In addition, we studied viscoelasticity and structural dynamics with rheology and X-ray photon correlation spectroscopy (XPCS), respectively. Although the salt concentration had a significant effect on structure, the only effect on viscoelasticity and structural dynamics was due to changes in structure. The surprising observation of structural dynamics in an ordered block copolymer is thought to be due to grain rotations. In order to evaluate this hypothesis, we have attempted to control grain size using thermal and solvent vapor annealing. In particular, solvent vapor annealing [2-4] was used by casting polymer solutions under conditions in which the solvent evaporation rate was controlled. The optical appearance of films dried in 1 hour versus those exposed to solvent vapor for 1 week are dramatically different, indicating that this approach can be successfully used to control structure. Small- and wide-angle X-ray scattering (SAXS & WAXS) were used to investigate block copolymer morphology, grain size, and crystallinity over a wide range of evaporation rates. These complement efforts to determine BCP structure with atomic force and electron microscopies. Grain dynamics were probed with XPCS at the Advanced Photon Source at Argonne National Lab. In particular, the effect of structure on dynamics was examined in two sets of block copolymers with three different morphologies. In one set, the majority phase is highly mobile, while in another set the majority phase is glassy. Both ion and small molecule transport through polymers are dictated by polymer dynamics. Therefore, this work has relevance to polymer electrolytes for batteries and polymer membranes for separations.

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Student 3-minute Presentation #20

Comparing the Bone Regeneration Capacity of Extracellular Vesicles Isolated from Bone Marrow-Derived and Adipose-Derived Mesenchymal Stem Cells

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While the general risk of fracture nonunion is approximately 1.9%, this can rise significantly to over 9% in certain patient populations [1], including the elderly, smokers, those with chronic disease such as diabetes mellitus, and severe anemia, and those taking specific classes of medications [2]. Fracture nonunion may result in permanent disability and/or huge healthcare costs [3]. Mesenchymal stem cell (MSC)-based therapies have demonstrated tissue repair and regeneration capacity in various preclinical bone healing models [4]. These therapeutic effects have recently been largely attributed to the paracrine effects of the MSC secretome, including proteins and extracellular vesicles (EVs) [5]. EVs are cell-secreted nano-sized vesicles with lipid bilayer membranes that facilitate cell-cell signaling [6]. Treatments based on MSC-derived EVs are beginning to be explored as an alternative to MSC transplantation-based therapies due to their similar effects on angiogenesis, osteogenesis, and immunomodulation [7]. However, it remains to be determined which MSC source produces EVs with the greatest clinical therapeutic potential. While the most widely used MSC type is bone marrow- derived MSCs (BMMSCs) [8], there has been increasing interest in the clinical use of adipose- derived MSCs (ADMSCs) [9]. This study compares the bone healing efficacy of EVs derived from BMMSCs and ADMSCs via *in vitro* and *in vivo* assays.

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Awardees of Student Presentations

Thirty-minute Presentation

1st place Richard Jeske and Peter Rassolov (tie)

Three-minute Presentation

1st place Stephanie F. Marxsen

2nd place David Quashie Jr.

3rd place Carlos Germosen Polanco