EDITORIAL

Focus on the physics of the cell membrane

Patricia Bassereau\textsuperscript{1}, Rob Phillips\textsuperscript{2,4} and Petra Schwille\textsuperscript{3}

\textsuperscript{1} Institut Curie, CNRS, Laboratoire Physico-Chimie Curie, Université Pierre et Marie Curie, 75248 Paris, Cedex 05, France
\textsuperscript{2} Division of Engineering and Applied Science, California Institute of Technology, Pasadena, CA 91125, USA
\textsuperscript{3} Biophysics/BIOTEC, Technische Universität Dresden, Tatzberg 47/49, 01307 Dresden, Germany
E-mail: phillips@pboc.caltech.edu

New Journal of Physics \textbf{14} (2012) 055021 (4pp)
Received 5 March 2012
Published 21 May 2012
Online at http://www.njp.org/
doi:10.1088/1367-2630/14/5/055021

Abstract. This focus issue on membrane biophysics presents a collection of papers illustrating new developments in modern biophysical research on cell membranes. The work described here addresses questions from a broad range of areas, including cell adhesion, membrane trafficking and activation of cells of the immune system. It also presents recent views on membrane mechanics, the effect of electric fields, as well as on the interplay of mechanics and chemistry and organization at many different scales.

The molecular biology revolution has made it possible for scientists to manipulate the DNA within many organisms. One of the consequences of these advances is the concomitant ability to manipulate the proteome of these cells, thereby altering their functions and metabolism in ways that would have been sheer fantasy only fifty years ago. At this point, these great advances of molecular biology have even made their way into most biophysics laboratories as part of the routine business of biophysical research. These overwhelming advances in engineering biology have recently stimulated a new field with great promise for analytical and quantitative approaches: synthetic biology, one of its perspectives being the construction of biological systems from the bottom up. Notably, however, in spite of the long tradition of membrane research in biophysics, engineering of biological membranes has lagged behind, in part because of the absence of tools with similar reach to those that allow us to alter genes and genomes.

\textsuperscript{4} Author to whom any correspondence should be addressed.
Nevertheless, biological membranes that are the seat of interactions between cells and the rest of the world are increasingly considered to be one of the most important functional parts of cellular systems, and it is high time to provide a flavor of the way physics touches on these important problems.

In this focus issue, leaders from the field of membrane biophysics illustrate the breadth and depth of modern biophysical research on membranes through a diverse set of case studies. The work described here runs the gamut from questions of how the cells of the immune system are activated as a result of cell–cell contacts through questions of ‘pattern formation’ at membranes to the behavior of falling membrane droplets. Further, many themes that permeate modern biology, such as the importance of adhesion, the interplay of mechanics and chemistry and organization at many different scales, all play a role in these papers.

In the first paper by Evans and Smith [1], an experimental study is presented of how the lipid bilayers that make up membranes fail under tension. The paper unites two techniques pioneered by Evans, namely, the use of a pipette to apply a well-controlled state of tension on a giant unilamellar vesicle [2] and the application of ideas on the relation between rupture and the rate at which tensions are prescribed. The result of this kind of careful kinetic measurements is highlighted.

Multicellular organisms are characterized by enormous diversity in their multitude of different cell types. One of the critical questions, which is only now being subjected to systematic experimental scrutiny, is how the molecular content and structure of the membranes in these different cell types differ. The second paper from the team of Simon Scheuring [3] reports on elegant studies using the atomic-force microscope to examine the junctions between the cells making up lenses in the mammalian eye.

Of course, one of the difficulties faced as biophysicists attempt to take stock of the membranes in different cell types is the lack of complete information on these systems combined with their staggering complexity. In the third paper in the collection [4], Sackmann describes how cells in the immune system known as T-cells are activated as a result of immunological insults. One of the interesting perspectives brought to the problem in this work is to link, in the context of the immune system, chemical reactions and cellular signaling to biophysical processes such as cellular adhesion and membrane and cytoskeleton reorganization.

There are a number of different fundamental shapes seen in biological membranes, two of the most important being spheres and cylinders, the latter in the form of tubules with nanometer scale radii. Spheres at many different sizes have been studied extensively both experimentally and theoretically, and it is now also possible to measure the behavior of individual tubules. In the paper of Shlomovitz et al [5], a theoretical analysis is made of how the protein dynamin nucleates on such tubules, forming helical structures.

In the interesting simulation study of Vliegenthart and Gompper [6], the behavior of thin shells subjected to external pressure and indentation is examined. Using a physical model of the free energy cost of deformation, this paper shows how the rate of deformation in addition to mechanical properties impacts on the final shape of the shell.

A feature of biological membranes that has attracted considerable attention in recent years is the existence of nanoscale lipid domains, which result from local unmixing within very heterogeneous lipid compositions, and which segregate and locally recruit membrane proteins (for a recent review see [7]). The paper of Ehrig et al [8] uses coarse-grained simulations to show how critical fluctuations close to lipid phase transitions result in anomalous diffusion, as observed in cell membranes and attributed to nanodomains.
A very pleasing study that also relates to the formation of membrane tubes is motivated by the response of cells, such as red blood cells, that are subject to hydrodynamic flows. Here, Viallat and her team show that a floppy giant vesicle can form tubes under simple sedimentation [9]. The paper provides a series of experimental measurements of this phenomenon and a corresponding model that describes, on an intuitive basis, how membrane deformations are induced by the flow.

Mechanical properties of membranes can be influenced greatly not only by the insertion of proteins, but also of peptides, and many pathogens use this aspect to unfold their destructive potential. Shchelokovskyy et al [10] discuss how the HIV-1 fusion peptide influences the mechanical properties of membranes, and may impact on leaflet coupling.

Membrane interactions and adhesion are often mediated by the binding of ligand–receptor pairs on the two opposing membranes (for a review, see [11]). A theoretical study by Reister et al [12] focuses on the coupling between these ligand–receptor interactions and the fluctuations in the membranes themselves. It reveals that membrane roughness can induce correlations between the positions of the adhesion molecules, controlling their local density and thus the adhesion.

Biological membranes are teeming with activity, with constant changes in topology and function [13]. One of the signature processes of biological membranes is the fusion between distinct membranes, which occurs during membrane trafficking or upon synaptic activity. In the work presented here, Ghosh et al use a number of different x-ray techniques to explore the effect of an important lipid, namely PIP$_2$, and the structural changes that accompany fusion events between synaptic vesicles and membranes [14].

Wang and Deserno [15] address the critical question of how to construct molecular-level simulations of lipid bilayers, which are at once faithful to the underlying chemical specificity conferred by different types of lipid molecules, and yet are computationally practical. This is an important task for a detailed understanding of membrane biophysics. Their paper reports on how coarse-grained interactions between ‘effective’ lipid molecules can be constructed; they also describe the extent to which such effective interactions are transferable from one molecular situation to the next.

The distribution of ligands and receptors of different lengths in adhering membranes has been modeled by Różycki et al in order to describe the adhesion zone of immune cells [16]. This paper shows that both the molecular length differences and the membrane fluctuations have a crucial role in the final organization and thus in the adhesion between the two membranes.

Ziebert and Lacoste’s paper [17] is a theoretical contribution, which uses the Poisson–Boltzmann theory to assess the response of a lipid bilayer membrane in an electric field. They go beyond earlier work [18, 19] by accounting for the nonlinearities present in the Poisson–Boltzmann, in contrast with the linearized approach taken in the Debye–Huckel theory.

Kaizuka and Groves [20] report on the very interesting ways in which phase separation in lipid membrane induces deformations that in turn produce macroscopic mechanical interactions and large-scale patterns.

Taken together, the papers presented here provide a valuable and lively snapshot of a field that is in rapid development. Further, the diversity of problems illustrated here demonstrates how themes such as self-assembly and organization, dynamics of adhesion, molecular recognition and pattern formation all play out in membrane biophysics.

New Journal of Physics 14 (2012) 055021 (http://www.njp.org/)
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