Preface

This book offers a survey of the theoretical description of and experimental evidence for micro- and nanostructures in biological systems. The book is novel in the sense that biophysical methods are used to describe and manipulate clinically relevant problems which have hitherto been largely described as purely biochemical phenomena.

In the theoretical description, a unifying approach is used starting from the single-particle energy, deriving the free energy of the system and finally determining the equilibrium state by minimizing the system free energy. This approach is basic, transparent and simple so that different systems and interactions can be considered. The method is then applied in describing different electric and elastic phenomena in biological and lipid nanostructures.

Orientational ordering of anisotropic system constituents is found to be an essential mechanism of stabilization of the system configuration in ionic solutions and biological membrane structures. Further, in models based on lattice statistics, a method considering the Boltzmann probability of energy averaged over rotational states is introduced as an improvement over the free energy minimization method.

Experimental evidence for theoretically predicted membranous nanostructures and mediated attractive interactions between these structures is presented. Possible applications in medicine, toxicology and nanotechnology are given, such as the use of the results and methods in the clinically relevant problem of blood clot formation or the fabrication of nanostructured biocompatible implant surfaces.

The book consists of eighteen chapters devoted to the biophysics and biology of biological micro- and nanostructures. Chapter 1 gives a brief review of the basic statistical thermodynamic principles and equations which are then used throughout the book in theoretical description of biological micro- and nanostructures, which are composed of a large number of constituents. The chapter starts with a short survey of the physics involved where some basic definitions of the physical quantities relevant in theoretical consideration of biological systems, like field and potential, are also given. Chapter 2 briefly describes the basic properties of lipid bilayers and biological membranes. Chapter 3 describes lipid vesicles as experimental tools. Different types of lipid vesicles can be used and their preparation and the interpretation of the results is presented. Among the most recent applications of lipid vesicles in scientific studies is their use in the field of nanobiology and nanotoxicology where interactions between nanoparticles and biological systems are investigated. Understanding nanoparticle-induced defects in biological membranes is among the major challenges of bio-nano-related fields of research. In Chapter 4 some basic microscopic techniques for studying the structure and properties of vesicles ranging from direct visualisation (optical or electron microscopy) or scattering techniques (light scattering, LS; small-angle neutron scattering, SANS; small-angle X-ray scattering, SAXS) to polarisation light microscopy; freeze fracture transmission electron microscopy, FF-TEM; and atomic force microscopy. The selection of methods depends on the aim of the study. These methods give information about the morphological features of vesicles and the structural characteristics of lipid bilayers.

In the continuum approach, biological surfaces (e.g., membrane surfaces) may be in the first approximation considered as smooth surfaces that can be theoretically described using the mathematical theory of differential geometry, as shown very briefly in Chapter 5 of the book. Further Chapter 6 describes the polymorphism of lipid nanostructures, including lipid nanotubes, and introduces the concept of anisotropic intrinsic shapes of lipid molecules. Chapter 7 is dedicated to the physics of lipid micro- and nano structures, starting with the concept of the single-lipid molecule energy. Applying the methods of statistical physics, the free energy of a lipid monolayer and bilayer is derived, taking into account the anisotropic shape of lipid molecules. The lipid monolayer and bilayer deviatoric bending energy due to average orientational ordering of lipid molecules is discussed. The influence of lipid anisotropy on the stability of planar, inverted spherical and inverted cylindrical lipid monolayer nanostructures and lipid bilayer nanotubes is presented in detail. At the end of the chapter the shape equation for closed lipid bilayer vesicles is derived and solved in order to describe theoretically the experimentally observed budding transitions of phospholipid vesicles. Chapter 8 gives a derivation of the energy of a single flexible membrane nanodomain. Flexible membrane nanodomains are defined as small complexes composed of proteins and lipids. The so-called membrane raft elements of biological membranes may fall into this category. Membrane nanodomains (inclusions) may also be induced by a single rigid globular membrane protein. Some membrane embedded peptides may induce such nanodomains.

Formation of tubular membrane bilayer structures (nanotubes) is a common phenomenon in both artificial lipid membranes and cellular systems. In Chapter 9 the formation and stability of tubular membrane structures is considered experimentally and theoretically. In Chapter 10 the physical mechanisms of the formation and stabilization of highly curved spherical membrane buds are experimentally and theoretically considered, with special emphasis on the stability of the narrow neck connecting the budding vesicle to the parent membrane. Chapter 11 is dedicated to fusion of a vesicle with the target plasma membrane. Experimental results, along with a theoretical model, are presented to provide a new interpretation of repetitive, transient fusion neck events with narrow neck diameters stabilized by anisotropic membrane components. As the suggested fusion neck stabilization mechanism is nonspecific and as there is no a priori reason why the membrane constituents should be in general isotropic, it could be expected to take place in any cell type. In Chapter 12 we discuss the influence of the intrinsic shape of membrane-attached nanoparticles on the elastic properties of bilayer membranes.

Chapter 13 is devoted to the electrostatic properties of biological systems. It starts with the definition of electrostatic energy and derivation of the configurational entropic part of the free energy of a system composed of finite-sized ions. Then a functional density theory of the electric double layer (EDL) which assumes constant dielectric permittivity is used to derive the standard Poisson–

Boltzmann (PB) equation and the modified PB, i.e., the Bikerman equation. Most models describing the EDL assume constant dielectric permittivity throughout the system. But actually, close to the charged surface, the water dipoles are oriented thus leading to a varying dielectric permittivity. Therefore in this chapter we derive the Langevin Poisson–Boltzmann (LPB) equation for point-like ions, where the orientational ordering of water molecules is taken into account. In order to develop an integrating framework to clarify the factors influencing the relative permittivity, the LPB model within the generalized Langevin–Bikerman model is upgraded to take into account the cavity field as well as the finite size of the molecules.

Subsequently, in Chapter 14 the attraction between like-charged biological surfaces, mediated by spherical macroions are described theoretically and illustrated by different examples observed experimentally, such as the attraction between a negatively charged nanostructured surface and osteoblasts. Chapter 15 briefly describes simulations of the encapsulation of spherical macroions, while in Chapter 16 the electrostatics and mechanics of hydrophilic pores in biological membranes is given. Chapter 17 is dedicated to the role of membranous nanostructures as in cell-to-cell transport mechanisms, where the recently discovered nanotube-mediated mechanism of cell-to-cell communication is described. Chapter 18 presents the liquid crystal mosaic model of the biological membrane as a result of the above generalizations. A pool of membranous nanstructures is biologically important; some clinically relevant mechanisms involving this pool are presented and possible manipulation of these mechanisms in medicine is suggested.

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