2025 GCSC Symposium: Chemical Dynamics in Materials and Living Systems

May 7 (Wed) – 9 (Fri), 2025

Organized by

Global Science Research Center for Systems Chemistry

https://www.gcsc.cau.ac.kr

Venue: Room 207 Building 303, Chung-Ang University, Seoul, Korea

Invited Speakers

Cao, Jianshu (MIT)
Chang, Rakwoo (University of Seoul)
Chen, Peng (Cornell University)
Cho, Hae Sung (Chung-Ang University)
Choi, Jeong-Mo (Pusan National University)
Cosa, Gonzalo (McGill University)
Cui, Qiang (Boston University)
Deeds, Eric (UCLA)
Jang, Joonkyung (Pusan National University)
Jung, YounJoon (Seoul National University)
Kim, Ji-Hyun (Chung-Ang University)
Kim, Philip M. (Toronto University)
Kim, Sungjee (POSTECH)
Koh, Hye Ran (Chung-Ang University)
Lee, Nam Ki (Seoul National University)
Lee, Sang Hak (Pusan National University)
Lee, Sang Uck (Sungkyunkwan University)
Lim, Mi Hee (KAIST)
Matyushov, Dmitry (Arizona State University)
Pressé, Steve (Arizona State University)
Ringe, Stefan (Korea University)
Roux, Benoit (University of Chicago)
Saito, Shinji (Institute for Molecular Science)
Shim, Sang-Hee (Korea University)
Sohn, Chang Ho (KAIST)
Son, Chang Yun (Seoul National University)
Son, Minjun (Chan Zuckerberg Biohub)
Straub, John (Boston University)
Sugita, Yuji (Riken)
Xiao, Jie (Johns Hopkins)
Yethiraj, Arun (UW-Madison)
Yoo, Joo-Yeon (POSTECH)
Yoon, Sungho (Chung-Ang University)
York, Darrin (Rutgers University)
Yu, Kui (Sichuan University)

Organizers

Jaeyoung Sung (Director, GSRC for Systems Chemistry)
Rakwoo Chang (University of Seoul)
Jeong-Mo Choi (Pusan National University)
Wonpil Im (Lehigh University)
YounJoon Jung (Seoul National University)
Ji-Hyun Kim (GSRC for Systems Chemistry)

Timetable

	5.6 (Tue)	5.7 (Wed)	5.8 (Thu)	5.9 (Fri)	5.10 (Sat)
Session		Session 1	Session 5	Session 9	
Chair		Jie Xiao (JHU)	YounJoon Jung (Seoul Natl. Univ.)	Peng Chen (Cornell Univ.)	
09:00 - 09:30		Peng Chen (Cornell Univ.)	Jie Xiao (JHU)	Gonzalo Cosa (McGill Univ.)	
09:30 - 10:00		Nam Ki Lee (Seoul Natl. Univ.)	Steve Pressé (Arizona State Univ.)	Sang-Hee Shim (Korea Univ.)	
10:00 - 10:30		Minjun Son (CZ Biohub)	Jianshu Cao (MIT)	Hye Ran Koh (Chung-Ang Univ.)	
10:30 - 11:00		Coffee Break	Coffee Break	Coffee Break	Excursion
Session		Session 2	Session 6	Session 10	
Chair		John Straub (Boston Univ.)	Wonpil Im (Lehigh Univ.)	Juyong Lee (Seoul Natl. Univ.)	
11:00 - 11:30		Arun Yethiraj (UW-Madison)	Benoit Roux (Univ. of Chicago)	Darrin York (Rutgers Univ.)	
11:30 - 12:00		Joonkyung Jang (Pusan Natl. Univ.)	Yuji Sugita (RIKEN)	Philip Kim (Univ. of Toronto)	
12:00 - 12:30		Jaeyoung Sung (Chung-Ang Univ.)	Rakwoo Chang (Univ. of Seoul)	Ji-Hyun Kim (Chung-Ang Univ.)	
12:30 - 14:30		Lunch + Poster	Lunch + Poster	Lunch + Poster	
Session		Session 3	Session 7	Session 11	
Chair		Dmitry Matyushov (Arizona State Univ.)	Bong June Sung (Sogang Univ.)	Philip Kim (Univ. of Toronto)	
14:30 - 15:00		John Straub (Boston Univ.)	Dmitry Matyushov (Arizona State Univ.)	Eric Deeds (UCLA)	
15:00 - 15:30	**Registration**	Joo-Yeon Yoo (POSTECH)	Shinji Saito (IMS)	Chang Ho Sohn (KAIST)	
15:30 - 16:00		Qiang Cui (Boston Univ.)	YounJoon Jung (Seoul Natl. Univ.)	Mi Hee Lim (KAIST)	
16:00 - 16:30		Coffee Break	Coffee Break	Coffee Break	
Session		Session 4	Session 8	Session 12	
Chair		Hae Sung Cho (Chung-Ang Univ.)	Hyonseok Hwang (Kangwon Natl. Univ.)	Ji-Hyun Kim (Chung-Ang Univ.)	
16:30 - 17:00		Wonpil Im (Lehigh Univ.)	Stefan Ringe (Korea Univ.)	Sang Hak Lee (Pusan Natl. Univ.)	
17:00 - 17:30		Kui Yu (Sichuan Univ.)	Chang Yun Son (Seoul Natl. Univ.)	Sang Uck Lee (Sungkyunkwan Univ.)	
17:30 - 18:00		Sungho Yoon (Chung-Ang Univ.)	Jeong-Mo Choi (Pusan Natl. Univ.)	Hae Sung Cho (Chung-Ang Univ.)	
18:00 - 20:00	Reception	Dinner	Dinner	Banquet	

Poster presentation venue: Rm. 1102, R&D center (BLDG. 102), Chung-Ang Univ.

Program

May 6th (Tue)

15:00~18:00	Registration for Invited Speakers (GLAD Hotel Yeouido)
18:00~20:00	Reception

May 7th (Wed)

08:00~08:50	Registration
08:50~09:00	Opening Remarks
Session 1 - Chair: Jie Xiao (Johns Hopkins University School of Medicine)	
09:00~09:30	Peng Chen (Cornell University) Single-cell imaging of energy conversion pathways in bacteria
09:30~10:00	Nam Ki Lee (Seoul National University) Observing endogenous motor proteins in a living cell
10:00~10:30	Minjun Son (Chan Zuckerberg Biohub) Input dynamics processing by the inflammatory (NF-kB) signaling network
10:30~11:00	Coffee Break
Session 2 - Chair: John Straub (Boston University)	
11:00~11:30	Arun Yethiraj (University of Wisconsin-Madison) Machine learning phase diagrams
11:30~12:00	Joonkyung Jang (Pusan National University) Structure and Phase of Interfacial Water
12:00~12:30	Jaeyoung Sung (Chung-Ang University) Chemical Dynamics, Statistical Thermodynamics, and Transport Theories for Complex Materials and Biological Systems
12:30~14:30	Lunch and Poster Session

Session 3 - Chair: Dmitry Matyushov (Arizona State University)	
14:30~15:00	**John Straub (Boston University)** **Exploring the equilibria and kinetics of transmembrane protein association**
15:00~15:30	**Joo-Yeon Yoo (POSTECH)** **Dynamics of membrane-bound biomolecular condensates**
15:30~16:00	**Qiang Cui (Boston University)** **Lipid Membrane Remodeling by Proteins and Peptides: Mechanistic insights from multi-scale analysis**
16:00~16:30	**Coffee Break**
Session 4 - Chair: Hae Sung Cho (Chung-Ang University)	
16:30~17:00	**Wonpil Im (Lehigh University)** **WHAT CAN CHARMM-GUI DO FOR YOU?**
17:00~17:30	**Kui Yu (Sichuan University)** **Prenucleation Clusters of ZnSe Assisting Formation of Photoluminescent CdSe Magic-Size Clusters under Mild Conditions**
17:30~18:00	**Sungho Yoon (Chung-Ang University)** **Development and Demonstration of a CO_2 Conversion System for Valuable Chemical Production Using Heterogenized Catalysts**
18:00~20:00	**Dinner**

May 8th (Thu)

08:00~09:00	**Registration**
Session 5 - Chair: YounJoon Jung (Seoul National University)	
09:00~09:30	**Jie Xiao (Johns Hopkins University School of Medicine)** **Single-molecule studies of chromosome organization and transcription regulation by DNA supercoiling**
09:30~10:00	**Steve Pressé (Arizona State University)** **Transcriptional dynamics with Bayesian nonparametrics: from dense 3D RNA spot localization/classification to gene network inference**
10:00~10:30	**Jianshu Cao (MIT)** **Non-equilibrium Conformational Fluctuations in Driven Chemical Networks**
10:30~11:00	**Coffee Break**
Session 6 - Chair: Wonpil Im (Lehigh University)	
11:00~11:30	**Benoit Roux (University of Chicago)** **Using Computer Simulations to Advance our Understanding of Biological Systems at the Atomic Level**
11:30~12:00	**Yuji Sugita (RIKEN)** **How to regulate protein condensation with highly charged HERO proteins**
12:00~12:30	**Rakwoo Chang (University of Seoul)** **Computer Simulation Studies of Chlorosulfolipids and Lung Surfactant Membrane Systems**
12:30~14:30	**Lunch and Poster Session**

Session 7 - Chair: Bong June Sung (Sogang University)	
14:30~15:00	Dmitry Matyushov (Arizona State University) Wet and Warm: Nonergodicity, Mobility, and Interfacial Polarization in Molecular Biology
15:00~15:30	Shinji Saito (Institute for Molecular Science) Unveiling microscopic mechanisms of dynamic slowdown in supercooled liquids
15:30~16:00	YounJoon Jung (Seoul National University) Far-from-Equilibrium Phase Transitions and Charge Transport in Disordered Systems
16:00~16:30	Coffee Break
Session 8 - Chair: Hyonseok Hwang (Kangwon National University)	
16:30~17:00	Stefan Ringe (Korea University) Towards a first-principles multi-scale understanding of CO_2 reduction
17:00~17:30	Chang Yun Son (Seoul National University) Classical and quantum charge transport in advanced electronic materials
17:30~18:00	Jeong-Mo Choi (Pusan National University) Stickers and Spacers in Biomolecular Condensation
18:00~20:00	Dinner

May 9th (Fri)

08:00~09:00	**Registration**
Session 9 - Chair: Peng Chen (Cornell University)	
09:00~09:30	**Gonzalo Cosa (McGill University)** **A window into lipid peroxyl radicals, peroxidation and electrophilic stress in cells**
09:30~10:00	**Sang-Hee Shim (Korea University)** **Fluorescence-free single-molecule Raman spectroscopy**
10:00~10:30	**Hye Ran Koh (Chung-Ang University)** **Molecular Insights into RNA Binding and Cleavage by CRISPR-Cas13a**
10:30~11:00	**Coffee Break**
Session 10 - Chair: Juyong Lee (Seoul National University)	
11:00~11:30	**Darrin York (Rutgers University)** **AI and free energy methods for drug discovery**
11:30~12:00	**Philip Kim (University of Toronto)** **Machine learning methods for protein and peptide design**
12:00~12:30	**Ji-Hyun Kim (Chung-Ang University)** **Integrated method for identifying the optimal descriptor of acute critical illness: Development of septic infection related risk index (SIRRI) and investigation into patient's fate dynamics along SIRRI**
12:30~14:30	**Lunch and Poster Session**

Session 11 - Chair: Philip Kim (University of Toronto)	
14:30~15:00	Eric Deeds (UCLA) A lack of distinct cellular identities in scRNA-seq data: revisiting Waddington's landscape
15:00~15:30	Chang Ho Sohn (KAIST) Fixative-eXchange (FX)-seq: scalable single-nucleus RNA-seq for FFPE clinical tissue
15:30~16:00	Mi Hee Lim (KAIST) Chemical Strategies to Study Multiple Facets in Dementia
16:00~16:30	Coffee Break
Session 12 - Chair: Ji-Hyun Kim (Chung-Ang University)	
16:30~17:00	Sang Hak Lee (Pusan National University) Anion and cation in Neurodegenerative diseases
17:00~17:30	Sang Uck Lee (Sungkyunkwan University) Machine Learning Potential assisted Energy Materials Research
17:30~18:00	Hae Sung Cho (Chung-Ang University) Physicochemical understanding of adsorption in porous crystals
18:00~20:00	Banquet

May 10th (Sat)

10:30~20:00	Excursion

Poster session

Poster No.	7 May (Wed.)	Poster No.	8 May (Thu.)	Poster No.	9 May (Fri.)
P1	Donghee Kim (Chung-Ang Univ.)	P19	Namho Kim (Kangwon Natl. Univ.)	P31	In-Chun Jeong (Chung-Ang Univ.)
P2	Jingyu Kang (Chung-Ang Univ.)	P20	Sungjun Lim (Kangwon Natl. Univ.)	P32	Seong Jun Park (Chung-Ang Univ.)
P3	Seyong Choi (Pusan Natl. Univ.)	P21	Yeonho Song (Ewha Womans Univ.)	P33	Jinhyung Kim (Chung-Ang Univ.)
P4	Minho Lee (Chung-Ang Univ.)	P22	Jay-Hak Lee (Seoul Natl. Univ.)	P34	Ji-Su Lim (Chung-Ang Univ.)
P5	Jaeyoung Kim (Pusan Natl. Univ.)	P23	Minseo Kim (Pusan Natl. Univ.)	P35	Sangmin Ji (Chung-Ang Univ.)
P6	Susung Kim (Chung-Ang Univ.)	P24	Chan-Gyu Kim (Pusan Natl. Univ.)	P36	Jaehyuk Won (Chung-Ang Univ.)
P7	Bo-Hee Choi (Pusan Natl. Univ.)	P25	Tae Seung Lee (Pusan Natl. Univ.)	P37	Hajin Lee (Molcube, Inc.)
P8	Ho-Jun Park (Pusan Natl. Univ.)	P26	Yubin Song (Univ. of Seoul)	P38	Gayoung Kim (Ewha Womans Univ.)
P9	Juhyeong Jeon (DGIST)	P27	Chan Young Joe (Univ. of Seoul)	P39	Nahyun Chi (Ewha Womans Univ.)
P10	Rajeev Kumar (Pusan Natl. Univ.)	P28	Jongchan Yoon (Kangwon Natl. Univ.)	P40	Seonghui Kim (Ewha Womans Univ.)
P11	Jeongveen Park (Seoul Natl. Univ.)	P29	Sangjin Han (POSTECH)	P41	Nayoung Kim (KAIST)
P12	Gyeongseon Min (Chung-Ang Univ.)	P30	Jonghyun Son (POSTECH)	P42	Duc Tai Nguyen (KAIST)
P13	TaeHwan Kim (Pusan Natl. Univ.)			P43	Janhee Hong (Univ. of Seoul)
P14	Khongorzul Enkhtaivan (Chung-Ang Univ.)			P44	Mohamed Elgawish (Korea Univ.)
P15	Eun Seo Lee (Chung-Ang Univ.)			P45	Kunwoo Kim (Sungkyunkwan Univ.)
P16	Gyunam Park (Chung-Ang Univ.)			P46	Minsoo Kim (Sungkyunkwan Univ.)
P17	Jonghwa Han (Chung-Ang Univ.)			P47	Jaemin Yoo (Sungkyunkwan Univ.)
P18	Gyeongpil Jo (Sungkyunkwan Univ.)			P48	Yubeen Kim (Seoul Natl. Univ.)
				P49	Yongin Cho (Seoul Natl. Univ.)
				P50	Ae-Ji Park (Pusan Natl. Univ.)

Oral Session

Abstract

(Session 1-1)

Single-cell imaging of energy conversion pathways in bacteria

Peng Chen*

Department of Chemistry and Chemical Biology, Cornell University, Ithaca, NY 14850, USA

This talk will present our recent work in using multimodal single-cell functional imaging to interrogate the energy conversion pathways in bacteria, especially on exchanging electrons with external environments. One part of the talk will be on studying microbe-semiconductor biohybrids that integrate microbial enzymatic synthesis with the light-harvesting capabilities of inorganic semiconductors for solar-to-chemical conversion. We uncover and differentiate the critical roles of different hydrogenases in the lithoautotrophic bacterium *Ralstonia eutropha* for bioplastic formation, discover this bacterium's surprisingly large nanoampere-level electron-uptake capability, and dissect the cross-membrane electron-transport pathways [1]. Another part of the talk will be on studying the extracellular electron transfer (EET) pathways of *Shewanella oneidensis*. We discover how the spatial and temporal reorganization of the inner-membrane electron-transfer hub protein CymA controls the cell's EET during anaerobic respiration.

Reference

[1] B. Fu,† X. Mao,† Y. Park, Z. Zhao, T. Yan, W. Jung, D. H. Francis, W. Li, B. Pian, F. Salimijazi, M. Suri, T. Hanrath, B. Barstow, P. Chen* "Single-cell multimodal imaging uncovers energy conversion pathways in biohybrids" *Nature Chem.* **2023**, *15*, 1400-1407.

(Session 1-2)

Observing endogenous motor proteins in a living cell

Nam Ki Lee[1*]

[1] *Department of Chemistry, Seoul National University, Seoul 08826, Korea*

Fluorescence imaging is a powerful technique for studying proteins within a living cell. However, its effectiveness is hampered by the prerequisite of fluorescently labeling the protein of interest. Thus, most fluorescence imaging approaches are confined to observing exogenous proteins. This limitation prompted the development of a novel method presented herein, enabling the observation of endogenous proteins without the need for cloning or gene modification. Our method uses the photoconversion of cyanine dyes [1]. Using this method, we successfully tracked the movement of endogenous dynein in live cells. Notably, our method has several advantages over conventional methods, as it eliminates the necessity for cloning, UV illumination, and potentially harmful cell-toxic additives. We also applied our method in studying transcription. Transcription, a process of mRNA generation by RNA polymerase (RNAP), is highly coupled with translation by the ribosome in bacteria. We directly observe the dynamics of transcription and the movement of the subcellular localization of genes actively transcribed by RNAP in living cells at the sub-diffraction limit resolution [2]. Our observation will provide new insight into the role of the coupling between transcription and translation on the effective expression of genes in E. coli [3].

Reference

[1] Y. Cho, An HJ., Kim T., Lee C., Lee N.K. (2021) J. Ame. Chem. Soc. 2021, 143, 14125
[2] S. Yang, S. H. Kim, D.-K. Kim, H. J. An, J. B. Son, A. H. Gynnå, N. K. Lee,(2019) Nat. Commun. 10, 5131
[3] S. Park et al. Under Revision (2025).

(Session 1-3)

Input dynamics processing by the inflammatory (NF-kB) signaling network

Minjun Son [1*]

[1]*Chan Zuckerberg Biohub Chicago, Chicago, IL, USA*

Cells within tissues operate in dynamic microenvironments where the timing, concentration, and sequence of signaling molecules continuously fluctuate. Despite this highly dynamic nature of inflammatory signaling, it remains unclear how these signals are encoded and decoded, or whether individual cells retain memory of past exposure to inflammatory molecules. In particular, the NF-κB pathway responds to dozens of signals from pathogens and tissue-resident cells and plays a vital role in processing proinflammatory inputs. We employed high-throughput microfluidics to investigate the regulation of the NF-κB network in diverse spatial and temporal contexts; then, we analyzed single-cell responses using various mathematical methods, including ODE-based modeling, information theory, and machine/deep learning. Our findings indicate that the NF-κB network responds sensitively to changes in the level of signal molecules (rather than to the magnitude of the level itself) and retains memories of previous signals. In addition, our co-culture experiments simulating the tissue environment demonstrated that these dynamics-sensing capabilities enable individual cells to capture detailed information about the spatial distance to signal sending source. Collectively, our results demonstrate that the NF-κB network encodes signal dynamics, allowing it to interpret various spatial and temporal changes in the environment and regulate inflammation accordingly.

(Session 2-1)

Machine learning phase diagrams

Arun Yethiraj

University of Wisconsin-Madison

The phase behavior of complex mixtures is important in many applications and understanding them from a molecular perspective is of fundamental importance. Molecular simulation of complex fluids has become feasible, even at the atomistic level, and elucidating the phase behavior of these systems is significant. Traditional simulations methods require the insertion and deletion of molecules, which is difficult in a dense molecular system. In this work we describe machine learning (ML) methods for the phase behavior of complex fluids. Unsupervised ML methods are particularly attractive because they do not require prior knowledge of the existence of a phase transition. We show that a robust input feature is the local affinity, where the value of the feature at each site is determined by the identity of the site and its neighbors. When coupled with a variational auto-encoder, the method can predict the phase behavior of a variety of lattice and continuous-space models in quantitative agreement with conventional simulations. The choice of activation functions in the auto-encoder is crucial, and this requires physical insight into the nature of the phase transition.

(Session 2-2)

Structure and Phase of Interfacial Water

Joonkyung Jang[1*]

[1] *Department of Nanoenergy Engineering Pusan National University, Busan 46241, Korea*

Several examples are presented for an interfacial water drastically different from the bulk in structure and phase behavior. Using molecular simulation and theory, we examine the molecular structure and phase behavior of interfacial water. Atomic force microscopy and vibrational-sum-frequency-generation spectroscopy are used to probe the molecular structure of an interfacial water. We show a molecular simulation is helpful for a clear interpretation of these experiments [1]. Controlling the wettability of a surface with an array of the micro(nano)scale pillars finds wide applications. We study the wetting transition of the interfacial water contacting a nano-corrugated surface. We uncover the metastable and transition states in the wetting transition [2]. The wettability of a pillared surface is quantified by the contact angle (CA) of a water droplet. It is desired to know the CA prior to construction of pillars, in order to obviate the trial-and-errors of experimenting with different topographies. By employing a three-dimensional descriptor of the surface topography, we show that a convolutional neural network model can predict experimental CAs within errors comparable to the experimental uncertainties in measuring CAs [3].

Reference

[1] K. Kim, S. Choi, Z. Zhang, L. Bai, S. Chung, and J. Jang, J. Phys. Chem. C **126**, 8967 (2022).
[2] Z. Zhang, M. Zhao, Y.Ahn, and J. Jang, J. Mol. Liq. **335**, 116276 (2021)
[3] S. Choi, K. Kim, K. Byun, J. Jang, Langmuir **39**, 117471 (2023)

(Session 2-3)

Chemical Dynamics, Statistical Thermodynamics, and Transport Theories for Complex Materials and Biological Systems

Jaeyoung Sung[1,2,3]

[1]*Global Science Research Center for Systems Chemistry,*

[2]*Creative Research Initiative Center for Chemical Dynamics in Living Cells,*

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We will introduce new chemical dynamics models and theories useful for quantitative investigations into complex reaction networks in living cells [1]. Next, we will talk about a novel transport equation whose solution provides a quantitative explanation of non-Gaussian, thermal motion in various complex fluids and solid electrolytes [2]. We will also discuss statistical thermodynamics and diffusion-influenced chemical dynamics of mesoscopic systems, along with their applications to nuclei seed formation and phase separation [3]. Combined with modern cutting-edge experimental and computational techniques, including machine learning, these works enable quantitative predictions regarding dynamics of complex materials and living systems on the basis of fundamental principles in physics and chemistry.

Reference

[1] Park et al., The Chemical Fluctuation Theorem governing gene expression, Nature Communications 9, 297 (2018); Song et al., Frequency spectrum of chemical fluctuation: a probe of reaction mechanism and dynamics, PLoS Comp. Biol. 15, e1007356 (2019); Kang et al., Stochastic kinetics of Nanocatalytic Systems, Phys. Rev. Letters 126, 126001 (2021).

[2] Song et al., Transport Dynamics in Complex Fluids, Proc. Nat. Acad. Sci. 116, 12733 (2019); Kang et al., Real-space imaging of nanoparticle transport and interaction dynamics by graphene liquid cell TEM, Sci. Adv. 7, 49 (2021); Poletayev et al., Defect-driven anomalous transport in fast-ion conducting solid electrolytes, Nat. Mater. 21, 1066 (2022); Lee et al., Transport dynamics of water molecules between lipid membranes J. Phys. Chem. Letters 15, 4437 (2024).

[3] Kim et al., Multiphasic growth dynamics of nanoparticle ensembles, ChemRxiv (2024); Kang et al., Supersaturation, Nucleation, and Phase Separation of Mesoscopic Systems (submitted) (2025).

(Session 3-1)

Exploring the equilibria and kinetics of transmembrane protein association

Ayan Majumder, Sangram Prusty, Seulki Kwon, and John E Straub[1*]

Department of Chemistry, Boston University, Boston, Massachusetts 02215

The accurate simulation of realistic biomembranes is a long-term goal in the field of membrane biophysics. Efforts to simulate increasingly complex lipid bilayers, consisting of multiple lipid types and proteins, have been hindered by the shortcomings of current coarse-grained and all-atom force fields. Due to the fundamental importance of protein dimerization to cellular signaling and protein trafficking, the study of protein-protein association and the related dimerization free energies has received significant attention in both simulation and experiment. Detailed comparisons of simulation results with NMR, crystallography, and FRET studies have served to test of the accuracy of simulation methods and provided insight into the underlying structural distributions and thermodynamic driving forces. These comparisons have led to the conclusion that existing state-of-the-art simulation methods have failed to effectively sample the equilibrium between associated and dissociated states, resulting in inaccurate estimates of binding constants and the misrepresentation of the associated structural ensembles. We will discuss the drawbacks of previously used protocols and our systematic development of methods for the identification of collective variables for use in enhanced sampling simulations. The resulting methods exhaustively sample the native and non-native dimer conformations and lead to precise estimates of the associated equilibrium binding constants. Our conclusions identify the most important current challenges to the field.

Reference

[1] “On computing equilibrium binding constants for protein-protein association in membranes,” A. Majumder and J.E. Straub, J. Chem. Theor. Comp. 18, 3961-3971 (2022).

[2] “Efficient calculation of the free energy for protein partitioning using restraining potentials,” S. Kwon, G.A. Pantelopulos, and J.E. Straub, Biophys. J. 122, 1-12 (2023).

[3] . “Machine learning derived collective variables for the study of protein homodimerization in membrane,” A. Majumder and J.E. Straub, J. Chem. Theor. Comp. 20, 5774-5783 (2024)

[4] “Exploring free energy landscapes for protein partitioning into membrane domains in all-atom and coarse-grained simulations,” S. Kwon, A. Majumder, and J.E. Straub, J. Chem. Theor. Comp. 20, 9687-9698 (2024)

(Session 3-2)

Dynamics of membrane-bound biomolecular condensates

Joo-Yeon Yoo [1*]

Department of Life Sciences, POSTECH

Liquid–liquid phase separation (LLPS) enables macromolecules to de-mix in solution, forming reversible intracellular compartments without membranes. While most studies on biomolecular condensates have focused on their assembly and biological roles in fluidic 3D cellular environments, recent findings highlight their presence near, on, or integrated with organelle membranes.

Our research investigates the molecular condensation of SCOTIN, an integral membrane protein with antiviral functions. SCOTIN expression is induced by interferon (IFN) stimulation or DNA-damage. Its condensation along membranes is closely linked to key cellular processes, including ER-Golgi vesicle transport[1], endosome-ER tethering[2], regulation of isolation membrane-ER contact during autophagosome biogenesis[3], and the ER stress responses[4].

To explore the dynamics of membrane-associated molecular condensates, we monitored the behavior of chimeric Sec61b-PRD-mEmerald on the ER membrane. In this talk, I will discuss its dynamics, membrane interactions, and regulatory mechanisms.

Reference

[1] Kim N, Kim TH, Kim C, Lee JE, Kang MG, Shin S, Jung M, Kim JS, Mun JY, Rhee HW, Park SY, Shin Y, **Yoo JY**. **2023**. Intrinsically disordered region-mediated condensation of IFN-inducible SCOTIN/SHISA-5 inhibits ER-to-Golgi vesicle transport. ***Dev. Cell*** 58(19):1950-1966.e8.

[2]Yun H, Jung M, Lee H, Jung S, Kim T, Kim N, Park SY, Kim WJ, Mun JY, **Yoo JY**. **2023**. Self-Assembly of SCOTIN controls endosome dynamics via ER membrane contact regulation. ***EMBO Report*** 24(8):e56538

[3] Lee JE, Kim N, Jung M, Mun JY, Yoo JY. **2022**. SHISA5/SCOTIN restrains spontaneous autophagyinduction by blocking contact between the ERES and phagophore. ***Autophagy***. 18:1613-1628

[4] Jo AR, Jung M, Mun JY, Kim YJ, Yoo, JY. **2025**. Membrane-tethered SCOTIN condensates elicit an endoplasmic reticulum stress response by sequestering luminal BiP. ***Cell Rep***. 44(2):115297

(Session 3-3)

Lipid Membrane Remodeling by Proteins and Peptides: Mechanistic insights from multi-scale analysis

Qiang Cui

Departments of Chemistry, Physics and Biomedical Engineering, Boston University

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We will discuss the analysis of membrane remodeling by proteins and peptides using multi-scale computational methods; these include mainly molecular dynamics simulations at atomistic and coarse-grained levels, although we will also touch upon analyses using lattice models and a mean- field theory. The discussions will cover several systems that we have analyzed in recent studies, which include the SAR1 protein from the COPII machinery and the ESCRTIII complex; we will also briefly discuss how protein condensates interact with lipid membranes, especially in terms of their mutual influence on morphology and phase behaviors. These examples illustrate different molecular properties and mechanisms that are potentially relevant to membrane remodeling, as well as the values and limitations of various computational methodologies in such context.

Reference

[1] Lysine-rich motif of synaptotagmin 1 regulates Ca 2+ binding via liquid-liquid phase separation, N. Mehta, S. Mondal, E. T. Watson, Q. Cui, and E. R. Chapman, Nat. Commun., 15, 262 (2024)

[2] Coacervation induced remodeling of nanovesicles, S. Mondal and Q. Cui, J. Phys. Chem. Lett. 14, 4532 (2023).

[3] Sensitive and Selective Polymer Condensation at Membrane Surface Driven by Positive Co- operativity, Z. Liu, A. Yethiraj and Q. Cui, Proc. Natl. Acad. Sci. U.S.A., 120, e2212516120 (2023)

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[5] Coacervation of poly-electrolytes in the presence of lipid bilayers: Mutual alteration of structure and morphology, S. Mondal and Q. Cui, Chem. Sci., 13, 7933-7946 (2022)

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(Session 4-1)

WHAT CAN CHARMM-GUI DO FOR YOU?

Wonpil Im

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Since its original development in 2006, CHARMM-GUI (https://www.charmm-gui.org) has proven to be an ideal web-based platform to interactively build complex molecular systems and prepare their simulation inputs with well-established and reproducible simulation protocols for state-of-the-art molecular simulations using widely used simulation packages with various force fields. The CHARMM-GUI development project has been widely adopted for various purposes and now contains a number of different modules designed to set up a broad range of molecular simulation systems. Our philosophy in CHARMM-GUI development is less about providing the nuts and bolts of molecular modeling, but instead focused on helping users to achieve a task, such as building a membrane system or solvating a protein, by providing a streamlined interface. This design principle helps us to think of the workflow critically when designing the interface and new modules, which leads CHARMM-GUI to be accessible to users with little experience in modeling tools and remains useful to experts, especially for batch generation of systems. The CHARMM-GUI development project is still ongoing. CHARMM-GUI will continue to help expert and non-expert researchers from a broader range of the modeling and simulation community to build the complex molecular systems of their interest and prepare the input files for any general and advanced modeling and simulation through the large and unique scope of CHARMM-GUI functionality, allowing the research community to carry out innovative and novel molecular modeling and simulation research. In this talk, I will present the past, present, and future of the CHARMM-GUI development project, and some applications of specific modules will be also discussed.

(Session 4-2)

Prenucleation Clusters of ZnSe Assisting Formation of Photoluminescent CdSe Magic-Size Clusters under Mild Conditions

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An outstanding demand for photoluminescence (PL) colloidal semiconductor nanocrystals is low-temperature approaches to surface passivation. When a shell growth is performed at elevated temperatures, core nanocrystals may undergo undefined changes. In this presentation I will show that surface passivation of CdSe magic-size clusters (MSCs) can be carried out at mild conditions such as at 25 C, when a prenucleation-stage sample of ZnSe is used. The ZnSe sample has prenucleation clusters (PNCs). Mixed with the ZnSe sample, PL-inactive MSCs of CdSe (purified) become PL-active, to which a core/shell structure of CdSe/ZnSe is assigned, based on our extensive characterization with TEM, XRD, SEM-EDX, and XPS. The two types of MSCs of CdSe (~2.3 nm) and CdSe/ZnSe (~3.0 nm) display an almost-identical doublet of optical absorption, which peaks at 421 and 450 nm. The PL-active ones exhibit a dual band emission. One band-edge PL signal peaks at 460 nm and is sharp with FWHM of ~15 nm and PL lifetime of ~1 ns. Another trap PL signal peaks around 505 nm and is much broader, with PL lifetime of ~6 ns. We suggest that the ZnSe shell growth at 25 C proceeds via the addition of ZnSe monomers, which are from the ZnSe PNC. The shell growth features the principle of isodesmic reactions, where the number of M−Se bonds (M = Cd and Zn) cleaved in the reactant (CdSe + ZnSe) is similar to that formed in the product (CdSe/ZnSe). Our study paves an avenue to surface passivation under mild conditions, narrows the knowledge gap of the pathway of the shell growth, and provides an in-depth understanding of the synthetic application of the PNC at mild conditions.

(Session 4-3)

Development and Demonstration of a CO_2 Conversion System for Valuable Chemical Production Using Heterogenized Catalysts

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The conversion of CO_2 into valuable chemicals is a crucial strategy for carbon neutrality and sustainable chemical production. In this study, we present a highly efficient heterogenized Ru molecular catalyst supported on bpyTN-30-CTF for continuous CO_2 hydrogenation to formic acid in a trickle-bed reactor. The unique structure of bpyTN-30-CTF enhances porosity and provides abundant metal anchoring sites, enabling superior catalytic performance. The Ru/bpyTN-30-CTF catalyst demonstrates excellent activity with a high formic acid productivity of 669.0 g_form. g_cat^{-1} d^{-1} and CO_2 conversion of 44.8% under optimized conditions. [1] Additionally, the catalyst exhibits outstanding stability, maintaining performance for over 30 days with a total turnover number (TON) of 524,000 without significant deactivation. This work establishes a viable pathway for formic acid production via CO_2 hydrogenation, highlighting the potential for commercial-scale implementation.

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(Session 5-1)

Single-molecule studies of chromosome organization and transcription regulation by DNA supercoiling

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Classic gene regulation dogma shows that transcription factor binding to specific DNA sequences regulates gene expression. In recent years, an increasing number of studies have shown that the supercoiling state of chromosomal DNA is a fundamental factor that impacts transcription. The topological organization of chromosomal DNA into individual domains, between which the diffusion of supercoiling is prohibited, thus plays an important role in gene regulation. In this talk, I will discuss our recent effort in developing in silico, in vivo, and in vitro single-molecule approaches to probe how DNA supercoiling impacts chromosome organization and transcription. We have built a synthetic supercooling domain platform to control topological domain formation at will in single E. coli cells. We used single-molecule fluorescence in-situ hybridization (smFISH) to probe the expression and correlation of two genes enclosed in the domain and a third gene outside the domain under altered topoisomerase activities. We then developed a corresponding in vitro single-molecule transcription assay to probe how DNA's supercoiling state affects transcription kinetics and the cooperation of neighboring RNA polymerase molecules. Finally, we combine these experimental studies to construct a quantitative computational model depicting the relationship between supercoiling and transcription regulation.

(Session 5-2)

Transcriptional dynamics with Bayesian nonparametrics: from dense 3D RNA spot localization/classification to gene network inference

Maxwell Schweiger[1,2], Rory Kruithoff[1,2], Zeliha Kilic[1,2], Sina Jazani[1,2], Camille Moyer[3], Douglas Shepherd[1,2], Steve Pressé[1,2,4*]

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Gene expression models are essential for understanding cellular regulation and single-cell transcriptional dynamics. While RNA data provide key insights, existing methods require predefined gene states and connectivity before estimating rate parameters. We introduce a method that jointly infers gene states, interactions, and rate parameters directly from single-molecule RNA counts using a Bayesian non-parametric framework. Validated on E. coli lacZ and S. cerevisiae STL1 pathways, our approach also proves robust on synthetic data [1].

If time allows, we will discuss inference of 3D RNA localization and classification from iterative FISH, particularly when diffraction-limited spots overlap [2]. Current methods rely on linear error-correcting codes and additional imaging rounds, but separate localization and classification can cause cascading errors. To improve efficiency, we propose a Bayesian nonparametric method that integrates both tasks, leveraging hierarchical modeling to account for dye properties and other complexities. This approach enhances accuracy, works with error-correcting codes like MERFISH, and may dramatically reduce imaging requirements through dense barcodes.

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(Session 5-3)

Non-equilibrium Conformational Fluctuations in Driven Chemical Networks

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The talk first discusses the influence of conformational dynamics on enzymatic networks and then presents a broad perspective on statistical kinetics and nonequilibrium thermodynamics of driven processes.

Single enzyme experiments reveal conformational fluctuations on multiple time scales, but the measured turnover rate still follows the simple Michaelis-Menten (MM) equation. To resolve this puzzle, we establish the generalized rate equation for an arbitrary enzymatic network, which reduces to the MM form when conformational detailed balance is obeyed. The generalized MM expression reveals a relation between non-MM corrections and non-equilibrium conformational currents and predicts allosteric effects in monomeric enzymes.

Our analysis of the enzymatic networks motivated a general study of the kinetics and thermodynamics of driven biomolecular systems. (i) Technically, a pathway approach allows us to decompose and combine complex chemical networks using kinetic motifs. (ii) Conceptually, for a dynamically disordered biomolecular machine regulated by a hidden process, a time-based fluctuation theorem no longer applies to the observable first-passage time; however, its validity can be restored in the absence of hidden currents (e.g., conformational detailed balance). (iii) Our analysis of chemical networks and the fluctuation theorem sheds new light on the validity of the course-graining procedure widely adopted in molecular modelling.

(Session 6-1)

Using Computer Simulations to Advance our Understanding of Biological Systems at the Atomic Level

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Classical molecular dynamics (MD) simulations based on atomic models play an increasingly important role in a wide range of applications in physics, biology and chemistry. The approach consists of constructing detailed atomic models of the macromolecular system and, having described the microscopic forces with a potential function, using Newton's classical equation, F=MA, to literally "simulate" the dynamical motions of all the atoms as a function of time. While great progress has been made, producing genuine knowledge about biological systems using MD simulations remains enormously challenging. Among the most difficult problems is the characterization of slow conformational transitions that underlies biological function. Most computational strategies require the knowledge of a suitable reaction-coordinate, which have traditionally been constructed using human intuition. To tackle increasingly difficult problems, it is important to develop more objectively robust approaches. Transition path theory, combining free energy methods, string method, transition pathway techniques, stochastic Markov State Models, and Machine Learning techniques based on artificial Neural Networks, offers a powerful paradigm to address these issues [1-6]. With a mixture of history and background, these concepts will be formally introduced and illustrated with previous computational studies of K+ channels, Src tyrosine kinases, and the P-type ion pumps.

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(Session 6-2)

How to regulate protein condensation with highly charged HERO proteins

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Liquid-liquid phase separation (LLPS) forms protein/RNA condensates in the cell. The molecular mechanisms for the condensate formation have been studied experimentally and computationally. However, molecular mechanisms for deformation or regulation of the condensate have not been elucidated so far. Here, we discuss functions of HERO (Heat-resistant obscure) proteins to study the regulation of protein condensates [1]. HERO proteins have several unique features: (1) They are highly charged, either positively or negatively. (2) Each HERO protein has its client proteins to avoid their aggregations. (3) Chargeless mutations cause the dysfunction of HERO proteins. Using GENESIS software, we carried out coarse-grained (CG) simulations of HERO11 with its client, TDP-43 [2]. In the MD simulation, HERO11 does not form condensates, while TDP-43 can form condensates at the same temperature. The mixture of HERO11 and TDP-43 dissolves TDP-43 condensate, as shown in the experiment. The trajectory analysis suggests that HERO11 functions both inside of the condensate and outside. Also, there is a possibility of avoiding the growth of TDP-43 condensates from small to larger ones. The slab model, which has been used in the MD simulation studies of LLPS, may not be sufficient to examine the fusion of protein condensates. Therefore, we have developed a new domain decomposition scheme for large-scale CG MD simulations and implemented it in CGDYN, a new MD program of GENESIS. We successfully simulated smaller droplet to a larger one, which can be explained with the Oswald-ripening mechanisms.

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(Session 6-3)

Computer Simulation Studies of Chlorosulfolipids and Lung Surfactant Membrane Systems

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In this talk, I will discuss computer simulation studies of two biological membrane systems: chlorosulfolipids and lung surfactant membranes. As the first example, chlorosulfolipids (CSLs) are major components of flagellar membranes in sea algae. Unlike typical biological lipids, CSLs contain hydrophilic sulfate and chloride groups in the hydrocarbon tail; this has deterred the prediction of the CSL membrane structure since 1960. In this study, we combine coarse-grained (CG) and atomistic molecular dynamics (MD) simulations to gain significant insights into the membrane structure of Danicalipin A, which is one of the typical CSLs. It is observed from the CG MD that Danicalipin A lipids form a stable monolayer membrane structure wherein the hydrocarbon moieties are sandwiched by hydrophilic sulfate and chloride groups in both the head and tail regions. Based on the mesoscopic structure, we have built the corresponding atomistic model to investigate the integrity of the CSL monolayer membrane structure. The monolayer membrane comprising bent lipids shows high thermal stability up to 313 K. The gel−liquid crystalline phase transition is observed around 300 K. The second topic, polyhexamethylene guanidine (PHMG), has recently been the most infamous chemical in South Korea because it caused several fatalities while used as a humidifier disinfectant. In a mouse experiment on the toxic effects of inhalation, it was confirmed that inhalation of these toxic components could cause increased mortality, hyperplasia of alveoli and bronchioles, alveolar emphysema, and pulmonary fibrosis. In this study, we have performed MD simulation to study effects of PHMG on lung surfactant membranes. The lung surfactant was modeled as a monolayer of dipalmitoylphosphatidylcholine (DPPC), which is the main component of the lung surfactant membrane. In addition, a water droplet containing PHMG mimicking aerosol and a bare PHMG were used to investigate the effects of water droplets upon the PHMG permeation into the blood stream. From MD simulations of around 100 ns, we have observed that the water droplet smeared into the water phase leaving PHMG behind in the membrane region in dilute concentration. On the other hand, it was also observed that PHMG induces endocytosis in high concentration. We have additionally examined structural effects of PHMG on DPPC monolayer by calculating translational and orientational pair correlation functions.

(Session 7-1)

Wet and Warm: Nonergodicity, Mobility, and Interfacial Polarization in Molecular Biology

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Efficiency of biology has both time and energy dimensions: events have to occur within a given time while spending less energy. Both requirements are achieved by enzymes accelerating reactions by many orders of magnitude without demanding much free energy input. Can this acceleration be captured by standard recipes of thermodynamics and Gibbsian statistics? It turns out that the observed speed of electron transport in biological energy chains is only possible when Gibbsian statistics are broken (becoming nonergodic) by dynamical constraints [1]. Much of this complexity comes from the protein-water interface defined by the competition of van der Waals (vdW) and electrostatic interactions. They turn out to be remarkably strongly correlated as is seen from mobility of molecular solutes and proteins in water: both vdW and electrostatic forces relax on the same time scale of several nanoseconds, separated by five-six orders of magnitude from the relaxation time of the total force [2]. Polarization of complex interfaces does not follow the rules of conventional dielectric theories. Standard linear theories of dielectric friction are grossly inapplicable to translational and rotational diffusion and interfacial polarization of water is characterized by a low dielectric constant [3]. I will discuss how these findings shape an emerging understanding of functionality of biological energy chains and manipulation of proteins in solution.

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(Session 7-2)

Unveiling microscopic mechanisms of dynamic slowdown in supercooled liquids

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When a liquid is rapidly cooled below its melting point while avoiding crystallizing, its molecular motions slow down. This slowdown is a universal phenomenon observed across various liquids. However, the temperature dependence of relaxation time varies among liquids: some, such as silica, classified as “strong” liquids, exhibit Arrhenius behavior, whereas others, including water above ~200 K, known as “fragile” liquids, follow a super-Arrhenius temperature dependence. Despite extensive research, the fundamental mechanism underlying this slowdown remains complex and is not yet fully understood.[1] To elucidate the microscopic origins of dynamic slowdown in supercooled liquids, we have conducted molecular dynamics simulations. Our analysis reveals that the jump dynamics, which drive structural rearrangements, deviate from Poisson statistics at lower temperatures. This deviation arises from the influence of slow variables that compete with the jumping motions, a phenomenon known as dynamic disorder.[2] We further identify the primary slow variables responsible for dynamic disorder. Additionally, by analyzing the survival probability and static amorphous order length scales, we characterize the temperature dependence of molecular cooperativity. These results provide new insights into the microscopic mechanisms governing the slowdown in supercooled liquids.[3]

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(Session 7-3)

Far-from-Equilibrium Phase Transitions and Charge Transport in Disordered Systems

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Understanding nonequilibrium dynamics in disordered materials is crucial for both fundamental science and technological applications. In this talk, we discuss our two recent studies in these aspects. First, we investigate dynamical phase transitions in stochastic and atomistic systems using trajectory ensemble methods. Specifically, we study 1D Ising and kinetically constrained models (KCMs), as well as the Kob-Andersen glassy system, through an energy-activity double-biasing approach. Our results uncover anomalous behaviors such as freezing-by-heating and permanent liquid states, offering insight into cooperative dynamics in soft materials. To efficiently compute large-deviation statistics, we employ Tensor Network methods, particularly the Matrix Product State (MPS) formalism, and develop a parallel spatio-temporal Monte Carlo algorithm for rare trajectory sampling. Building on our interest in complex dynamics of disordered systems, we also explore charge transport in organic semiconductors using a multiscale modeling framework that integrates atomistic morphology, kinetic Monte Carlo simulations, and machine learning techniques. This approach enables efficient prediction of key electronic parameters and provides molecular-level insights into exciton transport in OLED materials. Together, these efforts reflect a broader goal of understanding emergent behaviors in soft and disordered systems by combining nonequilibrium statistical mechanics with advanced computational methods.

(Session 8-1)

Towards a first-principles multi-scale understanding of CO_2 reduction

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Electrochemical CO2 reduction (CO_2RR) has become a promising pathway toward sustainable carbon feedstocks. Over the last years, the focus for electrolyzer performance optimization has shifted from catalyst design to interfacial and multi-scale design. In this presentation, the latest efforts of our group are shown for entangling the multi-scale nature of CO_2 RR to develop new engineering design concepts. At first, this refers to the solid-liquid interface and its impact on the surface composition and structure, directly affecting catalytic performance. Our research shows that the electric double layer plays a crucial role in this, and binding to metal surfaces should be treated using beyond-DFT methods. Second, this refers to the multi-scale nature of electrochemical systems, with multi-phase mass transport playing a crucial role in electrolyzer optimization, such as for state-of-the-art gas diffusion electrode systems.

(Session 8-2)

Classical and quantum charge transport in advanced electronic materials

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Charge transport plays a fundamental role in a wide range of advanced electronic materials, governing their efficiency and functionality. From energy storage and conversion to biological processes, charge carriers—ions, protons, and electrons—move through complex environments where their transport properties are dictated by molecular interactions, structural heterogeneity, and quantum effects. In this talk, I will present our efforts to model charge transport across diverse systems using advanced computational techniques, bridging classical and quantum descriptions to capture the underlying mechanisms.

Particularly, three ongoing development stories will be discussed: (1) developing first-principles based predictive polarizable force fields to model ion transport in highly charged liquid electrolytes and polymer electrolytes, where strong polarization and heterogeneous solvation environment produces complex correlated ion motion such as negative cationic transference number, (2) a novel hybrid Monte Carlo/molecular dynamics (MD) simulation approach to efficiently model proton transfer event in large scale condensed phase systems applicable to membrane fuel cell and biophysical channel proteins. (3) multi-scale simulation approach to the conjugate polymer interfaces at molecular level, including a CP-carbon nanotube (CNT) interface for thermoelectric application, and a CP-water interface for photocatalytic application. Through this, we offer novel insights for designing functional electronic materials in highly charged environments through advanced simulation techniques.

(Session 8-3)

Stickers and Spacers in Biomolecular Condensation

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The stickers-and-spacers framework, proposed in 2018 [1-2], provides insights into the collective behaviors of heteropolymers, particularly biomolecules such as proteins and nucleic acids. Inspired by the associative polymer theory, this model categorizes polymer constituents into two groups: those engaging in chain-chain interactions (*stickers*) and those that do not (*spacers*). The model has garnered significant interest due to its explanatory power regarding the role of intrinsically disordered proteins/regions (IDPs/IDRs) in biomolecular condensation. Notably, the existence of a hierarchy of stickers, based on their contributions to chain-chain interactions, has been suggested. However, the model has also sparked misunderstandings and critiques. In this presentation, I will elucidate the framework and its modifications and present recent findings that offer a non-canonical illustration of the stickers-and-spacers framework [3].

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(Session 9-1)

A window into lipid peroxyl radicals, peroxidation and electrophilic stress in cells

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In this presentation I will describe fluorogenic (off to on) probes we have developed to monitor electron transport [1], lipid peroxidation [2], and electrophilic stress [3], in lipid membranes. I will portray live cell imaging work where we exploit newly developed activatable fluorogenic antioxidants [2] and state-of-the-art imaging methodologies to monitor lipid peroxyl radicals under a series of pathological conditions. Secondly, I will touch upon the ability of cells to detoxify increasing lipid derived electrophile (LDE), exploring the link between lipid hydroperoxide accumulation, LDE formation and cell death. Here, I will describe a recently developed assay (ElectrophileQ) that enables live-cell assessment of the glutathione-mediated LDE conjugation and adduct export steps of the LDE detoxification pathway [3]. The body of work provides molecular insight on the onset and progression of a series of conditions where lipid peroxidation and or electrophilic stress are exacerbated.

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(Session 9-2)

Fluorescence-free single-molecule microscopy by independently tunable, resonance stimulated Raman scattering

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Single-molecule vibrational spectroscopy has been demonstrated with near-field amplification as in surface-enhanced Raman spectroscopy (SERS) or fluorescence detection as in stimulated Raman excited fluorescence (SREF) and bond-selective fluorescence-detected infrared-excited spectro-microscopy (BonFIRE).[1-2] However, these methods involve complex sample preparation or produce high backgrounds, limiting their practicality. To address these issues, we enhanced electronic resonance stimulated Raman scattering (ER-SRS) to achieve single-molecule sensitivity in far-field vibrational microscopy without relying on fluorescence detection. ER-SRS has encountered difficulties due to large electronic backgrounds.[3] For effective optimization of the signal-to-background ratio, we employed Raman-amplified nonfluorescent molecular probe (RANMP) alongside our synchronously pumped, independently tunable double optical parametric oscillators.[4] The new probes and new light source allowed us to successfully detect ER-SRS signal from single particles in solution and from single molecules embedded in polymer matrix.

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(Session 9-3)

Molecular Insights into RNA Binding and Cleavage by CRISPR-Cas13a

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The CRISPR system, originally discovered as an adaptive immune system in prokaryotes, has emerged as a powerful tool for gene editing and molecular diagnostics due to its programmability. Among CRISPR effectors, Cas13a specifically targets single-stranded RNA (ssRNA) in complex with a guide RNA (gRNA), making it highly applicable to RNA-based technologies. Despite its growing applications, the molecular mechanisms underlying its RNA binding and cleavage remain elusive. Here, we investigated the real-time dynamics of RNA binding and cleavage by the Cas13a-gRNA complex using single-molecule Forster resonance energy transfer. Notably, Cas13a-gRNA effectively binds target RNA independent of Mg^{2+} ions and exhibits robust *trans*-cleavage activity, efficiently degrading nearby ssRNAs even in the absence of prior *cis*-cleavage. This mechanism distinguishes Cas13a from dsDNA-cleaving Cas proteins and underscores its unique cleavage dynamics. By examining the interplay between RNA binding, *cis*-cleavage and *trans*-cleavage, our findings provide key insights into the molecular mechanisms of Cas13a-RNA interactions, advancing our understanding of Cas13a's function and its potential in RNA-targeted applications.

(Session 10-1)

AI and free energy methods for drug discovery

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Alchemical free energy (AFE) simulations for prediction of small molecule-target binding affinities are an indispensable tool for drug discovery. A critical barrier to progress are challenges that limit the ability of these methods to achieve high precision, accuracy and throughput. This talk summarizes the latest new and emerging methods for AFE simulation and analysis using AMBER/AMBER Drug Discovery Boost. Methods to enhance the robustness and precision of calculations will be presented. A new quantum deep-potential interaction (QDPi) model force field will be demonstrated to enhance the accuracy of protein-ligand binding predictions. The precision, accuracy and throughput afforded by these simulations provides the foundation from which to design target-specific machine learning models capable of prediction of up to millions of ligands.

(Session 10-2)

Machine learning methods for protein and peptide design

Philip Kim

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The field of protein and peptide modeling and design has been transformed in the last few years by the advent of machine learning methods. I will summarize the contributions of my group to this revolution, starting with the development of graph neural networks for protein sequence design [1] and the application of diffusion or score-based generative models to protein backbone design [2]. I will also cover methods that attempt to model dynamics and also our efforts to design therapeutics based on peptides or proteins.

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(Session 10-3)

Integrated method for identifying the optimal descriptor of acute critical illness: Development of septic infection related risk index (SIRRI) and investigation into patient's fate dynamics along SIRRI

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Acute critical illnesses, particularly sepsis, pose significant challenges due to their sudden life-threatening nature and heterogeneous pathologies, demanding early detection and appropriate treatment. The lack of a golden standard for early sepsis diagnosis has driven the exploration of deep learning (DL) methods for diagnostic and prognostic purposes, despite their opaque decision-making processes. Here, we propose a systematic and transparent method that integrates a DL module for early sepsis diagnosis, an explanation module for assessing feature importance and selecting key features, and a module for constructing multidimensional spaces defined by features generated through the application of mathematical operators to the key features. Using this integrated method, we establish the septic infection-related risk index (SIRRI), comprising only eight infection- or inflammation-related biomarkers, as the optimal descriptor characterizing the severity of pathology in sepsis patients. In addition, we develop a white-box prognosis model based on multi-stage reaction-diffusion equations in SIRRI coordinates, enabling quantitative prediction of time-dependent mortality or recovery rates of sepsis patients based on their SIRRI values at the onset of sepsis, with applicability across multiple datasets. These findings demonstrate the utility of SIRRI as a novel effective index for both diagnosis and prognosis in clinical practice, with potential applications extending beyond sepsis to other acute critical illnesses.

(Session 11-1)

A lack of distinct cellular identities in scRNA-seq data: revisiting Waddington's landscape

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Single-cell RNA sequencing is revolutionizing our understanding of development, differentiation and disease. Analysis of this data is often challenging, however, and tasks like clustering cells to uncover distinct cellular identities sometimes yields results that fail to align with existing biological knowledge. We analyzed publicly available data where the cell identity for each cell is known a priori, and found that cells of very different types and lineages do not occupy distinct regions of gene expression space. Rather, cells from different lineages overlap extensively with one another, significantly complicating attempts to recover distinct identities within the data. Indeed, our analysis of available epigenetic data for a wide variety of tissues, organisms and technological measurement techniques revealed these data are not consistent with the predictions of Waddington's landscape, suggesting a need to revisit our picture of gene expression changes during differentiation and development.

(Session 11-2)

Fixative-eXchange (FX)-seq: scalable single-nucleus RNA-seq for FFPE clinical tissue

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Clinical formalin-fixed paraffin-embedded (FFPE) samples are valuable for genomics research but challenging for single-nucleus RNA sequencing (snRNA-seq) due to poor RNA quality and reverse transcription efficiency [1-4]. We introduce Fixative-eXchange (FX)-seq, a scalable method for heavily fixed and FFPE samples. We validated this approach by analyzing over 500,000 nuclei from PFA-fixed tissues, FFPE blocks, and H&E-stained sections from mouse brain and human cancer specimens. We successfully applied FX-seq to FFPE samples from gastrointestinal stromal tumor, colorectal cancer, Ewing sarcoma, and lung cancer, generating transcriptomic data that provides insights into cancer development and metastasis. FX-seq advances both basic and clinical research by enabling transcriptome profiling of archival specimens, with significant implications for diagnosis and therapeutic development.

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(Session 11-3)

Chemical Strategies to Study Multiple Facets in Dementia

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Alzheimer's disease (AD), associated with degeneration of neurons and synapses in the brain, leads to motor impairment and eventual fatality. Neurodegeneration could be related to various interconnected features, including (i) plaque formation from amyloid-β (Aβ) peptide fragments, (ii) metal ion dyshomeostasis and miscompartmentalization, as well as (iii) inflammation and increased oxidative stress due to overproduction of reactive oxygen species (ROS). The inter-relations between some of these pathological factors have been investigated. Metals are found entangled in the Aβ plaque and likely contribute to Aβ neurotoxicity and oxidative stress. ROS have been shown to increase the rate of Aβ plaque formation. Our understanding of the correlation between these elements and AD neuropathogenesis has been very limited, however. There is currently no cure for AD; therapies are focused on symptomatic relief targeting the decrease in the levels of acetylcholine, only one of the multiple factors causing the disease.[1-3] To find a cure for AD, we require a better understanding of the relationship between various causative factors of this devastating disease. Towards this goal, we have been developing suitable chemical tools capable of targeting and regulating multiple underlying factors or identifying the pathogenic networks composed of their direct interactions and reactivities.[4-13]

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(Session 12-1)

Chemical framework for understanding Neurodegenerative Diseases

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The study of non-bonding interactions has transcended the exclusive domain of physical chemists employing spectroscopy and computer simulations. With the advent of molecular biology, non-bonding interactions have emerged as pivotal factors in comprehending the structures and functionalities of biomolecules, including DNA and proteins. Among these non-bonding interactions, ionic interactions stand out as the most robust forces mediating interactions between anionic and cationic molecules. When scrutinizing the intracellular milieu, non-bonding interactions, particularly those of the ionic nature, wield significant influence over protein-protein and DNA-protein interactions. Consequently, we hypothesized that protein aggregation or phase separation, known contributors to neurodegenerative diseases such as Alzheimer's, Parkinson's, and Lou Gehrig's diseases, may also be governed by these ionic interactions. Given the highly charged nature of disease-related proteins, a substantial charge disparity exists, making self-aggregation in the absence of cofactors a formidable challenge. Our research has yielded a compelling insight: small (negatively or positively) charged biomolecules play a pivotal role in facilitating the formation of protein condensates through ionic interactions within cellular environments.

(Session 12-2)

Machine Learning Potential assisted Energy Materials Research

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With the advancement of computational resources and methodologies, computational materials science has significantly reinforced experimental efforts and accelerated materials research and development. However, a significant disparity exists between experimental observations and theoretical calculations, primarily because of the structural simplifications often employed in computational models to enhance feasibility. Bridging this gap is challenging, especially when dealing with large, complex systems such as nanoparticles and interfaces. This requires solutions that extend computational simulations to emulate actual systems. Recently, machine learning techniques have emerged as powerful tools for assisting and enhancing the ability to solve complex problems beyond conventional computational methods. In this study, we propose a method that utilizes the moment tensor potential (MTP) combined with active learning techniques for highly reliable and large-scale simulations of alloy nanoparticle catalysts and reactive dynamics at electrode interfaces.

For alloy nanoparticles, our study presents a novel approach for estimating the HER catalytic activity of complex spherical nanoparticles (SNPs) of realistic sizes. We systematically investigated the catalytic behaviors of the most stable SNPs across various sizes and compositions from a macroscopic perspective. Regarding reactive dynamics, we performed long-time and large-scale simulations at the Li metal-Argyrodite interface using machine learning, elucidating structural decomposition and interphase formation mechanisms. Our findings demonstrate that machine learning potentials provide a practical and reliable approach for simulating large-scale, realistic, and complex systems, offering significant insights into energy materials research.

(Session 12-3)

Physicochemical understanding of adsorption in porous crystals

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Gas adsorption isotherm is one of general approach to characterize porous materials and develop their applications, but it does not directly give critical information concerning the adsorption behavior of gases in porous materials even they provide knowledge of the overall gas uptake within a material [1]. To solve this limitation, X-ray diffraction (XRD) coupled with gas adsorption measurements (in-situ gas adsorption XRD) has been developed, which can serve the information about total electron charge distribution, positions and numbers, contributed from both adsorbates and the crystal. In this presentation, I will demonstrate the approach involving the measurement and analysis of in-situ gas adsorption XRD data, termed as “gas adsorption crystallography”, and show how the interactions among adsorbates and substrate, controlled by the pore environment and species of adsorbates, influence on the adsorption behavior [2-5]. These works conclusively lead to a rigorous physicochemical understanding of the adsorption behaviour, which can help to design of adsorbents with guest selectivity and uptake capacity.

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Poster Session

Abstract

(Poster 1)

Supersaturation, Nucleation, and Phase Separation of Mesoscopic Systems

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Supersaturation, nucleation, and phase separation are ubiquitous phenomena of great interest in both science and industry. However, a unified, quantitative understanding of these phenomena has yet to be achieved for mesoscopic systems. Here, we present a set of general equations that determine the monomer saturation degree, the size distribution and free energy of mesoscopic systems, as well as their phase transition conditions. These equations reveal that, under supersaturation, the largest cluster size (LCS) is an important state-variable; the supersaturation degree decreases with the LCS, approaching unity in the macroscopic limit. We identify the critical supersaturation condition, above which the nuclei undergo the phase transition to form large crystals. Below this critical supersaturation, the nucleus size distribution is either a unimodal function or a monotonically decreasing function of size, depending on system and temperature. We also predict the most probable nucleus size and the direction of spontaneous changes of the LCS. This work will serve as a general theoretical framework for understanding, predicting, and designing nucleation and phase transitions in mesoscopic systems.

(Poster 2)

Multiphasic size-dependent growth dynamics of nanoparticle

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Colloidal nanoparticles are widely studied in science and industry, yet their thermodynamic mechanisms and growth dynamics remain elusive. Here, we investigated hundreds of in-situ growth paths of a nanoparticle group using liquid-phase TEM, uncovering size-dependent multiphasic growth dynamics inconsistent with current theories. Based on these observations, we developed a novel model and theory for growing nanoparticle ensembles, offering a comprehensive, quantitative understanding of time-dependent size averages, fluctuations, and size-dependent growth rates across diverse nanoparticle systems. Our findings indicate significant deviations from the Gibbs-Thomson equation in small nanoparticles, illuminating its role in governing size-dependent growth dynamics.

(Poster 3)

Structure and Phase of the Hydration Layer Probed by SFG Spectroscopy with Neural Network Potentials

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Hydration layers (HLs), structured water molecules at solid-liquid interfaces, play a crucial role in various properties such as wetting, nucleation, and reactivity. HLs form universally under ambient or aqueous conditions, even on hydrophobic surfaces. [1-3] Sum-frequency generation (SFG) spectroscopy, which has high interface selectivity, is a powerful tool for investigating the anisotropic molecular-level structure and phase of HLs. [4,5] However, interpreting the molecular structural dynamics that contribute to the SFG spectrum remains a challenge in experimental studies.

First-principles simulations, such as ab initio molecular dynamics, offer valuable insights into the molecular-level contribution to the SFG spectrum. Nonetheless, calculating the SFG spectrum demands substantial computational resources, and the system sizes that can be studied are inherently limited. This computational limitation hinders the ability to perform large-scale simulations, especially when studying systems involving complex molecular dynamics and large numbers of atoms.

To address these limitations, we built a neural network potential (NNP) model [6], trained on first-principles data. This approach significantly reduces computational costs while maintaining high accuracy, enabling the simulation of larger systems and providing deeper insights into the molecular structure and dynamics of HLs.

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(Poster 4)

Effects of Divalent Cations on Structure and Dynamics of Water Confined Between Lipid Bilayers

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Membrane-water interfaces host various chemical reactions that are vital for cellular functions. Among these, ion binding at the membrane-water interface plays a crucial role in modulating the structural properties of interfacial waters, such as their hydrogen-bond network and dipole alignment [1,2], which are critical for cellular processes. However, the influence of ion binding on dynamics of interfacial water molecules remains poorly understood [3]. Here, we employ molecular dynamics (MD) simulations to systematically investigate how varying concentrations of biologically relevant divalent cation salts [4] affect the transport dynamics of water molecules confined between lipid bilayers composed of 1,2-Dimyristoyl-sn-glycero-3-phosphocholine (DMPC). We find that the presence of divalent cation salts causes the displacement distribution of confined water molecules to deviate from Gaussian significantly. Using recently proposed theory of transport dynamics of complex fluids [5], we extract the magnitude and relaxation dynamics of the diffusion coefficient fluctuation from the non-Gaussian displacement distribution. While the relaxation time increases with the cation concentration regardless of cation species, the mean and variance of the lateral diffusion coefficient exhibit qualitatively different dependencies on cation concentration depending on the cation species.

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(Poster 5)

Computational Approach to the Identification of Visfatin-Derived Angiogenic Peptides

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Angiogenesis is a process essential for the healing of blood vessels and capillaries. It is also known to play an important role in various physiological processes, such as embryogenesis, tissue repair, and organ regeneration [1-5]. Visfatin was originally known as pre-B cell colony enhancing factor (PBEF) that promotes the growth of B-lymphocytes precursor cells [6]. Several recent studies have shown that Visfatin not only induces the production of the vascular endothelial growth factor (VEGF), but also stimulates angiogenesis, including proliferation, migration, and metastasis of vascular endothelial cells [7-9]. However, Visfatin has several inherent disadvantages as a drug itself due to its high molecular weight. In our previous study, we identified two peptides based on the active site of Visfatin using computational approach [10]. In this study, computational alanine scanning was used for additional peptide design and screening. Molecular dynamics simulations were conducted to investigate the structural stability of Visfatin-peptide complexes. Additionally, the toxicity and angiogenic properties of peptides were predicted using in silico tools.

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(Poster 6)

Synthesis and characterization of ferromagnetic MFI zeolite

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Organic wastes, produced as by-products of industrial activities, are released into lakes and oceans, disrupting aquatic eco-system and posing risks to human health. Among the various remediation methods explored, adsorption of wastes has gained attention for its cost-effectiveness, high efficiency and ease of application. Unfortunately, adsorption methods often face challenges in recovering adsorbents after use, and improper separation of dispersed adsorbents could induce additional contamination. Utilizing ferromagnetic adsorbents addresses these issues by allowing simple removal of the adsorbents by magnet.

Zeolites, crystalline microporous aluminosilicates, are among the well-known pollutant adsorbents due to their well-defined pore size, large surface area, and compositional tunability.[1] Ferromagnetic zeolites are generally synthesized by oxidation of magnetites (Fe_3O_4) onto the surface of pre-synthesized zeolite in magnetite precursor solution (i.e., co-precipitation method). However, this approach has drawbacks such as deterioration of adsorption performance and the separation of magnetites from zeolite in the solution due to formation of magnetites on the outer surface of zeolites.[2]

In this presentation, we introduce an approach to addressing the limitations of conventional ferromagnetic zeolites by direct conversion of zeolite precursor gel with magnetites. Directly synthesized ferromagnetic zeolites showed same framework structure, crystallinity and porosity as conventional zeolites. In addition, the leaching of magnetites from the surface of zeolite particles was suppressed due to directly incorporating magnetites into the zeolite frameworks. We expect that this work can be served as a general strategy for direct synthesis of functional ferromagnetic zeolites for pollutants removal. Furthermore, this strategy could be extended to the other nanoparticles incorporated into zeolites with various properties.

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(Poster 7)

Crowder Chemistry in Biomolecular Phase Separation

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Liquid-liquid phase separation (LLPS) plays a crucial role in cellular organization by facilitating the rapid assembly and disassembly of biomolecular condensates. In vitro, crowding agents such as polyethylene glycol (PEG) are commonly used to mimic the dense intracellular environment, yet their precise influence on phase behavior remains unclear. Here, we investigate how different synthetic polymers modulate the phase separation propensity of a simple multi-domain LLPS driver protein. Using turbidity measurements and spin-down assays, we determine phase separation thresholds under various polymer-induced crowding conditions. Additionally, we examine how these polymers influence the material properties of the protein-rich phase. We hope that these insights will advance our understanding of biomolecular phase separation in complex cellular environments.

(Poster 8)

Interplay of Biomolecular Phase Separation and Fibrillation: Graph-Based Percolation Simulation

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Recent studies suggest that the phase separation of specific pathological biomolecules can act as a precursor to fibrillation, which is implicated in the development of neurodegenerative diseases such as Alzheimer's. To address this, we developed a coarse-grained model based on the stickers-and-spacers framework, implemented as a graph-based system to simulate collective behaviors due to multivalent interactions. We first analyzed the percolation behavior of a system in which stickers can only induce phase separation, identifying characteristic features of condensate formation. We then introduced a fibrillation mechanism into the model to investigate and explain the interplay between phase separation and fibrillation. We anticipate that this study provides insights into the fundamental principles governing both biomolecular phase separation and fibrillation and may contribute to a better understanding of cellular processes and disease mechanisms.

(Poster 9)

Accurate Conformational Ensembles of Intrinsically Disordered Proteins using Reweighting based on NMR Chemical Shift

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Intrinsically disordered regions and proteins (IDR/Ps) underpin a wide range of vital biological processes but exhibit dynamic and heterogeneous conformations. Currently, many computational efforts seek to elucidate the structural ensembles of these disordered proteins, yet most methods still struggle to fully capture their conformational diversity. Here, we integrate structural libraries of various IDR/Ps—derived from coarse-grained molecular dynamics simulations and machine learning models—with experimental data obtained from NMR chemical shifts. Through a maximum entropy reweighting approach, we obtain reliable ensembles that more accurately reflect observed chemical shifts and reveal transient states. Our results highlight the importance of comprehensive sampling strategies for capturing diverse conformational states. Furthermore, we demonstrate that these weighted ensembles faithfully track conformational rearrangements under various environmental conditions, which are not fully captured by experiments alone. In addition, we provide dataset encompassing each IDP's specific structures along with their ensemble weights, offering a robust foundation for systematically exploring IDR/P structural landscapes, refining our understanding of their functional roles, and shedding light on processes related to misfolding and aggregation.

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(Poster 10)

Metal Substitution in Semi-constrained Systems: DFT Study on a Metalloenzyme

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Metal complexes with constrained or semi-constrained geometry play a crucial role in the coordination chemistry of metalloenzymes by imposing structural limits on the ligands. These constraints result in a pre-distorted coordination geometry, forming an entatic state of the protein. The entatic state of a metalloenzyme directly influences the thermodynamic and kinetic aspects across a broad range of chemical reactions by facilitating faster electron transfer and reaction kinetics. In this work, we selected the catalytic active center of human carbonic anhydrase II (CA II) and its four metal variants containing Co^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+} as the model system and conducted a density functional theory (DFT) study on their coordination chemistry. We imposed structural constraints on the active site to mimic the entatic state of the protein and tested various functional and basis set combinations to find the optimal combination for reproducing the experimental structures. We found that the native metal ion in metalloenzymes does not always exhibit the strongest binding, but the trend follows the Irving-Williams series, and that structural constraints make the energy landscape of the metal complexes more rugged. We anticipate that our findings can be utilized to design and tune the entaticity of the active site in artificial metalloenzymes.

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(Poster 11)

MORC2 is a phosphorylation-dependent DNA compaction machine

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The Microrchidia (MORC) family of chromatin-remodelling ATPases is pivotal in forming higher-order chromatin structures that suppress transcription. However, the exact mechanisms of MORC-induced chromatin remodelling have been elusive. Here, we report an *in vitro* reconstitution of full-length MORC2, the most commonly mutated MORC member, linked to various cancers and neurological disorders. MORC2 possesses multiple DNA binding sites that undergo structural rearrangement upon DNA binding. MORC2 locks onto the DNA using its C-terminal domain (CTD) and acts as a sliding clamp. A conserved phosphate-interacting motif within the CTD was found to regulate ATP hydrolysis and cooperative DNA binding. Importantly, MORC2 mediates chromatin remodelling via ATP hydrolysis-dependent DNA compaction *in vitro*, regulated by the phosphorylation state of its CTD. These findings position MORC2 CTD phosphorylation as a critical regulator of chromatin remodelling and a promising therapeutic target.

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(Poster 12)

Engineering Conjugated Polymer Nanoparticles for Enhanced Photodynamic Effects

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Conjugated polymers have garnered significant attention as a promising class of materials due to their diverse optoelectronic properties and high photostability. Previous studies have demonstrated that nanohybrids comprising a conjugated polymer donor (PCPDTBT), an acceptor (N2200), and gold nanoparticles—fabricated via a dispersion process using a phospholipid with a hydrophobically modified polar head group (D8PE-Ac)—exhibit markedly enhanced photothermal and photodynamic effects [1]. This enhancement arises from PCPDTBT acting as an energy harvester under 808-nm laser irradiation, absorbing light and exciting electrons, thereby facilitating charge and energy transfer to N2200. This process promotes the production of reactive oxygen species (ROS) for photodynamic cancer therapy, while simultaneous energy transfer from PCPDTBT to gold nanoparticles elevates the local temperature for photothermal therapy. However, the strong self-aggregation tendency of N2200 has hindered the formation of uniform nanoparticles, limiting its incorporation to less than 10 mol% relative to PCPDTBT and preventing optimization of compositions for maximal therapeutic performance. Moreover, efforts to enhance biocompatibility by incorporating polyethylene glycol (PEG) onto the surface of the nanohybrids have faced considerable challenges. To address these limitations, PEGylated phospholipids (D8PE-PEG) were introduced to improve biocompatibility and facilitate the formation of smaller, more uniform nanoparticles, thereby enabling compositional optimization and enhancing phototherapeutic efficacy.

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(Poster 13)

Analysis of Intramolecular Network in Protein Structure

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Detailed structural information about a protein is crucial for understanding its function. The structure of a protein is determined by non-covalent interactions between different amino acid residues, and these interactions form an intramolecular network. By analyzing the intramolecular network, the stability and functional characteristics of the protein can be systematically examined. During evolution, protein intramolecular networks adapt in response to physical and biological constraints. Therefore, it is important to understand the general principles governing intramolecular networks of proteins.

In this study, we analyzed the intramolecular networks within protein structures from five phylogenetically distant organisms: a virus, E. coli, Thermoprotei, Homo sapiens, and a mouse. These organisms were chosen due to their distinct features, such as evolutionary rates and widespread use as model organisms in biological research. We examined network topology by dividing the networks into subnetworks and calculating key metrics, such as network size and average degree, which are indicative of the structural complexity and connectivity within the protein. We further explored evolutionary characteristics by calculating sequence space free energy, a measure that reflects the stability and adaptability of protein structures over evolutionary time. Our analysis revealed significant differences in these metrics across the phylogenetically distant organisms, suggesting that the evolution of protein structure is influenced by specific biological and physical constraints unique to each lineage. This study demonstrates the potential of integrating statistical mechanics and network science to deepen our understanding of protein structure evolution.

(Poster 14)

Engineering Hybrid Vesicles for Targeted Drug Delivery in Triple-Negative Breast Cancer

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Triple-negative breast cancer (TNBC), defined by the absence of estrogen receptor (ER), progesterone receptor (PR), and HER2 expression, is one of the most aggressive and treatment-resistant subtypes of breast cancer. Despite the increasing need for targeted therapies, current delivery platforms face limitations in molecular specificity and stability. In this study, we developed hybrid vesicles through membrane fusion of bacterial extracellular vesicles (BEVs) and liposomes to deliver drugs selectively to PD-L1–positive TNBC cells. The hybrid vesicles were characterized using TEM, DLS, NTA, and FRET to evaluate their size distribution, fusion efficiency, and colloidal stability. Western blot analysis confirmed the retention of key BEV-associated protein markers in the hybrid structure. Preliminary in vitro results showed efficient and selective drug delivery to PD-L1–expressing TNBC cells with minimal off-target effects. These findings suggest that the BEV-liposome hybrid platform could serve as a promising next-generation nanotherapeutic system for TNBC treatment. [1-2]

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(Poster 15)

Hemicyanine-Coumarin Conjugates for Real-Time Simultaneous Detection of H_2S and H_2O_2 in Pathological Redox Analysis

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Hydrogen sulfide (H_2S) and hydrogen peroxide (H_2O_2) are particularly involved in cellular redox balance. For examples, H_2S is overexpressed in ROS-induced oxidative stress conditions. Accordingly, it is important to develop H_2S and H_2O_2 sensitive dual-sensing fluorescent probes to image production and extinction of H_2S and H_2O_2 within cells.

Until now, many single-detection-based probes capable of detecting either H_2S or H_2O_2 individually have been reported, but dual-detection probes capable of simultaneously detecting both are very rare. In this study, we aim to develop a dual-detection fluorescent probe that can simultaneously detect H_2S and H_2O_2 while providing independent detection signals for each. Using this system, we intend to monitor and image the quantitative changes of H_2S and H_2O_2 in cells in real time under various pathological conditions.

(Poster 16)

Counterintuitive distance-dependent bias in synaptic vesicle motion toward fusion sites in stimulated neurons

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Neuronal communication occurs through exocytosis of synaptic vesicles (SVs). However, dynamics of SVs undergoing exocytosis during stimulation is poorly understood. Here, we investigated real-time, three-dimensional motion of SVs undergoing exocytosis in presynaptic terminals during electrical stimulation and established a model that quantitatively explains the stimulation-dependent SV dynamics. We found both the straightness of SV trajectories and mean velocity toward their fusion sites increase about tenfold during electrical stimulation compared to their pre-stimulation values. Interestingly, SVs located farther from the fusion domain tend to move faster toward the fusion domain upon electrical stimulation. This causes a counterintuitive weak correlation between fusion times and the distances from the fusion site. The trajectory straightness of SVs and their distances from fusion sites exhibit strong heterogeneity, resulting in a broad distribution of SV fusion times. This allows neurotransmitters to be released gradually over an extended period of time, ensuring sustained neurotransmission without synaptic fatigue.

(Poster 17)

Elucidation of Equilibrium Size Distribution of Nanoparticles and Biomolecular Condensates

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Supersaturation and nucleus seed formation are universal processes that precede all phase transitions. Despite extensive research on nucleation, our understanding on supersaturation, and nucleus seed formation remains rudimentary. In this poster, we present the exact statistical thermodynamic formula for the saturation degree, the most-probable size distribution of mesoscopic nuclei, and their phase transition, introducing the mesoscopic state defined by temperature, the total monomer concentration, and the largest cluster size (LCS). These results show that supersaturation emerges even at equilibrium for mesoscopic nuclei systems and decreases with the LCS. The size-distribution of nucleus seeds is either a unimodal or a monotonically decreasing function of size, depending on the system and temperature. There exists a critical supersaturation condition under which nucleus seeds undergo a phase transition, during which the most probable size exhibits an abrupt change. In addition, we found that our non-classical nucleation theory fit well in real systems; Gold Nanoparticle, InP Quantum dot, FePt Nanoparticle, PRM-SH3-6His aggregate, mutant p53 aggregate, and IDP-2Yx2A micelle. This work can be extended to investigate diverse nucleation and phase transition phenomena prevalent across nature and industry.

(Poster 18)

Extensive Molecular Dynamics Simulations Reveal the Critical Role of Intrinsically Disordered Regions of Human Apurinic/Apyrimidinic Endonuclease in Diffusion Mechanisms

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The diffusion of DNA-binding proteins plays a vital role in biological processes such as DNA modification, transcription, and repair, as individual enzymes must efficiently locate and act upon multiple target sites. A prime example is human apurinic/apyrimidinic endonuclease 1 (hAPE1), which participates in the repair of DNA base excisions through diffusion-mediated mechanisms. hAPE1 comprises 318 amino acids, with its first 60 residues forming an intrinsically disordered region (IDR). While single-molecule studies have shown that hAPE1 locates its target sites via diffusion mechanisms, such as one-dimensional sliding and three-dimensional hopping, the molecular interactions between the IDR and DNA remain poorly understood. Structural biology approaches have provided detailed insights into the complex structure of the folded protein domains and DNA, but the specific role of the IDR in diffusion and target recognition is yet to be fully elucidated.

To address this knowledge gap, we conducted extensive molecular dynamics (MD) simulations using the AMBER force field with CUFIX corrections, significantly enhancing the accuracy of protein-DNA interactions. Over five independent 20-microsecond MD trajectories, we observed dynamic diffusion events characterized by diffusion coefficients on the order of $\mu m^2/s$. While the catalytic domain remained in contact with DNA during sliding, the IDR exhibited dynamic conformational fluctuations on the nanosecond timescale, continuously adjusting its contact points with DNA. Detailed analyses revealed that the IDR is crucial for the initial recognition of target sites, facilitates sliding along the DNA, and enables "monkey-bar" hopping between adjacent DNA molecules. To the best of our knowledge, this is the first atomistic MD simulation study to demonstrate the IDR-mediated control of hAPE1's diffusive behavior.

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(Poster 19)

Molecular Dynamics Study of Doxorubicin-Induced Cardiotoxicity: Unveiling the Role of Cardiolipin in Drug Membrane Permeation

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Doxorubicin (DOX) is a widely used chemotherapeutic agent, but its clinical use is limited by cardiotoxicity. Although DOX induces cardiomyocyte death via DNA intercalation and mitochondrial ROS production, the underlying molecular mechanism remains unclear. In this work, we applied all-atom molecular dynamics (AAMD) simulations to explore how cardiolipin (CL) lipids contribute to DOX-induced cardiotoxicity. Considering the heart-specific abundance of tetralinoleoyl cardiolipin (TLCL) within the mitochondrial membranes of cardiomyocytes[1], we developed outer (OMM) and inner (IMM) mitochondrial membrane models with variable TLCL levels. Additionally, we constructed a TLCL-enriched IMM (CL-IMM) model to reflect the crista junction microdomains of the IMM and analyzed the free energy landscapes governing DOX permeation through these membrane models. Given that DOX tends to be protonated under the acidic conditions of the mitochondrial intermembrane space, we investigated both its neutral (DOX0) and protonated (DOXP) forms to evaluate their differential permeation behaviors. Our simulations revealed that increasing TLCL content lowered the energy barriers for both forms of DOX during membrane translocation. Notably, the most prominent energy differences among membrane models appeared at the water-lipid interface, emphasizing the critical role of lipid head group interactions over those involving hydrophobic acyl chains. Furthermore, elevated TLCL levels induced membrane area expansion driven by changes in lipid head group orientation, regardless of DOX presence. We also observed a marked decrease in lateral membrane pressure on the surface of CL-IMM, likely attributable to increased electrostatic repulsion between negatively charged lipid head groups. Although DOXP exhibited stronger interactions with TLCL lipids, its higher permeation energy barrier compared to DOX0 suggests that deprotonation is a prerequisite for efficient membrane permeation. These findings provide new mechanistic insights into DOX-induced cardiotoxicity and highlight the possibility of modulating DOX protonation states as a potential therapeutic approach to alleviate its cardiotoxic effects.

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(Poster 20)

Effect of Cationic Lipid Composition on the Stability and Membrane Partitioning of AMP within Lipid Bilayers

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Cationic lipids are widely used in gene delivery systems for their ability to bind negatively charged nucleic acids.[1] In this study, we performed molecular dynamics (MD) simulations to investigate how the composition of cationic lipids affects the positional stability and permeation of adenosine monophosphate (AMP) through lipid bilayers composed of DOTAP (1,2-dioleoyl-3-trimethylammonium-propane), a cationic lipid, and DOPC (1,2-dioleoyl-sn-glycero-3-phosphocholine), a zwitterionic lipid. The potential of mean force (PMF) profiles were calculated to evaluate the free energy landscape of AMP across bilayers with varying DOTAP content.[2] To investigate the stability and energetics of AMP in the system, we analyzed thermodynamic integration (TI) energy components and examined bilayer properties such as area per lipid, hydrophobic thickness, and order parameters. These results demonstrate that increasing cationic lipid content enhances stability and membrane partitioning of AMP within the bilayer, providing insights into the rational design of lipid-based delivery systems.

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(Poster 21)

Characterization of the DNA Catenane: A Molecular Dynamics Simulation Approach

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Catenanes are mechanically interlocked molecules widely utilized in the construction of molecular machines, including molecular switches and motors, within the field of supramolecular chemistry. In this study, we studied the properties and behaviors of mechanical bonds in catenanes composed of small double-stranded DNA (dsDNA) minicircles using molecular dynamics (MD) simulations. Our findings reveal that due to the elliptical shape of the DNA minicircle, which has distinct long and short axes, the time correlations of relative translation and ring twisting exhibit double exponential decay. Additionally, we investigated that the rotational dynamics of the DNA minicircles are approximately 5 degrees per nanosecond. To neutralize the large negative charges of the PO4- groups in minicircle DNA, Na+ ions predominantly occupy the confined region between the two minicircles. These results provide essential insights into the fundamental properties of DNA catenanes, paving the way for their potential applications.

(Poster 22)

Exploring Dynamical Phase Transition via Double-Bias Trajectory Ensemble

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In this work, we explore far-from-equilibrium dynamics through a double-bias trajectory ensemble framework that simultaneously applies conjugate fields to both dynamical activity (s) and time-integrated energy (g). This method allows controlled sampling of non-equilibrium trajectories and reveals rich dynamical behavior beyond equilibrium predictions. Applied to the one-dimensional Ising model [1] and kinetically constrained models (KCMs) [2-3], our approach uncovers novel dynamical phase transitions, including energy-activity decoupling and counterintuitive phenomena such as “freezing-by-heating.” We further extend the method to the atomistic Kob-Andersen binary Lennard-Jones model, a realistic representation of metallic glass, constructing a g–T phase diagram that exhibits a first-order dynamical transition with upper and lower critical points [4]. Complementary structural analyses reveal changes in microscopic organization across phases, offering insight into the interplay between structure and slow dynamics. These results demonstrate the power of the double-bias ensemble in elucidating glassy behavior and complex non-equilibrium phenomena in both minimal and realistic systems.

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(Poster 23)

Chain Properties of Supercharged Proteins

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Supercharging a protein, by introducing a significant amount of charge, leads to extensive unfolding and stretching of the protein. However, the chain properties of the protein cannot be described by a simple polymer model, mainly due to the conformational constraints in the dihedral space. In this work, we utilized atomistic Monte Carlo simulations to understand the chain properties of supercharged proteins. We focused on proteins with a single intramolecular disulfide bond, which forms a tadpole-like structure after supercharging. We systematically changed the sequence composition and the position of the disulfide bond, spanning various topologies and sequences. By analyzing several measures of the global chain properties, we found that the dihedral angle distribution has no significant effect on determining the chain properties, and that the tail part is more crucial than the ring part for the overall properties. We anticipate that this work will contribute to a deeper understanding of the polymeric features of proteins, and that our findings will be extended to unfolded and intrinsically disordered proteins.

(Poster 24)

Design and Engineering of Phase Separation Driver Proteins

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Liquid-liquid phase separation (LLPS) plays a crucial role in the spatiotemporal compartmentalization of eukaryotic cells, with emerging interest in its underlying mechanisms. A significant subset of LLPS-driving proteins comprises multi-domain proteins characterized by folded domains linked by disordered segments. Based on the established knowledge of LLPS, we designed phase separation drivers by constructing trimers of fluorescent proteins, and investigated their LLPS behaviors. We quantified the phase separation propensity of these trimers through saturation concentration measurements and assessed the material properties of resulting condensates. We compared the LLPS propensity of three fluorescent protein trimers with different binding affinities by measuring their saturation concentration using three distinct methods: turbidity assay, spin-down assay, and imaging assay. Consequently, we observed a correlation between binding affinity and LLPS propensity. We propose that our system can serve as a minimalistic model for investigating the molecular principles of phase separation driver proteins. Our findings contribute to a deeper understanding of LLPS phenomena and may inform the development of strategies for modulating cellular organization and function.

(Poster 25)

Towards Accurate Determination of Binding Free Energy Using Molecular Dynamics Simulations

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The binding free energy between a protein and its ligand partner is crucial for predicting medicinal effects in pharmacology. To computationally obtain binding affinity data, various methods based on molecular dynamics simulations have been developed. Among them, umbrella sampling is a widely used technique for calculating binding free energy by sampling along the association/dissociation process. However, it has been reported that binding free energy is highly sensitive to the sampling method; factors such as the initial structure, number of samples, and dissociation path can significantly influence the results. In this work, we performed umbrella sampling with varying sampling times to investigate changes in the potential of mean force (PMF) and its relationship with the number of sampling windows. Our findings indicate that PMF is influenced by sampling time. Furthermore, we identified specific window regions that have a pronounced impact on the PMF. Based on these results, we propose a sampling method that enhances the efficiency and reproducibility of PMF calculations. We believe that our method can improve the accuracy of binding free energy estimations, thus contributing to advancements in computational drug design and engineering.

(Poster 26)

Elucidating $LiPF_6$ Ion Pairing Behavior in DMC and PC : A Molecular Dynamics Simulations

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This study investigates the solvent-dependent binding characteristics of lithium hexafluorophosphate ($LiPF_6$) to elucidate how ion-pair dissociation affects the performance of lithium-ion battery electrolytes [1]. Molecular dynamics (MD) simulations and the umbrella sampling method were employed to quantitatively evaluate the binding free energy of two $LiPF_6$ ion pairs in dimethyl carbonate (DMC, $\varepsilon \approx 3.1$) and propylene carbonate (PC, $\varepsilon \approx 65$), which differ significantly in their dielectric constants (ε) [1–2]. The results show that in the low-ε environment of DMC, $LiPF_6$ ion pairs form strong associations, making solvation difficult and potentially reducing ionic conductivity and battery performance. In contrast, in the high-ε PC solvent, the ion pairs are more loosely bound and readily dissociate, leading to enhanced ion mobility and solvation behavior [2–4]. This study demonstrates that the physicochemical properties of organic solvents directly influence ion-pair formation and dissociation in electrolytes, providing a fundamental understanding of the development of high-performance and high-stability electrolytes [1–2].

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(Poster 27)

Exploring In-Context Learning in Large Language Models for Molecular Property Prediction

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Recent advances in transformer-based large language models (LLMs) have shown remarkable capabilities across scientific domains, including chemistry [1–4]. This study explores the use of in-context learning (ICL) in LLMs for predicting molecular properties from SMILES strings. A 50-shot prompt format was used to evaluate the model across eight tasks: molecular weight (MW), LogP, topological polar surface area (TPSA), molecular refractivity (MolMR), fraction of sp^3-hybridized carbons (sp3), and three graph-based indices (Balaban J, Hall–Kier Alpha, and Chi1v), using the ESOL dataset [5]. Property values were computed using RDKit [6], and model performance was assessed using mean absolute error (MAE) and R^2 scores [7]. The LLM demonstrated strong performance across most tasks, often comparable to or exceeding that of traditional machine learning models. To probe the boundary between retrieval and reasoning, a linearly transformed version of MW was introduced, with results suggesting that the model engages in nontrivial inference from contextual examples. Furthermore, statistical distributions of each property (mean, standard deviation, skewness, kurtosis) were analyzed and visualized using t-SNE [8]. This projection revealed a separation between tasks where LLMs performed well and those favoring machine learning baselines, indicating that underlying distributional characteristics may influence task difficulty in ICL settings. Overall, this study offers insights into both the potential and limitations of LLMs for molecular property prediction using example-driven reasoning.

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(Poster 28)

Molecular Dynamics Simulation of the Effect of Cholesterol on the Interaction Between Lipid Bilayer and Micelle

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Micelle is one of the methods used for drug delivery, and its unique properties make it an effective option. Micelle has advantages of transporting drugs regardless of hydrophilicity or hydrophobicity, as well as easy maintenance with low cost. Anionic surfactants are commonly used to form a micelle, and in this study, we used SLES, which is less harmful to the human body, to create a micelle for our experiments. While numerous studies have explored the interaction between a surfactant micelle and a cell membrane, research on how cholesterol in the cell membrane influences this interaction has been lacking. In this study, we made both ceramide and DMPC bilayers, and by varying the cholesterol mole fractions for each, we created a total of six systems to investigate the effect of cholesterol on the interaction between lipid bilayers and the SLES micelle. To analyze this, we calculated the structural characteristics of the micelle and the lipid bilayer when the micelle approached the bilayer at different cholesterol mole fractions. Additionally, the umbrella sampling method was used to compute the potential of mean force (PMF) profiles for the micelle approaching to the lipid bilayer surface and for surfactant transfers from the micelle to the lipid bilayers. Through this study, we identified the effect of cholesterol on the interaction between a micelle and a lipid bilayer. In a lipid bilayer composed of ceramide alone, the micelle maintained a hemispherical shape. However, when cholesterol was included, several surfactants in the micelle were observed to insert into the bilayer, with a higher mole fraction of cholesterol leading to greater incorporation of SLES molecules. In a DMPC bilayer, the micelle retained its spherical shape as the cholesterol mole fraction increased, but the bilayer's fluidity decreased.

(Poster 29)

Excitonic Behaviors of 2D Tetracene Crystals Using Absorption and Emission Spectroscopies

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Recent studies on two-dimensional molecular crystals (2DMCs) revealed their unique physical, electrical, chemical, and optical properties distinct from their bulk counterparts. Molecular crystals are expected not only to manifest such size effects like the conventional inorganic 2D systems, but also enable diverse future applications. In this work, we exploited top-down mechanical exfoliation to form 2D tetracene (Tc) crystals and investigated their geometric and electronic structures using scanning probe microscopy and variable-temperature photoluminescence spectroscopy, respectively. Significant variations in absorption and emission spectra were induced as a function of temperature and thickness. The origins of the spectral changes will be explained in terms of phase transitions, trap states and electron-phonon couplings. We will also discuss the fate of molecular excitons confined in the 2D systems based on time-resolved photoluminescence measurements. The unique photophysical properties of two-dimensional Tc revealed in this work will lead to a deeper understanding of excitonic behaviors in low-dimensional molecular solids

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(Poster 30)

Electronic Davydov Splitting in Exfoliated 2D Tetracene Crystals

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2D molecular crystals grown by physical vapor deposition using inorganic 2D crystals as assembly templates have revealed intriguing novel photophysical [1, 2] and electrical [3] properties. In this work [4], we report on a mechanical exfoliation, a top-down approach, to form 2D crystals of various polyaromatic molecules. This approach, compared to the conventional bottom-up method, can offer advantages in structural quality and thickness control besides less limitation on supporting substrates. We evaluated both methods by quantifying the crystallinity of 2D Tetracene (Tc) crystals using wide-field photoluminescence (PL) imaging. Polarimetric analysis, based on two orthogonal polarization components, revealed long-range order that spanned more than several microns. Polarized absorption also showed thickness-dependent Davydov splitting, which can be attributed to varying crystalline structures and mixing of Frenkel and charge transfer exciton states [5]. We measured diffraction patterns by transmission electron microscope (TEM) to compare the structure of exfoliated and evaporated Tc crystals. The $\vec{a}$ of exfoliated Tc is 7% bigger than reference value [6] and 4% bigger than evaporated one. This subtle structural difference in the sub-Å range may change the contribution of the charge transfer state [7]. Thus, Davydov splitting is differentiated according to two methods. This study demonstrates that mechanical exfoliation can be applied to various molecular systems to generate their 2D crystal forms, potentially leading to new findings and applications. Also, it highlights the connection between molecular crystal structure and optical properties, which has been absent from molecular crystal research.

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(Poster 31)

Artificial intelligence-based prediction of septic patient's fate dynamics

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Acute critical illnesses, particularly sepsis, pose significant challenges due to their sudden life-threatening nature and heterogeneous pathologies, demanding early detection and appropriate treatment. The lack of gold standards for early sepsis diagnosis has led to the exploration of deep learning (DL) methods for diagnostic and prognostic purposes, despite their opaque decision-making processes. Here, we propose a systematic and transparent artificial intelligence (AI)-based prediction model, which integrates a DL module for early sepsis diagnosis, an explanation module for assessing feature importance and identifying key features, and a module for constructing the optimal descriptor, a function of key features, which is useful for prediction of the patient-state dynamics. Our optimal descriptor, named the Septic Infection-Related Risk Index (SIRRI), is composed of eight features related to infection and inflammation biomarkers, effectively representing the severity of pathology in sepsis patients. In addition, we develop a prognosis model based on a set of reaction-Fokker Planck equations that govern the time evolution of the SIRRI distributions for patients at various pathological stages. Our model provides accurate predictions for the time-dependent mortality and recovery rates of sepsis patients, based on their SIRRI values at the onset of sepsis. We propose SIRRI as an effective descriptor for both diagnosis and prognosis in clinical practice, with potential applications that extend beyond sepsis to other acute critical illnesses.

(Poster 32)

Time evolution of delayed birth-death processes

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The occurrence of birth and death is ubiquitous throughout the universe. In many situations, a product or customer undergoes “birth” through two processes: creation and maturation. During maturation, another creation process begins, followed by the annihilation of the product. This process can be referred to as a delayed birth-death process since maturation delays birth. In this study, the transient distribution of the number of products or customers undergoing a delayed birth-death process is presented. The integro-differential equation governing the time evolution of a delayed birth-death process was obtained after determining the number distribution of the product or customer at an arbitrary time. Herein, the derivation of the transient distribution considers all the cases associated with the system size (corresponding to the number of products or customers undergoing birth-death processes) at a specific time. Furthermore, the statistics of the system size for delayed birth-death processes were derived based on the transient distribution of the system size. The analytic formulas were consistent with previous results and were confirmed to be accurate in a stochastic simulation. This work contributes to the quantitative understanding of the transient dynamics of delayed birth-death processes.

(Poster 33)

Quantitative Understanding of Cell Signal Propagation and Adaptative Gene Expression Dynamics: Beyond Classical Systems Biology

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Cellular adaptation to environmental changes involves a series of complex biochemical processes. These processes are complex time-delayed processes, making it challenging to quantitatively describe their dynamics using the conventional chemical kinetics based on rate constant concepts. Here, we propose a new type of chemical dynamics model for the cell signal propagation and adaptation network that is composed of several submodules, including sensing and signal transduction, adaptive gene expression, post-translational modification or protein maturation, and protein degradation. In this model, dynamics of each network module is characterized by its own reaction time distribution. Starting from our model, we obtain the Chemical Fluctuation Theorem for the signal propagation and adaptive gene expression, which shows how the mean and variance of the signal-induced gene expression levels are related to the reaction time distributions of the modular networks composing the entire network. In particular, our theory predicts that the time-delayed dynamics of the adaptation initiation module, comprising signal sensing and propagation and gene activation governs the cellular signal response dynamics but little affects the steady-state mature protein level; in contrast, the protein maturation dynamics strongly affects the cell-to-cell variability in the mature protein level, which exhibits a non-monotonic dependence on the maturation time randomness. Our theory provides a unified, quantitative explanation for the dynamic responses of various *E. coli* genes to antibiotic stresses and transcriptional induction.

(Poster 34)

Effects of *Lactobacillus gasseri* on the Suppression of Muscle Loss: Analysis of Protein Synthesis and Degradation Pathways in a Mouse Model and Cellular Model of Sarcopenia

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Sarcopenia is a condition characterized by a loss of skeletal muscle mass and muscle function due to a variety of causes, including ageing, cancer, chronic disease and poor nutrition. In this study, we investigated the anti-sarcopenic effects and mechanisms of *Lactobacillus gasseri* isolated from human milk using animal and cellular models of sarcopenia. The animal study used the Balb/c model in which muscle atrophy was induced with the synthetic glucocorticoid dexamethasone and *L. gasseri* was administered orally for 21 days. Measurements of muscle mass and function in dexamethasone-injected mice showed a significant decrease in skeletal muscle mass and function, which were significantly restored in mice orally treated with *L. gasseri.* Dual-energy X-ray absorptiometry (DXA) showed that *L.gasseri* inhibited dexamethasone-induced loss of lean body mass both in the whole body and in the hindlimb. In cellular studies, C2C12 cells were used as a model of sarcopenia. C2C12 myoblasts were differentiated into myotubes and treated with *L. gasseri* culture supernatant (1.25-10%) and dexamethasone (100 μM) for 2 days. Myotube width was reduced by dexamethasone treatment, which was prevented by *L. gasseri* culture supernatant. Signaling pathways involved in protein synthesis and degradation in muscle tissue and C2C12 myotube cells were analyzed by qPCR, Western blot, ELISA and immunofluorescence. The levels of MyoD, a myogenesis-related transcription factor, and MyHC, a muscle contractile protein, were significantly increased in the *L. gasseri*-treated group. It was found that the phosphorylations of Akt and mTOR were increased along with increased IGF-1 expression, confirming that the protein synthesis pathway was activated. Conversely, the expressions of MAFbx/Atrogin-1 and MuRF1, which induce myoprotein degradation, along with their transcription factor FOXO, were decreased in the *L. gasseri*-treated group, suggesting that the protein degradation pathway was inhibited. In conclusion, this study suggests that *L. gasseri* may be a promising probiotic candidate for the suppression of sarcopenia.

(Poster 35)

Cas12a-based gene detection using single-molecule fluorescence imaging

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Some CRISPR-associated (Cas) proteins exhibit *trans*-cleavage activity, which non-specifically cleaves single-stranded DNA or RNA. The *trans*-cleavage activity of Cas12a has been widely used to develop sensitive gene detection methods due to its multiple-turnover enzymatic capability. Most Cas12a-based gene detection methods accompany with a pre-amplification step. However, a pre-amplification step often suffers from the tedious design of primers and inevitable base substitution errors by polymerases, making it unsuitable for quantitative analysis. Here, we report a single-molecule fluorescence assay for ultrasensitive and quantitative gene detection utilizing the trans-cleavage activity of Cas12a without pre-amplification. We immobilized a hairpin DNA probe with a stem-loop structure, where the single-stranded DNA loop can be cleaved by *trans*-cleavage of Cas12a. A fluorophore and quencher pair was attached at the end of the stem, producing fluorescence only in the presence of target gene that activates *trans*-cleavage. The appearance of fluorescent spots, visualized through single-molecule fluorescence imaging, was proportional to the amount of target gene, enabling its quantification. To enhance the detection sensitivity, we optimized various experimental conditions, including Cas12a variants, ion concentrations, and hairpin DNA probe sequence, and successfully detected the E gene of SARS-CoV-2 down to sub-picomolar levels without any pre-amplification steps.

(Poster 36)

Quantifying Bacterial Stress and Recovery through New Chemical Dynamics

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Microorganisms survive harsh environments by dynamically reprogramming transcription through competition between the housekeeping sigma factor RpoD and alternative sigma factors. During stress, RpoS—a key regulator of the general stress response—accumulates and activates protective genes. After stress removal, RpoS levels decline while RpoD regains control, enabling cellular recovery and growth.

Here, we present a chemical dynamics model that captures this post-stress regulatory transition in *Escherichia coli*. Calibrated with experimental measurements of the timing of the first cell division after stress, the model quantitatively reproduces population-level regrowth dynamics.

Our results underscore the central role of sigma factor switching in bacterial adaptation and persistence, providing a mechanistic understanding of how cells restore normal physiology following stress. This framework offers potential insights for designing strategies to combat persistent infections and improve antimicrobial efficacy.

(Poster 37)

MolCube-APPs: An Integrated Platform for Automated Preparation of Molecular Dynamics Simulation Systems

Hajin Lee and Wonpil Im

MolCube, Inc

Efficient and accurate preparation of input systems for molecular dynamics (MD) simulations remains a significant bottleneck in computational research workflows.

We present **MolCube-APPs**, a comprehensive, modular platform designed to automate and streamline the construction of simulation-ready molecular systems.

MolCube-APPs offers a series of interoperable modules tailored for distinct stages of system preparation:

- **PDB Reader** enables the import, correction, and modification of biomolecular structures from public repositories or custom sources, supporting CHARMM, AMBER, and Martini force fields.
- **Ligand RM (Reader & Modeler)** facilitates ligand structure modeling, alignment to reference structures, and force field parameterization based on 2D/3D inputs.
- **Solution Builder** and **Membrane Builder** construct solvated and membrane-embedded systems, respectively, offering customizable solvent conditions, ion concentrations, lipid compositions, and box geometries.
- **Ligand Docker** supports automated setup for protein-ligand docking simulations by defining docking boxes and managing ligand placement.
- **AFES (Alchemical Free Energy Simulator)** enables generation of simulation-ready input files for relative and absolute binding free energy (RBFE/ABFE) calculations across major MD engines, including GROMACS Non-eq TI, AMBER-TI, and BLaDE.

In addition, **MolCube-Simulator** facilitates job submission to designated cloud systems and efficient management of simulation tasks, while **MolCube-Analyzer** provides simulation trajectory analysis capabilities within the SaaS environment.

MolCube-APPs is delivered entirely through a **cloud-based SaaS model**, providing users with seamless access to scalable computational resources for large-scale MD simulations.

The platform maximizes user convenience through automated environment setup, intuitive interfaces, and robust data security measures, ensuring protection of intellectual property (IP) while enabling rapid, reproducible, and flexible drug discovery research.

(Poster 38)

Curvature-dependent lipid domain patterning in phase-separating liposomes

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The phase behavior of lipid mixtures in planar membranes is well-characterized. However, how lipid domains organize in highly curved systems, such as exosomes, remains poorly understood. In this study, we investigated the influence of curvature on the spatial arrangement of lipid domains within phase-separating liposomes. Our study employed ternary lipid mixtures comprising saturated lipids (1,2-dipalmitoyl-sn-glycero-3-phosphocholine, DPPC), unsaturated lipids (1,2-dilinoleoyl-sn-glycero-3-phosphocholine, DIPC), and cholesterol (CHOL) at a ratio of 50:30:20. To investigate these systems under varying curvature conditions, coarse-grained molecular dynamics simulations were conducted using MARTINI 2.0 force field.

By applying compression along the z-axis, we transformed liposomes into discoidal structures with fixed heights of 12, 16, and 20 nanometers. The results reveal a clear relationship between the degree of compression and the positioning of lipid domains. At lower curvature with height of 20 nm, lipid domains showed no significant preference for either flat or curved surfaces. Under moderate compression with height of 16 nm, DPPC/CHOL-rich domains were observed to localize at the curved edges, while under strong compression with height of 12 nm, DIPC-enriched domains preferentially occupied the same regions.

These findings indicate that domain segregation in compressed liposomes arises from a combination of several factors, including internal pressure variations, pore formation and closure, and lipid-dependent bending modulus. Remarkably, in case of strong compression with a height of 12 nm, the discoidal vesicles preserved their shape and distinct domain segregation even after the compressive force is removed, suggesting irreversible pattern formation. This study emphasizes the potential of external compression as a effective strategy for the development of lipid domain patterns on soft nanostructures. By curvature effects, lipid domain positioning can be precisely controlled, opening new possibilities for developing functional nanomaterials based on lipid vesicles.

(Poster 39)

Evaluating Molecular Dynamics Approaches for Melting Point Prediction of Organic Crystals

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Predicting melting points with high accuracy is fundamental to understanding the molecular-scale mechanism of crystal growth and phase transition in molecular dynamics (MD) simulations. In this study, we used direct MD simulations to estimate the melting points of nitromethane and acetic acid, focusing on three primary objectives: first, evaluating the predictive performance of widely used force fields (CGenFF, OPLS, GAFF); second, examining the effectiveness of different MD simulation strategies, including solid/liquid, vapor/solid/liquid/vapor, vapor/solid/vapor, and solid alone systems; and third, analyzing the role of timescale and anisotropy in crystal melting and growth dynamics. Our results demonstrate that melting points are not accurately predicted by any of the widely used force fields, emphasizing the need for improvement. Consistent melting points were obtained across all MD Simulation approaches except for the solid-alone simulation, while continuous heating in the vapor/solid/vapor system proved to be effective. Significant differences were observed in the timescales of crystal growth and melting, with nitromethane melting in 20 ns and acetic acid requiring 200 ns. Anisotropy in both crystal growth and melting is evident, being considerably more pronounced in acetic acid than in nitromethane. This study serves as guideline for MD-based melting point predictions of molecular crystals.

(Poster 40)

Analysis of tracer diffusion confined in a dynamic network

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Particles confined within polymer networks exhibit subdiffusion at short timescales and normal diffusion at long timescales. To better understand the subdiffusive behavior of tracer particles in polymer networks, we utilized Brownian dynamics simulations to investigate their diffusion within a simplified model of a dynamic network. This model is composed of small network particles located at each lattice point, oscillating under the influence of a harmonic potential, resulting in the network flexibility modulated by the harmonic force constant. To elucidate the microscopic origins of subdiffusive behaviors, we analyzed the hopping dynamics and the percolation of tracers within the dynamic network. Our findings demonstrate that the onset of subdiffusion is closely linked to the hopping dynamics and the network percolation. This study provides physical insights into the subdiffusion phenomena observed in various condensed materials, including hydrogels and cell nuclei.

(Poster 41)

Chemo-Metabolic Single-Cell Nanoencapsulation and Construction of Enzyme-Powered Cell Microrobots

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Inspired by cryptobiosis in nature, chemists have developed various strategies to construct cell-in-shell nanobiohybrids, which enhance cellular protection and endow cells with exogenous functions. However, the approaches still lack the biological autonomy observed in natural cellular responses to environmental changes. Here, we present a chemo-metabolically coupled method for forming cell-in-shell structures in cell growth media. Specifically, the strategy integrates alcohol fermentation by *Saccharomyces cerevisiae* with a shell-forming reaction, aided by an extrinsic catalytic cascade reaction involving alcohol oxidase and horseradish peroxidase. Notably, shell formation occurs in parallel with cell proliferation, yielding anisotropic cell-in-shell structures. The anisotropic nanobiohybrids are further tailored for the construction of enzyme-powered cell microrobots, upon conjugation with urease.

(Poster 42)

Synthesis of Janus Particles with Metal-Organic Complexes in Biphasic Water-Oil Systems

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Janus particles hold significant potential for advanced applications in drug delivery, bioimaging, sensing, and therapeutics.[1-3] However, their synthesis from homogeneous precursors typically involves multistep procedures and harsh conditions. Here, we present a one-step, one-pot strategy for synthesizing Janus microparticles via biphasic interfacial self-assembly of supramolecular metal–organic complexes (MOCs) in vortex-assisted water–oil systems.[4,5] This method enables partial MOC coating of individual microparticles, with the coating ratio easily tunable by changing the oil phase. Furthermore, our platform supports both simultaneous and sequential orthogonal functionalization of the two distinct faces of the Janus particles with functional entities, such as proteins and DNA. This facile and scalable approach provides an efficient route for the synthesis of multifunctional Janus microparticles with broad applicability in bioengineering and nanomedicine.

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(Poster 43)

Enhanced Sampling of Complex Molecular Systems via Hybrid All-Atom/Coarse-Grained Resolution Exchange Molecular Dynamics

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Systems such as intrinsically disordered proteins (IDPs), ionic liquids, and polymers often exhibit complex energy landscapes with substantial energy barriers between conformational states, making them challenging to simulate using conventional molecular dynamics (MD) techniques. Traditional approaches namely, all-atom (AA) and coarse-grained (CG) models offer trade offs between resolution and efficiency: AA models provide detailed molecular interactions but struggle with transitions over high energy barriers, while CG models facilitate faster sampling but sacrifice atomic-level detail. To overcome these limitations, we propose a hybrid simulation framework that integrates AA and CG models within a resolution exchange molecular dynamics (REMD) protocol. This method enables dynamic resolution switching between AA and CG representations, enhancing sampling efficiency while preserving structural accuracy when needed. We applied this hybrid REMD approach to a binary mixture system and evaluated its effectiveness by comparing the observed mixing behavior with that obtained from conventional AA-only simulations. The results demonstrate that our method successfully captures complex system behavior while improving computational efficiency.

(Poster 44)

Redesigning UnaG-Bilirubin Fluorogenicity: Self-Renewable NIR Tags for Super-Resolution Microscopy

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Fluorophores with reversible and exchangeable properties hold great promise for extended live-cell imaging, enabling dynamic visualization of intracellular processes over time. UnaG, a ligand-dependent fluorescent protein derived from the Japanese eel, fluoresces brightly upon binding the endogenous metabolite bilirubin. With a high quantum yield (0.51) and emission at 527 nm, UnaG is well-suited for super-resolution microscopy (SRM). However, its blue-green emission and reliance on high-intensity excitation limit its utility in long-term live-cell imaging due to photobleaching and background autofluorescence. To overcome these challenges, we engineered a red-shifted, self-renewable UnaG–bilirubin system by chemically modifying bilirubin while preserving its strong non-covalent interaction with UnaG. By targeting the propionate residues near UnaG's binding cavity, we successfully extended the emission into the red and near-infrared range without disrupting binding affinity. Bilirubin was conjugated to PEG-diamine and further linked to red-emitting fluorophores such as Rhodamine B and Alexa Fluor 647, producing probes that mimic the photophysics of native bilirubin while emitting at longer wavelengths. Importantly, these red-emitting probes do not require reducing agents or oxygen scavengers, and demonstrate robust fluorescence both *in vitro* and in live-cell environments. This innovative system not only reduces the need for high-power lasers but also enhances photostability and imaging depth, making it ideal for prolonged single-molecule localization microscopy under physiological conditions. Our approach paves the way for expanded applications of UnaG in far-red SRM, enabling multiplexed, long-term imaging in complex biological systems.

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(Poster 45)

Diffusion-Based Generative Model of Protein-DNA Complex Ensembles

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Traditional sequence-to-structure models based on AI, such as AlphaFold[1], primarily sample native-like conformations, limiting their ability to capture the full conformational landscape of biomolecules. Inspired by the transition from text-to-image to text-to-video models, which are cutting-edge in the AI field, we develop a sequence-to-ensemble model[2] that generates diverse conformations beyond the native state. Our diffusion-based approach learns the underlying conformational distribution from extensive molecular dynamics simulations, enabling accurate sampling of biologically relevant structural ensembles. This method proves particularly effective for complex biomolecular interactions, such as protein-DNA binding, where structural dynamics plays a crucial role. Furthermore, our model achieves robust performance even with limited training data, making it suitable for systems with sparse structural information. By capturing the dynamic nature of biomolecules, our framework enhances structure-based predictions and provides valuable insights into functionally important conformational transitions.

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(Poster 46)

DeepFold-PLM: Accelerating Protein Structure Prediction with Optimized Homolog Detection and Protein Language Models

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Deep neural network-based methods such as AlphaFold have demonstrated remarkable accuracy by leveraging evolutionary information from multiple sequence alignments (MSAs). However, generating MSAs can be both time-consuming and resource intensive. DeepFold-PLM offers a novel approach to protein structure prediction by addressing the computational challenges of conventional MSAs. DeepFold-PLM integrates protein language models (PLMs) from ESM and Ankh to convert sequences into high-dimensional vectors. These models are fine-tuned through contrastive learning optimizing the clustering of homologous sequences. This strategy enables rapid homolog detection without relying on progressive alignment or dynamic programming. Benchmarking on CASP15 targets shows that DeepFold-PLM achieves TM-scores comparable to AlphaFold 2 and JackHMMER while offering near-constant time scaling in its MSA search pipeline. Furthermore, the capability to generate dense vectors offline significantly enhances retrieval speeds, making the pipeline highly scalable. Overall, DeepFold-PLM presents a robust, high-throughput solution for protein structure prediction, particularly beneficial for processing large datasets with reduced computational overhead.

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(Poster 47)

Refining ff19SB-OPC for Super Accurate MD Simulations of Proteins, Nucleic Acids, and Their Complexes

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Accurate molecular dynamics (MD) simulations depend critically on the underlying force field. However, many commonly used force fields tend to overestimate intermolecular attraction, leading to artificially low diffusion and restricted dynamical sampling in simulations. While the latest AMBER ff19SB with the OPC water model (ff19SB-OPC) offers enhanced stability and accuracy in many systems, we observed that it can still overestimate intermolecular attractions. In this work, we refined the original ff19SB-OPC force field to improve its accuracy across a broad range of biomolecular systems, including proteins and nucleic acids. Our approach involved adjusting the Lennard-Jones parameters, guided by osmotic pressure data obtained from over 40 different small molecule systems. Using this refined protocol, a 100-microsecond simulation of the TrpCage protein captured multiple folding–unfolding events, with the resulting free energy of folding agreeing with experimental measurements within 1 kT. For proliferating cell nuclear antigen (PCNA), a 10-microsecond simulation under the original force field produced a diffusion coefficient of 0.5 $\mu m^2/s$, significantly lower than the experimental value of 2.3 $\mu m^2/s$. However, the refined force field corrected this discrepancy, yielding diffusion properties much closer to experiment. Moreover, comparison with other commonly used AMBER and CHARMM force fields revealed clearer improvements in diffusion predictions, demonstrating the robustness of our refinements. Collectively, these results highlight the enhanced predictive power of the updated ff19SB-OPC parameter set, offering a more reliable framework for MD simulations of proteins, nucleic acids, and their complexes.

(Poster 48)

ComMat: Protein loop structure prediction by community-based deep learning and its application to antibody CDR H3 loop modeling

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As of now, more than 60 years have passed since the first determination of protein structures through crystallography, and a significant portion of protein structures can be predicted by computers. This is due to the groundbreaking enhancement in protein structure prediction achieved through neural network training utilizing extensive sequence and structure data. [1, 2] However, substantial challenges persist in structure prediction due to limited data availability, with antibody structure prediction standing as one such challenge. In this paper, we propose a novel neural network architecture that effectively enables structure prediction by reflecting the inherent combinatorial nature involved in protein structure formation. The core idea of this neural network architecture is not solely to track and generate a single structure but rather to form a community of multiple structures and pursue accurate structure prediction by exchanging information among community members. Applying this concept to antibody CDR H3 loop structure prediction resulted in improved structure sampling. Such an approach could be applied in the structural and functional studies of proteins, particularly in exploring various physiological processes mediated by loops. Moreover, it holds potential in addressing various other types of combinatorial structure prediction and design problems.

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(Poster 49)

Energy-Based Machine Learning for Continuous Free Energy Surface Estimation and Infinite-Horizon Variational Path Sampling

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Elucidating the exact and useful relation between controllable parameters and intractable but interesting quantities is central in theoretical chemistry, as well as in the development of new methodology for multi-scale computational chemistry. We present a new variational principle for inferring free-energy surfaces from multiple canonical ensembles and associated thermodynamic work. Classical free-energy estimators are ill-posed or computationally intractable for continuous or multivariate collective variables, while generative model-based methods improve tractability but use only data, neglecting the biasing potential information necessary for Boltzmann statistics. To address this gap, we rederive classical estimators within a statistical learning framework that models the joint configuration–control parameter distribution using the principle of minimum discrepancy. Motivated by this new viewpoint, we introduce a family of statistically consistent and tractable estimators. This approach extends the equipartition theorem, introduces transferable bottom-up coarse-graining techniques, and proves effective in estimating free-energy surfaces in cases with sparse sampling and multivariate spaces where existing methods struggle. We apply this methodology to model the effective Hamiltonian describing water density fluctuations with multiple observation volumes, and fluctuations in atomic electrode charges of an ionic-liquid nanocapacitor.

Motivated by the relation between force, free-energy, equilibrium distribution and their estimators, in the latter part, we propose a relation between policy, value, and steady-state distribution in reinforcement learning (RL) applied to sampling *s,g*-path ensemble. RL—a broad family of variational sequential decision-making—has recently been applied to sampling rare trajectories. However, understanding of the physical meaning in the statistically learned elements: policy and value, as well as the more direct relation between them, is limited. Here, we argue equivalence in the characterization of optimal policy and optimal drift force, and express optimal drift with gradient of the optimal value function and the current-like observable coupled to the *s*-control parameter. This also implies that the steady-state probability density of the *g*-ensemble with overdamped Langevin dynamics is computable from the learned value function. We verify this relation through numerical experiments and offer a more sample-efficient variational path sampling alternative to the existing algorithms.

(Poster 50)

Phase Separation of Amino Acid Derivatives and Water: Molecular Dynamics Study

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Biological systems utilize the phase separation of biomolecules in cells. This mechanism plays a crucial role in regulating biological reactions and facilitating the spatiotemporal separation of biomolecules in vivo. Phase separation can induce the local accumulation of particular molecules, hence acting as a catalyst for biological reactions. Thus, it is important to understand the molecular principles of biomolecular phase separation.

To obtain insight into biomolecular phase separation, we employ a simple model system that can undergo phase separation and simulate its phase behavior using molecular dynamics (MD) simulations. The key player in our model system is an amino acid protected by the Fmoc group. The Fmoc-protected amino acid contains both hydrophobic (Fmoc) and hydrophilic (amino acid) groups, and the balance between them can be easily controlled by using different side chains. When mixed with water, the Fmoc-protected amino acid exhibits rich phase behaviors, depending on its side chain.

This study investigates the impact of amino acid polarity on phase separation. By combining molecular dynamics (MD) simulations with the simulated annealing method, we successfully reproduced experimental results and analyzed the phase separation mechanisms driven by polarity differences at the molecular level. Our findings demonstrate that even subtle differences in polarity can significantly influence collective behaviors and phase separation patterns, providing important insights into the principles underlying complex phase separation processes in biological systems. This study highlights how discoveries in simple molecular systems can serve as a foundation for understanding the mechanisms governing biomolecular behavior and offers new directions for research on molecular dynamics.