

This book is the 46th volume of this review series. A variety of timely topics are covered in 17 reviews, written by experts working in their respective fields. The reviews cover a broad range of individual topics in pharmacology and toxicology. Each will be of great value to medicinal chemists working in fields directly related to the topics covered. Select reviews likely to be of most direct interest to medicinal chemists in specific fields of drug discovery include (1) Peroxisome Proliferator-Activated Receptors; How Their Effects on Macrophages Can Lead to the Development of a New Drug Therapy against Atherosclerosis; (2) Cannabinoid Receptors as Therapeutic Targets; (3) Accessory Proteins for G Proteins: Partners in Signaling; (4) The Proteasome and Proteasome Inhibitors in Cancer Therapy; (5) Regulation of Platelet Functions by P2 Receptors; (6) Molecular Mechanism of 7TM Receptor Activation—A Global Toggle Switch Model.

All reviews are well written and informative. The subject index is thorough. Citations for most reviews are extensive and up to date. This book contains a short but useful list of reviews in other annual review publications that are related to topics in this volume. The present volume is a welcome addition to this long-standing series, providing concise summaries of advances in pharmacology and toxicology. It is notable that this book is located online at <http://pharmtox.annualreviews.org>. In addition, additional Annual Reviews series are located at [www.annualreviews.org](http://www.annualreviews.org).

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**Modern Biopharmaceuticals. Design, Development, and Optimization. Volumes 1–4.** Edited by Jörg Knäblein. Wiley/VCH Verlag, Weinheim, Germany. 2005. cxxxviii + 1886 pp. 17.5 × 24.5 cm. ISBN 3527331184. \$535.00.

This series of four volumes is an ambitious attempt to define the current state of biopharmaceuticals. Perhaps the biggest challenge with such a series is to define what is meant by the term and where the boundaries are with “traditional pharmaceuticals”. In the introduction, Gary Walsh defines biopharmaceuticals as “protein or nucleic acid based pharmaceuticals used for therapeutic or in vivo diagnostic purposes and produced by means other than direct extraction from a nonengineered biological source”. This defines the boundaries in Dr. Walsh’s contribution, but the entire four-volume set with 186 contributing authors is not encumbered by this definition. Topics run the gamut, from overviews of protein based and nucleic acid based therapeutics and therapeutic candidates to cell therapy, diagnostics, pharmacogenomics, analytical techniques, regulatory approval issues for pharmaceuticals, and drug delivery. It is a strikingly ambitious attempt to define and describe a burgeoning field of exciting research and development at the interface of science and commerce.

Individual contributions are somewhat variable in their scope and utility to a general reader, but such a series is likely to be a fine addition to library shelves in academic and corporate libraries. For the uninitiated in the field, this four-volume set will be somewhat overwhelming except for selected chapters.

The 100+ pages of introductory materials before the first chapter include short vignettes about virtually every contributor and topic. All in all, this is an impressive snapshot of the field.

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**G Protein-Coupled Receptors as Drug Targets: Analysis of Activation and Constitutive Activity. Methods and Principles in Medicinal Chemistry. Vol. 24.** Edited by Roland Seifert and Thomas Wieland. Wiley-VCH, Weinheim, Germany. 2005. xxvii + 275 pp. 17.5 × 24.5 cm. ISBN 3527308199. \$170.00.

The current installment of the Methods and Principles in Medicinal Chemistry series is a comprehensive treatment of the theory, study, and therapeutic applications of constitutive activity, a fundamental, underappreciated principle of G-protein-coupled receptor function. Although originally perceived as a simple ligand-operated on/off switch for activating cellular G-proteins, G-protein-coupled receptors (GPCRs) are now understood to possess varying degrees of ligand-independent or constitutive activity. In compiling *G Protein-Coupled Receptors as Drug Targets: Analysis of Activation and Constitutive Activity*, editors Roland Seifert and Thomas Wieland have assembled an international cast of experts to weigh in on diverse topics related to constitutive receptor activity in an accessible format.

The first half of the book gives detailed reviews of the structural, biochemical, and physiological basis for and implications of constitutive GPCR activity, beginning with an accessible description of mechanistic and mathematical models for inverse agonists and constitutive activation. Structural determinants that affect constitutive GPCR activity are reviewed, including splice forms, naturally occurring mutants, and G-protein coupling. Potential pathological roles for aberrant constitutive activity, as well as the potential therapeutic use of inverse agonists, are also presented in this section. The basic concepts section of the book ends with a thorough discussion of techniques commonly used to define constitutive GPCR activity, including thoughtful analysis of the limitations of the approaches.

The second half of this book examines the constitutive activity of various GPCR systems in greater depth, in most cases including structural, chemical, pharmacological, and physiological aspects and implications. Highlighted systems include  $\alpha$  and  $\beta$  adrenergic receptors, muscarinic acetylcholine receptors, histamine receptors, serotonin receptors, and chemokine receptors.

The chapters of this book were designed to stand alone as sovereign units such that they can be read à la carte. This is helpful for use as a quick reference, although it does lead to some redundancy (each chapter has an introduction to basic concepts) and a few inconsistencies. However, extensive cross-referencing between chapters helps to tie together concepts and make the book more cohesive. In summary, this book is an excellent review of the body of evidence describing constitutive GPCR activity. It is of general interest to pharmacologists, structural biologists, biochemists, and medicinal chemists with an interest in GPCR signaling pathways and as such would be