Engineering Membrane Division: A Short-Cut Strategy

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Living matter, such as cells, extracellular matrix, and tissues, exhibits remarkable organizational patterns. These patterns typically emerge from a network of controlled, hierarchical biomolecular interactions and are subsequently propelled by a multitude of physical forces [1]. How do physical forces, emerging within a network of disordered molecules, drive their controlled organization? Is it possible to design new physical principles to reverse-engineer the assembly of bio-inspired materials? My research objective is to develop a computational, synthetic biology-based approach to address these questions.

My talk will focus on the novel design of minimal biomimetic models of bilayer membranes, engineered to emulate the level of mechanical work typically performed by complex cellular machinery at nanoscale. The remodeling of bilayer membranes is an integral part of emerging cellular events, leading to the formation of highly curved membrane geometries and corresponding sub-compartments (e.g., during cell division, endo- and exocytosis). These events are largely driven by controlled physical forces, the origins of which are often not fully understood. By harnessing the strength of coarse-grained, minimally reconstituted model membranes, we could reverse-engineer membrane remodeling events and subsequently probe the underlying physical forces [2-6]. I will discuss my recent efforts to reconstitute minimal models of membrane division [2,3] and membrane endocytosis [5]. Our findings reveal that the mechanical forces driving membrane remodeling during these events can be precisely controlled by tuning the individual leaflet tension of the membrane bilayer. This adjustment can be achieved by tuning the trans-bilayer asymmetry, which in turn controls the magnitude of intrinsic membrane curvature. Our findings challenge the conventional belief that membrane remodeling events can only be triggered by complex cellular machinery. Instead, our study demonstrates an alternative, non-trivial mechanism of membrane remodeling, emerging from the fundamental principles of membrane curvature elasticity. These insights can be leveraged in a scalable manner in synthetic experimental procedures to design the controlled formation of membrane sub-compartments in nanovesicles or liposomes, thereby opening up exciting possibilities in biomaterial engineering. In the concluding part of my talk, I will outline my future research vision on engineering assembly patterns in soft biomaterials, with a focus on probing the mechanical forces that propel these patterns into formation. By combining physics-driven and machine-learning-based modeling strategies, my overarching vision is to develop alternate design principles for autonomous, synthetic nano-cells, capable of sustaining minimal metabolism, regeneration, internal content transportation, and signal transduction, thereby aiming to contribute to novel nanomaterial engineering and biomedical technology.

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