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Marta Filizola  
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# G Protein-Coupled Receptors - Modeling and Simulation

 Springer

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## Preface

G protein-coupled receptors (GPCRs) are membrane proteins of significant interest in pharmaceutical research owing to their involvement in several important biological processes, including those leading to some serious medical conditions. In spite of focused research, progress towards the discovery of effective therapeutics for GPCRs has long been hampered by the lack of high-resolution structural information about these receptors. Although the number of high-resolution crystal structures of GPCRs has grown significantly in the past few years, the information they provide is limited. Not only are we still far from a comprehensive structural coverage of the GPCR superfamily, but the available structures refer to static, heavily engineered, and generally inactive conformational states of receptor subtypes stripped out of their natural lipid environment. Furthermore, it has become increasingly clear that a full understanding of GPCR structure and function requires dynamic information at a level of detail that is likely to require integration of experimental and computational approaches.

Significant progress has been made over the past decade in the development and application of computational approaches to the large family of GPCRs. A dedicated book that discusses in depth this important topic is lacking but strongly needed owing to: (a) the critical (but sometimes unappreciated) impact that these computational approaches have on understanding the molecular mechanisms underlying the physiological function of GPCRs in support of rational drug discovery, (b) the recent advances in theory, hardware, and software, and (c) the potential for much-improved applications using newly available experimentally-derived structural and dynamic information on GPCRs. Thus, I sought the help of experts with an established reputation in the development and/or application of computational methods to GPCRs, and asked them to contribute their state-of-the-art views on modeling and simulation of this important family of membrane proteins. I am indebted to the highly distinguished authors of this book for agreeing to participate in this project and to provide chapters for four different sessions: a first one describing the impact of currently available GPCR crystal structures on structural modeling of other receptor subtypes, a second one reporting on critical insights from simulations, a third one focusing on recent progress in rational ligand discovery and mathematical modeling, and a fourth one providing an overview of bioinformatics tools and resources that are available for GPCRs.

Heartfelt thanks also go to the several anonymous reviewers of the chapters, and to Thijs van Vlijmen from Springer for the opportunity he offered me to edit this volume. I believe this book adds a unique facet to the “Advances in Experimental Medicine and Biology” series, and I hope the reader will find it both fascinating and of enduring interest.

New York, NY, USA  
June 3, 2013

Marta Filizola, Ph.D.

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