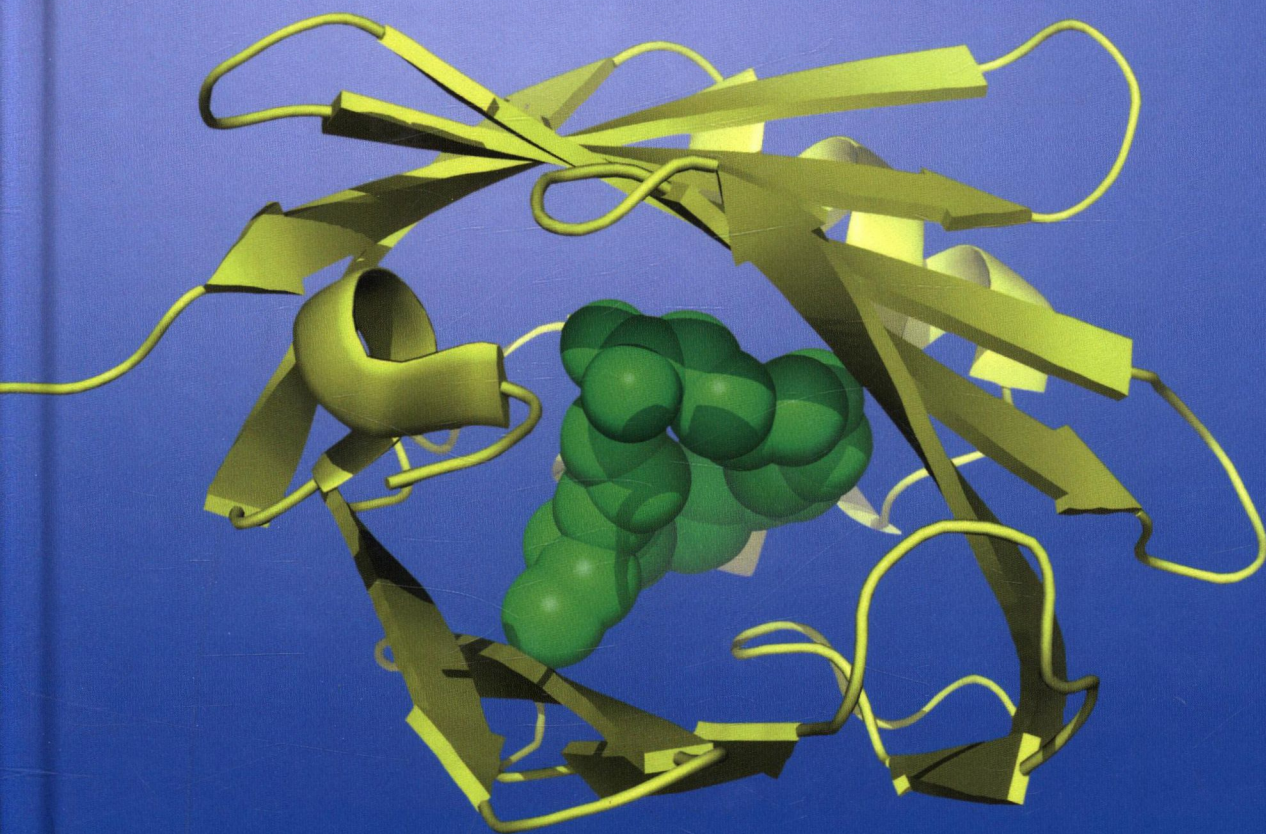


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Andrea Bellelli and Jannette Carey

Reversible Ligand Binding

Theory and Experiment



Presents the physical background of ligand binding and instructions on designing and analyzing experiments

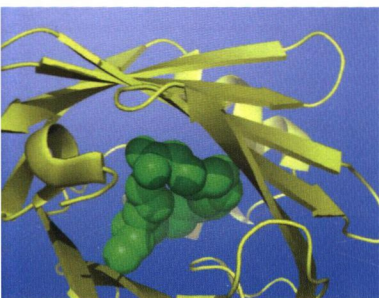
Reversible Ligand Binding: Theory and Experiment discusses the physical background of protein-ligand interactions—providing a comprehensive view of the principles that govern reversible, as well as irreversible, ligand binding. Special consideration is devoted to enzymology, a field usually treated separately from ligand binding, but actually governed by identical thermodynamic relationships. Attention is given to the design of experiments, including how to uncover evidence of biochemical features that may otherwise escape notice. Classical experiments are reviewed in order to further highlight the importance of the experimental design. Overall, the book supplies students with understanding necessary for interpreting ligand binding experiments, formulating plausible reaction schemes, and analyzing the data according to a chosen model.

Topics covered include: theory of ligand binding to monomeric proteins; practical considerations and commonly encountered

problems; oligomeric proteins with multiple binding sites; ligand binding kinetics; hemoglobin and its ligands; single-substrate enzymes and their inhibitors; two-substrate enzymes and their inhibitors; and rapid kinetic methods for studying enzyme reactions.

- Bridges theory and experiment in ligand binding and allostery
- Applies historical and physical insight to provide clear understanding of ligand binding
- Written by renowned authors with long research and teaching expertise in the areas of ligand binding and allostery

Reversible Ligand Binding: Theory and Experiment is an ideal text for students and scientists involved in biophysical chemistry, physical biochemistry, biophysics, molecular biology, protein engineering, drug design, pharmacology, physiology, biotechnology, or bioengineering.




Andrea Bellelli, PhD is a Professor of Biochemistry at the University of Rome Sapienza. He chaired the Department of Biochemical Sciences "A. Rossi Fanelli" and currently chairs the Medicine and Surgery "B" school at the same University. His research focuses on structural and functional properties of oxygen carrying proteins.

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Reversible Ligand Binding

Theory and Experiment

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Reversible Ligand Binding

A.B. dedicates this book to Maurizio Brunori, teacher, mentor and friend for thirty-eight years until now and with more to come.

Preface

Ligand binding is a crucial event in virtually every biological phenomenon. Detailed understanding of many biologically relevant events including enzymatic catalysis, transport, and molecular recognition requires quantitative description of ligand binding. Such description may prove exquisitely complex because biological macromolecules may bind multiple ligands at once or alternatively and their reactions may present several types of thermodynamic linkage. The scope of this book is to provide a comprehensive view of the various biochemical considerations that govern reversible as well as irreversible ligand binding. Special attention is devoted to enzymology, a field usually treated separately from ligand binding, but actually governed by identical thermodynamic relationships.

This book is intended for PhD students and researchers, and aims at providing the understanding necessary to interpret ligand-binding experiments, formulate plausible reaction schemes, and analyze the data according to the chosen model(s). Attention is given to the design of the experiment because a properly designed experiment may provide clear evidence of biochemical features that can otherwise escape notice. Classical experiments are reviewed in order to further highlight the importance of the design of the experiment.

The book includes treatment of thermodynamic relationships that are most often left to the specialized literature, for example, ligand-linked dissociation. To make the book accessible to a general audience, we simplified the analysis of these relationships to the maximum possible extent, for example, whenever possible we adopted homodimeric proteins as model systems instead of more complex macromolecular assemblies. This choice allowed us to explore a large range of effects with minimally complex equations. Our scope throughout the book has been to present all the essential and distinguishing aspects of the phenomena we describe rigorously, but at the same time in the simplest possible form. Indeed, we are confident that every reader having competence in elementary algebra may take advantage of our work.

Acknowledgments

The authors of scientific books always contract debts with many people who, directly or indirectly, contributed ideas, suggestions, and comments. This book contains considerations and ideas that we elaborated over many years, long before our decision to write, and the list of people we would like to thank is very long. Moreover, the background of the authors being different, our two lists sum without overlapping.

We acknowledge the innumerable hours of education on the subject matters discussed in this book by our teachers and mentors. A.B. expresses his thanks to Maurizio Brunori, Eraldo Antonini, Bruno Giardina, Gino Amiconi, and Quentin H. Gibson.

We enjoyed many long and fruitful discussions with our colleagues, that often shaped our views as expressed in this book. Thanks are due to W.A. Eaton, S.J. Gill, T. Yonetani, M. Coletta, P. Ascenzi, G. Antonini, P. Sarti, F. Malatesta, E. Henry, P. Brzezinski, J.S. Olson, W.F. Xue, S. Linse, G.K. Ackers, and many others.

We express our thanks to our marvelous students, whose questions made us grow. Many of them are now well reputed researchers and close friends: R. Ippoliti, E. Lendaro, G. Boumis, A. Brancaccio, S. Santanché, A. Arcovito, F. Angelucci, L. Jin, B. Harish and R. Grandori. Special thanks are due to F. Saccoccia and A. Di Matteo who read the manuscript more than once and pointed out errors and unclear passages: their contribution has been invaluable.

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