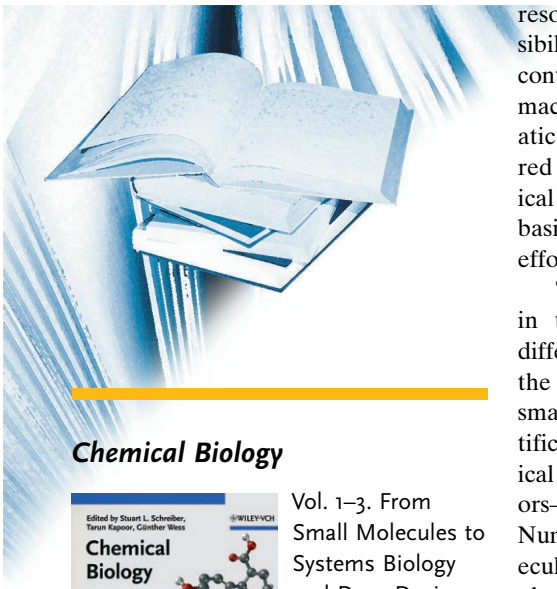
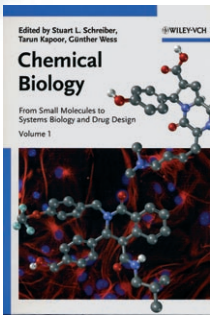


Chemical Biology



Vol. 1–3. From Small Molecules to Systems Biology and Drug Design. Edited by *Stuart L. Schreiber, Tarun Kapoor* and *Günther Wess*. Wiley-VCH, Weinheim 2007. 1206 pp., hardcover € 479.00.—ISBN 978-3-527-31150-7

The relatively new field of chemical biology encompasses research approaches that employ chemical synthesis and chemical methodology to understand biological processes. The prevalent strategy is to exert a chemical perturbation on the biological system, e.g., by inhibition or activation of biological macromolecules, signaling pathways, cellular processes, or whole organisms. By this definition, the wide scope of chemical biology is reflected by the diversity and complexity of the processes under study.

In this book, Schreiber, Kapoor, and Wess undertake the first attempt to combine the research areas of chemical biology in a comprehensive collection. The main focus is on the identification and application of small molecules as binders of cellular proteins. This corresponds to the research activities of the editors, and also to the most prominent aspect of chemical biology research. Compared to classical genetic and molecular biology approaches, the advantages of directly targeting proteins as mediators of most biological processes are, amongst others, the high-resolution temporal control, the reversibility, and the doseability that can be controlled in the experiment. This pharmacological approach is, in its systematic application, nowadays often referred to as "chemical genetics and chemical proteomics", and seamlessly links basic research with drug discovery efforts in the pharmaceutical industry.

The book contains 39 contributions in the form of review articles. The different aspects of the quest towards the development of biologically active small molecules—synthesis, target identification, most relevant targets, chemical informatics, and industrial endeavors—are all appropriately represented. Numerous examples of how small molecules have been used to dissect complex pathways are found throughout the book. Many chapters also describe current efforts to rationalize the parameters that increase the likelihood of a small molecule displaying the desired properties. The aim is to lay the foundations for a mathematical model to predict, on the one hand, the most interesting molecular structures out of the virtually infinite chemical space, and on the other hand the proteins, protein families, and binding sites that offer the most promising drug targets. A mathematical description of the complex cellular processes is the goal of system biology, which is represented in articles on genome-wide expression analyses and modeling of signaling pathways. Another significant proportion of the book is concerned with chemical genetic approaches that combine an engineering step with the use of a small-molecule ligand. These approaches have been developed partly because there is at present no specific small molecule for each protein. According to the concept "one ligand–many proteins", the protein of interest is first manipulated by a genetic intervention to render it susceptible to an otherwise biologically inert molecule. Thus, for example, there are chapters on allele-selective protein kinase inhibitors, fusion proteins for chemical modification, and bidentate ligands that act as chemical inducers of dimerization. Finally, several chapters are devoted to new strategies for the synthesis or chemical modification of proteins and carbohydrates. Here, chemical synthesis is often crucial to understanding the function of these biological macromolecules on a molecular level, or to obtaining homogeneous material for biochemical studies. From my point of view, some important approaches are missing from the selection of contributions, in particular those based on nucleic acids, involving, for example, ligand-dependent ribozymes, riboswitches, and aptamers, which have already proved to be useful research tools. Apart from this, the chapters are coherent and the descriptions of the techniques are well balanced.

The strength of the book clearly lies in the high quality of the articles, which have been almost exclusively written by the leading scientists from both academic institutions and industry. The articles have a consistent structure, beginning with an explanation of the background for the motivation and an introduction that is comprehensible to the non-expert. The book contains numerous figures, many of which are colored, and the articles provide extensive and up-to-date references to the literature. The table of contents is useful for navigating to the chapters; however, one has to realize first that the section headings are completely wrong, clearly because of an error in the production. A minor flaw is the subject index, which, although extensive, is not well-constructed. For example, there is no entry for "FK506", and only one for "chemical space", despite the fact that both terms appear in many of the chapters.

I found the book very stimulating, also in fields where I do not feel at home. It can also be used as a reference book for the areas of chemical biology that are covered. I recommend it for a readership that extends from the advanced PhD student with an interest in the subject to scientists already working in the field.

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