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		Sungho Yoon (Chung-Ang Univ.)	Hyonseok Hwang (Kangwon Natl. Univ.)	Hae Sung Cho (Chung-Ang Univ.)	
16:30 - 17:00		Kui Yu (Sichuan Univ.)	Stefan Ringe (Korea Univ.)	Sang Hak Lee (Pusan Natl. Univ.)	
17:00 - 17:30		Sungjee Kim (POSTECH)	Chang Yun Son (Seoul Natl. Univ.)	Sang Uck Lee (Sungkyunkwan Univ.)	
17:30 - 18:00		Hae Sung Cho (Chung-Ang Univ.)	Jeong-Mo Choi (Pusan Natl. Univ.)	Sungho Yoon (Chung-Ang Univ.)	
18:00 - 20:00	Reception	Dinner	Dinner	Banquet	

Program

May 6th (Tue)

15:00~18:00	Registration
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: Sungho Yoon (Chung-Ang University)	
16:30~17:00	Kui Yu (Sichuan University) Prenucleation Clusters of ZnSe Assisting Formation of Photoluminescent CdSe Magic-Size Clusters under Mild Conditions
17:00~17:30	Sungjee Kim (POSTECH) Nanoclusters and Quantum Dots
17:30~18:00	Hae Sung Cho (Chung-Ang University) Physicochemical understanding of adsorption in porous crystals
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: Hae Sung Cho (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	**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	**Banquet**

May 10th (Sat)

10:30~20:00	**Excursion**

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

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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)

[4] Molecular mechanism of GTP binding- and dimerization-induced enhancement of Sar1-mediated membrane remodeling, S. Paul, A. Audhya and Q. Cui, Proc. Natl. Acad. Sci. U.S.A., 120, e2212513120 (2023)

[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)

[6] Delineating the shape of COPII coated membrane bud, S. Paul, A. Audhya and Q. Cui, PNAS Nexus, 3, 305 (2024)

[7] Sequence sensitivity in membrane remodeling by polyampholyte condensates, S. Mondal, Q. Cui, J. Phys. Chem. B, 128, 2087-2099 (2024)

(Session 4-1)

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

Kui Yu

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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 4-2)

Nanoclusters and Quantum Dots

Sungjee Kim

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Magic sized clusters (MSCs) are thermodynamically stable intermediate nanoclusters often captured during the growth of semiconductor nanoparticles (NPs). MSCs can be isolated as intermediates in quantum dot (QD) synthesis, and they provide pivotal clues in understanding QD growth mechanisms. We report syntheses for two families of heterogeneous-atom-incorporated InP MSCs that have halide or zinc atoms. All the MSCs could be directly synthesized from conventional molecular precursors. Alternatively, each series of MSCs could be prepared by sequential conversions. As the conversion proceeded, evolution from uni-molecule-like to QD-like characters was observed. Early stage MSCs showed active inter-state conversions in the excited states, which is characteristics of small molecules. Later stage MSCs exhibited narrow photoinduced absorptions at lower-energy region like QDs. The crystal structure also gradually evolved from polytwistane to more zinc-blende. We also introduced halide atoms (Cl, Br, I) as dopants into MSCs. Chiroptical activities of III-V group QD growth intermediates, or MSCs, will be addressed as suggesting chiral MSCs as prospective materials on designing chiroptical nanomaterials. InP nanoparticles and nanostructures synthesized from InP MSCs will be also discussed.

(Session 4-3)

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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(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

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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)

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.

Reference

[1] CO_2 hydrogenation to formic acid over heterogenized ruthenium catalysts using a fixed bed reactor with separation units, Green Chem., 2020, 22, 1639-1649

Poster Session

Abstract