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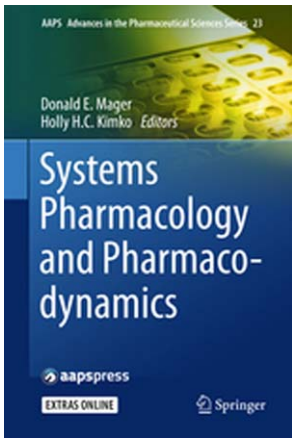
BOOK REVIEW

Book Review: *Systems Pharmacology and Pharmacodynamics*



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In 2008 and 2010, the National Institute of General Medical Sciences of the National Institutes of Health sponsored two workshops that resulted in the 2011 white paper "*Quantitative and Systems Pharmacology in the Post-genomic Era: New Approaches to Discovering Drugs and Understanding Therapeutic Mechanisms*,"[1] which is widely accepted to be a milestone marking the birth of the discipline of quantitative systems pharmacology (QSP). As early as 2004, the National Institute of General Medical Sciences had already coined an initiative to revive integrative and organ pharmacology as "Systems Pharmacology"[2] and, as far as I am aware, van der Greef & McBurney[3] were the first to propose the term in 2005 in the context of drug discovery. Since then, various (mainly overlapping) definitions of QSP have been proposed, the most pragmatic one that "systems pharmacology can be regarded as an approach to integrate the desirable features of the various model types spanning the spectrum between systems biology and pharmacometrics."[4] *Systems Pharmacology and Pharmacodynamics*, edited by Don Mager and Holly Kimko, has used this definition as its framework and, as a result, is the first textbook that provides an introduction to QSP accessible to both systems biologists as well as pharmacometricians.

The book is divided in three sections: Part I is an introduction to systems modeling for the pharmacometricians; Part II is an introduction to pharmacodynamics for the system biologists; and Part III is on multiscale models of drug action for both audiences.

Part I contains several high-level introductory chapters, which provide a generic overview of the status and role of QSP in academia and drug discovery, development, and also regulatory drug approval, which will provide a useful background for those new to the field. The final three chapters in this section delve deeper into the areas of discrete and kinetic dynamic modeling of networks and control systems, which will be of greater interest to readers already familiar with the general principles of QSP.

Part II is the mirror image of Part I and provides an introduction to pharmacodynamics and pharmacometrics for systems biologists. The editors should be applauded for achieving this task and managing to condense most basic pharmacokinetic/pharmacodynamic and pharmacometric principles into a handful of chapters. I found the chapter on "Detecting Pharmacokinetic and Pharmacodynamic Covariates from High-Dimensional Data" particularly interesting as a view on how to adopt well-established pharmacometric methods to the new world of big data.

Part III illustrates with case studies what the result of combining the approaches presented in Parts I and II looks like in the context of drug development. Compelling examples of the use of "multiscale models" are provided in the areas of the central nervous system, inflammation, cardiac toxicity, infectious diseases, oncology, and diabetes.

This is an excellent first of its kind general introduction to QSP, which will be of particular interest to those new to (the aspects of) the field. Given the rapid uptake of QSP in drug discovery and development, I expect that a second edition will include an even wider range of case studies demonstrating the impact of mechanistic modeling in research and development of decision making.

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