Poster Session A, Wednesday June 12th, 12-1:15PM, Singh Center for Nanotechnology

Phase Separation in Living Matter
Author list: Hongbo Zhao, Amy Strom, Clifford Brangwynne, Sujit Datta, Andrej Kosmrlj
This poster explores the complexity of phase separation in two distinct biological systems: membraneless intracellular compartments in the cell nucleus and the collective behavior of bacteria. These systems are characterized by their complex interplay of mechanical interactions and nonequilibrium activities. Our work reveals how competition between elasticity and capillarity influences the structural and mechanical properties of chromatin networks, and how motility-induced phase separation coupled with movements along chemical gradients result in novel emergent phenomena in active systems. Looking forward, the theory and methodologies I developed for phase separation in fiber networks and active matter hold immense potential for unlocking new biophysics of living matter in complex and nonequilibrium environments.

Getting in shape—unraveling the morphodynamics of microbial communities
Authors: Alejandro Martínez-Calvo, Tapomoy Bhattacharjee, Carolina Trenado-Yuste, R. Kōnane Bay, Hyunseok Lee, Hao Nghi Luu, Anna M. Hancock, Jeff Gore, Ned S. Wingreen, and Sujit S. Datta
In nature, microbial organisms often self-organize into spatially structured communities, with distinct groups of cells occupying distinct spatial domains in 3D space. This spatial arrangement significantly influences diverse biological functions, including stability, nutrient access, and diversity; and yet, how exactly multicellular microbial communities get their shape and spatial structure remain poorly understood. Here, we first study how growing 3D bacterial colonies get their shape, a morphodynamical process that remains underexplored despite the prevalence of 3D environments in nature, e.g., soils and hosts. Using experiments in transparent 3D granular hydrogel matrices, we show that dense colonies generically become morphologically unstable and roughen as they consume nutrients and grow beyond a critical size—eventually adopting a characteristic broccoli-like morphology independent cell type and environmental conditions. This behavior reflects a key difference between 2D and 3D: while a 2D colony may access the nutrients needed for growth from the third dimension, a 3D colony inevitably becomes nutrient limited in its interior, driving a transition to unstable growth. We elucidate this instability using a continuum model that treats the colony as an “active fluid” whose dynamics are driven by nutrient-dependent cellular growth. We find that when all dimensions of the colony substantially exceed the nutrient penetration length, nutrient-limited growth drives a 3D morphological instability that recapitulates essential features of the experimental observations. Additionally, we extend our work to unveil the morphodynamics of multispecies communities, in which different microbes form monoclonal domains that compete for space and resources. What determines the shape of the interface between such domains—which in turn influences the interactions between cells and overall community function? Using a related model, we establish quantitative principles describing when different interfacial behaviors arise, and find good agreement both with the results of previous experimental reports as well as new experiments performed here. Altogether, our work thus provides a framework to predict and control the organization of proliferating colonies—as well as other forms of growing active matter, such as tumors and engineered living materials—in 2D and 3D environments.

Observing bacterial dynamics in transparent soil microcosms
Authors: Ahmed Al Harraq, Joshua Shaevitz, Sujit Datta.
Observing the dynamics of soil-dwelling bacteria in their environment is pivotal for our understanding of microbial survival and resource utilization. Soil presents a complex and heterogeneous environment which forces bacteria to adapt their growth and motility based on the morphology of their surroundings. Traditional methods of studying bacterial behavior in soils are inaccessible due to the opacity of natural soil matrices. To address this challenge, we create a transparent porous medium that emulates the structural heterogeneity found in natural soils. Unlike previous studies employing hydrogel-based porous media, our model incorporates cryolite, an impermeable mineral with a refractive index equivalent to water. This enables us to directly visualize bacteria using confocal microscopy in a structured environment that more accurately mimics soils by confining both the microbes and their nutrients. These cryolite-based porous media provide a minimalistic microcosm to test microbial responses to physicochemical changes such as

varying soil texture and chemical environment. Our results provide insights into bacterial proliferation and chemotactic migration within soil-like environments, bypassing the issue of opacity of natural soils.

Anomalous elastic behavior in soft fiber networks
Andrei Zakharov, Myra Awan, Arvind Gopinath, Sang-Joon John Lee, Anand K. Ramasubramanian, and Kinjal Dasbiswas
The mechanical properties of soft and fibrous biological materials play a crucial role in their function. However, understanding how these materials respond to external stress and internal cell traction remains a challenge. In this study, we investigate the nonlinear elastic behavior of blood clots using a combination of microscopy, rheology, and an elastic network model. This model considers the stretching, bending, and buckling of fibrin fibers, the structural components of blood clots. By inhibiting fibrin cross-linking, we observe an unexpected softening regime in the macroscopic shear response of clots, along with a decrease in platelet-induced clot contractility. Our model, supported by experimental evidence, attributes these findings to the bending stiffness of individual fibers. Our study offers insights into the nonlinear elastic properties of blood clots and provides a framework for understanding similar behaviors in other active biopolymer networks.

Ion-specific effects on charge transport in nanoconfined surfactant mesophases
"Author list: Christopher Johnson, Ranadeb Ball, Lizhu Zhang, Solmi Oh, Keira Culley, Jessica Anna, Amish Patel, Karen Winey, Chinedum Osuji
Ion exchange polymer membranes are a key component of our progress towards next-generation clean energy and water purification systems. To improve performance for use cases where ions have similar sizes but different chemical properties, we require understanding of the fundamental nature of ion motion in nanoscale spaces. By investigating highly ordered nanoconfined mesophases, we can deduce structure-property correlations for specific morphologies and ions. In this work, we polymerize a resilient quaternary ammonium surfactant monomer in a direct hexagonal (HI) mesophase for the purposes of ion conduction and diffusion. Using a combination of electrochemical impedance spectroscopy (EIS), two-dimensional infrared spectroscopy (2DIR), and molecular dynamics (MD), we investigate the motion of free anions within our membrane and track their interactions with cationic and polar charge centers. EIS shows us that there are differences in ionic behavior as a function of both hydration and the temperature within the system. Activation energies of highly polarizable I- and SeCN- are significantly higher than species like Br- and N3-. 2DIR and MD confirm the idea of these ion-specific interactions, and indicate that ions that strongly coordinate with positively charged centers have significantly hampered motion. Studies on nanoconfined restriction show that mesophase limiting dimensions are impactful so long as one considers a hydration shell a limiting dimension of transport. This work suggests that using precisely structured soft materials can provide new fundamental insight into ionic behavior and provide design rules for the next generation of ion-specific separation membranes."

Defect dynamics of colloidal antiferromagnetic tetratic phase confined in quasi-2d
Michio Tanaka, Yihao Chen, Arjun Yodh
We experimentally realize an antiferromagnetic tetratic phase with short-range translation order and quasi-long-range four-fold bond orientational order. The experiments employed hard-sphere micron size colloidal particles confined between parallel plates. We verify theoretical predictions (PHYSICAL REVIEW LETTERS 128, 255501 (2022)) of topological order resulting in bound pairs of oppositely-oriented dislocations and free dislocation pairs (FDPs) oriented at 90 degrees. FDPs move predominantly in the direction of their (total) Burgers vector unless in contact with another perpendicularly-oriented FDP. FDPs spontaneously form and annihilate only in oppositely oriented sets, conserving total topological charge. Further, FDPs have a tendency to align along an axis perpendicular to their (total) Burger's vector. We identify a region with significant defect movement resembling a ""free dislocation gas"" as well as a region of less activity resembling a Low Angle Grain Boundary in which ""cage-like"" dynamics are observed."

Instabilities and Twinning in Porous Elastomers

Peter Caulfield, Pedro Ponte Castañeda

Porous elastomers actuated pneumatically are an interesting candidate for soft active materials. Here we explore the behavior of porous elastomers under plane strain conditions, building on previous estimates [Lopez-Pamies & Ponte Castañeda, 2004, J. Elasticity 76, 247] derived from nonlinear homogenization theory for an incompressible neo-Hookean elastomer containing aligned cylindrical voids distributed randomly and isotropically. The incremental homogenized response was previously found to lose strong ellipticity for certain loading conditions, leading to the development of an instability in its mechanical response. We investigate the relaxed response by means of a generalized Maxwell procedure, corresponding physically to the formation of lamellar domains, or twins, and giving rise to soft modes of deformation, which can be advantageously exploited for actuation purposes.

Cholesteric Liquid Crystal Elastomers (CLCEs) Coating for Enhanced Impact Resistance of 3D Shellular Structures

Shangsong Li, Ziting Tian, Kunyu Wang, Zhengdan Lin, and Shu Yang, Department of Materials Science and Engineering, University of Pennsylvania
Marcos Reyes-Martinez, and Edwin Chan, Materials Science and Engineering Division, National Institute of Standards and Technology
Doksoo Lee, and Wei Chen, Department of Mechanical Engineering, Northwestern University

Shellular structures with assembled empty cells on a continuous surface have both light weight and high strength, with different curvatures and subdivided cell densities making their properties variable. However, their toughness is yet to be enhanced. Liquid crystal elastomers (LCEs) are good energy absorber by mechanism of stress-induced LC molecules reorientations. Further, cholesteric LCEs (CLCEs) have surface twisted lamellar structure showing shiny color for photonic devices, with potential toughness enhancement unexplored previously. Here, CLCE films are coated on 3D shellular structures, showing vivid structural color with controlled and tunable color distribution. At nano scale, the lamellar structures in CLCE showed enhanced modulus in indentation tests compared to LCE. At macro scale, the impact resistance of CLCE coated shellular structures are greatly increased for different curvatures and cell densities. As an innovative combination of CLCE assembly at nano scale and shellular structures at macro scale, this research is promising for applications such as biomimetics, shock absorbing materials, and functional building materials.

Spontaneous assembly of condensate networks during the demixing of structured fluids.

Christopher Browne and Chinedum Osuji.

Phase separation plays an important role in industrial separations and biological compartmentalization. However, little is known about such condensation in structured fluids. We demonstrate how some structured fluids can form filamentous condensates, which grow, tangle, and knot. By controlling these dynamics, we can direct the self-assembly of dynamic condensate networks, which remain “living” for hours by constant self-remodeling.

Coalescence of Sessile Radial Nematic Droplets

Slaughter, Charlotte1*; Ettinger, Sophie; Chen, Yihao; Feng, Zhe; Zhang, Rui; Collings, Peter and Yodh, A.G.
1 University of Pennsylvania, Philadelphia, PA

We report on experiments that demonstrate coalescence of two “largely” radial nematic liquid crystal (NLC) droplets with homeotropic anchoring. Previously, extensive theoretical work has suggested that coalescence of two NLC radial droplets is prevented by the energy barrier for formation of a topological defect between the two droplets [1, 2]. Our experimental work suggests that droplet wetting and deformation lowers this energy barrier. We describe the spontaneous formation of a Q = −1 defect at the neck between two sessile droplets, and the subsequent annihilation of defects to generate a single radial hedgehog droplet with a Q = +1 defect. Using polarized optical microscopy (side and top views), we are able to observe droplet merging and defect and director evolution, as well as characterize how the drop contact angle influences likelihood of coalescence. Simulations were also employed to build connections with the POM images and director configurations, as well as to calculate the change in energy due to distortion of the director field, which suggests that the coalescence energy barrier is lowered.

[1] Heppenstall-Butler , M. , Williamson , A. M. and Terentjev , E. M. 2005 . Liq. Cryst. , 32 : 77

[2] Terentjev , EM . 1995 . Europhys. Lett. , 32 : 607

Enzyme chemotaxis and non-reciprocal interactions

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Enzyme chemotaxis is the directional motion of enzyme molecules towards or away from a gradient of their respective substrates and products. The phenomenon has wide-ranging implications for not just modern-day applications, such as drug delivery and disease detection, but also for determining the physiochemical driving force behind the origin of life and its subsequent evolution. We show two factors: 1) kinetic asymmetry, the difference between the unbinding rates of the substrates and the products and 2) diffusion asymmetry, the difference in the diffusivities of the unbound and the bound form of the enzyme, govern the direction of enzyme chemotaxis. Our model captures the non-equilibrium distribution of enzyme molecules while being consistent with the dynamics of low Reynold's number regime. Further, we show that enzyme chemotaxis can generate nonreciprocal interactions between complementary enzymes, such as a pair of kinase and phosphatase. Nonreciprocal interactions are common in living systems such as predator-prey interactions, flocking of birds, and swarming of fish. Our work provides a molecular origin for nonreciprocal interactions which may explain the collective motion of enzymes such as metabolon formation and throw light on the origin of life.

Fat is more rigid & physically disruptive than you might think.

Ivanovska, Tobin, Georgiou, Discher.

We had first noticed years ago that fat droplets in stem cells undergoing adipogenesis have nuclei that are heavily indented by micron-sized lipid droplets filled with fat. No one seems to have measured the effective interfacial tension of such fat-filled lipid droplets taken from tissue, and our measurements conform to typical oil-water systems. Imaging of fat cells in tissue show one large droplet per cell that displaces and deforms the nucleus and cytoskeleton, but they are imperfect spheres consistent with Law of Laplace. The results align with higher levels of collagen in fat compared to softer tissues such as brain. Cell culture studies further show that fat droplets can even rupture the nucleus, increase DNA damage, and undermine cell cycle, confirming the mechanically disruptive nature of fat.

A Braess paradox analog in optimal search networks.

Georgios Gounaris, Eleni Katifori

What is the optimal network architecture to minimize the time it takes for a random walker to find a randomly selected target node? A low first encounter time is the key to successful exploration both for diffusion in real space, like the motion of a protein inside a living cell and for the stochastic transitions in an energy landscape. Intuition suggests that adding a shortcut between the random walk's starting and target nodes will reduce the pair's mean first passage time. Considering the mean first passage time between all pairs, one would assume that a topologically well-connected network would be optimal. Counterintuitively, we find that this is not always the case. We show a Braess paradox analog in the case of diffusive exploration in spatially embedded graphs in which the transit time through an edge scales as the mean squared displacement of the random walk through the edge. For regular diffusion a shortcut longer than the average edge length of the graph can deteriorate the overall search efficiency of the network, although it bridges topologically distant nodes. Ultimately, to investigate the interplay between the graph structure and anomalous diffusion, we propose an optimization scheme according to which each edge can adapt its conductivity until the graph's average pairwise mean first passage time is minimized. The optimization reveals a crossover in the network's architecture: for super-diffusive motion, the optimal graph is small-world, while for sub-diffusive propagation short-range networks are optimal. We believe that this optimization approach might give insights to investigate the mechanisms that highly optimized biological systems employ to solve the problem of efficient exploration in various length scales.

Mechanical prions: Self-assembling microstructures
Mathieu Ouellet, Dani S. Bassett, Lee C. Bassett, Kieran A. Murphy, Shubhankar P. Patankar.
Prions are misfolded proteins that transmit their structural arrangement to neighboring proteins. In biological systems, prion dynamics produce a variety of complex functional outcomes. Yet, an understanding of prionic causes has been hampered by the fact that few computational models exist that allow for experimental design, hypothesis testing, and control. Here, we identify essential prionic properties and present a biologically inspired model of prions using simple mechanical structures capable of undergoing complex conformational change. We demonstrate the utility of our approach by designing a prototypical mechanical prion and validating its properties experimentally. Our work provides a design framework for harnessing and manipulating prionic properties in natural and artificial systems."

Matrix stiffness genomic instability and variation in cancer spheroids
Alişya A. Anlaş*, Brandon H. Hayes, Mai Wang, Markus Sprenger, Steven Phan and Dennis E. Discher
University of Pennsylvania, Department of Chemical and Biomolecular Engineering, Department of Bioengineering
Genomic instability, the inability of a cell to pass on its genetic information accurately, is a hallmark of cancer. Aneuploidy, or an abnormal number of chromosomes, is observed in approximately 85% of solid tumors. During cancer progression, changes in the mechanical microenvironment can physically restrict cancer cells and induce errors in DNA replication or mitosis. Using chromosome reporter cell lines, we investigated whether a three-dimensional (3D) tumor microenvironment contributes to aneuploidy and found that increased matrix stiffness increases mitotic aberrations that may lead to chromosome missegregation. Our findings indicate that stiff microenvironments suppress mitosis, increase micronucleus formation, and enhance chromosome loss, thus highlighting a potential role for mechanical confinement in chromosome segregation. We also find that inhibiting myosin-II increases chromosome loss without affecting spheroid growth. The variance in chromosome loss across cancer spheroids increases per Luria-Delbruck's theory of heritable genetic change and is also consistent with the emergence of colonies with chromosome loss. Overall, our findings indicate that increased matrix stiffness increases heritable genomic instability and tumor heterogeneity -a deeper understanding of which could contribute to synergistic treatments for cancer.

Multiscale soft matter physics in baseball gripping
Pradeep Shravan, University of Pennsylvania

Pan-tissue percolation scaling of viscoelasticity with tissue collagen reflects strain-inhibited fibril degradation
K. Saini1, S. Cho1, M. Tewari1, A. Jalil1, M. Wang1, S. Belt1, B. Lee1, B. Taichman1, A. Kasznel1, K. Yamamoto2, D. Chenoweth1, K. Margulies1, and D. E. Discher1
1 University of Pennsylvania, Philadelphia, PA 19104, USA; 2 University of Liverpool, UK
Many processes in mature and developing solid tissues are impacted by tissue physical properties. Such physical properties often exhibit characteristic power-law scaling similar to polymer network properties with polymer density and reflect an underlying gelation transition. Here, we show rigidity percolation of the collagen-fiber networks within living tissues provides a robust framework to predict pan-tissue scaling of biophysical properties while reflecting contractile-strain driven collagen degradation. Progressive degradation of collagen-fibers in diverse adult tissues is imaged by label-free second harmonic generation (SHG) and paired with viscoelasticity measurements to reveal a gel-to-sol critical transition brought about by small reductions of fiber density above critical levels. Importantly, a pan-tissue percolation exponent ($z \sim 1.4$) predicts a similar power-law exponent for scaling of elasticity, viscosity, and plasticity with collagen-fiber density across adult and embryonic tissues – including perturbations to tissue contractile-strain. Pan-tissue scaling of tissue stiffness with Collagen-I levels, measured by SHG and by mass-spectrometry (MS), exhibits a sub-linear scaling that aligns with results from cellularized gels of Collagen-I but not acellular gels. Water content and cell-density variations across tissues also indicate a rigidity transition. Verification of collagen-I protein scaling with SHG signal forms the basis for a contractile-strain stabilized feedback loop, which predicts scaling of tissue stiffness with collagen-I RNA. Importantly, the inhibition of cellular contractile strains fits the scaling, and combination with inhibitors of matrix metalloproteinases (MMPs) show collagenase activity is strain - not stress - suppressed in tissues. Universality of collagen-fiber percolation together with stiffness scaling based on 'use-it-or-lose-it' kinetics not only provides matrix-based metrics for

live tissue health, pathology, and regeneration but also provides insight into organ-size scaling with body-weight while suggesting contractility-driven therapeutics.

Morphodynamics of mixed bacterial communities proliferating in three dimensions
Authors: Meera Ramaswamy, Carolina Trenado Yuste, Alejandro Martínez-Calvo, Ned S. Wingreen, Sujit S. Datta
Abstract: In nature, bacteria often grow as communities in three-dimensional (3D) environments, with multiple different cell types cooperating or competing for resources. While many studies have investigated how proliferation drives the spatial organization of multi-strain/species communities in two dimensions, little is known about the morphology of these communities in three dimensions. Here, we use two different strains of E. coli suspended in a transparent jammed packing of microgel particles to investigate the morphodynamics of communities with multiple cell types proliferating in 3D. Unexpectedly, even though the strains are initially well-mixed, we find that they proliferate into segregated microcolonies within the overall community, with the size and shape of each microcolony determined by the initial cell density and colony width. We rationalize these results by considering the interplay between proliferation, competition for space, and competition for nutrients. Taken altogether, our results help to shed new light on the morphodynamics of mixed microbial communities, as well as other forms of proliferating active matter, in 3D.

Poster Session B, Wednesday June 12th, 5-7PM, Singh Center for Nanotechnology

Modeling Exogenously and Endogenously Controlled Bioinspired Materials,
Author List: Michael Norton, John Berezney, Katsu Nishiyama, Seth Fraden, Zvonimir Dogic, Mike Hagan, Aparna Baskaran, Piyush Grover,
Active fluids comprised of reconstituted biopolymers and motor proteins are self-driven materials that exhibit rich spatiotemporal dynamics. In microtubule-based active nematics, these dynamics are characterized by buckling instabilities and the proliferation of topological defects in orientational order. These defects drive material flows and give the microtubule system its characteristic texture and chaotic dynamics. One of the grand challenges of active soft physics is aimed at engineering such materials to exhibit desired spatiotemporal patterns. In my poster, I'll outline progress towards two kinds of control strategies: those that come from external fields and those that are generated from within the material itself and governed by reaction-diffusion processes. This work is supported by the Brandeis MRSEC (DMR-2011846) and a DOE grant lead by University of Nebraska-Lincoln (DE-SC0022280).

Exploring evolutive dynamics in three-dimensional bacterial colonies and beyond.
Authors: Alba García Vázquez (presenter), Namiko Mitarai, Liselotte Jauffred.
Genetic fluctuation on the expanding front is a key process driving evolution during range expansion. When a bacterial population attached to a surface is expanding, random fluctuations in the growth of the pioneers at the front line cause a strong de-mixing of genotypes. Extensive studies of range expansions in surface-attached colonies of fluorescently-labeled microorganisms have significantly contributed to our understanding of fundamental evolutionary dynamics. However, experimental studies on genetic fluctuations in three-dimensional range expansions have been sparse, despite their importance for understanding tumour or biofilm development. Here, we provide a novel and simple model to investigate dynamics in three-dimensional bacterial colonies. The method consists in encapsulating populations of cells in inoculation agarose beads. The confined cells can grow when embedded in a matrix with nutrients and develop in quasi-spherical three-dimensional colonies with well-defined sectors. We characterized how cell concentration in the inoculation droplet controls sectors and growth rate. We complement these experimental results with a modified 3D Eden growth model and point out qualitative differences between radial and spherical range expansions in bacterial neutral competition experiments. Our novel technique, due to its simplicity, extends competition assays from two to three dimensions. The method is not restricted to bacterial cells but can also be applied to other cell types such as yeasts and potentially mammalian cells. We are confident that this method will shed light upon the development and evolutive dynamics in three-dimensional environments.

Hierarchical assembly is more robust than egalitarian assembly in synthetic capsids.
Wei-Shao Wei, Anthony Trubiano, Christian Sigl, Stefan Paquay, Hendrik Dietz, Michael F. Hagan, Seth Fraden.
Self-assembly of complex and functional materials remains a grand challenge in soft material science. Efficient assembly depends on a delicate balance between thermodynamic and kinetic effects, requiring fine-tuning affinities and concentrations of subunits. By contrast, we introduce an assembly paradigm that allows large error-tolerance in the subunit affinity and helps avoid kinetic traps. Our combined experimental and computational approach uses a model system of triangular subunits programmed to assemble into T=3 icosahedral capsids comprising 60 units. The experimental platform uses DNA origami to create monodisperse colloids whose 3D geometry is controlled to nanometer precision, with two distinct bonds whose affinities are controlled to kBT precision, quantified in situ by static light scattering. The computational model uses a coarse-grained representation of subunits, short-ranged potentials, and Langevin dynamics. Experimental observations and modeling reveal that when the bond affinities are unequal, two distinct hierarchical assembly pathways occur, in which the subunits first form dimers in one case, and pentamers in another. These hierarchical pathways produce complete capsids faster and are more robust against affinity variation than egalitarian pathways, in which all binding sites have equal strengths. This finding

suggests that hierarchical assembly may be a general engineering principle for optimizing self-assembly of complex target structures.

Machine learning that predicts well may not learn the correct physical descriptions of glassy systems

Arabind Swain, Sean Ridout, and Ilya Nemenman

The complexity of glasses makes it challenging to explain their dynamics. Machine Learning (ML) has emerged as a promising pathway for understanding glassy dynamics by linking their structural features to rearrangement dynamics. Support Vector Machine (SVM) was one of the first methods used to detect such correlations. Specifically, a certain output of SVMs trained to predict dynamics from structure, the distance from the separating hyperplane, was interpreted as being linearly related to the activation energy for the rearrangement. By numerical analysis of toy models, we explore under which conditions it is possible to infer the energy barrier to rearrangements from the distance to the separating hyperplane. We observe that such successful inference is possible only under very restricted conditions. Typical tests, such as the apparent Arrhenius dependence of the probability of rearrangement on the inferred energy and the temperature, or high cross-validation accuracy do not guarantee success. We propose practical approaches for measuring the quality of the energy inference and for modifying the inferred model to improve the inference, which should be usable in the context of realistic datasets.

Enhancing bone tissue regeneration through mechanical, chemical, and biological regulation of bone extracellular matrix.

Micaila Curtis, Georgetown University

Bone fractures caused by injuries due to aging and stress require reconstruction to restore tissue function. As we age, current grafting-based treatments are limited by supply and donor match rates. Additionally, there are limited options for bone tissue regeneration for bone diseases such as osteoporosis, leaving these individuals with high risks of fractures and health decline. Most bone homeostasis declines due to aging as the tissue undergoes changes in its extracellular matrix (ECM) composition, impacting the bone cells that contribute to bone mineralization and strength. To overcome such limitations in treatments and intervention methods, we will incorporate calcium phosphate and vitamin C to 3D-bioprintable bone ECM for bone regeneration.

For a deeper understanding of the role of aging in bone ECM, we will develop a 3D microphysicological system recapitulating the 3D composition/structure of bone ECM. Specifically, to engineer the 3D bone matrix, 1-5% w/v hydroxyapatite (HA) was dissolved in 4-25% w/v Ascorbic Acid (AA). The HA/AA solution was mixed with collagen at final concentration of 3mg/ml and fibronectin at concentration of 5µg/ml. Human primary osteoblasts (HOBs) at density 0.1 million/ml are embedded in the ECM and human umbilical endothelial cells (HUVECs) are used to mimic the bone microvasculature. The structure roughness, porosity, composition, viscoelasticity, and other mechanical properties of the ECM are measured by SEM, FTIR, AFM, and rheology. Finally, the biocompatibility of the ECM and bioprinting on HOBs is measured by apoptosis staining for caspase 3/6 in vitro and by implanting 3D-bioprinted scaffolds into C57Bl/6 mice. Mechanical properties were evaluated in young (passage <4 cells) and aged (passage >4 cells), as well as in secondary osteoporotic models as established by treatment of devices or mice using glucocorticoids.

Our results from SEM, FTIR, and rheology demonstrated differences in 3D ECM porosity, roughness, stiffness, and viscoelastic behavior. Specifically, AA in the ECM supported the formation of COL bundles and improved matrix mechanical properties for cellular health.

Overall our 3D micro physiological systems permit us to fine-tune the microenvironment that cells are sensing and measure the dynamic changes of bone regeneration in vitro, avoiding animal studies. Finally, these platforms will enable us to identify new molecular mechanisms in aging bone diseases and develop new bioengineered tools for bone tissue regeneration, such as implantable bone scaffolds.

Acknowledgments: This work was supported by Georgetown Funding (91252), the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health (R21AR076497), and the Georgetown University Aging and Alzheimer's Research Training NIH T32 Program (GR414768).

The role of facilitation in the glass transition in polymers
Peter D Olmsted, Matthew Reynolds, Daniel L Baker, Johan Mattsson
The glass transition temperature Tg(M) of polymers depends strongly on the molecular weight M. We have shown that Tg(M) may have a universal functional form, independent of chemical details, for polymers with high internal dihedral barriers. We will discuss how this can be understood in terms of facilitation, and report on recent measurements of the characteristic size of dynamical heterogeneties. We propose a scheme for understanding this in terms of facilitation that is consistent with Tg(M).

Memory of shear flow in soft jammed materials
Authors: H. A. Vinutha, Manon Marchand, Marco Caggioni, Vishwas V. Vasisht, Emanuela Del Gado, and Veronique Trappe
The mechanical properties of complex fluids are well known to depend on their shear history. However, the mechanisms through which memory is imparted to the material remain poorly understood. In this study, we combine experiments and simulations to investigate the memory of shear flow in flow cessation tests. Our findings reveal that shear flow imprints a memory of spatial correlations in the dynamics of neighboring particles as well as a memory of local particle configurations. Both aspects contribute to distinctive characteristics in the stress relaxation process observed upon flow cessation.

Introducing Amigami
Noah Toyonaga, L. Mahadevan;
We name amigami the art of constructing shape morphing structures from a lattice of scissor mechanisms. we demonstrate that such lattices can be designed using a closed form local rule and use our algorithm to build desktop-scale toys with controlled curvature and geometry

Postural control of an upright “standing” snake
Ludwig A. Hoffmann, Petur Bryde, Ian C. Davenport, S Ganga Prasath, Bruce C. Jayne, L Mahadevan
Posture and its control is a fundamental aspect of behavior. Here we investigate an extreme example of posture control, that of a slender snake that can ``stand'' upright, with 3/4 of its length being almost vertical, as it moves from one perch to another. Inspired by observations of the shape and stability of this posture in tree snakes and juvenile pythons, we provide theoretical frameworks for this phenomena combining the physics of active filaments with the principles of optimal control theory. We start from the simple perspective of an active filament that can exert (non-local) muscular torques to characterize the posture of a standing snake, before moving to a control-theoretic model posed as an optimization problem, and finally close with a discussion of the dynamic stability of the snake in this precarious pose. Our results are qualitatively consistent with observations, and lead to a phase diagram for the stability of standing snakes and their robotic mimics.

Signatures of energy dissipation in chemotaxis signaling pathways
David Hathcock, Qiwei Yu, Yuhai Tu
Chemotaxis signaling pathways in Escherichia coli are driven out of equilibrium by ATP hydrolysis, which enables the phosphorylation of messenger proteins that carry signals from the chemoreceptors on the cell surface to the motors that control the bacteria’s swimming motion. Two recent measurements of chemosensory response and dynamics that reveal subtle, but clear signatures of this underlying dissipation. First, adaptation by methylation of chemoreceptors shifts the downstream intracellular response by two orders of magnitude in ligand concentration, which is disproportionately larger than the adaptive shifts in ligand binding response. Second, even in the absence of external stimuli, cells spontaneously switch between active and inactive kinase states, with dynamics that break time-reversal symmetry. To understand these behaviors, we introduce nonequilibrium allosteric and lattice models of the chemoreceptor array that resolve these experimental observations and explain they how arise from dissipative collective dynamics. Our models also provide new insights into the microscopic mechanisms underlying of the chemosensory array and the role of energy dissipation in enhancing cooperative sensing and adaptation.

Controlling flow patterns and topology in active emulsions.
Authors: Louise C Head, Giuseppe Negro, Livio N. Carenza, Tyler N. Shendruk, Davide Marenduzzo, Giuseppe Gonnella, Adriano Tiribocchi.
Active emulsions and liquid crystalline shells are intriguing and experimentally realisable types of topological matter. Here we numerically study the morphology and spatiotemporal dynamics of a double emulsion, where one or two passive small droplets are embedded in a larger active droplet. We find activity introduces a variety of rich and nontrivial nonequilibrium states in the system. First, a double emulsion with a single active droplet becomes self-motile, and there is a transition between translational and rotational motion: both of these regimes remain defect-free, hence topologically trivial. Second, a pair of particles nucleate one or more disclination loops, with conformational dynamics resembling a rotor or chaotic oscillator, accessed by tuning activity. In the first state a single, topologically charged, disclination loop powers the rotation. In the latter state, this disclination stretches and writhes in 3D, continuously undergoing recombination to yield an example of an active living polymer. These emulsions can be self-assembled in the lab, and provide a pathway to form flow and topology patterns in active matter in a controllable way, as opposed to bulk systems that typically yield active turbulence."

Cell motility self-regulated by secreted footprints
Authors: Perez Ipiña, E., d'Alessandro, J., Ladoux, B., Camley, B. A.
Abstract: Eukaryotic cell migration is essential to biological processes like embryonic development, immune response, wound healing, or cancer metastasis. During migration, there is a complex interplay between cells and their environment, as cells respond to environmental signals and actively alter their surroundings. Recent experiments observed that MDCK epithelial cells, when placed on 1D fibronectin micropatterned stripes, leave a footprint on the substrate that modifies their own motility, resulting in oscillatory motion. This talk will explore how footprint secretion affects cell motility patterns by combining mathematical modeling and experiments. We assume that cells secrete a footprint that activates signaling pathways that regulate cell polarity. The model reproduces the observed oscillatory motion and predicts new 2D motility patterns, which are experimentally verified. We show that minor changes in footprint interactions can cause cells to switch from confinement to complex exploratory dynamics. This study highlights the potential of cells to self-regulate their motility using footprints and provides insight into the mechanisms guiding cell migration.

Taming Active Nematic Topological Chaos Through Defect Pinning on Sharp Boundary Features
Brandon Klein, Kevin A. Mitchell, Linda S. Hirst, Daniel A. Beller
In active nematic liquid crystals, topological defects drive chaotic flows in the bulk. Confined geometries with uniform curvature have been shown to produce ordered defect motion and flows. However, little is known about ordered defect motion enabled by boundaries with varying curvature. To explore how varying curvature can control the active steady state, we simulate an active nematic system using active Beris-Edwards nematodynamics with curved boundary walls. In particular, we investigate the effects of varying bulk topological charge via pinning defects on boundary features. We show that locally convex and concave boundary features have defect pinning effects on positive and negative topological charge respectively, and demonstrate a scheme to tune the strength of defect pinning, expanding the possibilities of ordered states. Using tools from braid theory, we characterize the trajectories and topological entropy associated with fluid mixing resulting from ordered defect motion and show that active nematics can generate maximally mixing braids in their confining geometries. Our findings suggest routes to controllable bulk active flows utilizing boundary features.

Serial flow cytometry as a method to measure membrane elasticity
Leroy Jia, Sydney Lee, Matthew DiSalvo, Paul Patrone, Gregory Cooksey
Flow cytometry, in which cells or other kinds of particles are flowed through a microchannel and measurements of attached fluorescent biomarkers are made, has been used to detect, count, and sort particles with extremely high accuracy and repeatability. We built upon this technology and invented a robust method to measure the elasticity of cell membranes. High-speed neuromorphic cameras were used to accurately image the deformations of membranes as they traveled through the instrument. An asymptotic theory based on perturbing coupled Stokes equations allows us to calculate the deformations in terms of spherical harmonics and determine the focusing positions of particles. We demonstrate that this information allows us to determine the elasticity and other physical properties of the cell with controlled uncertainty.

Exploring the geometry of the energy landscape of jammed packings
Mathias Casiulis, Praharsh Suryadevara, Stefano Martiniani

Emergent Activity
Authors: Ella M. King, Mia C. Morrell, Jacqueline B. Sustiel, Matthew Gronert, Hayden Pastor, David G. Grier
Active matter, a form of matter with components that consume energy and convert it to motion, has already spurred the discovery of new materials properties. Thus far, active matter has been limited to systems with individually driven components. Here, we uncover a new form of activity that emerges as a collective property of the system. While individual particles remain stationary, clusters of particles gain the ability to transduce energy from the environment and use it to propel their motion.
This emergent activity arises in systems of particles immersed in a wave. Scattering of the incident wave off the particles induces an effective force that is not reciprocal: the force of one particle on a second particle is not necessarily equal to the force of the second particle back on the first. This apparent violation is allowed because the system is not closed. However, as a result of this nonreciprocal force, clusters of particles exhibit several modes of motion, including rotation and translation. The motion can be tuned via readily accessible experimental parameters, such as particle configuration, size, and density, making the system well-poised for inverse design of complex dynamics.

Intermittency and clogging in complex fluid flows through confined geometries
Sara Hashmi, Northeastern University
Intermittency and clogging of complex fluids flowing through small spaces can occur nearly anywhere: in the porous media of the earth, in industrial flows through hoppers, in water filters, 3D printing nozzles, and in some of the worst instances, in our blood vessels. These examples include flows of colloidal particles, granular material, crosslinking polymers, and multicomponent systems. Despite the differences in the type of complex fluid involved, some aspects of clogging are universal, like its stochastic nature and the importance of the constituent material properties. Our research explores intermittency, clogging, and flow in micro- and macroscopic flows. In colloidal and granular flows, we vary the softness of the constituent particles and the fraction of soft particles in a mixture. In this way we elucidate how softness controls phenomena like clogging and avalanches. Polymers crosslinking in situ in flow through microchannels also exhibit intermittent dynamics reminiscent of avalanches. In these flows, gelation, deposition, and ablation can occur repeatedly and persistently. Intriguingly, despite the low-Re nature of the flow, we find signatures of chaotic behavior as conditions approach regions of complete failure. This model system might represent situations encountered in polymer flows in 3D printing applications, or, in a greatly simplified way, two of the final steps in the coagulation cascade.

Emergent Mesoscale Correlations from Noisy Chiral Dynamics in Active Solids
Amir Shee, Silke Henkes, Cristián Huepe
Across scales, from molecules to tissues, dense biological systems can exhibit collective dynamics driven by noise-induced activity and elastic interactions, including flocking transitions and long-range spatiotemporal order. In this work, we consider active solid composed of densely packed systems of active Brownian particles with intrinsic individual chirality from a theoretical perspective, showing that these can lead to the emergence of a variety of states, including collective rotating mesoscopic order. Using dual analytical approaches—one based on normal modes and the other on continuum elasticity—this study provides a comprehensive understanding of the states that can be observed in the systems, matching very well our numerical simulations. Our findings suggest that the collective rotating states that we identify may generically appear in natural and artificial active solids.

Mechanically guided self-patterning of confined three-dimensional growing biofilms
Changhao Li, Japinder Nijjer, Jing Yan, Sulin Zhang
Active nematics are the non-equilibrium analogue of passive liquid crystals. They consist of anisotropic units that consume free energy to drive emergent behaviour. As with liquid crystal molecules in displays, ordering and dynamics in active nematics are sensitive to boundary conditions. However, unlike passive liquid crystals, active nematics have the potential to regulate their boundaries through self-generated stresses. Here we show how a three-dimensional, living nematic can actively shape itself and its boundary to regulate its internal architecture through growth-induced stresses, using bacterial biofilms confined by a

hydrogel as a model system. We show that biofilms exhibit a sharp transition in shape from domes to lenses in response to changing environmental stiffness or cell–substrate friction, which is explained by a theoretical model that considers the competition between confinement and interfacial forces. The growth mode defines the progression of the boundary, which in turn determines the trajectories and spatial distribution of cell lineages. We further demonstrate that the evolving boundary and corresponding stress anisotropy define the orientational ordering of cells and the emergence of topological defects in the biofilm interior. Our findings may provide strategies for the development of programmed microbial consortia with emergent material properties.

Nucleation pathways of multicomponent biomolecular condensates: a cautionary tale of the classical nucleation theory
Qiwei Yu, Yury Polyachenko, Ned S. Wingreen, Mikko Haataja, William Jacobs, Andrej Košmrlj
Intracellular phase separation plays a crucial role in regulating important biological processes, such as transcription and DNA organization. In certain cases, condensates assemble via processes analogous to nucleation and growth in abiotic systems (e.g. first-order liquid-gas phase transition). However, a quantitative description of the nucleation landscape must also account for both the multicomponent nature of bimolecular condensates and the crowded intracellular environment.
Here, we address this question by combining theory, molecular simulation, and continuum-scale numerical methods. To illustrate the idea, we consider a 3-component system where the third component occupies only a minority volume fraction but can lower the free-energy barrier for nucleating one of the two majority components. We find that, at low mobilities and in the presence of significant thermal fluctuations, the preferred nucleation pathway can deviate significantly from predictions of Classical Nucleation Theory (CNT), in terms of both the concentration profiles and the free-energy barrier. We will discuss scenarios in which this discrepancy becomes important and the resulting biological implications."

Block-copolymer stabilized lipid nanoparticles: A novel platform for targeted gene delivery,
Nikhil Subraveti, Princeton University

Pattern Formation for Functionality in Soft Matter Systems – Buckled Phononic Crystals and Liquid-Liquid Phase Separation in Flow
Authors: Tejas Dethe, Howard A. Stone, Andrej Košmrlj
Pattern formation as a result of spontaneous symmetry breaking, beyond its visual appeal, not only can mediate biological function but also be harnessed to create novel materials. Our work focuses on two different systems – elastic phononic crystals and phase separating flows – to elucidate how patterns arising in soft matter can be used to create functional materials.
Elastic phononic crystals are soft, deformable metamaterials that have periodic modulations in their materials properties, which are used to control the propagation of acoustic waves for applications such as filtering and wave-guiding. The wave propagation properties, represented via band diagrams, are not only affected by materials properties, but also by symmetry properties of the crystal. These properties can influence the formation of directional as well as complete band gaps. We have developed a group representation-based framework to explain the effects of unit cell symmetries in the band diagram for undeformed elastic phononic crystals. We are now extending the group theoretic framework to account for symmetry-breaking bifurcated patterns in deformable crystals caused by buckling. This generalized symmetry-based analysis can be used to formulate rational design rules for acoustic metamaterials as well as be used to study generalized problems in soft matter physics via group-theoretic considerations.
Phase separating flows, on the other hand, can lead to patterns based on nonequilibrium thermodynamics. These patterns can be used to create multilayered multicomponent droplets, as has been shown by previous researchers in Oil-Water-Ethanol systems. We study the problem of phase separation caused by the selective diffusion of one component (ethanol) out of a ternary mixture, making the mixture unstable to perturbations that lead to spinodal decomposition. In a simplified 1D Flory-Huggins type model with Cahn-Hilliard kinetics, we see the emergence of a concentration-dependent interaction parameter that guides which spatial regions of the ternary mixture have the potential to undergo phase separation. We are now characterizing the properties of an associated phase separating front, by exploring the front velocity and spectral properties of the patterns created. Our analysis can then be used for phase separation in microchannel co-flow systems, which can help design material fibers or droplets by controlling the underlying pattern-forming phase separation processes.

Physical constraints and adaptive potential of natural immunity

Authors: Hongda Jiang, Milos Knezevic, Qing Xu, Pavel Tolar, and Shenshen Wang*

The adaptive immune system of vertebrates is able to learn from past experiences to better suit an unforeseen future. This is made possible by a diverse and dynamic repertoire of lymphocytes expressing unique antigen receptors and capable of rapid Darwinian-like evolution within an individual. However, naturally occurring immune responses exhibit limits in efficacy, speed and capacity to adapt to new challenges. Strikingly, antigen recognition taking place at the cell-cell interface is strongly physical and manifests an inside-out feedback control exerted by an active cellular interior. Here we present conceptual and computational frameworks for exploring functional impacts of non-equilibrium antigen recognition under physical constraints. We show that activity-driven signal transfer via synaptic contacts between cells can reach far to influence the adaptive potential of the lymphocyte repertoire. Considering information propagation from receptor to repertoire and back lets us rethink what is fitness, and the logic behind proofreading, in a dynamical system that demands precision and balance while being immersed in perpetual disturbances.

The Intrinsically disordered region of Drosophila Canoe facilitates dynamic coupling of adherens junctions to cytoskeleton during epithelial morphogenesis

Authors: Yufei Xiao, Corbin C. Jensen, Noah J. Gurley, Emily D. McParland, Kevin C. Slep, and Mark Peifer (Department of Biology, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599)

Embryogenesis requires robust linkage between cell-cell adhesive junctions and the actomyosin cytoskeleton to allow self-organized cell movements without disrupting tissues. Drosophila Canoe (Cno) and its mammalian homolog Afadin are crucial scaffold proteins that couple the adherens junctions to the actin cytoskeleton, enabling dynamic cell-cell adhesion during epithelial morphogenesis. Both share the same domain structure with five folded domains and a long intrinsically disordered region (IDR), comprising over a third of the protein. IDRs are known to mediate multivalent protein interactions, and are implicated in phase separation, but its mechanism and biological function remain unclear. We found that deleting the IDR severely disrupts Canoe's localization from the apical junctions to the nucleus. It also impairs junctional function, leading to tissue defects. Surprisingly, despite low sequence conservation, Afadin IDR can largely rescue Canoe's role. We're now dissecting the IDR to define functional regions. Alphafold predicts two conserved helices in the middle of the IDRs of both Canoe and Afadin. The C-terminal region contains a conserved proline-rich motif, potentially acting as an SH3 binding motif. The C-terminal is longer and more polar in amino acid composition compared to the N-terminal, which is more prion-like. We have made mutants individually deleting the conserved helices, the C-terminal or the N-terminal to the helices. Unexpectedly, all are dispensable for viability, and all mutant proteins localize to cell junctions. Sensitized assays suggest the C-terminal region may be more essential. We also generated a mutant in which we deleted both the N- and C-terminal regions, leaving the helices. This mutant is strongly impaired, with the mutant protein re-localized to the nucleus and function strongly reduced. Together, these findings underscore the IDR's indispensable role in Canoe's function. However, its sequence composition and identifiable motifs like helices or proline-rich regions only partially explain its morphological effects. In ongoing work, we will test the hypothesis that the IDR's entropic volume, rather than specific motifs, contributes to functional differences observed between mutants. Future efforts integrating insights from IDR biophysics and adhesion complex biology may unravel the mechanism of Canoe IDR function, such as in tension sensing and molecular assembly. "

Ion Channels in Critical Membranes: Clustering, Cooperativity, and Memory Effects

Author List: Antonio Suma, Daniel Sigg, Seamus Gallagher, Giuseppe Gonnella, Vincenzo Carnevale

Much progress has been made in elucidating the inner workings of voltage-gated ion channels, but lessunderstood is the influence of lipid rafts on gating kinetics. Here we propose that state-dependent channelaffinity for different lipid species provides a unified explanation for the experimentally observed behaviors ofclustering, cooperativity, and hysteresis. We develop models of diffusing lipids and channels engaged in Ising-like interactions to investigate the collective behaviors driven by raft formation in critical membranes close to thedemixing transition. The model channels demonstrate lipid-mediated long-range interactions, activation curvesteepening, and long-term memory in ionic currents. These behaviors likely play a role in channel-mediatedcellular signaling and suggest a universal mechanism for self-organization of biomolecular assemblies.

Homeocurvature adaptation of phospholipids underlies pressure-specialization of deep-sea invertebrates

Sasiri Vargas Urbano, Jacob Winnikoff, Steve Haddock, Itay Budin, Edward Lyman

The deep ocean is dark, cold, and pressurized—pressure increases by 1 bar for every 10 m depth. How does marine life adapt to this extreme environment? Given that lipid membranes are sensitive to both temperature and pressure (they are the most compressible biological material in a cell), one expects to find adaptations in the lipidomes of organisms that are specialized for life at high pressure. Here, we explore this question using the ctenophores as a model organism. Ctenophores make up a marine invertebrate phylum that is the oldest distinct lineage on the metazoan tree, and different species have adapted independently to many pressure and temperature regimes. Building on years of work by the Haddock lab collecting different ctenophore species from different marine environments, and on recent work by the Budin lab obtaining ctenophore lipidomes, we use MD simulations to study how ctenophore lipidomes adapt to maintain critical material properties within a narrow range. We find that depth strongly predicts plasmalogen abundance, with deep-adapted ctenophore lipidomes containing as much as 73 mol% phosphatidylethanolamine plasmalogen. Our simulations and analysis suggest that plasmalogen maintains membrane deformability at high pressure, so that vital cellular functions (e.g., endo- and exocytosis) can still be performed under deep-sea conditions. These results imply that in addition to other more widely appreciated membrane properties (such as fluidity), lipid intrinsic curvature is also subject to natural selection in the deep sea.

Flexicles: Individual and Collective Behaviors of Active Cell-like Microrobots

Philipp W.A. Schönhöfer, Sophie Y. Lee and Sharon C. Glotzer, University of Michigan

Although the boundary between the functionality of synthetic active microparticles and their biological counterparts becomes increasingly blurred, we still lack the fundamental understanding to recreate the key facets of autonomous behavior exhibited by microorganisms or macroscopic robots. In this study, we propose a model for a three-dimensional self-driven, deformable cellular robot composed of self-propelled colloids confined to a flexible membrane - a superstructure we call a “flexicle”. Using molecular dynamics simulations, we investigate the behavior and reaction mechanisms of individual flexicles within complex environments or a collective. We show that flexicles can adapt to their surroundings by exhibiting intricate shape changes. This coupling between morphological adaptability and particle propulsion gives rise to a diverse set of behaviors from motility-induced phase separation phenomena and the spontaneous flow of flexicles in multi-flexible systems to curvature-sensitive dynamics of single flexicles. Our findings establish a foundation for controlling the migration of cell-like active particles and designing autonomous robotic behaviors in vesicular systems.

Sequence programmable nucleic acid condensates

Sumit Majumder (Whitehead Institute) and Ankur Jain (Whitehead Institute, MIT Biology)

Nature uses bottom-up self-assembly to build structures with remarkable complexity and functionality. Understanding how molecular-scale interactions translate to macroscopic properties remains a major challenge and requires systems that effectively bridge these two scales. Here, we generate DNA and RNA liquids with exquisite programmability in their material properties. Nucleic acids are negatively charged, and in the presence of polycations, they may condense to a liquid-like state. Within these liquids, DNA and RNA retain sequence-specific hybridization abilities. We show that intermolecular hybridization in the condensed phase cross-links molecules and slows down chain dynamics. This reduced chain mobility is mirrored in the macroscopic properties of the condensates. Molecular diffusivity and material viscosity scale with the intermolecular hybridization energy, enabling precise sequence-based modulation of condensate properties over orders of magnitude. Our work offers a robust platform to create self-assembling programmable fluids and may help advance our understanding of liquid-like compartments in cells.

Poster Session C, Thursday June 13th, 12-1:15PM, Singh Center for Nanotechnology

It takes two to tango: Unraveling trophic interactions in the phycosphere.
Carolina Trenado-Yuste, Alejandro Martínez-Calvo, Xi Li, Bruce Wang, Anushree Malik, Ned S. Wingreen, and Sujit S. Datta.
In nature, microbes frequently self-organize into spatially structured communities, where different types of cells inhabit distinct spatial domains. This spatial arrangement plays a pivotal role in influencing various biological functions, including community growth, stability, metabolite cross-feeding, and diversity. An important example is the phycosphere—the region around phytoplankton (e.g., cyanobacteria, microalgae) in the ocean, in which trophic interactions with surrounding bacteria strongly influence carbon/nutrient cycling and aquatic food webs. Laboratory studies typically focus on these microbial systems in well-mixed cultures, which provide valuable information on cellular processes, but do not capture the spatial arrangement of different cell types often found in nature. Thus, here, we address this gap in knowledge using direct visualization of spatially-structured bacteria-cyanobacteria communities in transparent hydrogel matrices. Our experimental platform enables byproduct exchange, mirroring the interactions and spatial organization found in diverse marine and terrestrial ecosystems. Our experiments reveal the emergence of complex dynamical spatio-temporal interactions between bacteria and cyanobacteria, driven by the exchange of byproducts. These dynamics strongly depend on environmental conditions, cell motility, and cell density, which we recapitulate with a minimal theoretical model. Our results provide quantitative principles to predict and control the trophic interactions in the phycosphere that play crucial roles in the environment and global ecology.

Microbial life in complex fluids
Authors: Sebastian Gonzalez La Corte, Ned Wingreen, and Sujit Datta
Bacteria often live in complex macromolecular fluids, such as mucus in the body, exopolymers in the ocean, and cell-secreted extracellular polymeric substances (EPS) that encapsulate biofilms. However, studies of bacteria typically focus on cells in simple fluids. As a result, despite their prevalence, how macromolecules influence bacterial behavior remains poorly understood. Here, we address this gap in knowledge by studying how non-motile bacteria proliferate in macromolecular solutions.
First, we show that in mucus-like polymer solutions, when the polymer is sufficiently concentrated, cells form large-scale “cables”' as they proliferate in a colony—in stark contrast to forming a random dispersion, as in the conventionally-studied polymer-free case. This characteristic colony morphology arises independent of variations in cell type and polymer composition across three different species of bacteria and seven different polymer solutions, including mucins, a key component of mucus in the body. By combining experiments, theoretical modeling, and agent-based simulations, we trace the origin of cable formation to an interplay between polymer-induced entropic attraction between pairs of cells and their hindered ability to diffusively separate from each other after growing and dividing in a viscous polymer solution.
Next, given that some bacterial habitats can have liquid crystalline order, we also study proliferation in nematic liquid crystals. In this case, we find that cells again form large-scale cables that are more slender, only one cell in width. These cables are initially aligned with the local nematic director field; however, upon reaching a critical length, they undergo a mechanical instability and buckle. Again by combining experiments, theoretical modeling, and simulations, we show that this behavior is determined by the competition between the energetic cost associated with deforming an anisotropic medium and the energy released by a growth-induced compression.
Taken altogether, our work suggests a pivotal role of macromolecules in shaping proliferating microbial colonies, and provides quantitative principles to predict and control these morphodynamics more broadly.

The flow thickens: predicting macroscopic flow resistance of viscoelastic fluid flow in porous media
Emily Y. Chen, Simon J. Haward, Amy Q. Shen, and Sujit S. Datta
Flows of viscoelastic polymer solutions in porous media are ubiquitous in industrial and environmental applications. Despite their shear thinning nature in bulk rheology, these fluids can exhibit anomalous flow thickening above a threshold flow rate in porous media, marked by a drastic increase in flow resistance. The precise mechanisms for flow thickening have remained a puzzle since the first reports in the 1960s.

Previous studies have suggested mechanisms including extensional viscosity, added viscous dissipation associated with elastic instabilities, and chemical adsorption or pore clogging; however, direct quantification of these mechanisms remains lacking. Here, we show that a mechanical power balance incorporating the added viscous dissipation arising from the onset of an elastic flow instability coupled with resistance from extensional viscosity can capture the macroscopic flow resistance of polymer solution flow in 2-D and 3-D ordered porous media. Our model directly links pore-scale flow fields obtained using confocal microscopy to the macroscopic flow resistance with no additional fitting parameters. Further, we find that stagnation point-driven extensional flows can be well-captured by a resistance-per-stagnation point in ordered geometries. Our work thus improves understanding into the mechanisms driving flow thickening and provides guidelines towards controlling macroscopic flow resistance in applications.

Up, up, and away: Entrainment by biogenic bubbles enables long-range microbial dispersal
Babak Vajdi Hokmabad, Hao Nghi Lou, Meera Ramaswamy, Sujit Datta,
Microbial communities usually inhabit confining 3D environments, such as soils and sediments, foods, and gels and tissues in the body. While some microbes can disperse in their surroundings using motility, many are non-motile and can only grow and proliferate locally. Here, we show how even these non-motile microbes can break free of their local microenvironments and disperse over long ranges by riding bubbles they produce through metabolism. We study non-motile yeast growing in transparent 3D granular hydrogel matrices. Through fermentation, the yeast produce bubbles of carbon dioxide that grow, deform the surrounding matrix, and ultimately rise, entraining yeast cells in their wake over large vertical distances. The motion of these bubbles leaves a lasting imprint in the matrix, acting as a nucleation site for subsequent bubbles. The sequential entrainment by the train of rising bubbles ultimately culminates in the formation of a conduit within the matrix, encapsulating the colony and giving rise to a distinct columnar morphology. Our study provides a quantitative insight into the entrainment process driven by biogenic bubbles and demonstrates its connection to the microbial dispersal. It underscores the pivotal role of biogenesis in the proliferation and transport of living matter within complex environments, which mirrors many biogeological processes in nature.

Nonlinear Classification Without a Processor
Sam Dillavou, Benjamin D Beyer, Menachem Stern, Marc Z Miskin, Andrea J Liu, Douglas J Durian
We build 'learning metamaterials', systems of simple repeated self-adjusting elements whose collective dynamics produce desired global functionality of a system. That is, they are analog electronic networks that perform machine learning, but without a companion processor -- they train themselves. They are extremely energy efficient and robust to physical damage, making them an exciting new paradigm for machine learning hardware, the only physical analog we have to emergent (non-centralized) learning outside of biology and simulation, as well as a fascinating physical system in their own right, We discuss their construction, emerging abilities (e.g. nonlinear classification), and types of tasks, as well as future prospects.

Mechanics of confluent biological tissues as a learning problem
Sadjad Arzash, Indrajit Tah, Andrea J. Liu, M. Lisa Manning
During embryonic development, tissues undergo substantial transformations to sculpt the organism's body plan. This remarkable morphogenesis is facilitated by the tissue's ability to shift from a solid-like to a more fluid-like state, enabling extensive movement. Simple vertex models have been successful in capturing the mechanical properties of epithelial tissues, such as these solid-to-fluid transitions. These models have parameters like target cell perimeters that dictate the tissue's mechanical behavior. Typically, tissues in these models are described by a distribution of these inherent cellular parameters, defined by a mean and a standard deviation. Inspired by the success of physical learning algorithms in resistor and spring networks used to create materials capable of learning, we explore the possibility that biological tissues might adjust their intrinsic properties to meet certain design objectives. To examine this hypothesis, we introduce the cell-scale parameters within vertex models as new learning degrees of freedom. We maintain the overall distributions of these new degrees of freedom fixed but allow their spatial reassignment and minimize a simple objective function—total mechanical energy. By including these degrees of freedom alongside the physical ones represented by vertex positions, we alter the high dimensional energy landscape of the system. We find that as we introduce the target cell perimeters as transient degrees of freedom, the system can find a lower energy state, so that the rigidity transition occurs at a lower average value of the target perimeters. Moreover, there is an optimal width of the target perimeter distribution to facilitate learning.

Adding target areas as transient degrees of freedom has a similar effect in fluidizing tissues. Adding perimeter or area stiffnesses as new degrees of freedom, on the other hand, does not change the rigidity transition of tissues.

Cage Escapes Cause Cage Escapes
Rahul Chacko, University of Pennsylvania
A persistent question regarding the dynamics of supercooled liquids and glasses is whether the increasing strength and range of spatiotemporal correlations in these dynamics as temperature decreases is causal, with local plastic rearrangements perturbing their neighborhoods and causing new rearrangements to occur nearby, or merely correlational, resulting from correlations of hidden variables in the structure that might be predicted via a purely thermodynamic theory. We introduce a simple test which shows that while correlations of structure likely to influence the dynamics are present, these can only account for a tiny fraction of the dynamical correlations seen in particle simulations.

Experimental Demonstration of Coupled Learning in Elastic Networks
Doug Durian (UPenn), Menachem Stern (UPenn), Andrea Liu (UPenn), Shivangi Misra (UPenn), Cynthia Sung (UPenn)
Coupled learning is a contrastive scheme for tuning the properties of individual elements within a network in order to achieve desired functionality of the system. It takes advantage of physics both to learn using local rules and to “compute” the output response to input data, thus enabling the system to perform decentralized computation without the need for a processor or external memory. We demonstrate a proof-of-concept mechanical network that can learn simple tasks via iterative tuning of individual spring rest lengths. We also explore the potential of robotically controlled tunable-stiffness springs as a building block for adaptive prosthetics and manipulable actuators. These mechanical networks could feasibly be scaled to solve increasingly complex tasks, hinting at a new class of “smart” metamaterials.

Designing disordered truss network based mechanical metamaterials using a spectral method;
Authors: Niranjan Sarpangala, Sean Fancher, Prashant K. Purohit, Eleni Katifori;
Mechanical metamaterials are materials with non-trivial mechanical properties such as the negative Poisson ratio and tunable acoustic filtering. While such properties are absent in natural bulk materials, innovative network structures have emerged as a pathway to realizing them artificially. Several pioneering studies employed periodic network structures for this purpose, but recent studies, partly inspired by biological systems like disordered bone tissue, have turned attention to non-periodic or disordered networks because of their higher tunability and better functionalities. This is further encouraged by recent breakthroughs in additive manufacturing technologies that make it possible to synthesize disordered networks with intricate structures on the sub-millimeter scale. To fully leverage the advancements in manufacturing technology, it is crucial to be able to compute network responses and optimize the networks efficiently. Here we develop and use a spectral method for designing dissipative disordered metamaterials that is both fast and accurate. Our method is based on truss structures where one can neglect the bending of the filaments. This allows us to assume purely uniaxial stresses on the filaments reducing the computational cost. This method considers uniform mass distribution along filaments. We show that it is more accurate than the beads and springs models while running faster than more detailed finite element methods. Currently, we are applying this model to design a material capable of effectively channeling and uniformly dissipating mechanical energy.

Scaling Laws in Physical Learning
Authors: Marcelo Guzmán, Andrea J. Liu

Morphology, tension and core size of disclination lines in twisted nematic liquid crystals
Yihao Chen, Mina Mandic, Michio Tanaka, Charlotte Slaughter, Jay Kikkawa, Peter Collings, and Arjun G. Yodh
We deploy confocal microscopy and a non-invasive method with magnetic field to characterize the three dimensional morphology, tension and disclination core radius of disclination lines in twisted nematic liquid crystal cells. The disclination lines form loops separating regions with two different twisting directions after the sample is quenched to the nematic phase. The disclination lines exhibit two configurations: some parts of the disclination lines are pinned to surface and have irregular shapes, while the other parts are free from

the surface and form bending profiles perpendicular to the surface. The profiles are successfully captured by a model minimizing the total disclination line energy between two pinned ends and it shows the tension decreases towards the middle of the sample cell. The free disclination lines extend and form arcs parallel to the surface under a magnetic field that induces an energy difference in the two regions of different twisting directions, and the curvature of the arcs increases as the strength of magnetic field increases. Tension of the disclination line is obtained through the relation between curvature and the magnetic field via a model of energy balance, and has a logarithmic relation with the thickness of the sample cell. Assuming an isotropic disclination core, a core radius is extracted from both the bending profile of free disclination lines and the logarithmic dependence of tension on the cell thickness via previous theoretical predictions.

Dynamics of the surface growth resulted from falling spherical particles in a Hele–Shaw cell
Vahideh Sardari, Feyzollah Ghavami, Fatemeh Safari, Bita Olamaei, and Maniya Maleki
We investigate the dynamics of surface growth resulting from falling spherical granular particles in an air or liquid environment, using experiments and simulations. In the experimental part, spherical polystyrene particles are poured down from the top of a vertical Hele–Shaw cell and form a 1 + 1-dimensional growing surface. The surface roughness is obtained from the images, and the growth and roughness exponents are measured. In the numerical simulation part, the surface growth process is simulated using the discrete element method, considering the interactions between the grains, and the exponents are calculated. In this method, unlike conventional simulation models, instead of a discrete deposition law, the dynamics of the individual particles throughout the process are obtained, considering different forces acting on the particles. Finally, the simulation results are compared with the experiment, and we see a very good agreement between them. We find values for the exponents that are different for liquid and air and are not consistent with standard scaling models.

Exploring Ribosomal Dynamics: A Theoretical Model for Translation and Frame-Shifting Phenomena
Authors: Meysam Chitsazha, Farshid Mohammad-Rafiee
Abstract: Protein molecules in cells are synthesized by macromolecular machines called ribosomes. Understanding the ribosomal translation process, particularly under external forces and through RNA structures, is crucial for elucidating cellular dynamics. In this study, we propose a theoretical model that considers frame-shifting possibilities to express ribosomal activity in six distinct states. Our model reveals insights into translation rates and the frame-shifting phenomena. We suggest that frame-shifting occurs in two states of the translation process: the accommodation state, characterized by tRNA-induced structural shifts, and a displacement state, marked by ribosomal subunit rotations. Our model enables investigation of the impact of downstream RNA structures on frame-shifting rates. We performed dynamical Monte Carlo simulations using the Gillespie algorithm to study the dynamic features of translation during the elongation phase. We used some experimental data, particularly from studies on HIV-1 virus mRNA, to tune the parameters of our model. By bridging theoretical modeling with experimental findings, our study provides a clearer understanding of ribosomal dynamics during translation, offering insights into cellular processes and potential implications for biomedical research.

Oscillatory Flow Networks with Valves
Authors: Aaron Winn, Martin Brandenbourger, Eleni Katifori
When subject to unfavourable pressure gradients, an alternative mechanism is needed in biological transport networks to pump fluid. The time-reversibility of Stokes flow makes static asymmetric structures incapable of rectifying flow. However, if those asymmetric structures are also flexible, deforming in response to fluid forces (i.e. valves), the flow can be rectified. Similarly, propagating contraction waves in the walls of a vessel (i.e. peristalsis) can induce directional transport. While biological valves and peristalsis have been thoroughly studied separately, less attention has been given to the interplay between these two pumping mechanisms, which is relevant for understanding transport in the lymphatic system.

Branching, crowding, and packing of the embryonic kidney epithelium
Louis Prahl, Ronald Canlla, Alex Hughes
The human kidney must establish a network of ~1 million nephrons and collecting tubules during embryonic development to meet the blood filtration and homeostasis demands of adult physiology. These are built by an embryonic tissue-building program called branching morphogenesis, where an epithelial tissue invades

the nearby mesenchyme and forms a tree-like tubule network through iterative rounds of branching bifurcations. Mouse embryology experiments and computational modeling reveal that branching tubule tips become densely packed at the kidney surface and must progressively restructure to accommodate increasing tip number while avoiding organizational defects. Tip packing correlates with bulk tissue stiffening, while laser cutting experiments at the scale of individual niches indicate periodic changes in local stress linked to the branching cycle. Stem cell clusters within the niche receive local mechanical cues, which influence their condensation and differentiation into early nephrons concurrently with the branching cycle. Finally, we describe ongoing work to investigate the biochemical regulation of branching using explanted kidney tissue, in vitro cell culture, and optogenetic signaling tools. Together, our results reveal fundamental insights into how branching and nephron formation are coordinated at the cell-to-organ scale and highlight a design pathway to control tubule organization in engineered kidney tissue.

Methods for nanoscale characterization of soft and living matter with electron and ion microscopy
Author: Eric Stach

Gastrovascular network flow models in Jellyfish
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Jellyfish are interesting sea creatures that provide insight into the evolution of cardiovascular networks; while complex organisms such as mammals are characterized by a centralized heart that allows the distribution of resources in the body through pulsatile pumping, jellyfish lack such a centralization. However, they also have complex vascular structures, with gastrovascular canals that extend throughout their bodies from their open mouths to their stomach pouches and back in 4-fold symmetrical fractal branching patterns that increase in complexity as they age and develop. Flow through these networks is generated through swimming motion, involving a muscle contraction leading to deformations of these canal networks. Here, we build a mathematical model using principles from fluid dynamics and network theory to simulate the flow through these networks during contraction, looking at three different variations of swimming motions. Future directions include comparing the flow generated through simulation to experimental data, increasing the biological accuracy and complexity of the model, and incorporating the effects of cilia on the flow in our model.

Post-loading lipid nanoparticles: A feasible route for RNA delivery
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Lipid nanoparticles (LNPs) have recently emerged as effective vehicles for delivering messenger ribonucleic acid (mRNA) in vaccine formulations. LNP-based mRNA vaccines for COVID-19, such as those developed by Moderna and Pfizer, are among the most notable examples. A major limitation of these vaccines is their requirement for cold chain handling (-20 °C for Moderna and -70 °C for Pfizer). Current formulations involve precipitating four different lipids together with mRNA through a fast-mixing process. Although this method efficiently forms mRNA-loaded LNPs, the electrostatic binding between cationic ionizable lipids and the negatively charged nucleic acid enhances RNA degradation, necessitating extreme freezing to suppress degradation kinetics. To overcome this, we propose a ""post-loading"" approach, where ""empty"" LNPs (eLNPs) are produced and later loaded with RNA at healthcare facilities. Using Confined Impinging Jet (CIJ) mixers, we tune conditions to produce colloidally stable eLNPs and develope a technique for loading RNA while maintaining LNP size under 100 nm. Our study shows post-loaded LNPs are as effective as traditional formulations in delivering mRNA to model cancer cells. X-ray and neutron scattering analyses confirm similar internal structures in both methods, supporting their comparable performance. This approach allows for premade eLNPs and RNA cargo to be stored and shipped under mild cooling conditions, enhancing vaccine accessibility and distribution."