Any eukaryotic cell is enclosed by a membrane that separates the intracellular fluids and organelles from the extracellular environment. The cell membrane is composed of diverse macromolecules – primarily lipids and proteins of various types – which govern numerous biological processes, including tissue formation and repair, nutrient uptake, neuronal communication, and immune responses. The spatial distribution of these macromolecules in the cell membrane is typically inhomogeneous and dynamic.

Diverse biological processes involve changes in the shape of the cell membrane. They are also accompanied by redistributions of the macromolecules that constitute the cell membrane. Among the major problems of contemporary biophysics is to explain how these dynamic rearrangements of cell membranes – which typically occur at the length scales of micrometers – are induced by such molecular events as protein-protein binding and protein conformational transitions, which take place within the cell membrane at the length scales of Angstroms and nanometers. Solving this general problem is a central objective of our research. In particular, we want to elucidate the molecular mechanisms that underlie the multi-scale rearrangements in cell membranes resulting from their adhesion.

Adhesion of cell membranes arises from the binding of membrane-anchored receptor proteins to their ligands anchored in the apposing membrane. Importantly, biological cells use the membrane-anchored receptor proteins to physically interact and, thereby, identify and communicate with other cells. For this reason, the adhesion of cell membranes is essential for numerous processes, including immune responses, tissue formation, and cell signaling.

The binding of the membrane-anchored receptors to their membrane-anchored ligands can be a cooperative process, which can be explained as follows. The formation of the receptor-ligand complexes in the space between the apposing membranes suppresses fluctuations in the separation between the two membranes. The suppression of membrane fluctuations, in turn, facilitates the formation of additional receptor-ligand complexes between the apposing membranes. The feedback between the suppression of membrane fluctuations and the formation of receptor-ligand complexes leads to an effect of fluctuation-induced cooperative binding. This effect has been discovered in recent experiments on membranes adhering *via* the binding of multi-domain proteins CD47 and SIRPα. We will study the cooperative binding of CD47 to SIRPα using multi-scale molecular dynamics simulations. The combination simulations and experiments will allow us to gain a detailed understanding of the molecular mechanisms that give rise to the dynamic and cooperative behavior of membranes adhering *via* the binding of CD47 to SIRPα.

Importantly, the binding of CD47 to SIRPα has been found to play important roles in phagocytosis, auto-immunity, and host defense. As such, CD47 and SIRPα have been recognized as a potential therapeutic target in cancer and inflammation. Therefore, our studies on the cooperative interactions between CD47 and SIRPα may have a direct influence on the advancement of new cancer treatments.

We will also use the multi-scale molecular dynamics simulations to study the binding of the SARS-CoV-2 spike protein to the human ACE2 receptor. This binding process initiates the attachment of the coronavirus particles to human cells. Our studies will deepen the understanding of how the coronavirus particles interact with host cells and, thus, may have a direct impact on the development of new vaccines and anti-viral drags.

Cell membranes contain fluctuating nanoscale molecular clusters, or domains, enriched in sphingolipids, cholesterol, and proteins. These nanodomains are commonly termed lipid rafts. They can be stabilized and made to coalesce, forming platforms that function in membrane signaling and trafficking. There are possibly many physical mechanisms that cause the stabilization and coalescence of lipid rafts, which is a subject of intense research. We will use state-of-the-art methods of statistical and computational physics to investigate how membrane adhesion affects the distribution of lipid rafts in adhering membranes. We will also study the interplay between the membrane adhesion and the aggregation of raft-associated membrane receptors. Understanding these processes will be particularly relevant in the context of trans-membrane signaling because receptor aggregation is a ubiquitous process triggering intracellular signals.

Taken together, our research is interdisciplinary as it applies diverse methods of computational physics and chemistry to relevant problems at the frontiers of membrane biophysics and molecular biology. Our studies will have impact not only on developments in computational biophysics but also on future advancements in other biological sciences, including molecular immunology.