Biomimetic Lipid Membranes: Fundamentals, Applications, and Commercialization

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Editors

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To my beloved mother, Nursen Kok –
Dr. F. N. Kok

To Duru and Hakan, my beloved family, nothing would be possible without their support and encouragement – Dr. A. Arslan Yildiz

To my grandparents, Şamil – Gülizar Inci and Neşet – Şehzade Çiftci, who always believed in my ability to be successful in the academic arena. They are gone but their constant source of support and encouragement have made this journey possible. Regrettably, angels deserve to die . . . – Dr. F. Inci

Preface

The cell, the smallest living unit, interacts with its surroundings via cell membrane and creates a unique biointerface that is vital for cellular processes and cell survival. Better understanding of such a tiny yet complex system is not only crucial for basic research, but also to design advanced platforms for a variety of applications, particularly in medical field. Development of less complex model systems, i.e., biomimetic lipid membranes, is highly needed, but these models need to sustain fluidity of the lipid bilayer and mimic native dynamic complexity to some extent and retain their structure for the intended duration. Over the years, different techniques have been proposed for the construction of the model systems (chapter "Structural and Mechanical Characterization of Supported Model Membranes by AFM"). In particular, atomic force microscopy (AFM), an elegant technology, has enabled not only structural but also mechanical characterization of membrane systems with different compositions at nanoscale resolution (chapter "Structural and Mechanical Characterization of Supported Model Membranes by AFM"). Biomimetic membranes also offer a platform for the reconstitution of membrane proteins *in vitro* milieu, and AFM imaging has further enabled to probe various membrane proteins *in situ* through their density and spatial distribution (chapter "To Image the Orientation and Spatial Distribution of Reconstituted Na+,K+-ATPase in Model Lipid Membranes"). Nevertheless, the existing biomimetic membrane models are mostly insufficient to mimic all crucial properties on a single platform and do not reflect the asymmetry present in actual biological membranes. Moreover, the lipid content and distribution are essential in the structure and function of most biological membranes. Recently, an intense effort has been focused on deploying this asymmetry into model membrane systems (chapter "Asymmetric Model Membranes: Frontiers and Challenges"). This emerging field has addressed some of the challenges associated with production of asymmetric vesicles, and thereby, more realistic biomimetic membranes could be constructed for practical applications. As aforementioned, dynamics of biomimetic membranes is pivotal in the function. The experimental techniques combined with computational tools provide essential information and help researchers interpreting the experimental data. Molecular dynamics methodology is mainly used for this purpose, and not only the membrane itself (chapter "Modeling of Cell Membrane Systems"), but also its interactions with other structures, such as nanoparticles (chapter "Molecular Dynamics Studies of Nanoparticle Transport Through Model Lipid Membranes"), can be evaluated. In addition, model membranes are key tools to understand cell–cell and cell–surface interactions, and when functionalized with bioactive molecules, supported lipid membranes (SLBs) can be utilized to study membrane-mediated cellular processes and to investigate cell behavior on various surfaces (chapter "Investigation of Cell Interactions on Biomimetic Lipid Membranes"). For larger transmembrane proteins spanning the lipid bilayer, SLBs are not adequate as they are constructed directly on the surface and they lack of submembrane space, leading to denaturation and malfunctioning of transmembrane proteins. In this regard, tethered bilayer lipid membranes (tBLMs) offer a promising strategy to leverage the lipid bilayer from the surface and precisely fine-tune the thickness of this space, facilitating the construction of membrane proteins on the biosensor platforms (chapter "Tethered Lipid Membranes as Platforms for Biophysical Studies and Advanced Biosensors"). When integrated with immunoassays and micro- and nanoarray formats, SLBs, tBLMs, and liposomes have provided prominent applications for clinical use (chapter "Biomedical Applications: Liposomes and Supported Lipid Bilayers for Diagnostics, Theranostics, Imaging, Vaccine Formulation, and Tissue Engineering"). Owing to their native-like biophysical properties, liposomes, on the other hand, carry their cargo like small lipid vesicles found in cells, and when loaded with vaccines, contrast agents, or drugs, they become very effective delivery vehicles (chapter "Biomedical Applications: Liposomes and Supported Lipid Bilayers for Diagnostics, Theranostics, Imaging, Vaccine Formulation, and Tissue Engineering"). While applying them into microfluidics realm, dynamics and significant utility of SLBs and liposomes can be efficiently investigated in a confined small volume. Furthermore, integrating bioprinting tools, e.g., nozzles and spraying modules, with microfluidic-stemmed strategies creates high throughput, automation, and scale-up for the future applications (chapter "Lipid Bilayers and Liposomes on Microfluidics Realm: Techniques and Applications"). Biomimetic lipid membranes are also very powerful for designing drug screening platforms since the majority of therapeutic agents interact with either cell membranes or membrane proteins (chapter "Biomimetic Model Membranes as Drug Screening Platform"). All these instances clearly point out the potential of biomimetic lipid membranes in medical and pharmaceutical fields. Biomimetic membranes are also being used in other distinct fields, including water filtration and food and environmental pollutant monitoring. Aquaporins, membrane proteins with unique selectivity toward water, embedded in biomimetic membranes have been tested for water purification purposes (chapter "Biomimetic Membranes as an Emerging Water Filtration Technology"), while their functionalization with different biomolecules can be used in the detection of various analytes, including phenols, pesticides, heavy metals, toxins, allergens, antibiotics, microorganisms, hormones, dioxins, and genetically modified produce (chapter "Applications of Lipid Membranes-based Biosensors for the Rapid Detection of Food Toxicants and Environmental Pollutants"). In sum, the unique and admirable characteristics of biomimetic membranes have extended our fundamental knowledge on cell membranes and their organization with milieu and ultimately opened new horizons for other disciplines at the intersection of chemistry, physics, materials science, engineering, biology, and medicine. Exclusively, their applications in the field of medicine and other conjunctive realms have gained immense interest in recent years by screening diseases and therapies, therefore expediting clinical management through prevention studies. In the near future, further engineered biomimetic membranes, in combination with the existing developments, will spectacularly impact greater than their current status in the health-care system through elucidating the fundamental understanding of disease biology and mechanism, leading to synergetic medical solutions to the real-world problems.

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