
Preface

Membrane proteins play key roles in numerous cellular processes, in particular, mediating cell-to-cell communication and signaling events that lead to a multitude of biological effects. This functional diversity is achieved through a variety of different membrane proteins, encoded by some 30 % of genes in typical genome. Membrane proteins have also been implicated in many critical diseases such as atherosclerosis, hypertension, diabetes, and cancer. Therefore the three-dimensional structure and dynamics of membrane proteins and their relationship to the function of the proteins remain an important field of research in molecular biology, biochemistry, and biophysics. Researchers have worked relentlessly for many years to obtain sufficient quantities of purified proteins and structural information using several different biophysical techniques, such as X-ray crystallography, NMR, and other spectroscopic methods. In the last few years there has been a gold rush of structures published especially for the superfamily of membrane proteins known as the G-protein coupled receptors, providing the scientific community with insight into the inner workings of cell signaling through this largest class of membrane proteins. These structures also serve as the starting point for drug design targeting these receptors. However, individual experimental techniques often provide incomplete information on the structure and dynamics of membrane receptors, especially due to the difficulty in working with membrane proteins experimentally as a result of their hydrophobic nature. Thus, different biophysical and structural techniques are increasingly used together in exploiting their complementary information content. Increasingly sophisticated computational techniques are becoming available to bridge the gap in connecting the fragmented structural information obtained from different techniques, to generate and test biological hypotheses. In particular, mechanistic questions related to ligand binding and activation of membrane proteins tremendously benefit from computational analyses of membrane protein structures. The integrated cycle of experimental data generation, computational prediction, and experimental validation is now an established approach to rational drug design in both academia and pharmaceutical industries. It is the goal of this volume to highlight the numerous advances in both experimental and computational approaches to the study of structure, dynamics, and interactions of membrane proteins.

This volume is divided into two sections. Section A brings to light the details of the procedures used for measurements of structure and dynamics of membrane proteins using X-ray crystallography, nuclear magnetic resonance spectroscopy, mass spectrometry, ultraviolet/visible spectroscopy, infrared spectroscopy, and Fluorescence Resonance Energy Transfer methods. The elucidation of numerous examples of ligand protein dynamics as well as protein–protein interactions of the complexes that the receptors form upon activation using these approaches is highlighted to demonstrate the functional significance of these structural and spectroscopic studies. Section B of this volume contains a survey of the computational methods that have played a critical role in membrane protein structure prediction as well as in providing atomic level insight into the mechanism of the dynamics of membrane receptors. Thus, this section has been inspired by the usage of computational methods that tie several fragmented experimental data from structural and spectroscopic

studies and provide an integrated visualization of the mechanism of activation of membrane receptors. It is intended to provide a resource on the current state-of-the-art techniques available in the computational area for studying membrane protein structure, dynamics, and drug design.

Numerous experts in this area have contributed chapters to this volume. We thank them all for taking their time writing the detailed procedures that would serve as a laboratory guide to all researchers in this field. Given the broad range of expertise covered by the authors and their authoritative status in each specific area, we are sure that this volume will be an invaluable resource to all readers interested in membrane protein structure and function.

We both thank our respective families for putting up with us working through times normally reserved for them, including the many lonely dinners they had without mom at the table. Editing this volume with chapters from varied fields has been a learning experience for both of us. We thank John Walker for giving us this opportunity and all at Humana Press, especially David Casey and Monica Beaumont, for their generous help offered to make this volume useful.

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