Summary of thesis: Mesoscopic structural dynamics and mechanics of cell membrane models

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Cellular membranes are mainly composed of phospholipid bilayers, in which a number of key biochemical reactions take place. From the viewpoint of physics, membranes can be generalized as quasi-two-dimensional fluid, the mode of deformation of which is both plastic and elastic. This enables them to maintain excellent mechanical stability during the formation of highly curved structures with both positive and negative curvatures, such as the deformation of mitochondrial membranes and endocytosis. Despite the large number of studies enlightening specific interactions at the molecular level, quantitative studies concerned with the structural dynamics and mechanics of cell membranes in the presence and absence of external molecules (proteins and saccharides) are still missing.

The primary aim of this thesis is to quantify the mechanical properties of lipid membranes accompanied with biologically relevant functions. The study focuses on quantification of two systems, i.e., lipid nanotubes observed in the presence and absence of proteins (positive local curvature), and glycolipid membranes, which are known to undergo endocytosis in contact with toxins (negative local curvature) from the experiments in real space and reciprocal space, respectively.

In Chapter 3, the dynamics of single soft nanotubes of pure phospholipid membranes with a thickness of several tens to hundreds of nanometers were examined with fluorescent microscopy. The confinement of nanotubes in quasi-two dimensional fluidic environments (chamber height ~ 2 μm) enabled us to determine the structural dynamics of individual tubes within the theoretical framework of semi-flexible polymer chains. A simple elastic model was constructed which enabled us to precisely calculate the thickness of individual nanotubes on a mesoscopic length scale that is beyond the optical resolution, which cannot be achieved with standard phenomenological image analysis. This simple but straightforward strategy was further extended to naturally occurring nanotubes formed by the association of proteins with F-BAR domains during filopodia formation and cytosis. Quantitative analysis revealed that the mode of tubulation dynamics and the bending modulus of membranes can be classified with respect to their similarities

with F-BAR proteins as determined from a rooted phylogenetic tree.

In Chapter 4, the impact of surface saccharide groups on membrane mechanics was investigated in reciprocal space using off-specular neutron scattering. Synthetic lipids with Gb3 headgroups were selected, since Gb3 is known to invaginate Shiga toxins by creating a mesoscopic membrane pocket with negative curvature (endocytosis). Owing to the planar geometry of membrane stacks deposited on solid substrates, the free energy of interacting membranes could be described by a discrete smectic elastic theory. In contrast to analytical, and thus semi-quantitative, approaches, the introduction of a finite sample size (parameterized by a "cut-off radius") allowed full calculation of two principal mechanical parameters of membranes, bending rigidity and compression modulus, of biologically relevant glycolipid membranes. Precise measurements of membrane mechanics in reciprocal space and systematic comparisons with the mechanical properties of pure phospholipids and other glycolipids (intermediate compounds) demonstrated for the first time that very minor changes in the length and conformation of saccharide groups significantly alter the mechanics of membranes. These findings will help shed a "mechanical" light on the key question in biology, "why nature dynamically modulates the expression of various surface saccharides on cell surfaces".