Research Summary

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Overview

I am currently pursuing my Ph.D. at Caltech, where I specialize in developing computational tools for simulating polymeric systems. My research centers on the fundamental physics of aqueous polyelectrolyte and multi-valent ion complexation, with the goal of enhancing our understanding and predictive abilities in fields like water remediation and drug delivery. To achieve this, I employ various computational methodologies, including enhanced sampling molecular dynamics, density functional theory, and machine learning, which have yielded academically and industrially relevant insights.

Beyond my research, I have also developed a passion for software engineering and data science. Version control, unit testing, and continuous integration serve as the foundation of my research projects and aid in the reproducibility, as well as maintainability, of my work. I am proficient in Python and its data science stack and have experience developing parallelized workflows. My focus on efficient computing has led me to extend open-source molecular dynamics analysis tools to run on high-performance computing clusters, which members of my research group have adopted. In the following sections, I will briefly describe my research projects and publications.

Research at Caltech (Advisor: Prof. Zhen-Gang Wang)

Aqueous polyelectrolytes are commonly employed to chelate multi-valent ions, serving a crucial function in drug delivery, water softening, and mineralization control. In particular, polyanions are highly effective at chelating multi-valent cations like Ca^{2+}, which form scale deposits within water pipes. At sufficient ionic strength, ion-mediated interactions between polyelectrolyte chains can result in the precipitation of polyelectrolyte-ion complexes. This phenomenon, known as "like-charge attraction", also underlies the effects of "salting in" and "salting out" in protein solutions. Both experimental and theoretical studies have posited that ion bridging is the primary driver of this counterintuitive phenomenon; however, the specific molecular mechanisms remain elusive.

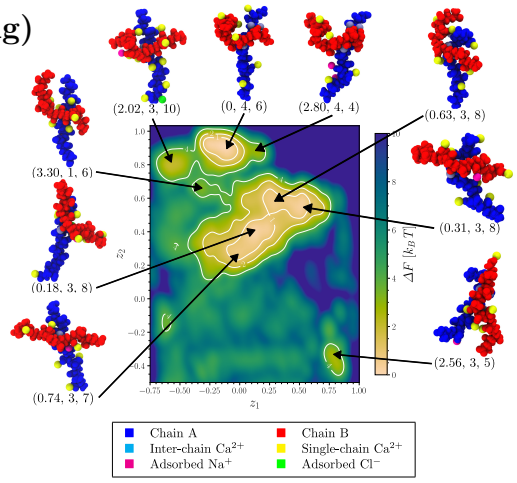

Figure 1: Free energy landscape of the autoencoder latent space for two associated 16-mer PAA chains with 32 Ca^{2+}. The tuple below each conformation displays the relative free energy, number of bridging Ca^{2+}, and number of single-chain adsorbed Ca^{2+}.

I utilized all-atom molecular dynamics simulations to probe the molecular mechanisms of like-charge attraction between two poly(acrylic acid) (PAA) chains in a $CaCl_2$ salt solution. PAA serves as a model polyelectrolyte and is widely used in water softening. In addition to studying PAA, we have explored its copolymers with vinyl acetate and vinyl alcohol, which exhibit greater stability in high ionic strength solutions. We have also investigated polypeptides of aspartate and glutamate for their potential applications in drug delivery. I employed a hybrid enhanced sampling approach combining well-tempered metadynamics and Hamiltonian replica exchange to traverse the substantial free energy barriers in the polymer conformational and ion binding landscape. Interestingly, I found that increasing concentrations of Ca^{2+} did induce attraction between PAA chains; however, the binding energy of the chains was not contingent on the number of ion bridges formed between them. Additionally, at high ionic strengths, electrostatic screening significantly reduced ion bridging between chains.

The observed chain-chain interactions were primarily influenced by correlations between the chelated ions rather than by the ion bridges themselves. To quantify these interactions, I utilized machine learning techniques, specifically an autoencoder neural network, to analyze the structure of ion-polyelectrolyte complexes. The network's latent space effectively differentiated the dominant polymer complex conformations, as demonstrated in Figure 1. Moreover, the latent space successfully distinguished between the number of ions bridging between chains and those adsorbed on single chains, which were the primary driving forces of chain-chain interactions at high ionic strengths. I am currently extending these methodologies to rationally design copolymer systems for water softening that can chelate multi-valent ions more efficiently than existing commercial solutions, without the downside of precipitation in the solution.

Research at Caltech (Advisor: Prof. John F. Brady)

My previous research at Caltech delved into hydrodynamic interactions between deformable bodies in both Stokes and potential flow regimes. I focused on "active" systems, wherein body deformations are internally driven, resulting in self-propulsion, as shown schematically in Figure 2. These active systems often display spontaneous self-organization, forming patterns such as schools of fish, flocks of birds, and growing bacterial colonies. I aimed to decipher the role of the fluid medium in these collective behaviors and to explore whether fluid dynamics alone could account for the emergent phenomena observed without the need for phenomenological interaction rules.

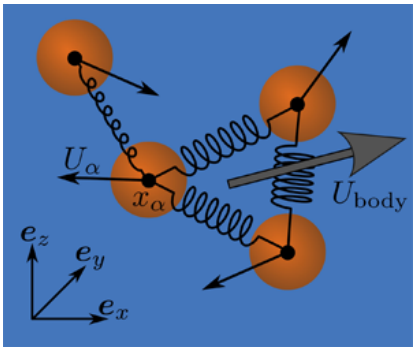

Figure 2: N spherical particles are connected together to form a deformable body. Each particle α is parametrized by its position $\boldsymbol{x}_\alpha$ and velocity $\boldsymbol{U}_\alpha$, leading to a net body velocity $\boldsymbol{U}_{\text{body}}$.

I initiated my investigation by constructing a theoretical framework based on potential flow theory to describe non-linear, many-body hydrodynamic interactions between deformable entities. This involved employing a multipole expansion technique for the flow field and solving a set of corresponding boundary integral equations. I found that the hydrodynamic interactions alone can lead to spontaneous self-propulsion without any net work. This result was surprising because it was thought that self-propulsion occurred through viscous dissipation, which is not present in potential flow.

I then expanded my theoretical model to incorporate arbitrary numbers of interconnected bodies. I also developed a molecular dynamics-like code using C++ to simulate their dynamics. The code was parallelized via both OpenMP and CUDA to make the simulation runtime feasible on high-performance computing clusters. Computational challenges posed by the construction and inversion of relevant tensors provided an opportunity to enhance my skills in efficient and parallel computing. My findings suggested that hydrodynamic interactions alone are sufficient to produce emergent structures. Additionally, I found that the fluid medium establishes a natural length scale that can be used to understand system dynamics, dependent on the body configuration and velocity.

Research at UC Berkeley (Advisor: Prof. Kranthi K. Mandadapu)

Biological lipid membranes make up the boundary of the cell, as well as many of its internal organelles. Such membranes are not simply static, semipermeable barriers protecting their internal contents but play a dynamic role in many cellular processes. While there is much experimental evidence for the dynamic behavior of lipid membranes in biological systems, the physical mechanisms governing membrane motion—and their coupling to membrane geometry—remained poorly understood. Lipid membranes are unique materials: lipids flow in-plane as a two-dimensional viscous fluid, yet the membrane bends out-of-plane as an elastic shell (see Figure 3).

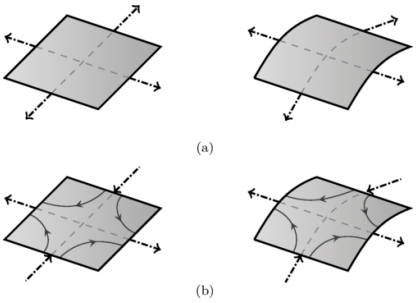

Figure 3: (a) Surface tension pulls the membrane at each edge, so a normal force arises when the shape is perturbed. (b) In an extensional flow (solid arrow), the tractions push and pull the fluid (dashed arrows) such that when the membrane is perturbed, a viscous force arises in the normal direction.

To shed light on these phenomena, I constructed a theoretical framework to understand the dynamics of lipid membranes across various geometries. My approach employed a balance law formulation and linear irreversible thermodynamics framework to model the transport phenomena. I observed that perturbed in-plane and out-of-plane quantities exhibit different length scale variations in systems where lipid flow is present. Upon performing a scaling analysis, I identified two critical dimensionless numbers governing the dynamics of lipid membranes: the Föppl-von Kármán number and a novel dimensionless number I introduced, which I termed the Scriven-Love number. The Scriven-Love number compares out-of-plane forces arising from the in-plane, intra-membrane viscous stresses to the familiar elastic bending forces. In contrast, the Föppl-von Kármán number compares tension to bending forces. Calculations of non-negligible Scriven-Love numbers in various biological processes and *in vitro* experiments show that in-plane intra-membrane viscous flows cannot generally be ignored when analyzing lipid membrane behavior.

Publication List

1. A. Glisman, S. Mantha, D. Yu, and Z.-G. Wang. "Multi-valent Ion Mediated Polyelectrolyte Association and Structure", *Manuscript in Review* (2022)
2. S. Mantha, A. Glisman, D. Yu, and Z.-G. Wang. "Adsorption isotherm and mechanism of Ca^{2+} binding to polyelectrolyte", *Manuscript in Review* (2022)
3. A. Glisman, and J. F. Brady. "Swimming in potential flow", *Journal of Fluid Mechanics* (2022) **952**, R5
4. A. Sahu, A. Glisman, A. Tchoufag, and K. K. Mandadapu. "Geometry and dynamics of lipid membranes: the Scriven-Love number", *Physical Review E* (2020) **101**, 052401