

MBN2026

MOLECULAR BIOPHYSICS IN THE NORTHEAST



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CONNECTICUT

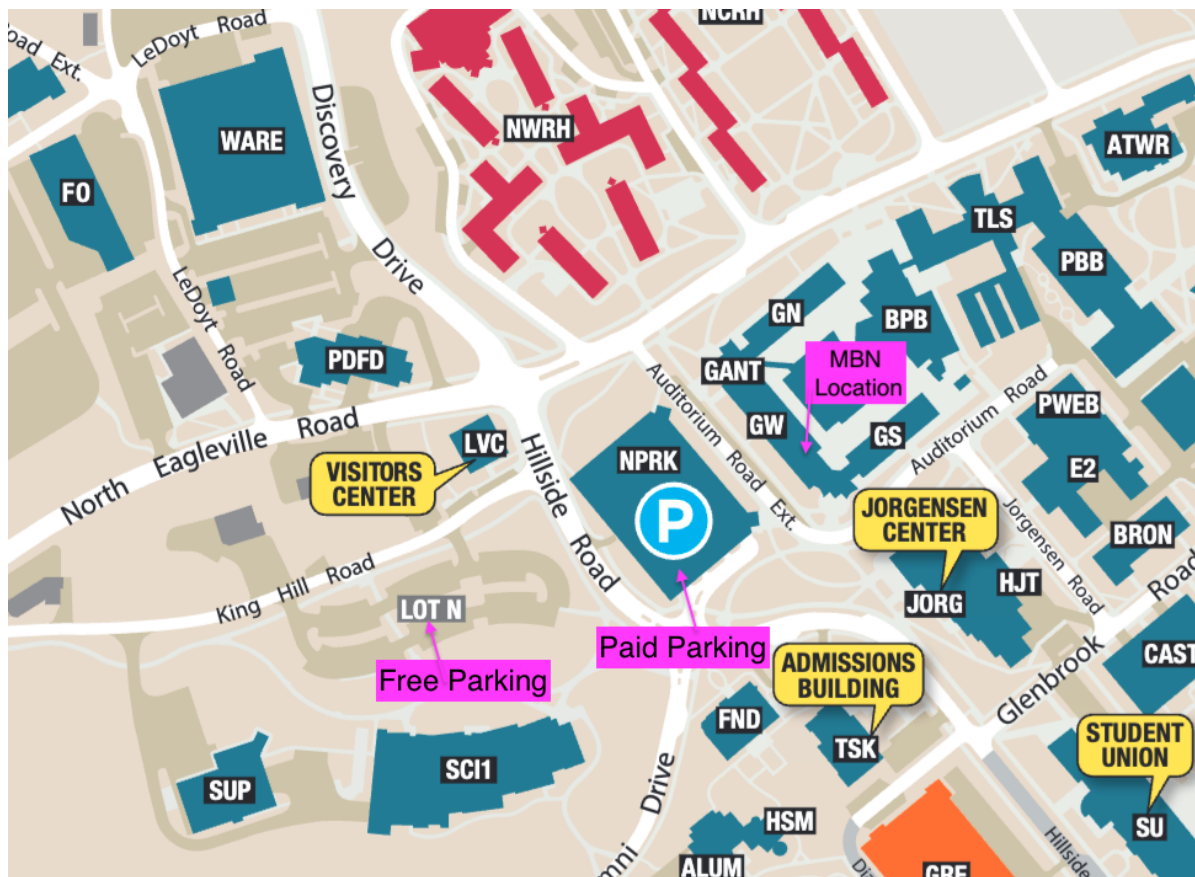
Saturday, October 3, 2026
Gant Science Complex, Room GW-002
University of Connecticut | Storrs, Connecticut

SUPPORTED BY

**Department of Molecular and Cell Biology (MCB)
Office of the Vice President for Research (OVPR)**

mbnmeeting.org

Parking and Venue



The meeting will be held in **Gant Science Complex, Room GW-002**. The closest paid parking is **North Parking Garage, 2152 Hillside Rd, Storrs, CT 06268**. Free parking is available in **Lot N, 25 King Hill Rd, Storrs, CT**, approximately a five-minute walk from Gant.

Presenter Information

Promoted talks are 10 minutes, followed by 5 minutes for questions and transition. Presenters may use their own laptop, a USB drive, or an online source and should test the setup before their session. Promoted talks are in addition to poster presentations; promoted speakers are expected to present their posters during the 12:25-2:30 lunch and poster session.

Contacts

Meeting chair: Eric May, eric.may@uconn.edu | Registration and website: Paul Whitford, p.whitford@neu.edu; Sirupa Chakraborty, s.chakraborty@neu.edu | mbnmeeting.org

Program at a Glance

TIME	PROGRAM
9:00-10:00	Check-in, coffee, and breakfast snacks
10:00-10:15	Introductory remarks
10:15-11:10	Session 1 - DNA and Nucleic-Acid Molecular Mechanisms (Chair: Eric May, University of Connecticut)
11:10-11:30	Morning coffee break
11:30-12:25	Session 2 - Molecular Simulation and Predictive Design (Chair: Paul Whitford, Northeastern University)
12:25-2:30	Lunch and poster viewing
2:30-3:25	Session 3 - Structural Heterogeneity and Therapeutic Targeting of Biomolecular Ensembles (Chair: Jianhan Chen, UMass Amherst)
3:25-4:00	Afternoon coffee break
4:00-4:55	Session 4 - Biomolecular Phase Behavior and Organization (Chair: Srirupa Chakraborty, Northeastern University)
4:55-5:00	Keynote introduction - George Makhatadze
5:00-5:45	Keynote address - Catherine Royer, Rensselaer Polytechnic Institute

Organizing Committee

Eric May, Chair (University of Connecticut) | Colin Smith (Wesleyan University) | Dylan Murray (University of Connecticut) | George Makhatadze (Rensselaer Polytechnic Institute) | Sean Edington (University of New Hampshire) | Srirupa Chakraborty (Northeastern University) | Sweta Vangaveti (University at Albany)

Supported by the UConn Department of Molecular and Cell Biology (MCB) and the UConn Office of the Vice President for Research (OVPR).

Scientific Program | Morning

Session 1 | 10:15-11:10 | DNA and Nucleic-Acid Molecular Mechanisms

Chair: Eric May, University of Connecticut

10:15-10:40	INVITED	Franziska Bleichert Yale University	License to replicate: biochemical and structural mechanisms of eukaryotic DNA replication initiation
10:40-10:55	PROMOTED TALK	Camila Molina Brown University	Atomic Details of the FnCRISPR-Cas12a Nuc Domain Reveal Allosteric Hotspots Affecting DNA Binding and Cleavage
10:55-11:10	PROMOTED TALK	Sara Mohamed Northeastern University	Retroviral intasome integration drives nucleosome disassembly: an atomic force microscopy study

11:10-11:30

Morning coffee break

Session 2 | 11:30-12:25 | Molecular Simulation and Predictive Design

Chair: Paul Whitford, Northeastern University

11:30-11:55	INVITED	Anna Tarakanova University of Connecticut	Elastin's function and dysfunction: from molecules to elastic fiber networks
11:55-12:10	PROMOTED TALK	Salah Hassan Northeastern University	Simulating Structural Transitions of HIV-1 Env Protein During Refolding
12:10-12:25	PROMOTED TALK	Lauren Intravaia UMass Chan Medical School	A Dynamics-Informed Machine Learning Framework for Inhibitor Optimization Against Quickly Evolving Targets to Avoid Resistance

Lunch and Poster Viewing | 12:25-2:30

Promoted speakers will also present their posters during the lunchtime poster session, providing additional time for discussion. All poster presenters should have their posters in place before lunch.

Scientific Program | Afternoon

Session 3 | 2:30-3:25 | Structural Heterogeneity and Therapeutic Targeting of Biomolecular Ensembles

Chair: Jianhan Chen, UMass Amherst

2:30-2:55	INVITED	David Punihaole University of Vermont	Structural Characterization of Amyloid Fibrils Across Molecular, Supramolecular, and Macroscopic Spatial Scales
2:55-3:10	PROMOTED TALK	Gabriel Brill Stony Brook University	Sequence Determinants of Amylin Amyloidogenicity Inform the Design of Improved Bioactive Analogs
3:10-3:25	PROMOTED TALK	Dan Fabris University of Connecticut	Hunting for new antivirals capable of disrupting the dynamic ensembles of regulatory RNAs

3:25-4:00

Afternoon coffee break

Session 4 | 4:00-4:55 | Biomolecular Phase Behavior and Organization

Chair: Srirupa Chakraborty, Northeastern University

4:00-4:25	INVITED	Shana Elbaum-Garfinkle City University of New York	Tunable multiphase dynamics of biomolecular condensates
4:25-4:40	PROMOTED TALK	Jacob Winnikoff Harvard University	Structural adaptation of lipids to support membrane topology change and life at extremes
4:40-4:55	PROMOTED TALK	Jessica Fong Ng UMass Amherst	Intermediate-Resolution Modeling of Dynamic DNAs and Their Phase Separation

4:55-5:00

KEYNOTE
INTRODUCTION
George Makhataдзе

5:00-5:45

Catherine Royer

Rensselaer Polytechnic Institute

Pressure-based mapping of the Arf nucleotide switch transitions

Poster Directory

Posters are listed by assigned number. Promoted speakers also present during the lunchtime poster session.

NO.	POSTER TITLE	PRESENTER / INSTITUTION
1	Towards structural biochemistry in biological environments	David Punihaole University of Vermont
2	Structural adaptation of lipids to support membrane topology change and life at extremes	Jacob Winnikoff Harvard University
3	pH-Dependent Regulation of T7 RNA Polymerase Revealed by Constant pH Molecular Dynamics	Masoud Keramati Northeastern University
4	Mechanistic Modeling of Aging Effects in Elastin Fiber Networks: Linking Microstructure to Mechanical Response	Zhaofan Li University of Connecticut
5	Structural Characterization of RGS9-1 Anchoring Protein (R9AP)	Michael Rizzi University of New Hampshire
6	Subtyping Kinase Inhibitor Binding Modes with Super-Resolution Nanopore Tweezers	Ly Nguyen UMass Amherst
7	Stabilizing the Transient Biophysical Signatures of the Disease-linked “oxMIF” Protein via Targeted Mutagenesis	Briana Mercado Brown University
8	Characterizing the role of (a)symmetry in Macrophage Migration Inhibitory Factor (MIF).	Isabel Varghese Brown University
9	Decoding Poly-ADP ribosylation: Single-molecule detection of post-translational modifications using biological nanopores	Susmita Dey UMass Amherst
10	Analysis of Disease-Linked USP7 Mutations in Hao-Fountain Syndrome	Kavitha Paramatmuni UConn Health
11	Restraining Interproton Angular and Distance Dynamics with KEnRef	Amr Alhossary Wesleyan University
12	Bringing Order to Disordered Proteins: How the HSPB8 Chaperone Modulates the Aggregation of TDP-43	Paul Braymen University of Connecticut
13	Structural and Functional Characterization of PXL: A Unique Binding Module of PML-1	Rebekah Sheih UConn Health
14	Biophysical characterization of NS4a-BRIL for structural determination of an essential Orthoflavivirus membrane protein	Ellie Lee UConn Health
15	Nanobodies as a Tool for Identification of Exploitable Exosites in Caspase-6	Thomas Bregnard UMass Amherst
16	A novel mechanism of host translation inhibition by ribocin	Emily Sholi UMass Chan Medical School
17	Investigating the Molecular Interactions of HuR, VEGF-A RNA, and MiR-29a	Madeline Clark Brown University
18	Quantifying and Engineering Electric Fields in Liver Alcohol Dehydrogenase	Justice Chinonso Eze University of Connecticut
19	Investigation of Elamipretide Translocation and Curvature Response in Inner Mitochondrial Membrane Models Using Molecular Dynamics Simulations	Hayden Yuan University of Connecticut
20	Biophysical characterization of anti-CRISPR II-C1 binding to a thermostable Cas9	Praise Lasekan Brown University

NO.	POSTER TITLE	PRESENTER / INSTITUTION
21	The Role of Intrinsically Disordered Head and Tail Domains of Type III Intermediate Filaments in Polymerization and Interaction	Joshua McDonald University of Connecticut
22	Atomic Details of the FnCRISPR-Cas12a Nuc Domain Reveal Allosteric Hotspots Affecting DNA Binding and Cleavage	Camila Molina Brown University
23	Multiscale Modeling Predicts the Interaction of AAC2 with the Mitochondrial Respiratory Super complex	Seyad Shefrin Naina Mohamed Basil University of Connecticut
24	Electrostatic switches remodel the Enterovirus D68 capsid during acidification and prime it for genome release	Mahmoud Sharawy University of Connecticut
25	Water as a Thermodynamic Driver of Elastin Structure and Function	Metehan Cam University of Connecticut
26	Detecting Sampling Errors in Membrane Permeation Free-Energy Profiles through an FEP-Based Cross-Validation	Rey Carten University of Connecticut
27	Membrane Composition–Dependent Cooperative Hydropathy Governs FHV γ Peptide Membrane Activity	Muhammed Umair University of Hartford
28	Computational Modeling of Age-Dependent Mechanical Deterioration in Elastin Fibers	Seyedmostafa Hosseini Nasab University of Connecticut
29	Tale of Two Tails: Thermodynamic Control of DIAPH1 Membrane Localization and Activity by the N- and C-Termini	Gregory Theophall Albert Einstein College of Medicine
30	Developing a nanopore assay to monitor interaction between the NS4B cytoplasmic loop and the NS3 helicase of Dengue virus	Moly Rani UMass Amherst
31	Characterizing the Physicochemical Diversity of Cell-Penetrating Peptides Through Unsupervised Learning	Anurag Upadhyaya Northeastern University
32	SAXS-Guided Evaluation of Tropoelastin Conformational Ensembles Across Molecular Dynamics Force Fields	Elika Shams University of Connecticut
33	VPS45 Regulates Rabenosyn-5 and Syntaxin 16 binding in Endosomal Membrane Trafficking	Helen Magana UMass Chan Medical School
34	Single-Molecule Biophysical Characterization of DM1 Repeat Hairpin Mechanics Using C-Trap and Molecular Dynamics Simulations	Shirin Mohammadian University at Albany
35	Hunting for new antivirals capable of disrupting the dynamic ensembles of regulatory RNAs	Dan Fabris University of Connecticut
36	Optimization and Validation of an Implicit-Water Model for Simulating O-Glycans and Glycoproteins at the Atomistic Scale	Simran Pandey Northeastern University
37	A molecular blue-print for mucin inspired biomaterials	Joshua Koja Aduampon Northeastern University
38	Retroviral intasome integration drives nucleosome disassembly: an atomic force microscopy study	Sara Mohamed Northeastern University
39	Amyloid Fuzzy Coat Atlas: a ensembles database for disordered region of amyloid fibrils	Clarice Stumpf UMass Amherst
40	Role of Spectrin Unfolding and Non-muscular Actomyosin in the Nonlinear Shear Response of the RBC Membrane Cytoskeleton	Salim Mirshahi University of Connecticut

NO.	POSTER TITLE	PRESENTER / INSTITUTION
41	Glycographer: An Open-Source Modeling Suite for Protein-Glycan Binding Landscape Characterization and Targeted Sequence Design	Jason Kantorow Northeastern University
42	How Magnesium Tunes Light Absorption in the Microbial Rhodopsin HwMR	Zanders Peraza University of Connecticut
43	SIMULATING STRUCTURAL TRANSITIONS OF HIV-1 ENV PROTEIN DURING REFOLDING	Salah Hassan Northeastern University
44	Characterizing the Binding Capability of Single-domain Kinases	Flora Wang Wesleyan University
45	Identification and characterization of atypical and novel zinc finger domains	Antonio Rua University of Connecticut
46	Uncovering a novel antifreeze protein from bulk genomic data	Joseph Faherty University of New Hampshire
47	Predicting and Improving Fluorescence in Mini Fluorescence-Activating Proteins	Maruf Hasan Wesleyan University
48	Coarse-grained modeling of TDP-43 LCD fibril elongation and HSPB8 chaperone effect	Xubo Luo University of Connecticut
49	Solid state NMR characterization of wild-type and mutant GFAP intermediate filament assemblies	Emily Faircloth University of Connecticut
50	Coordination and Energetics of tRNA Hybrid-State Formation in the Yeast 80S Ribosome	Eghosa Osazuwa Northeastern University
51	Elucidating LCD Fibril Structures- A Solid-State NMR Study of EWS LCD Fibrils	Sameena Shah University of Connecticut
52	Novel Generation of pHLIP Peptide	Craig Klumpp University of Rhode Island
53	PXL: a Nucleic Acid-Binding Module of the Promyelocytic Leukemia Protein	Daniel Fairchild UConn Health
54	A human-specific tau nanobody with avidity-enhanced recognition of multivalent tau epitopes	Ai Han Nguyen University of Connecticut
55	Anti-hnRNP A2/B1 Nanobodies with Defined Epitopes	Fatemeh Tashakori Asfestani University of Connecticut
56	What the LOX Is Going On? How Mutations Break a Crosslinking Enzyme	Yu-Bai Xiao University of Connecticut
57	Effects of Local Dynamics on Glass transition in Entangled and Cross-linked Melts of Large Polymers	Calvin Johnson University of Connecticut
58	A Dynamics-Informed Machine Learning Framework for Inhibitor Optimization Against Quickly Evolving Targets to Avoid Resistance	Lauren Intravaia UMass Chan Medical School
59	Intermediate-Resolution Modeling of Dynamic DNAs and Their Phase Separation	Jessica Fong Ng UMass Amherst
60	Combining SAXS and Reactive MD Simulations to Uncover the Structure and Assembly of Crosslinked Surfactant Nanoparticles	Patrick Corrigan University of Connecticut

NO.	POSTER TITLE	PRESENTER / INSTITUTION
61	Infrared signatures of lanthanide-specific binding in peptides	Harrison Vedrani University of New Hampshire
62	Spectroscopic signatures of scaffold rigidity and solvation in metal chelators	Arka Roy University of New Hampshire
63	ShapeAligner: Direct Molecular Superposition from Clique-Based Atom Correspondence	Umut Ozuguzel University of Connecticut
64	Analysing solvation effects on metal-ion coordination with optical spectroscopy	Diotima Bose University of New Hampshire
65	Spontaneous binding of pentagalloyl glucose stabilizes tropoelastin and reduces the exposure of cleavage sites	Teresa Carrolliny Rodrigues University of Connecticut
66	Molecular Modeling of Key Mitochondrial Proteins in Cardiolipin-Containing Membranes	Edgar Lopez Perez University of Connecticut
67	Molecular Mechanisms of Elastin Coacervation and Condensate Assembly During Elastogenesis	Chengeng Yang University of Connecticut
68	Sequence Determinants of Amylin Amyloidogenicity Inform the Design of Improved Bioactive Analogs	Gabriel Brill Stony Brook University
69	Kinetic Stability of Seed Proteins: Connecting Proteolytic Resistance, Digestive Persistence, and Allergen-Associated Proteins	Ashma Adhikari Rensselaer Polytechnic Institute
70	Effect Of Hao-Fountain Syndrome-Causing Hyperactive Variant Of USP7 On Its Structure And Conformational Dynamics	Nuala Peterman UConn Health
71	The Characterization of Human Ankle2: An important proviral factor in Orthoflavivirus infection	Kate Bruder UConn Health

Attendee Directory

Registered attendees are listed alphabetically by name. Total attendees: 116.

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Poster Abstracts

Abstracts are presented in poster-number order.

Poster 1 | Towards structural biochemistry in biological environments

David Punihaole | University of Vermont

Authors: Punihaole, David, University of Vermont

Abstract: Amyloid fibrils are insoluble, non-crystalline protein aggregates that are commonly associated with many diseases, such as Alzheimer's Disease (AD), Cerebral Amyloid Angiopathy (CAA), and Type II Diabetes. Amyloid fibrils exhibit structural polymorphism, which can influence their toxicity, how they grow, and propagate. Investigating how different fibril polymorphs aberrantly interact with their local biological environment is critical to understanding the clinical variations of diseases observed in patients. Unfortunately, investigating this is challenging, as there is a lack of biophysical methods to monitor the structure and dynamics of fibrils in their native biological environments. Here, we discuss our group's work in addressing this problem. We are developing characterization methods using Raman microscopy to quantitatively assess the molecular-level structure of fibrils. For example, we recently developed methods to measure important dihedral and bond orientation angles in fibrils. To determine the molecular-level structure of different polymorphs, we use these angular measurements as experimental constraints in molecular dynamics simulations. The resulting simulations from the production runs yield an ensemble of structures that are consistent with the experimental Raman data. We are working towards translating some of our methodologies towards Raman imaging applications to quantitatively assess amyloid fibril structures found in plaques from brain tissue of AD and CAA patients.

Poster 2 | Structural adaptation of lipids to support membrane topology change and life at extremes

Jacob Winnikoff | Harvard University

Authors: Winnikoff, Jacob R, Harvard University

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Girguis, Peter R, Harvard University

Lyman, Edward, University of Delaware

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Abstract: The structure of phospholipid headgroups and chains are well-established drivers of membrane elastic properties, but functions for different chemistries that join these moieties together are poorly understood. While canonical phospholipids feature ester linkages, alkyl ether- and plasmenyl-linked species emerged in prokaryotes, are highly abundant in metazoans, and have been implicated in neurodegeneration and aging. Ether phospholipid chemistry, and plasmenyl linkages in particular, arose independently several times in evolution, suggesting conserved functions in the structure of cell membranes. Here we combine experiments and molecular simulations to show that backbone linkage chemistry provides modular control of membrane mechanics and topology through a set of discrete handles. Ether linkages provide the first handle: by additively promoting negative intrinsic curvature, which destabilizes bilayers. They also decouple membrane stiffness from viscosity, softening membranes while maintaining packing in the hydrophobic core. The plasmenyl C=C bond represents a second, distinct handle that uniquely stabilizes the inverted hexagonal phase by relieving interstitial packing frustration. These results explain the fusogenicity of ether lipids, show how they regulate membrane topology through multiple physical mechanisms, and provide a rationale for convergent evolution of the complex plasmenyl linkage moiety.

Poster 3 | pH-Dependent Regulation of T7 RNA Polymerase Revealed by Constant pH Molecular Dynamics

Masoud Keramati | Northeastern University

Authors: Keramati, Masoud, Department of Bioengineering, Northeastern University, Boston, Massachusetts 02115, United States

Ondrechen, Mary Jo, Department of Chemistry and Chemical Biology, Northeastern University, Boston, Massachusetts 02115, United States

Abstract: T7 RNA polymerase (T7 RNAP), the workhorse of mRNA vaccine manufacturing, has a narrow optimum pH near 8.0. The molecular origin of this pH dependence is presented here. CpH-REMD simulations spanning pH 4.75 to 9.15 (2.88 μ s) reveal a pH sensing network coordinating structure and function.

His811 (pKa 5.9), adjacent to catalytic Asp812 in the palm subdomain, is the primary active site sensor: protonation at acidic pH creates an electrostatic trap that restricts flexibility required for nucleotide incorporation, while deprotonation at optimal pH permits productive geometry. Energy decomposition attributes C terminal repositioning to a pH dependent switch in electrostatic coupling, from protonated His545 and His790 at acidic pH to catalytic metal ions at pH 8. Glu148 (pKa 5.3) is a second structural sensor, stabilizing the specificity loop contact with subdomain H required for elongation complex formation. Aggregate charge analysis shows excess positive charge at acidic pH (+5 at pH 5 versus +2 at pH 8) raising an electrostatic barrier to promoter escape.

The C-terminal Ala883 to active site distance and the specificity loop to β hairpin spacing show opposing pH dependencies that converge only at pH 8.0, where Tyr639 positioning confirms active site competence. Optimal activity therefore requires simultaneous convergence of multiple structural parameters, guiding design of pH stable variants and IVT conditions.

Poster 4 | Mechanistic Modeling of Aging Effects in Elastin Fiber Networks: Linking Microstructure to Mechanical Response

Zhaofan Li | University of Connecticut

Authors: Li, Zhaofan, University of Connecticut

Tarakanova, Anna, University of Connecticut

Abstract: Elastic fiber networks, primarily composed of elastin, are essential to the mechanical function of many biological tissues but undergo substantial structural remodeling with aging. How these microstructural changes alter force transmission across the network remains incompletely understood. Here, we develop a three-dimensional coarse-grained model of elastin-like fiber networks to investigate the effects of aging-related structural changes on network mechanics. Fibers are represented as flexible chains connected by multifunctional crosslinkers, forming disordered network architectures that are subjected to tensile deformation. We examine three candidate mechanisms of aging: loss of network connectivity, increased inter-fiber cohesion and clustering, and fiber fragmentation. Simulations reveal highly heterogeneous stress distributions, with a subset of aligned, straight fibers carrying elevated tensile stress and forming connected load-bearing pathways. Network connectivity strongly regulates the organization and continuity of these pathways, whereas fiber fragmentation disrupts long-range load transmission and weakens the network. Comparisons with multiphoton imaging of elastic fiber networks further connect simulated aging mechanisms with experimentally observed structural remodeling. Together, these results provide a mechanistic framework linking aging-induced microstructural changes to altered force transmission and mechanical function in elastic fiber networks.

Poster 5 | Structural Characterization of RGS9-1 Anchoring Protein (R9AP)

Michael Rizzi | University of New Hampshire

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Wang, Xin, University of New Hampshire

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Varga, Krisztina, University of New Hampshire

Abstract: Retinal RGS9-1 Anchoring Protein (R9AP) is a membrane-bound protein that anchors the RGS9-1/G β 5L complex to the outer segment membranes of retinal photoreceptor cells. During visual excitation in rod and cone photoreceptors, rhodopsin activates the G-protein, transducin, causing its α -subunit (T α^* -GTP) to activate the cGMP phosphodiesterase (PDE6) that leads to membrane hyperpolarization. Termination of the photoresponse is primarily controlled by the rate of GTPase activity of T α^* which is accelerated by the R9AP/RGS9-1/G β 5L complex. Despite its central role in terminating the photoresponse, the atomic-level structure of R9AP has not been solved. Here we present progress toward structural characterization of R9AP using solution nuclear magnetic resonance (NMR) spectroscopy. We first optimized recombinant expression and purification of R9AP to achieve the high yield and purity required for biophysical studies. CD spectroscopy reveals that R9AP adopts α -helical secondary structure at low protein concentrations in NP-40, DHPC, and FC-12 micelles (but not sodium cholate), consistent with its predicted transmembrane topology. This α -helical character is maintained over a range of 50 to 300 mM NaCl, suggesting the secondary structure is robust to changes in electrostatic environment. However, R9AP undergoes concentration-dependent loss of α -helical content at elevated protein concentrations required for solution NMR. These results motivate further optimization of conditions (e.g., varying the detergent-to-protein ratio) as well as expressing a C-terminal truncated, soluble R9AP to eliminate detergents from solution NMR measurements of R9AP. The atomic-level resolution of R9AP structure and dynamics will assist in determining the molecular organization of this heterotrimeric inactivation complex, and provide insights into therapeutic strategies for treatment of bradyopsia caused by mutations in the human R9AP gene.

Poster 6 | Subtyping Kinase Inhibitor Binding Modes with Super-Resolution Nanopore Tweezers

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Abstract: Accurate determination of kinase inhibitor binding modes could provide essential information for understanding resistance mechanisms and accelerating drug discovery. While conventional structural methods such as X-ray crystallography, cryo-EM and NMR provide high-resolution information but are low-throughput and capture largely static snapshots of dynamic protein-ligand interactions. Here, we introduce a single-molecule nanopore tweezer platform that functionally subtypes ATP-competitive Abl kinase inhibitors by resolving distinct ionic current signatures of Abl-inhibitor complexes. This approach distinguishes Type I, Type IIA, and Type IIB inhibitors without structural determination. We further show how clinically relevant Abl variants (T315I and E255V) reshape inhibitor engagement and binding modes. By combining baseline probability features with wavelet-based time-frequency descriptors, ensemble machine-learning models

achieved 97.5% classification accuracy across seven kinase inhibitor binding modes at sub-angstrom resolution and enabled deconvolution of mixed-inhibitor samples at nanomolar concentrations. These results establish nanopore tweezers as a label-free, super-resolution platform for profiling kinase conformational states and inhibitor binding modes, complementing structural approaches and supporting precision oncology.

Poster 7 | Stabilizing the Transient Biophysical Signatures of the Disease-linked “oxMIF” Protein via Targeted Mutagenesis

Briana Mercado | Brown University

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Abstract: Macrophage migration inhibitory factor (MIF) along with its paralog, D-dopachrome tautomerase (DDT, MIF-2), are ubiquitous expressed cytokines. MIF and MIF-2 harbor a conserved proline-1 that confers tautomerase activity and a C-terminal motif that binds and activates the CD74 receptor. MIF and MIF-2 overexpression are implicated in inflammatory diseases, such as asthma. In these inflammatory settings oxidative conditions induce structural and biochemical changes in MIF, yielding an oxidized isoform (oxMIF). oxMIF displays reduced catalytic activity but enhanced CD74 activation, making it a therapeutic target. However, structural studies of oxMIF are hindered by conformational heterogeneity. Remarkably, a single point mutation (C80A) reproduces key structural and functional features of oxMIF without oxidation, suggesting mutations can mimic oxMIF-like states. I investigated the role of cysteine and methionine residues in MIF and MIF-2 by generating substitution mutations and conducting functional assays and structural NMR studies. These studies identified M101A, which is recognized by an oxMIF-specific antibody, suggesting additional mutations may stabilize oxMIF-like conformational states. Furthermore, several cysteine and methionine mutations altered MIF tautomerase activity, whereas analogous mutations in MIF-2 produced minimal functional effects, revealing distinct redox sensitivities between the two paralogs. These findings establish a framework for characterizing oxMIF states at atomic resolution by NMR.

Poster 8 | Characterizing the role of (a)symmetry in Macrophage Migration Inhibitory Factor (MIF).

Isabel Varghese | Brown University

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Abstract: Macrophage Migration Inhibitory Factor (MIF) is a pro-inflammatory cytokine implicated in numerous rheumatic and inflammatory diseases, including but not limited to various forms of cancer, asthma, arthritis, and lupus. Structurally, MIF is a homotrimer comprised of 12.5 kDa monomers organized around a central solvent channel. Despite its compact arrangement, MIF exhibits diverse biological activities, including receptor binding and activation, enzymatic activity, and insulin chaperoning. Prior work in our lab has linked the pleiotropic nature of MIF to conformational plasticity and allosteric regulation. However, the role of conformational plasticity and allostery in modulating the global symmetry of the protein remains unclear. Thus, this work will provide insight into ongoing efforts to develop a biophysical map of residues in MIF that are critical to stabilizing a symmetric trimer.

Preliminary data from computational simulations reveal subtle asymmetries at the trimer interface, suggesting these residues may play a key role in maintaining a stable trimer. Site-directed mutagenesis of these positions results in significant changes to the structural, dynamic, and functional properties of MIF, as characterized by nuclear magnetic resonance (NMR) spectroscopy. Notably, our findings raise the possibility of an asymmetric solution-state configuration of MIF, which has not been previously characterized. These insights provide a novel framework by which MIF can be regulated. Insights from this project will thus be critical in informing future therapeutic developments that specifically target MIF.

Poster 9 | Decoding Poly-ADP ribosylation: Single-molecule detection of post-translational modifications using biological nanopores

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Abstract: Poly(ADP-ribose) (PAR) is a unique post-translational modification built of repeating ADP-ribose units that plays a critical role in cellular physiology, particularly in DNA repair. The length and structural complexity of PAR polymers directly involved in DNA repair protein recruitment, chromatin condensation, and enzymatic activities. Unusual PAR accumulation shows a strong association with poor clinical outcomes in cancer and neurodegenerative diseases. Although biologically important, existing analytical methods still lack the resolution and precision required to comprehensively characterize PAR chain length distribution or identify modification sites at the single-molecule level in biological samples. A huge, largely unexplored area limits our understanding of how proteins interact with PAR chains of different lengths and

hinders translational advances in genome integrity and disease contexts. Using nanopore technology, we will develop a robust, high-resolution platform to directly profile PAR length and identify site-specific ADP-ribosylation. This innovative approach will help us to achieve precise characterization of PAR polymer architecture in native biological settings, overcoming a major methodological barrier. By developing a reliable platform for real-time detection and profiling of ADP-ribosylated peptides, our work aims to deepen understanding of PAR biology and open new avenues for novel therapeutic strategies in oncology and neurodegeneration.

Poster 10 | Analysis of Disease-Linked USP7 Mutations in Hao-Fountain Syndrome

Kavitha Paramatmuni | UConn Health

Authors: Paramatmuni, Kavitha, Research Intern

Abstract: Under the mentorship of Dr. Irina Bezsonova in the Department of Molecular Biology and Biophysics at UCONN health, my research contributes to investigating Hao-Fountain syndrome, a rare neurodevelopmental disorder. The disease is linked to mutations in the USP7 gene, which plays an essential role in regulating protein stability by removing ubiquitin tags that mark proteins for degradation. When mutated, the gene can no longer regulate the removal of these tags correctly, which can lead to the manifestation of intellectual and developmental disabilities from birth. To study these mutations, I designed primers encoding specific single-nucleotide substitutions and introduced them into plasmids carrying USP7. The mutated DNA plasmid was then transformed into BL21 cells for the protein to be expressed and grown in LB.

Once the mutant proteins are expressed and purified, crystallographic data can be collected to compare structural differences between the mutated and the wild-type protein. Gel electrophoresis was used to measure differences in the activity of the mutated USP7 proteins in comparison to the wild type. We saw how, as time passed, a certain mutation would show no growth in protein expression, while another mutation would show activity levels relatively similar to the wild type, which helped us conclude that that particular mutation was impacting the gene in some other way. By comparing these differences, we aim to understand how these mutations affect the function of these expressed proteins, which would help develop effective forms of therapy and treatment strategies.

Poster 11 | Restraining Interproton Angular and Distance Dynamics with KEnRef

Amr Alhossary | Wesleyan University

Authors: Amr Alhossary, Colin Smith

Abstract: Despite the increase in computational power, traditional NMR structure determination remains semiquantitative or even qualitative, especially because of the complicated mathematics involved in modeling the nuclear dipole–dipole interactions in nuclear Overhauser effect (NOE) spectra. Even advanced exact NOE (eNOE) and residual dipolar coupling (RDC) methods neglect the effects of interproton angular motion, limiting the physical realism of generated ensembles. We present KEnRef, an open-source C++ library implementing the Kinetic Ensemble approach to refine multistate protein structures using restraints that rigorously account for interproton distance and angular fluctuation. We introduce a loss function, using fractional exponents, that balances sensitivity across the target distance range. KEnRef interfaces with GROMACS to introduce forces calculated at each molecular dynamics time step. On synthetic ubiquitin data sets, single-structure simulations with a fractional exponent of 0.25 achieved an interproton RMSD of ≈ 0.2 Å and convergence time down to 2 ns. Two-structure ensembles showed 100-fold restraint energy decreases at high force constants and reproduced both rigid and dynamic behaviors with distance and angular fluctuation highly correlated to reference data ($R > 0.85$), validating KEnRef's capacity to capture localized motions. KEnRef enables integrated refinement of distance and angular fluctuations, yielding ensembles that faithfully model both structural and dynamic properties. Its performance on synthetic benchmark tests and modular design lay the foundation for ultraquantitative NMR-based ensemble refinement.

Poster 12 | Bringing Order to Disordered Proteins: How the HSPB8 Chaperone Modulates the Aggregation of TDP-43

Paul Braymen | University of Connecticut

Authors: Braymen, Paul, University of Connecticut

Corbett, Katherine, University of Connecticut

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Abstract: Proteins often fold into a well-ordered native structure, but some sequences are prone to disorder. Proteins with these intrinsically disordered regions (IDRs) play important roles in cells, acting as flexible linkers, promiscuously recognizing client proteins, scaffolding biomolecular complex formation, and nucleating biomolecular condensation. However, many of these proteins also form large, insoluble, and cytotoxic aggregates that are implicated in a wide variety of neurodegenerative diseases like amyotrophic lateral sclerosis (ALS). To better understand how cells prevent IDR-containing proteins from aberrantly aggregating, I am studying the interaction between TDP-43, the pathohistological marker of ALS, and the chaperone protein HSPB8. HSPB8 is known to delay the aggregation of TDP-43, but the mechanism by which this happens remains unknown. I am using chemical crosslinking to covalently link the proteins together and stabilize the heterodimeric complex. I will use biophysical techniques, such as ssNMR, size exclusion chromatography, and mass spectrometry, to characterize this complex. With these results, I hope to better understand the molecular interactions that lead to aggregation, as well as how chaperone proteins can prevent aggregation and maintain proteostasis.

Poster 13 | Structural and Functional Characterization of PXL: A Unique Binding Module of PML-1

Rebekah Sheih | UConn Health

Authors: Rebekah Sheih, Daniel Fairchild, and Irina Bezsonova

Abstract: Promyelocytic Leukemia Protein (PML) is a stress-response factor implicated in anti-cancer and anti-viral response. Under conditions of stress, PML can assemble into dynamic subnuclear components called PML nuclear bodies. These entities play an important role in transcriptome regulation, telomere maintenance, and genome stability through poorly understood mechanisms. We have recently shown that the most abundant isoform of PML, PML-1, contains a unique structured domain called PXL that can directly bind nucleic acids. This previously unrecognized functionality of PML may provide the missing mechanism.

Structural and functional characterization of the apo-PXL domain revealed an exo-nuclease-like fold with high specificity towards G-rich oligonucleotides that can form guanine quadruplexes. We hypothesize that PXL functions by directly recognizing DNA and/or RNA G-quadruplexes. These structures are often found in telomeres, gene promoters, and viral genomes that are targeted by PML. Here, we report biochemical assays that test whether PXL shows greater affinity for linear oligonucleotides or folded G-quadruplexes, and X-ray crystallography experiments to solve the structure of PXL in complexes with DNA and RNA. Our findings may provide a novel molecular mechanism for PML's role in genome regulation, tumor suppression, and anti-viral response.

Poster 14 | Biophysical characterization of NS4a-BRIL for structural determination of an essential Orthoflavivirus membrane protein

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Abstract: Zika virus (ZIKV) can cross the placental barrier, where its non-structural protein 4a (NS4a), a viral membrane protein essential for replication, interacts with human ANKLE2, a protein involved with cell cycle regulation and neurogenesis. Maternal ZIKV can lead to Congenital Zika Syndrome, with microcephaly being a hallmark manifestation. Despite these significant consequences on human health, the molecular interactions underlying ZIKV infection remain poorly understood. Structural characterization of NS4a is particularly challenging due to its small size, flexibility, and intrinsically disordered regions. As a result, no high-resolution, single-particle cryo-electron microscopy (cryo-EM) structure of NS4a is currently available. To address these challenges, we created a fusion construct in which the engineered protein BRIL was attached to NS4a to increase its molecular size and stability. We found that NS4a-BRIL can be expressed in *Escherichia coli* and solubilized in detergents, providing a foundation for purification, biophysical characterization, and eventual cryo-EM structure determination. Additionally, BRIL reduced cell toxicity of NS4a and appeared to stabilize higher-order oligomeric states. These findings support BRIL as a promising tool for the expression and structural characterization of challenging viral membrane proteins such as NS4a.

Poster 15 | Nanobodies as a Tool for Identification of Exploitable Exosites in Caspase-6

Thomas Bregnard | UMass Amherst

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Abstract: Caspase-6 is an apoptotic cysteine protease with additional roles in neurodegeneration. Caspase-6 may contribute to Alzheimer's and Huntington's diseases through cleavage of tau and huntingtin, respectively, while cleavage of DJ-1 by caspase-6 appears to protect against Parkinson's disease. While caspase-6 presents a tempting target for drug design, the ideal targeting strategy would selectively block deleterious substrate cleavage with minimal impact on beneficial substrate cleavage. We hypothesize that caspase-6 may bind its various neurodegeneration-relevant substrates through discrete, potentially druggable exosites. This project aims to use caspase-6-binding nanobodies for exosite identification. We have utilized a yeast surface display library to isolate candidate nanobodies and confirmed their binding to caspase-6 by flow cytometry and bio-layer interferometry. We are in the process of characterizing these nanobodies, focusing on their impact on substrate cleavage by caspase-6. Any nanobodies that selectively block cleavage of specific substrates may bind a caspase-6 exosite used by that substrate. We will solve structures of caspase-6 in complex with putative exosite-binding nanobodies and identify the binding interfaces on caspase-6, which constitute potential exosites.

Poster 16 | A novel mechanism of host translation inhibition by ribocin

Emily Sholi | UMass Chan Medical School

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Abstract: Control of host translation is a powerful strategy used by pathogens to promote their own survival and damage host tissues, increasing nutrient availability and facilitating further spread. *Pseudomonas aeruginosa*, a major bacterial cause of pneumonia, inhibits translation in human cells. We recently discovered a nuclease, termed ribocin, encoded by nearly all strains of *P. aeruginosa* which may help explain the impact of infection on host translation. We show that ribocin selectively cleaves eukaryotic 28S rRNA within helix 69 (H69),

inhibiting translation through a mechanism distinct from other pathogenic translation inhibitors such as ricin and diphtheria toxin. To define the consequences of H69 damage on translation dynamics, we used in extracto cryo-EM to characterize ribosome-state distributions in actively translating samples following ribocin treatment. We find that H69 damage shifts occupancy toward specific active states and stabilizes transient translation intermediates, revealing which stages of the translation cycle are most affected. In addition, our structural analyses revealed ribosome populations that are protected from H69 damage, uncovering the protective roles of cellular factors that are not involved in translation. Finally, using our high-resolution maps of a ribocin-bound ribosome complex, we identified key interactions between ribocin and eukaryote-specific translation machinery, explaining this virulence factor's selective inhibition of host (but not bacterial or "self") translation. Together, these results define a novel mechanism of translation inhibition by a bacterial pathogen and underscore the importance of ribosomal hibernation factors as defenses against disruption of human translation.

Poster 17 | Investigating the Molecular Interactions of HuR, VEGF-A RNA, and MiR-29a

Madeline Clark | Brown University

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Abstract: Human antigen R (HuR) is a ubiquitously expressed RNA-binding protein that plays a role in the post-transcriptional regulation of several mRNAs. In the context of peripheral artery disease, HuR binds and stabilizes vascular endothelial growth factor A (VEGF-A) mRNA, promoting its expression and subsequent increased angiogenesis in response to cardiac stress. In aged mice, the HuR binding and half-life of VEGF-A mRNA is reduced, as is angiogenesis following artery ligation. A microRNA, miR-29a, has recently been implicated in binding and stabilizing VEGF-A mRNA at a site adjacent to the HuR binding site. The goal of this project is to define the interactions between HuR, the 3' UTR of VEGF-A mRNA, and miR-29a via the use of nuclear magnetic resonance (NMR) spectroscopy, microscale thermophoresis (MST), and other biophysical techniques. These methods will be used to evaluate the impact of ligand binding (i.e. mRNA or miRNAs) on the conformation and dynamics of HuR to further define the molecular details of the interaction between HuR, VEGF-A mRNA, and miR-29a. The findings of this project will provide not only a deeper understanding of the complex regulation of angiogenesis, but also possible therapeutic targets for promoting angiogenesis in atherosclerotic conditions such as peripheral artery disease.

Poster 18 | Quantifying and Engineering Electric Fields in Liver Alcohol Dehydrogenase

Justice Chinonso Eze | University of Connecticut

Authors: Justice Chinonso Eze

Abstract: Electrostatic interactions are central to enzyme catalysis, stabilizing charge distributions along the reaction coordinate and modulating catalytic efficiency. The Vibrational Stark Effect (VSE) enables direct experimental measurement of electric fields projected along vibrational probes within enzyme active sites, revealing strong correlations between electric field magnitude and reaction rates. In liver alcohol dehydrogenase (LADH), VSE studies have demonstrated that active-site electric fields are key determinants of catalytic efficiency, and targeted mutations have been shown to enhance enzymatic activity. In this work, we employ quantum mechanics/molecular mechanics (QM/MM) simulations to quantify electric fields in LADH variants corresponding to experimentally characterized mutations. The computed electric fields successfully reproduce experimentally observed trends, validating the ability of the QM/MM framework to capture electrostatic contributions governing catalysis. Extending this approach, we predict additional mutations that are expected to further enhance catalytic activity. This study establishes a robust computational framework for quantitatively reproducing enzyme electric fields in agreement with experiment. By bridging experimentally measurable electric fields with atomistic QM/MM calculations, this work provides a predictive platform for electrostatics-driven enzyme engineering and rational mutation design.

Poster 19 | Investigation of Elamipretide Translocation and Curvature Response in Inner Mitochondrial Membrane Models Using Molecular Dynamics Simulations

Hayden Yuan | University of Connecticut

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Abstract: Elamipretide (SS-31) is a mitochondria-targeted tetrapeptide recently granted accelerated FDA approval for the treatment of Barth syndrome. Its alternating cationic and aromatic residues promote association with cardiolipin in the inner mitochondrial membrane (IMM). In models of mitochondrial dysfunction, elamipretide improves energy production, decreases reactive oxygen species generation, restores cristae morphology, and delays opening of the mitochondrial permeability transition pore. However, the molecular mechanisms linking peptide-lipid interactions to IMM curvature and dynamics remain poorly understood. Here, we use molecular dynamics simulations to investigate how elamipretide affects the organization, mechanical properties, and curvature response of cardiolipin-containing membranes. Membrane-buckling simulations are being used to determine how peptide concentration alters membrane bending behavior and the energetic cost of curvature. In parallel, free-energy calculations are being performed to characterize elamipretide translocation across the bilayer and determine whether redistribution between membrane leaflets could contribute to curvature remodeling. Together, these studies seek to establish a molecular-level connection between elamipretide binding and changes in IMM structure and dynamics.

Poster 20 | Biophysical characterization of anti-CRISPR II-C1 binding to a thermostable Cas9

Praise Lasekan | Brown University

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Abstract: Expansion of the CRISPR toolkit toward applications requiring prolonged stability, robust gene editing in human plasma, or unique targeting loci led to the discovery of a thermostable Cas9 (GeoCas9). A subsequent biochemical study reported inhibition of this same thermostable Cas by a mesophilic anti-CRISPR II-C1 (AcrIIC1), which is encoded by viruses to prevent destruction via the CRISPR-Cas immune system. However, molecular level information revealing how this Acr inhibits GeoCas9 is lacking.

Using a synergistic biophysical approach, we resolved the interaction between AcrIIC1 and GeoCas9. An X-ray crystal structure defined the binding interaction between the GeoCas9 HNH nuclease domain and AcrIIC1, which disrupts the electrostatic interactions within GeoHNH. NMR, mutagenesis, and DNA cleavage assays confirm the interaction between the proteins and the necessity of the crystallographically defined binding residues. Microscale thermophoresis demonstrates that the presence of AcrIIC1 allosterically modulates the binding affinity of GeoCas9 for its guide RNA.

Poster 21 | The Role of Intrinsically Disordered Head and Tail Domains of Type III Intermediate Filaments in Polymerization and Interaction

Joshua McDonald | University of Connecticut

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Abstract: Intermediate filaments (IFs) are components of the cytoskeleton that provide support to a variety of cellular processes. Despite the large number of IF proteins, they share a conserved structure: an α -helical coiled-coil rod domain flanked by intrinsically disordered head and tail domains. Although it is known that the head and tail domains play a role in the polymerization of these filaments, and that these proteins interact with other components of the cell, the structural mechanisms by which these processes occur is not fully understood. My work focuses on three such interactions and their effects on polymerization: oxidants, metal ions, and molecular chaperones. In the presence of oxidizing agents, IFs rapidly reassemble from networks of long filaments into dense puncta. Meanwhile, monovalent metal ions are necessary for the formation of full-size filaments, and divalent metal ions influence filament morphology and their association with one another. Finally, small heat shock proteins interact with IF proteins and can be found in pathological IF aggregates in the juvenile neurodegenerative condition Alexander Disease. Through a combination of biophysical techniques, including solid-state NMR and TEM, I hope to investigate these proteins to elucidate the fundamental structural characteristics that facilitate these processes.

Poster 22 | Atomic Details of the FnCRISPR-Cas12a Nuc Domain Reveal Allosteric Hotspots Affecting DNA Binding and Cleavage

Camila Molina | Brown University

Authors: Camila E. Molina, Mohd Ahsan, Aakash Saha, Anika Weling, Kyle W. East, Giulia Palermo, and George P. Lisi

Abstract: CRISPR-Cas technology has revolutionized gene editing with expansive applications including engineering disease models and personalized precision medicine. Years of extensive studies on CRISPR Cas enzymes have revealed several promising Cas effectors with the potential to expand CRISPR based applications. CRISPR-Cas12a is a RNA-guided endonuclease that achieves double-stranded DNA scission with a preference for T-rich genomic regions achieved by its preferred protospacer adjacent motif (PAM) sequence (TTTV, V=A, C, G). The unique cleavage mechanism of Cas12a produces staggered cuts resulting in DNA overhangs in the target DNA that can be leveraged for genome insertions via homology directed repair. DNA cleavage is controlled by the nuclease lobe of Cas12a, composed of RuvC and an uncharacterized NUC domain. RuvC is the only catalytically active domain responsible for cleaving both the target and non-target DNA strands. However, mutations in NUC have been shown to significantly impact dsDNA cleavage, highlighting its importance to the function of Cas12a. This work unveils the functional contribution of NUC in Cas12a and its inter-domain coordination with RuvC obtained by solution NMR. Our research sought to provide a potential biophysical characterization of NUC with atomic-detail to further optimize CRISPR-Cas12a as a gene editing tool.

Poster 23 | Multiscale Modeling Predicts the Interaction of AAC2 with the Mitochondrial Respiratory Super complex

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Abstract: The mitochondrial ADP/ATP carrier AAC2 facilitates nucleotide exchange across the inner mitochondrial membrane and is functionally related to human adenine nucleotide translocases. Although AAC2 can function independently, it has also been observed to associate with respiratory supercomplexes (RSCs) containing complexes III and IV in cardiolipin-rich membranes. However, the molecular basis of this association remains poorly understood. Here, we combined protein–protein docking with coarse-grained and all-atom molecular dynamics simulations to characterize interactions among AAC2, the RSC, and cardiolipin. During coarse-grained simulations, AAC2 consistently converged toward a common RSC-binding region despite starting from distinct docked configurations. Low-energy conformations identified from free-energy projections were converted to all-atom models, which maintained stable AAC2–RSC interfaces and revealed candidate residues contributing to the interaction. The preferred binding region was further evaluated using enforced-rotation simulations and umbrella-sampling free-energy calculations. Replicated coarse-grained simulations combined with PyLipID analysis also identified specific cardiolipin-binding sites on AAC2 and at the AAC2–RSC interface. Together, these results provide a structural model of AAC2 association with the RSC and suggest potential roles for cardiolipin in stabilizing the complex. The predicted interfaces and lipid-binding sites provide experimentally testable targets for mutagenesis studies of mitochondrial carrier–respiratory complex organization.

Poster 24 | Electrostatic switches remodel the Enterovirus D68 capsid during acidification and prime it for genome release

Mahmoud Sharawy | University of Connecticut

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Abstract: Enterovirus D68 (EV-D68) undergoes uncoating during endosomal acidification, and cryo-electron microscopy localizes the resulting capsid openings to specific symmetry axes. However, the protonation events that initiate this process remain unidentified because experiments cannot directly resolve ionization states within the assembled capsid.

We performed explicit-solvent constant-pH molecular dynamics simulations of a 1.1-million-atom EV-D68 partial capsid, titrating 393 Asp, Glu, and His residues across 48 pH replicas and 24 μ s of aggregate sampling. Acidification from pH 7.4 to 5.0 neutralized 32% of the net negative charge of an icosahedral asymmetric unit, with the changes concentrated at the capsid symmetry axes. Electrostatic switches operate at all three axes, combining titratable residues with neighboring residues that remain in fixed protonation states. At the fivefold vertex, protonation of Glu75 contracts four of the five modeled VP1–VP1 interfaces. At the twofold axis, His98, Asp61, and Glu238 act across the interface to expand the contact where capsid opening is observed by cryo-EM. Glu19 and Glu58 respond at the threefold axis exclusively on the capsid interior.

Acidification also altered the capsid's internal ionic environment: chloride accumulated while sodium was depleted. Protonated histidines recruited chloride into their first coordination shells, whereas protonated carboxylates reduced anion exclusion. Consequently, the genome-facing surface became less repulsive to RNA before any large-scale conformational change occurred. Together, these results reveal a hierarchical mechanism in which protonation first reorganizes capsid electrostatics and ion distributions and then remodels specific symmetry-axis interfaces, priming EV-D68 for genome release.

Poster 25 | Water as a Thermodynamic Driver of Elastin Structure and Function

Metehan Cam | University of Connecticut

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Abstract: Elastin is the extracellular matrix protein that provides arteries, lungs, and skin with reversible elasticity and resilience. Both elastin elasticity and coacervation are widely understood to be entropy-driven, yet whether the dominant entropy originates from protein conformational fluctuations or hydration water remains unresolved. Here, we use multi-microsecond all-atom molecular dynamics simulations to directly quantify protein and hydration-water thermodynamics during elastic deformation and elastin-like polypeptide (ELP) conformational transitions and assembly.

For an elastomeric region of tropoelastin, stretching produces only a modest loss of protein conformational entropy, whereas the dominant entropy penalty arises from hydration water. Extension recruits bulk water into a thin, low-entropy hydration layer and reorganizes water around exposed hydrophobic motifs, supporting a hydration-driven mechanism of elastic recoil. In complementary ELP simulations, we find that thermodynamic signatures associated with coacervation already emerge during single-chain conformational transitions and persist during multichain assembly. ELPs remain highly hydrated and largely disordered upon condensation, with substantial interstitial water retained within the assembled phase.

Together, these results identify water as an active thermodynamic participant linking elastin elasticity and coacervation and emphasize hydration-water thermodynamics as a central determinant of elastomeric protein function.

Poster 26 | Detecting Sampling Errors in Membrane Permeation Free-Energy Profiles through an FEP-Based Cross-Validation

Rey Carten | University of Connecticut

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May, Eric, University of Connecticut

Abstract: Passive permeation of drug-like molecules and other solutes across lipid bilayers is an important process in pharmacology and cell biology. Because spontaneous permeation occurs on timescales that are often inaccessible to conventional molecular dynamics simulations, membrane permeation is commonly characterized using umbrella sampling (US). In US, biased simulations sample a series of windows along a membrane-crossing reaction coordinate, which are then combined to reconstruct a potential of mean force (PMF). However, slow degrees of freedom orthogonal to this coordinate—particularly changes in membrane structure and solute orientation—can produce systematic sampling errors that are difficult to detect from the PMF alone. Here, we introduce a cross-validation procedure in which free-energy perturbation (FEP) is used to calculate the free-energy change associated with decoupling the solute from selected umbrella windows. Differences among these calculations are compared with the corresponding free-energy differences obtained from the US-derived PMF. Using ibuprofen permeation across a POPC bilayer as a model system, we demonstrate agreement between the US- and FEP-derived estimates at key positions along the permeation pathway. Agreement between these independent estimates provides a thermodynamic consistency test, whereas disagreement identifies regions of the PMF that may not be adequately converged. This framework provides a new approach for diagnosing systematic sampling errors in membrane-permeation calculations and may inform future strategies for correcting poorly converged free-energy profiles.

Poster 27 | Membrane Composition–Dependent Cooperative Hydropathy Governs FHV γ Peptide Membrane Activity

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Abstract: Membrane-active peptides from non-enveloped viruses play a central role in membrane disruption and genome release. The 44-residue γ peptide of Flock House Virus (FHV) provides a model system for understanding how peptide sequence and membrane composition regulate membrane activity. Here, we investigate residue-level membrane interactions of wild-type (WT) γ and the F402A mutant using PARCH-based hydropathy analysis derived from molecular dynamics simulations in neutral (PC), negatively charged (PG), and mixed (PCPG) membranes. Residue-wise hydropathy profiles reveal that WT γ exhibits a coordinated, region-specific response to membrane composition. The N-terminal region (1–21) shows strong membrane sensitivity, while the C-terminal region (31–44) displays cooperative responsiveness that is particularly enhanced in mixed PCPG membranes. Region-wise analysis further demonstrates that membrane composition redistributes hydropathy responses along the WT peptide, with mixed membranes amplifying C-terminal contributions. In contrast, F402A produces a more fragmented hydropathy profile, alters membrane-responsive behavior in the middle region, and reduces coordinated C-terminal responsiveness. Together, these results indicate that FHV γ membrane activity is associated with sequence-dependent cooperative organization across the peptide and that mutation of a critical C-terminal residue disrupts this organization.

Poster 28 | Computational Modeling of Age-Dependent Mechanical Deterioration in Elastin Fibers

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Abstract: Elasticity is one of the most important properties of vertebrate tissues, provided primarily by elastic fibers. These fibers have a long lifespan and low turnover, making them highly susceptible to progressive age-driven modifications. Yet the technical difficulty of isolating individual fibers leaves empirical mechanical data scarce, and macroscopic measurements may obscure underlying degradation mechanisms. To address this, we developed a lattice-spring model of an elastic fiber and implemented fragmentation through a biologically motivated protocol. Macroscopically, the fiber softens progressively with fragmentation but exhibits no clear transition before failure. Microscopically, a sharp transition appears: redistributed load initially recruits new load-bearing elements to compensate for those lost, but once this finite reserve is exhausted, the network can no longer offset continued damage. At this point, multiple structural and energetic descriptors undergo a simultaneous shift in rate, identifying a microstructural transition that can predict bulk properties long before failure. Our results indicate that microstructural analyses can resolve a degradation that is not apparent in the bulk response, suggesting that early elastin damage may be structurally well-defined yet mechanically subtle. The framework provides a route to represent elastic fibers more accurately at higher scales and to trace how age-driven modifications propagate across hierarchical biological structures.

Poster 29 | Tale of Two Tails: Thermodynamic Control of DIAPH1 Membrane Localization and Activity by the N- and C-Termini

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Abstract: DIAPH1 is a major actin polymerase involved in cell migration, phagocytosis, molecular trafficking and cytokinesis. In its resting state, DIAPH1 is autoinhibited through intramolecular interactions between the DIAPH1 inhibitory domain, DID, and the DIAPH1 autoinhibitory domain, DAD, and is activated by the Rho GTPase, RhoA. We recently employed a robust and reproducible method to produce milligram quantities of highly pure, isotopically labeled fragments of DIAPH1, allowing detailed biophysical and structural characterization of the DID-DAD complex. Analysis of DID-DAD in the presence of RhoA revealed that DIAPH1 activation is not governed by direct competitive displacement. Instead, activation proceeds through the formation of a negatively cooperative ternary complex, resolving the longstanding paradox of tight binding but low potency activation.

Building upon this success, we investigated the 66-residue N-terminus and the 76-residue C-terminus of DIAPH1, which includes DAD, both of which are predicted by AlphaFold to contain helical regions that may contribute to RhoA-mediated activation. Here, we demonstrate that both the N- and C- termini competitively interact with the DID through a multistep, negatively cooperative mechanism, to direct DIAPH1 localization to membranes enriched in phosphatidylinositol 4,5-bisphosphate. This provides an additional layer of spatiotemporal control that fine-tunes DIAPH1 activation and underpins its diverse biological functions.

Poster 30 | Developing a nanopore assay to monitor interaction between the NS4B cytoplasmic loop and the NS3 helicase of Dengue virus

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Abstract: Dengue virus (DENV) infection remains a major global health burden, with no approved direct-acting antivirals currently available. The nonstructural protein NS3 helicase, essential for viral genome replication, has been shown to interact with the cytoplasmic loop of NS4B, a transmembrane replication complex protein, suggesting that this interaction may play a regulatory role in the DENV-2 replication cycle. Disrupting this protein-protein interaction represents a promising, largely unexplored antiviral strategy. However, tools capable of characterizing this interaction in real time and at high resolution remain limited. Here, we propose the development of a nanopore-based single-molecule platform to investigate the interaction between the NS4B cytoplasmic loop and the NS3 helicase domain. Specifically, this study aims to: (1) monitor the interaction in real time using nanopore sensing, (2) determine the binding affinity between the two proteins, and (3) evaluate whether the NS4B cytoplasmic loop modulates ATP binding by the NS3 helicase. We hypothesize that nanopore-based single-molecule analysis will enable precise, real-time characterization of the binding kinetics and affinity of this interaction, and that NS4B binding may allosterically influence the ATP-binding activity of NS3 helicase. The anticipated outcomes of this research will establish nanopore technology as a robust and sensitive platform for studying dynamic protein-protein interactions within the DENV replication complex, and will generate mechanistic insight that can inform the design of small-molecule or peptide-based inhibitors targeting the NS4B–NS3 interface. Beyond dengue virus, this approach offers a generalizable framework for probing protein-protein interactions across other viral systems, supporting a broader strategy for antiviral discovery centered on the disruption of essential viral protein complexes.

Poster 31 | Characterizing the Physicochemical Diversity of Cell-Penetrating Peptides Through Unsupervised Learning

Anurag Upadhyaya | Northeastern University

Authors: Anurag Upadhyaya

Martin Shen Wang

Srirupa Chakraborty

Abstract: Cell penetrating peptides (CPPs) span diverse sequences and physicochemical properties, complicating their organization into interpretable groups. We developed an unsupervised contrastive learning framework using 2204 peptides (1149 CPPs, 1055 nonCPPs). Frozen ESM2-650M representations and trainable local sequence features were integrated into 128 dimensional embeddings, optimized with conservative sequence augmentation, and clustered using K-means. We assessed robustness across five initializations and characterized clusters using physicochemical descriptors, predicted secondary structure, and published cellular uptake data. Five clusters were preferred in four of five runs; the selected model achieved a silhouette score of 0.8734. Among CPPs, Cluster 0 was arginine rich, highly charged, and hydrophilic. Cluster 1 was longer, lysine containing, and hydrophobic. Cluster 2 was shorter and weakly cationic and Clusters 3 and 4 showed intermediate profiles. A descriptor based random forest recovered cluster labels with macro-F1 scores of 0.802 internally and 0.712 externally. Predicted structures showed the greatest helical tendency in Cluster 1 and predominantly coil like conformations in Cluster 2. Among 474 peptides with published cellular uptake data, median cell associated fluorescence was 219.1 RFU in Cluster 1 versus 8.7 RFU in Cluster 2. Together, these findings indicate that the learned CPP clusters reflect physicochemical and structural diversity associated with distinct experimental cellular uptake profiles and may inform drug delivery research.

Poster 32 | SAXS-Guided Evaluation of Tropoelastin Conformational Ensembles Across Molecular Dynamics Force Fields

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Abstract: Tropoelastin, a soluble precursor of elastin which provides elasticity to connective tissues, is a largely disordered protein whose biological function depends on its heterogeneous conformational ensemble. Accurately modeling this conformational ensemble is challenging because simulations of disordered proteins are sensitive to force field accuracy and environmental conditions. Here, we investigated how force field, ionic strength, and temperature influence tropoelastin ensembles and evaluated simulated conformations against experimental SAXS data.

Conformational ensembles of full-length tropoelastin were generated using long-timescale all-atom MD simulations using the CHARMM36m/TIP3P and a99SB-disp/TIP4P-D force field and water model combinations. The a99SB-disp was additionally simulated at 50 and 150 mM NaCl and at 283 and 300 K. Ensembles were characterized by radius of gyration, maximum molecular dimension, residue-pair distances, shape anisotropy, and generating theoretical SAXS profiles.

The CHARMM36m/TIP3P ensemble favored highly compact conformations and agreed poorly with experimental dimensions, whereas a99SB-disp/TIP4PD sampled broader, more extended ensembles and better reproduced SAXS data. Increasing salt concentration in simulations shifted the ensemble toward more compact conformations, whereas temperature had no significant effect.

These findings identify a99SB-disp/TIP4PD as the better choice for modeling full-length tropoelastin and highlight the importance of experimentally benchmarking force fields and environmental responses for a large, disordered protein.

Poster 33 | VPS45 Regulates Rabenosyn-5 and Syntaxin 16 binding in Endosomal Membrane Trafficking

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Abstract: Eukaryotic membrane trafficking is required for cell growth, signaling, and survival. Many proteins regulate vesicle trafficking to ensure cargo delivery to the correct location at the appropriate time. SNARE proteins, located on the vesicle and target membranes (v-SNAREs and t-SNAREs, respectively), control membrane fusion through the assembly of a four-helix SNARE complex. VPS45, a Sec1/Munc18 (SM) protein, is a regulator of endosomal membrane trafficking through its interaction with SNARE proteins. Point mutations in VPS45 are also associated with Severe Congenital Neutropenia 5 (SCN5), a devastating disease. VPS45 binds the syntaxin type t-SNARE, Syntaxin 16 (Stx16), through two binding modes: 1) the N-peptide of Stx16 and a hydrophobic pocket in VPS45, and 2) the cleft of VPS45 and the Habc domain + SNARE motif of Stx16. It is hypothesized that the interactions between VPS45 and Stx16 regulate membrane fusion. VPS45 also interacts with the endosomal Rab5 effector, Rabenosyn-5. The function and role of this complex in membrane trafficking is currently under investigation. Using recombinantly expressed, purified proteins, we examine interactions, and any possible competition, between VPS45, Rabenosyn-5, and Stx16. Additionally, the wildtype mechanism and modes of interaction will elucidate the dysfunctional VPS45 SCN5 mechanisms.

Poster 34 | Single-Molecule Biophysical Characterization of DM1 Repeat Hairpin Mechanics Using C-Trap and Molecular Dynamics Simulations

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Abstract: Expanded CTG repeats associated with myotonic dystrophy type 1 (DM1) can form heterogeneous hairpin structures that may contribute to abnormal nucleic-acid behavior. However, bulk measurements average over multiple conformational states and cannot resolve the mechanical behavior of individual molecules. Here, we combine single-molecule measurements using a LUMICKS C-Trap with molecular dynamics (MD) simulations to investigate the mechanics and structural heterogeneity of DM1 repeat hairpins. Force-extension measurements will characterize unfolding and refolding transitions, rupture forces, hysteresis, and intermediate states, while constant-force experiments will probe conformational hopping. Confocal fluorescence measurements will provide complementary information on molecular localization and conformational changes. MD simulations will resolve nucleotide-level interactions, including hydrogen bonding, base stacking, loop stability, and repeat-dependent structural deformation. By integrating single-molecule experimental observables with atomistic simulations, we aim to identify distinct repeat-hairpin conformational states and connect their mechanical signatures to the underlying molecular interactions.

Poster 35 | Hunting for new antivirals capable of disrupting the dynamic ensembles of regulatory RNAs

Dan Fabris | University of Connecticut

Authors: Dan Fabris

Abstract: In many RNA viruses, genomic sequences corresponding to regulatory (i.e., non-coding) domains can fold alternative conformations responsible for different biological functions. Disrupting their interconversion would represent an excellent strategy for inhibiting such functions and interfering with the viral lifecycle. Owing to the intrinsic challenge of resolving the structural heterogeneity of these RNA dynamic ensembles, traditional drug-discovery approaches have thus far failed to provide effective leads. The talk will illustrate a suite of approaches based on native mass spectrometry (nMS) and Ion Mobility Spectrometry (IMS) MS, which afford the ability to distinguish the individual members of an RNA ensemble and to assess the effects of ligand binding on their mutual distribution. The talk will discuss the unique features that make nMS capable of taking accurate snapshots of all unbound/bound species present at equilibrium in solution when putative ligands are mixed with target RNAs. It will also show that combining nMS with IMS allows one to monitor RNA conformational landscapes before and after addition of ligand, which is necessary to detect possible conformer selectivity. The information provided by these approaches will provide the foundations for developing conformer-specific antivirals with greatly reduced off-target toxicity.

Poster 36 | Optimization and Validation of an Implicit-Water Model for Simulating O-Glycans and Glycoproteins at the Atomistic Scale

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Abstract: Glycans are complex, heterogeneous chains of pyranose sugars, often covalently attached to proteins or lipids, that are essential to many biological processes and serve important protective and barrier functions. Explicit solvent simulations are the benchmark for glycan conformational analysis, but their cost limits application to large glycosylated systems such as mucin hydrogels, antibodies, and viral envelope glycoproteins. Implicit solvent approaches capture solvent-mediated effects at lower cost, yet they have not been validated for glycans against explicit models.

We optimized and benchmark the Generalized Born Implicit Solvent (GBIS) model with the CHARMM36 force field against explicit TIP3P simulations, using a peptide anchored O-glycan relevant to mucin-rich systems. Our analysis reveals a difference in the Chi (χ) rotamer populations between implicit and explicit solvent. This torsion (N-CA-CB-OG1 of threonine) involves the oxygen through which the O-glycan attaches to the peptide, making it critical for local conformation. We tune parameters, including coupled dihedral angles, via a CMAP-like approach evaluated against Replica Exchange with Solute Scaling (REST2) enhanced sampling. The corrected model recovers the explicit solvent χ populations, establishing GBIS as a viable solvent model for O-glycans and improving the feasibility of simulating large glycoprotein systems relevant to health and disease.

Poster 37 | A molecular blue-print for mucin inspired biomaterials

Joshua Koja Aduampon | Northeastern University

Authors: Joshua Mantey Kojo.A, Simran Pandey, Srirupa Chakraborty

Abstract: Mucin inspired biomaterials are a rapidly growing class of functional polymers designed to replicate the selective permeability and molecular recognition properties of biological mucus. MUC2, the dominant mucin of the intestinal barrier, it exceeds 5,000 amino acids in length, and O-glycans account for 40–80% of its total mass. Its size and glycan heterogeneity have made structural characterization difficult by experimental methods, leaving key questions about how glycosylation shapes mucin conformation unresolved.

We built a scaled atomistic model of MUC2 that preserves its glycosylation pattern, domain architecture, and key physical properties. Using all-atom molecular dynamics simulations, we characterized its polymer behavior across three glycosylation states: unglycosylated, mid-level glycosylated, and extensively glycosylated. We have determined the optimal model length and scale, then quantified chain extension, structural stiffness, and flexibility because of glycans. Glycosylation progressively expands and stiffens the polymer chain through steric and electrostatic repulsion between O-glycans, with the magnitude of this effect scaling directly with glycan density.

These results establish glycan density as the primary determinant of MUC2 chain architecture and conformational behavior. This provides a direct molecular basis for designing mucin inspired materials, offering an atomistically grounded framework for engineering glycopolymers for mucosal drug delivery and hydrogel scaffolds

Poster 38 | Retroviral intasome integration drives nucleosome disassembly: an atomic force microscopy study

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Abstract: Retroviral integration is a crucial step in the viral replication cycle, catalyzed by intasomes- integrase multimers bound to viral DNA ends. Following strand transfer, the host nucleosome is left with a single-stranded gap at each viral–host junction. However, how the nucleosome is then disassembled to allow gap repair is not fully understood. Using atomic force microscopy (AFM), we show that prototype foamy virus (PFV) intasome integration disassembles reconstituted 12-mer nucleosome arrays in a concentration-dependent manner, displacing histones far faster than the spontaneous rate. Array loss follows biexponential kinetics, with a fast, intasome-dependent phase and a slow, spontaneous phase. The fast disassembly rate is independent of intasome concentration ($\tau_{\text{fast}} = 29.8 [-2.9/+3.0]$ min); instead, intasome concentration sets the fraction of arrays committed to fast disassembly. We also observe similar nucleosome disassembly for the structurally distinct mouse mammary tumor virus (MMTV) intasome, indicating that the effect is not specific to the PFV intasome and may be a more general phenomenon of retroviral integration. Preliminary data suggest that intasome binding may also contribute to disassembly. Together, these results show that retroviral intasome integration, and possibly binding, disassembles nucleosomes without host chaperones or ATP-dependent remodelers.

Poster 39 | Amyloid Fuzzy Coat Atlas: a ensembles database for disordered region of amyloid fibrils

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Abstract: Amyloid fibril formation is a hallmark of numerous neurodegenerative and metabolic diseases, including Alzheimer's, Parkinson's, and Type 2 diabetes. While the structured cores are well-characterized, the fibrils are typically flanked by intrinsically disordered regions (IDRs) known as the “fuzzy coat.” This disordered shell plays a critical role in modulating fibril solubility, secondary nucleation, and pathological transmission, yet its high conformational flexibility renders it largely invisible to traditional structural determination techniques. To bridge this gap, we present the “Amyloid Fuzzy Coat Atlas”, a comprehensive database of fuzzy coat conformational ensembles. We employed the Hybrid Resolution (HyRes) coarse-grained protein model, refined against experimental measurements of amyloid proteins and their fibrils, to perform large-scale simulations to sample the fuzzy coat ensembles across diverse fibril architectures. This Atlas provides atomic-level ensembles alongside a characterization of the structural, dynamic, and thermodynamic landscapes of the fuzzy coat. The HyRes model and this database will offer a platform for further advancing the understanding of the role of fuzzy coats in pathological and physiological processes, offering new insights for therapeutic intervention.

Poster 40 | Role of Spectrin Unfolding and Non-muscular Actomyosin in the Nonlinear Shear Response of the RBC Membrane Cytoskeleton

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Abstract: The spectrin–actin cytoskeletal network and its interactions with active contractile components regulate the mechanical integrity of the red blood cell (RBC) membrane. To investigate the coupled effects of spectrin extensibility, dynamic actin–spectrin interaction, and actomyosin contractility under shear deformation, we developed a three-dimensional coarse-grained molecular dynamics (CGMD) model of the RBC membrane skeleton. In this model, actin junctional complexes act as dynamic cross-links with reversible binding, whereas spectrin tetramers are represented as multi-segment chains capable of unfolding and refolding in response to externally applied deformation. Actomyosin interactions are incorporated via a finitely extensible nonlinear elastic (FENE)-based potential to simulate contractile coupling between actin nodes. With unfolding forces in the range of ~25–35 pN and contour length increments of ~30 nm, our model reproduces the characteristic sawtooth force–extension response of spectrin unfolding and is validated against single-molecule atomic force microscopy measurements. We then applied shear deformation to the cytoskeletal network over a range of strain rates. Our simulations demonstrate that whereas spectrin unfolding and actin–spectrin dissociation reduce load-bearing capacity and promote mechanical softening, actomyosin contractility increases shear stiffness and shifts the stress–strain response toward higher stress levels. The transition from elastic deformation to structural failure is governed by the interplay among filament extensibility, bond rupture, and contractile forces. Together, these results provide quantitative and mechanistic insight into the multiscale mechanisms underlying the deformation and rupture of RBC membranes under severe mechanical strain.

Poster 41 | Glycographer: An Open-Source Modeling Suite for Protein-Glycan Binding Landscape Characterization and Targeted Sequence Design

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Abstract: Despite their ubiquity and potential in therapeutics development, molecular glycobiology and glycoengineering are vastly underrepresented in research due to glycan structure and dynamics often being refractory to experimental methods of study at the molecular level. While computational modeling and simulation have overcome many of these barriers, there is a lack of such resources for investigating glycans from the nanomedicine perspective. We present a solution to this lack of support in the form of Glycographer, a novel atomistic glycan modeling and computational design methodology powered by glycan fragment-based receptor characterization in a lectin-relevant multivalent context deployed through an open-source Python simulation package. In this work, we execute the full Glycographer protocol on the carbohydrate binding domain models of two clinically relevant lectins (DC-SIGN and SIGLEC-7). We show that Glycographer correctly ranks the binding preference of sampled probes compared to literature, recovers both known and experimentally predicted binding sites, and identifies physiochemically feasible theoretical binding sites for both the multimeric and monomeric lectin receptor models. This methodology promises to bridge a critical gap between atomistic glycan simulation techniques and the principles of computational drug design towards future clinical translation of glycan-based therapeutics.

Poster 42 | How Magnesium Tunes Light Absorption in the Microbial Rhodopsin HwMR

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Abstract: Microbial rhodopsins are light-driven transmembrane proteins that use a retinylidene Schiff base chromophore. In the halophilic archaeon *Haloquadratum walsbyi*, HwMR is the first identified light-driven magnesium transporter, but the molecular basis of its Mg^{2+} -dependent spectral tuning is not understood. In this work we combine molecular dynamics, QM/MM, and TD-DFT to compute the absorption maxima of wild-type HwMR and D84N HwMR at low and high $MgCl_2$ concentrations, and of the related proton pump HwBR. At low salt concentrations (0~M $MgCl_2$), a protonated Schiff base (RSBH⁺) reproduces the known experimental absorption value; interestingly, at high salt concentrations (2~M $MgCl_2$), a neutral, deprotonated RSB matches the experimentally observed blue shift; for wild-type HwMR, proton transfer to D84 gives the best agreement. In contrast to HwBR, where Schiff-base deprotonation occurs only in photocycle intermediates, HwMR undergoes ground-state RSB deprotonation at high Mg^{2+} . Electrostatic analysis shows that counterions D84 and D213 provide strong blue shifts, and the D84N mutation weakens this effect, explaining a 30~nm red shift. These results reveal a dual tuning mechanism, RSBH⁺ deprotonation at high Mg^{2+} and direct electrostatic modulation by bound Mg^{2+} , distinguishing HwMR from the proton pump HwBR and rationalizing its adaptation to hypersaline environments.

Poster 43 | SIMULATING STRUCTURAL TRANSITIONS OF HIV-1 ENV PROTEIN DURING REFOLDING

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Abstract: Membrane fusion is a crucial step in the HIV-1 viral entry process. The fusion process is mediated by the envelope glycoprotein (Env) gp120/gp41. gp120/gp41 is a heterotrimer that undergoes a series of large-scale conformational rearrangements during fusion. To gain a quantitative picture of this process, we employ molecular dynamics simulation using structural-based models (SMOG) to obtain a mechanistic, dynamical, and energetic description of the process. In this model, we include all non-hydrogen atoms and define the postfusion state of gp41 as energetically stable. We find that Env proceeds through many asymmetric intermediates during the fusion process. Upon CCR5-binding, the fusion peptide fires toward the host, followed by Env adopting an early pre-hairpin-like structure with all 3 gp120 subunits bound to gp41. This is followed by asymmetric shedding of gp120 subunits. During the shedding of gp120, HR2 helices begin to refold asymmetrically around HR1. After all gp120 subunits are shed, HR2 refolds completely around HR1, adopting the postfusion state of gp41. We integrate our MD approach with cryoET data by Schaefer et al (unpublished), monitoring the fusion in membranes to arrive at a quantitative description of the structural intermediates of HIV-1 Env.

Poster 44 | Characterizing the Binding Capability of Single-domain Kinases

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Abstract: Bacterial signal transduction pathways commonly involve histidine kinases (HKs) to regulate a diversity of cellular processes. While structurally homologous to the kinase domain of HKs, HK-like serine threonine kinases (HK-like STKs) are single-domain kinases without a separate substrate specificity domain. In *Bacillus subtilis*, there are two HK-like STKs that respectively regulate sporulation and the stress response by phosphorylating their cognate substrates. Previous studies identified conserved residues proposed to mediate interactions between HK-like STKs and their cognate substrates. We initially hypothesized that HK-like STKs exhibit strict substrate specificity that prevents stable binding to non-cognate substrates. However, results from biochemical pulldown assays and size exclusion chromatography showed that one of the HK-like STKs can interact with a non-cognate substrate in addition to its cognate substrate. Through computational analysis, we further identified and assessed differentially conserved residues in substrates that contribute to the kinase-substrate specificity. These findings lay a foundation for future analysis to understand specificity determinants across HK-like STKs.

Poster 45 | Identification and characterization of atypical and novel zinc finger domains

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Abstract: Zinc fingers (ZNFs) occur in multi-domain proteins with functions including transcription, ubiquitin ligation, and chromatin remodeling. These protein modules typically only fold and function upon binding Zn^{2+} . The sequences of ZNFs follow consensus rules, including strict spacing between zinc ligands, and conserved locations of nonpolar residues that form a rudimentary hydrophobic core. Differences from these sequence patterns confound prediction algorithms, so that atypical ZNFs are often mis-annotated as 'degenerate' non-functional domains. Using solution-state NMR, together with CD and UV-Vis spectroscopy, our lab investigated seven ZNFs that were improperly annotated as nonfunctional and identified an additional three novel functional ZNFs. Why were these ten domains misidentified? (i) The ZNF motif is more tolerant to sequence alteration than previously realized. (ii) Three of the ZNFs are missing the last of the four ligands for zinc. These tridentate ZNFs show increased dynamics, compared to their normal tetradentate counterparts, and display increased hydrolytic activity. We are currently using ZNF mutated in cancers to see if the substitution results in a DNase activity gain-of-function. Taken together, our results show that there remains much to learn about the versatile and ubiquitous ZNF folding motif.

Poster 46 | Uncovering a novel antifreeze protein from bulk genomic data

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Abstract: Antifreeze proteins (AFPs) are a group of proteins that help organisms survive freezing temperatures by controlling ice growth. AFPs are found in many organisms, including fish, insects, plants, bacteria, and fungi. Freeze-avoidant fish and insects are known to have AFPs, which often share well-characterized structural and sequence motifs. In contrast, AFPs from freeze-tolerant microbes are not well documented, and their structure and sequence composition differ considerably from other AFP types. Here, we present preliminary computational evidence for novel antifreeze proteins from permafrost bacteria. Our putative sequences originate from DNA extracted from Alaskan permafrost cores. The putative sequences were identified using comparative analysis of AlphaFold-predicted structures and aligned sequences. These sequences are predicted to have a 6-loop beta-solenoid structure, which is common in bacterial AFPs, and have many linearly arranged threonine residues on their binding faces. Characterizing novel AFPs could enhance our understanding of how biomolecules interact with ice, benefiting the development of cryoprotectants and ice-inhibiting materials for medical, agricultural, and aeronautic applications.

Poster 47 | Predicting and Improving Fluorescence in Mini Fluorescence-Activating Proteins

Maruf Hasan | Wesleyan University

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Abstract: De novo fluorescence-activating proteins provide a useful platform for understanding how designed proteins control small-molecule (fluorogen) behavior. These proteins bind fluorogen and increase fluorescence by shaping the local environment around the ligand. However, predicting why some designed variants are bright while others are dim remains challenging because fluorescence depends on both ligand binding and chromophore dynamics. In particular, the ability of the protein pocket to restrict chromophore motion after excitation can strongly influence fluorescence yield. This project develops a computational workflow to evaluate and improve fluorescence-activating protein systems across different chromophores and protein scaffolds. Quantum mechanical calculations are used to describe chromophore torsional energy landscapes, while molecular dynamics simulations are used to compare fluorogen dynamics in solution and in protein bound states, showing how protein binding influences chromophore motion and planar-state stability. These simulations provide rotation-based metrics that can be compared with experimental fluorescence trends. In parallel, mutation screening approaches based on molecular dynamics and Rosetta modeling are used to identify amino acid changes that may stabilize favorable chromophore-binding environments. Together, this work aims to improve the computational prediction, explanation, and design of brighter fluorescence-activating proteins for future applications in bioimaging, biosensing, and de novo protein engineering.

Poster 48 | Coarse-grained modeling of TDP-43 LCD fibril elongation and HSPB8 chaperone effect

Xubo Luo | University of Connecticut

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Abstract: Fibrillar aggregation of the TAR DNA binding protein 43 low complexity domain (TDP-43 LCD) is a potential therapeutic target in neurodegenerative diseases, and the small heat shock protein HSPB8 delays this process. We refined a putative multi-stage mechanism of fibril formation. To probe the stages of this mechanism, this work established a series of experiment-inspired coarse-grained models to evaluate fibril elongation with preexisting monomeric cores. Condensation and the propensity of fibril elongation were simulated using hydropathy scale (HPS) slab simulations for homogenous TDP-43 LCD and for 50:50 mixtures with monomeric HSPB8. All simulated states underwent liquid-liquid phase separation into condensates. However, only TDP-43 LCD bearing large planar cores in the N-terminal half assembled into well-aligned stacks, indicating a high propensity of fibril elongation consistent with experiment. HSPB8 co-condensed and mixed well with early-stage species but was excluded from fibril-competent late-stage states by microphase separation, indicating that it could act only before fibrils matured.

Poster 49 | Solid state NMR characterization of wild-type and mutant GFAP intermediate filament assemblies

Emily Faircloth | University of Connecticut

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Abstract: GFAP is a type III intermediate filament primarily found within astrocytes that maintains proper cell structure. Mutations in GFAP are implicated in the pathology of Alexander disease, a neurodegenerative disease characterized by cytoplasmic inclusions of protein. GFAP consists of a highly conserved alpha-helical rod domain bracketed by intrinsically disordered head and tail domains. While the general domain organization of GFAP monomers and the assembly process for tetramers is known, we lack an atomic resolution mechanistic understanding of GFAP assembly into mature filaments. Understanding the structure of GFAP filaments and how mutations disrupt this structure will provide insight into how mutations produce Alexander disease pathology. First, we characterized wild-type GFAP tetramers and filaments using solid state NMR. We observe uniformly rigid alpha helical structure and can resolve highly mobile intrinsically disordered regions, likely arising from the head and tail domains. Tetramers display increased mobility in these regions. We next characterized an assembly-deficient GFAP mutant, C294S. The rigid regions of this mutant are consistent with the wild-type GFAP, but there is an increase in highly mobile regions. Our results provide a foundation for developing solid state NMR approaches to characterize intermediate filament assembly mechanisms and the effect of disease mutations.

Poster 50 | Coordination and Energetics of tRNA Hybrid-State Formation in the Yeast 80S Ribosome

Eghosa Osazuwa | Northeastern University

Authors: Eghosa Osazuwa
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Whitford Paul

Abstract: During translocation, tRNA moves through the ribosome via hybrid states in which it simultaneously occupies different binding sites on the two subunits. The classical-to-hybrid ($P/P \rightarrow P/E$) transition involves intersubunit rotation, L1 stalk closure, and displacement of the tRNA 3'-CCA tail toward the E-site. Although these motions have been individually resolved by cryo-EM, their relative coupling strengths and the energetic landscape governing the transition have not been quantified in eukaryotic ribosomes.

Using all-atom structure-based simulations of the *Saccharomyces cerevisiae* 80S ribosome, we investigate this transition with two complementary approaches: single-basin simulations to capture the transition pathway, and multi-basin simulations to probe the equilibrium free-energy landscape. Across single-basin trajectories, we observe complete $P/P \rightarrow P/E$ transitions that sample intermediate CCA-tail configurations. Correlation analysis reveals a mechanical hierarchy in which body rotation controls both L1 stalk closure and CCA-tail displacement, while L1 position correlates more strongly with body rotation than with CCA movement, indicating that L1 closure is a mechanical response to rotation. Cross-correlation analysis confirms that L1 and CCA rearrangements occur simultaneously in most

Poster 51 | Elucidating LCD Fibril Structures- A Solid-State NMR Study of EWS LCD Fibrils

Sameena Shah | University of Connecticut

Authors: Sameena Shah, Upasana Sridharan, Katherine Corbett and Dylan T, Murray

Abstract: FET proteins have a conserved N-terminal low complexity domain (LCD), and C-terminal RNA binding domain. Single amino acid mutations within the LCDs of these proteins are implicated in their accumulation into fibrillar aggregates in neurodegenerative disorders like amyotrophic lateral sclerosis. LCDs have distinct amino acid compositions to that of other amyloid-forming proteins and are under-represented in the protein data bank. As such, we will use a combination of solid-state nuclear magnetic resonance (ssNMR) and cryo-electron microscopy to solve an EWS LCD fibril structure. Further, we will use EWS LCD fragments to probe the formation of secondary fibril cores. Thioflavin T (ThT) assays of full length EWS LCD, EWS 1-120, and EWS 99-199, indicate formation of cross-beta structures. Transmission electron microscopy (TEM) images suggest that both full-length EWS LCD and EWS 1-120 form similar fibril structures whereas EWS 99-199 has some morphological differences. Sharp resonances in cross polarization based ¹³C and ¹⁵N 2D spectroscopy of full-length EWS LCD indicate the presence of a homogeneous fibril core and further reveal the amino acid composition of that core. Our results will help establish the molecular interactions that dictate LCD fibril structure and will help identify common structural motifs for LCDs.

Poster 52 | Novel Generation of pHLP Peptide

Craig Klumpp | University of Rhode Island

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Abstract: pH Low Insertion Peptide (pHLP) technology is clinically utilized as a vehicle for targeted delivery of imaging and therapeutic payloads to solid tumors. pHLP technology is based on pH-triggered insertion of pHLP peptides into lipid bilayer of cellular membranes. pHLPs sense low pH at the surface of cancer and activated myeloid cells within tumor microenvironment, and deliver imaging and therapeutic agents both intracellularly (into cytoplasm) and extracellularly (to position at cell surface). We have designed and studied a second generation of pHLP peptides (Gen2.0) consisting of eleven novel pHLP variants. We characterized these peptides by studying their interaction with lipid bilayer models. To act as a payload, the near infrared dye indocyanine green (ICG) was conjugated to the membrane-inserting end of the peptides. These pHLP-ICG conjugates were used to test their cytotoxicity, plasma stability, human serum albumin interactions, tumor targeting and biodistribution in mouse models. Several pHLP variants exhibited superior properties and will be used in the design of improved pHLP-cargo conjugates for targeted cytoplasmic delivery in clinical applications.

Poster 53 | PXL: a Nucleic Acid-Binding Module of the Promyelocytic Leukemia Protein

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Abstract: The promyelocytic leukemia protein (PML) is a stress-response factor that assembles into PML nuclear bodies, dynamic subnuclear compartments involved in tumor suppression and antiviral defense. The most abundant isoform, PML-1, has been linked to transcriptional regulation, genome stability, and antiviral responses, yet the molecular basis of these functions remains unclear and is generally attributed to proteins associated with PML nuclear bodies. Here, we report that PML-1 itself harbors previously structurally uncharacterized nucleic acid-binding domain. The domain, termed PXL, is encoded by exon 9 of the PML gene and is unique to isoform 1. Its structure reveals an exonuclease III fold, but lacks the catalytic residues required for activity, defining PXL as a pseudo-exonuclease. Biochemical, structural, mutational and cellular analyses demonstrate that PXL specifically binds G-rich oligonucleotides implicated in G-quadruplex formation and displays a strong in vitro preference for polyUG RNA. Furthermore, deletion of the PXL domain significantly decreases PML colocalization with G-quadruplexes in cells, downregulates genomic maintenance pathways and modulates the expression of E2F target and interferon- α response genes. These findings provide molecular basis for previous observations implicating PML in nucleic acid-associated functions and establish a mechanistic framework for future studies of PML-mediated stress responses, nuclear organization, and gene regulation.

Poster 54 | A human-specific tau nanobody with avidity-enhanced recognition of multivalent tau epitopes

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Abstract: Alzheimer's disease (AD) is characterized by pathological tau assemblies in which repeated epitopes are presented at high local density. We sought to exploit this multivalency to develop nanobody-based constructs that preferentially recognize oligomeric or aggregated tau over soluble monomeric tau. Using an epitope-directed yeast surface display strategy, we identified Nb1, a human tau-specific nanobody targeting the HT7 epitope region. When expressed on the yeast surface, Nb1 showed weak binding to monovalent peptide, with no detectable interaction up to 10 μ M, whereas multivalent presentation of the same epitope on streptavidin enabled clear binding in the nanomolar range. Consistently, recombinant Nb1 purified from *E. coli* bound monovalent peptide weakly at 10–100 μ M, while both monomeric Nb1 and tandem Nb1-linker-Nb1 showed markedly stronger binding to multivalently presented peptide in the nanomolar range. Avidity-dependent enhancement became evident at 400 nM Nb1 but at 100 nM Nb1-linker-Nb1, indicating that linking two Nb1 domains strengthens multivalent recognition at lower construct concentrations. Nb1 also retained intracellular functionality, colocalizing with cytosolic and nuclear-localized EGFP-tau and reducing intracellular tau by 34% when fused to IpaH9.8. These results establish epitope multivalency as an exploitable pathological feature and support avidity engineering for preferential recognition of densely presented tau epitopes.

Poster 55 | Anti-hnRNP A2/B1 Nanobodies with Defined Epitopes

Fatemeh Tashakori Asfestani | University of Connecticut

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Abstract: RNA-binding proteins (RBPs) play important roles in regulating RNA metabolism, particularly during cellular stress. One of these proteins, heterogeneous nuclear ribonucleoprotein A2/B1 (hnRNP A2/B1), is involved in processes such as alternative splicing, mRNA transport, and microRNA sorting into extracellular vesicles. However, many of its cellular functions remain poorly understood, partly because of the difficulty of tracking and manipulating endogenous hnRNP A2/B1 in cells. Here, we screened a yeast-display nanobody (Nb) library against an hnRNP A2/B1-derived peptide and identified Nb19. Nb19 specifically bound the target peptide and colocalized with both EGFP-fused and endogenous hnRNP A2/B1 in mammalian cells. When fused to the E3 ligase domain IpaH9.8, Nb19 also reduced EGFP-hnRNP A2 levels by approximately 40%. We then used directed evolution to improve Nb19 binding and identified Nb19.3, which showed a 23-fold higher affinity ($K_d = 101$ nM) than Nb19 (~ 2.7 μ M). However, Nb19.3 formed punctate aggregates in the cytoplasm that did not colocalize with anti-hnRNP A2/B1 antibody stain. These results suggest that mutations that improve binding affinity can compromise intracellular stability, highlighting an important consideration when engineering nanobodies for intracellular applications.

Poster 56 | What the LOX Is Going On? How Mutations Break a Crosslinking Enzyme

Yu-Bai Xiao | University of Connecticut

Authors: Erika Shams, Biomedical Engineering, University of Connecticut
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Abstract: Lysyl oxidase (LOX) is an important enzyme responsible for generating the reactive precursors required for crosslinking two major structural proteins in the body: collagen and elastin. Through interaction with its lysyl tyrosylquinone (LTQ) cofactor, LOX oxidatively converts lysine into reactive allysine, which can subsequently participate in crosslink formation. Two LOX mutations, S280I and C291S, have been identified in patients with thoracic aortic aneurysm and dissection. So, the obvious question is: how do these mutations make LOX stop working properly? Experimental investigation is challenging because LOX is notoriously difficult to express and characterize recombinantly. Thankfully, previous homology-modeling studies have provided an atomic model that allows us to explore these mechanisms using molecular dynamics simulations. Our simulations suggest two distinct routes to catalytic-site burial. S280I promotes formation of a hydrophobic core that reorganizes the N-terminal region and surrounding protein structure, driving the catalytic site inward. In contrast, C291S disrupts the C291–C340 disulfide bond, altering the interaction network between loops 330–340 and 232–259 and likewise promoting catalytic-site burial. Together, these simulations provide new insight into how LOX works—and, perhaps more interestingly, how it stops working.

Poster 57 | Effects of Local Dynamics on Glass transition in Entangled and Cross-linked Melts of Large Polymers

Calvin Johnson | University of Connecticut

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Abstract: We study the effects of cross-linking and entanglements on the glass transition temperature (T_g) of polymer melts using molecular dynamics (M-D) simulations of Kremer-Grest polymers. While the increase of glass transition temperature from cross-linking is well documented in both experiment and simulation, entanglements have not shown the same increase contrary to theoretical expectations. Entanglements in polymer melts are typically characterized by equilibrated chain statics using primitive path analysis which results in the calculation of the number of monomers per chain overlap N_e . Instead of using chain statics to characterize the entanglements, deliberate loops were constructed between sets of two chains at their center for initialization in M-D. The cross-linked melt was created using the same initial atom coordinates, except the entanglement is replaced with a single bond between chains centers. Control uses the same coordinates, but without the bond. For chains with 1000 atoms in a dense melt, introduced entanglements produced a larger average T_g (0.4119 ± 0.0015) when compared to control (0.4068 ± 0.0061) in Lennard-Jones simulation units. Local dynamics are also explored around T_g , revealing heterogeneous behavior that increases replica variability for the control melt.

Poster 58 | A Dynamics-Informed Machine Learning Framework for Inhibitor Optimization Against Quickly Evolving Targets to Avoid Resistance

Lauren Intravaia | UMass Chan Medical School

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Abstract: Drug resistance often emerges through mutations that reshape protein conformational ensembles, allowing inhibitor potency to be altered without directly disrupting protein-ligand contacts. Consequently, the molecular determinants underlying these effects remain difficult to identify, hindering the design of inhibitors with durable potency against rapidly evolving drug targets. To address this challenge, we developed ROBUST, a physics-informed machine learning framework that identifies key energetic signatures of inhibitor potency. Using HIV-1 protease as a stringent model system for drug resistance, we determined 157 new inhibition constants and integrated them with prior measurements to establish a comprehensive experimental dataset of 364 protease-inhibitor pairs. Analysis of the corresponding molecular dynamics simulations revealed a compact network of energetic interactions that quantitatively explains the multidimensional resistance landscape. Machine learning models built from several dynamics-derived descriptors predicted binding free energies with high accuracy ($RMSE < 1$ kcal mol⁻¹) and generalized to unseen darunavir analogs. Importantly, these models accurately ranked unseen inhibitors by their average potency across resistant variants, demonstrating their utility for prioritizing analogs with improved resistance profiles. Together, these results demonstrate that resistance mutations and inhibitor chemistry converge on a compact energetic interaction network that governs potency and establish a mechanistically interpretable framework for designing robust inhibitors against rapidly evolving drug targets.

Poster 59 | Intermediate-Resolution Modeling of Dynamic DNAs and Their Phase Separation

Jessica Fong Ng | UMass Amherst

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Abstract: DNA is a fundamental biomolecule in eukaryotic cells, playing central roles in processes ranging from genome organization and transcription to innate immune signaling. Recent studies have revealed that DNA can undergo protein-free phase separation in the presence of divalent cations, yet the underlying molecular mechanisms, including the interplay of base stacking, base pairing, electrostatics, and ion interactions, remain poorly understood. Here, we introduce an intermediate-resolution model for condensates of DNAs (iConDNA) that can capture key local and long-range structural features of dynamic DNAs and simulate their spontaneous phase transitions. By introducing explicit base stacking and pairing interactions, iConDNA model not only reproduces major conformational properties of DNA homopolymers, while also folds DNA hairpins and duplexes and captures their thermodynamic properties. With an effective model of explicit Mg²⁺, iConDNA successfully captures the temperature and magnesium concentration dependence of DNA properties. Together, these features enable iConDNA to qualitatively recapitulate homotypic DNA phase separation. Notably, the model distinguishes the phase separation propensities of DNA and RNA CAG repeats, highlighting its sensitivity to chemical differences between the two nucleic acids. iConDNA thus provides a suitable tool for studying DNA homotypic phase separation in both biological and engineering contexts.

Poster 60 | Combining SAXS and Reactive MD Simulations to Uncover the Structure and Assembly of Crosslinked Surfactant Nanoparticles

Patrick Corrigan | University of Connecticut

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Dr. Jessica Rouge, Department of Chemistry

Abstract: Therapeutic Nucleic Acids (TNAs) are a promising new field of medicine but are limited by poor delivery efficiency. To help increase delivery, we designed the Nucleic Acid Nanocapsule (NAN), a TNA delivery vehicle consisting of a crosslinked surfactant nanoparticle (SNP) functionalized with the TNA cargo. The SNP is designed to be degraded upon entry into the cell, assisting in the intracellular delivery of the TNA. Previous work on surfactant assembly suggested our SNPs would have a micellar internal structure - however, transmission electron microscopy images showed our SNPs were far too large to be simple micelles. To determine the internal structure of our NANs, we combined small angle x-ray scattering (SAXS) with coarse-grained reactive molecular dynamics (MD) simulations. Our SAXS data indicated that our SNPs were multi-lamellar and contained up to 10 concentric layers of surfactant. Through the MD simulations, we were able to visualize the formation of SNPs up to 3 layers, corroborating the SAXS data and suggesting potential mechanisms for the formation of these multi-lamellar structures. Through this work, we have built a better understanding of our NAN and how it forms, allowing us to construct better design rules to build more efficient TNA delivery vehicles.

Poster 61 | Infrared signatures of lanthanide-specific binding in peptides

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Abstract: Ion-specific binding underpins the ion signaling and enzymatic processes central to many biological pathways. Despite its prevalence – up to one third of known proteins bind metal ions in some capacity – understanding of the relationship between binding pocket structure and ion specificity is still developing. In most biological binding sites, ion coordination is mediated by electrostatic interactions between the metal cation and anionic side chain carboxylate groups. As such, the vibrational transitions of these carboxylate groups provide a sensitive readout of binding site configuration. Thus, we utilize infrared spectroscopy to probe the specific binding site architectures that control changes to affinity in carboxylate-containing systems.

We have previously found that the carboxylate asymmetric stretching modes of ion-chelator complexes show blueshifts that are linearly proportional to the charge density of the bound ion, offering a tantalizing window into small site geometry changes difficult to otherwise resolve. This raises the prospect of using similar vibrational features to discern the determinants of selectivity in biological ion-binding architectures. As a first step towards investigating these features in signaling proteins, we exploit infrared spectroscopy of lanthanide-binding tags (LBTs) to investigate the binding site conformational changes that confer their exceptional ability to discriminate between rare-earth elements.

Poster 62 | Spectroscopic signatures of scaffold rigidity and solvation in metal chelators

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Abstract: Approximately 70% of enzymes require specific metal ions to function, yet the structural principles controlling ion selectivity remain unclear. To investigate these mechanisms, we simulated two small-molecule chelators: flexible EDTA and sterically restricted BAPTA, which chemically mimic key properties of biological binding pockets. We performed molecular dynamics (MD) simulations evaluating these chelators coordinated with divalent and trivalent ions in explicit water. To correlate coordination strain with vibrational shifts, harmonic IR spectra were computed from minimum-energy DFT structures using MD trajectory snapshots as a starting point.

Results demonstrate the accepted principle that, while chelators designed around flexible chemical backbones bind promiscuously, rigid scaffolds demand strict geometric complementarity. In such cases, suboptimal coordination induces dynamic instability, characterized by fluctuating chelator bonds and continuous solvent infiltration. Conversely, optimally sized or highly charged ions successfully lock restricted backbones into a stable conformation, effectively shielding the complex from bulk water.

Ultimately, forcing suboptimal ions into restricted backbones creates structural stress that weakens coordination and permits water to impair binding. Our work provides a direct spectroscopic signature for structural strain, elucidating the physical rules governing protein-metal

selectivity. This result will aid interpretation of IR spectra of more complex biological ion binding architectures.

Poster 63 | ShapeAligner: Direct Molecular Superposition from Clique-Based Atom Correspondence

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Abstract: Superposing one small molecule onto another is routine in ligand-based drug discovery. In atom-level correspondence methods, the pose the correspondence determines is only a starting point, and a subsequent search produces what is reported. We present ShapeAligner, a rigid aligner whose output pose is the superposition its maximal clique correspondence determines. Maximal cliques of an association graph over chemically typed heavy atoms each fix a reflection-free, equally weighted Kabsch transform in closed form. An analytic Gaussian shape-and-color volume overlap ranks the resulting poses. Nothing after the superposition moves the pose. Across 68,150 directed tasks from the LOBSTER cross-pair corpus, the top pose lands within 2.0 Å of the crystallographic pose in 30.98% of the tasks ShapeAligner covers, against 28.32% for the next-highest of six comparators. The median time is 0.214 s per task on one CPU core. Recovery depends strongly on the pair. It is highest when the larger ligand serves as the template, and the two ligands share at least 0.60 of the smaller ligand's volume. Below that threshold no method recovers more than 4% of the tasks it covers. The output is deterministic, and the correspondence it rests on is invariant to the input coordinate frame by construction. The implementation is released under the MIT license.

Poster 64 | Analysing solvation effects on metal-ion coordination with optical spectroscopy

Diotima Bose | University of New Hampshire

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Abstract: Binding and release kinetics are essential parameters of ion-signalling structures that regulate biological processes. These kinetics are largely controlled by subtle changes to coordination geometry and solvation structure, which are difficult to probe and thus remain poorly understood. Vibrational spectroscopy offers a sensitive view into these local binding environments. We use FTIR spectroscopy to investigate the spectral response of carboxylate (COO⁻) stretching modes in EDTA, EGTA and BAPTA upon binding a series of di- and trivalent ions. These chelators allow us to explore how changes to scaffold rigidity mediate solvent exposure in systems that are small enough to analyse with density functional approaches.

Although EDTA, EGTA and BAPTA are structurally similar, BAPTA's backbone rigidity leads to Ca²⁺ binding and release kinetics faster than those of the others. Similarly and surprisingly, BAPTA's COO⁻ stretching modes are markedly less sensitive to ion substitution than their counterparts in EDTA and EGTA. We interpret this puzzling spectroscopic result through the lens of density functional theory calculations and molecular dynamics simulations. Isothermal titration calorimetry provides a complementary view of the scaffold's role in modulating ion-solvent interaction. Our results suggest that BAPTA's ion-release kinetics and spectroscopic properties stem from increased solvent exposure driven by scaffold structure.

Poster 65 | Spontaneous binding of pentagalloyl glucose stabilizes tropoelastin and reduces the exposure of cleavage sites

Teresa Carolliny Rodrigues | University of Connecticut

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Abstract: This study evaluated how pentagalloyl glucose (PGG) affects monomeric tropoelastin in both intact and cleaved forms. The findings indicate that PGG shields tropoelastin, offering partial protection against cleavage by elastases while stabilizing its overall structure.

Following cleavage, PGG maintains association between the resulting fragments, preserving structural integrity. This was particularly evident at domain 30, located at the junction between Fragment III and Fragment IV: cleavage removes the continuous backbone that normally constrains this region, and cleaved tropoelastin without PGG showed substantially greater mobility, reflected in its high RMSD (1.824 ± 0.899 nm), whereas in the presence of PGG, RMSD was markedly reduced (0.659 ± 0.228 nm), consistent with PGG bridging the separated fragments and acting as a molecular clamp. Domain 30 also exhibited the highest normalized PGG occupancy (92.0%) and among the strongest nonpolar interaction energies (-14.59 kJ/mol per residue). Notably, the III–IV interface, which contains domain 30, showed substantially more bridging PGG molecules (10.16 ± 1.07) than either of the other two interfaces, corroborating its role as a preferential site for PGG-mediated fragment cohesion. PGG further reduced exposed cleavage sites from 27.45% to 5.95%. Overall, these results support a multi-site and adaptive binding mechanism of PGG that maintains structural stability through multiple, persistent interactions.

Poster 66 | Molecular Modeling of Key Mitochondrial Proteins in Cardiolipin-Containing Membranes

Edgar Lopez Perez | University of Connecticut

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Abstract: Mitochondrial membrane architecture is shaped by reciprocal interactions between proteins and a lipid environment enriched in cardiolipin. Using Martini 3 coarse-grained molecular dynamics simulations, we investigated protein–membrane coupling involving ATP synthase and endophilin B1 (Bif-1), proteins associated with mitochondrial membrane organization and remodeling. Protein-free cylindrical membranes exhibited pronounced leaflet asymmetry, with greater lipid density and a smaller area per lipid in the inner leaflet, illustrating the unequal packing stresses imposed by strong curvature. ATP synthase produced an asymmetric membrane response, with a larger local perturbation in the inner leaflet, consistent with coupling between the enzyme and the highly curved regions of mitochondrial cristae. In planar membranes, increasing tetraoleoyl cardiolipin (TOCL) content stabilized Bif-1 association, while TOCL accumulated near its N-terminal amphipathic helices during membrane contact. This local enrichment suggests that cardiolipin can help create a favorable environment for Bif-1 recruitment and membrane insertion. Together, the results support distinct but complementary mechanisms of mitochondrial membrane organization: ATP synthase couples to leaflet-specific curvature and packing, whereas Bif-1 association is promoted by cardiolipin-dependent lipid recognition and redistribution. These interactions may contribute to the formation and remodeling of specialized mitochondrial membrane domains.

Poster 67 | Molecular Mechanisms of Elastin Coacervation and Condensate Assembly During Elastogenesis

Chengeng Yang | University of Connecticut

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Abstract: Elastin is a highly flexible extracellular matrix protein that confers elasticity to connective tissues. It is deposited into elastic fibers through the hierarchical assembly of its soluble precursor, tropoelastin. A critical early step of elastogenesis is coacervation: a thermo-responsive liquid-liquid phase separation in which tropoelastin assembles into condensates at physiological temperature, exhibiting lower critical solution temperature (LCST) behavior, and these condensates subsequently mature into elastic fibers. Despite the central role of coacervation in elastogenesis, the molecular organization and phase behavior of elastin condensates remain poorly understood. Here, we develop thermally-responsive coarse-grained models of elastin condensates that reproduce SAXS-derived molecular dimensions of tropoelastin as well as experimental coacervation and imaging data. We find that hydrophobic interactions dominate phase separation, collectively forming an extensive intermolecular network that reflects both their favorable energetics and their high sequence abundance. We further show that prolyl hydroxylation, a naturally occurring post-translational modification of tropoelastin, delays coacervation by weakening hydrophobic intermolecular contacts, redistributing the interaction network toward hydroxyproline-mediated contacts, and reducing condensate connectivity. Using natural domain 18 and ten tandem repeats of the (GVVPG) motif as heterogeneous and homogeneous sequences, respectively, we demonstrate that sequence heterogeneity in elastin-like polypeptides promotes phase separation independently of average hydrophobicity, by generating localized hydrophobic hotspots that enhance intermolecular association. Together, these findings link LCST behavior, biomolecular condensation, and elastin assembly; provide a molecular basis for how regulated prolyl hydroxylation may tune elastogenesis; and offer a framework for the design of elastin-inspired biomaterials.

Poster 68 | Sequence Determinants of Amylin Amyloidogenicity Inform the Design of Improved Bioactive Analogs

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Abstract: Human amylin (also known as IAPP) is a therapeutic scaffold for diabetes and obesity whose amyloidogenicity complicates analog development. We combined evolutionary comparisons, aggregation assays, spectroscopy, microscopy, and cellular studies to identify sequence determinants of amyloid formation. Elephant amylin formed no detectable amyloid under the conditions tested, including exposure to human amylin fibril seeds or anionic lipid vesicles, and was markedly less toxic to INS-1 beta cells. Introducing elephant-derived T9R/R11H, V17H, or G24E substitutions into human amylin reduced amyloid formation and toxicity, with G24E producing the strongest suppression despite decreasing net positive charge. Structural modeling placed Glu24 in a solvent-exposed environment without obvious clashes in receptor-bound amylin models, supporting functional evaluation. Sequence-based predictions did not consistently match experimental aggregation behavior. Apo-cagrilintide, the unlipidated cagrilintide peptide, exhibited greater apparent solubility and lower beta-cell toxicity than human amylin but formed beta-sheet-rich fibrils at 500 μ M and pH 7.4. N14E/V17R, designed to stabilize helicity, slowed human amylin aggregation without preventing fibril formation. Together, these findings support targeting position-specific interactions that promote pathological self-assembly while testing preservation of receptor activity, rather than relying on net charge, presumed helicity, or delayed fibril formation alone.

Poster 69 | Kinetic Stability of Seed Proteins: Connecting Proteolytic Resistance, Digestive Persistence, and Allergen-Associated Proteins

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Abstract: Kinetic stability (KS) describes a protein's resistance to unfolding and degradation, allowing it to persist under conditions that normally destabilize proteins. We investigate whether KS contributes to seed protein persistence during proteolytic digestion and whether kinetically stable proteins (KSPs) correspond to proteins associated with limited digestibility and allergenicity. We characterized peanut, soybean, lupine, and sunflower seeds using electrophoretic KS-assays, proteinase K digestion, simulated gastrointestinal digestion, and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. KS-assays identified proteins resistant to thermal denaturation, while proteinase K digestion assessed proteolytic resistance, a predicted characteristic of kinetically stable proteins. Simulated gastrointestinal digestion was used to determine whether identified KSPs persist under gastric and intestinal conditions. KSPs were identified in all four seed types, including peanut Ara h 1, Ara h 2, and Ara h 3, and 11S proteins in soybean and sunflower, which have been associated with allergenicity and/or limited digestibility. Proteinase K assays demonstrated resistance among 11S proteins and additional unidentified proteins. Simulated gastrointestinal digestion revealed proteins that persisted following digestion, providing a basis for determining whether these correspond to identified KSPs. Preliminary processing studies showed decreased detectable KSPs following peanut roasting at 140°C and lupine heating at 100°C. These findings support KS as a potential molecular determinant of seed protein persistence and will help clarify its relationship with proteolytic resistance, digestive persistence, and allergenicity.

Poster 70 | Effect Of Hao-Fountain Syndrome-Causing Hyperactive Variant Of USP7 On Its Structure And Conformational Dynamics

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Abstract: Ubiquitin-specific protease 7 (USP7) is a key deubiquitinase essential for protein homeostasis and controlling levels of numerous protein targets. As it has only recently been found that heterozygous mutations cause the paediatric neurodevelopmental disorder Hao-Fountain Syndrome, mechanistic understanding and related treatments are lacking. To better understand the consequences of USP7 patient mutations on enzymatic function and link them to disease pathogenesis, we are currently investigating potential causes of enhanced catalytic activity of the N418S mutation by determining its crystal structure and investigating its conformational dynamics compared to WT. Using solution NMR spectroscopy, we probe conformational dynamics of N418S with CPMG relaxation dispersion experiments. The catalytic domain of USP7 was fully deuterated with its backbone amides and its Ile, Leu, and Val (ILV) methyl groups selectively isotopically labelled. Backbone 15N-CPMG and four ILV methyl CPMG experiments were used, including multiple- and single-quantum 13C CPMG, and single- and triple-quantum 1H CPMG. These experiments revealed dynamic regions within the catalytic domain that undergo significant conformational exchange. Comparing USP7 WT and N418S structures and dynamics provides insight into the nature of pathogenic

hyperactivity, hopefully leading to personalized therapies that aid the treatment of patients with Hao-Fountain Syndrome and potentially other Ubiquitin-Proteasome Pathway-related disorders.

Poster 71 | The Characterization of Human Ankle2: An important proviral factor in Orthoflavivirus infection

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Abstract: Zika is a prevalent and concerning virus for pregnant women. It can bypass the blood brain barrier and through vertical transmission, infect a fetus. My research is focused on the characterization of the interaction between Zika's nonstructural viral membrane protein 4a (NS4a) and human protein Ankle2 (which is membrane-bound). My goal is that by determining the structure of the complex between NS4a and Ankle2 I might be able to find ways to disrupt the interaction. Ankle2 is essential for cell division and the development of the immune system and neural progenitor cells. NS4a hijack's Ankle2, impairing neuronal development, leading to microcephaly (Shah et al. Cell, 2018; Fishburn et al. mBio, 2024). Due to Ankle2 being membrane-bound, coupled with large intrinsically disordered regions, NMR is the best technique employ for the characterization of this protein. I intend to characterize the structure of Ankle2, targeting residues 2-121. This is the region that has been known to interact with NS4a.