

*Book review by
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In its simplest form, a model may be defined as one thing that stands for another. The purpose of most pharmacokinetic/pharmacodynamic (PK/PD) models, and indeed virtually all scientific models, is to extract relevant information from the sea of data in which we are adrift (Boxenbaum, H. "Pharmacokinetics: Philosophy of modeling," *Drug Metabolism Reviews*, 24:89-120,1992)). In doing so, we distort one aspect of reality in order to enhance another, e.g., reducing the complexity of the mammalian body into two compartments, thereby allowing prediction of plasma concentration – time curves. However, losing information is only to our advantage if, and only if, the information gained is more valuable than the information lost.

If I were to select only one source of information on PK/PD modeling, this book would be it, since it is an extraordinary tome covering virtually all mathematical and conceptual perspectives inherent within the PK/PD modeling process. In its preface, the book lists the most common dysfunctions in PK/PD modeling: (1) unwarranted trust of software; (2) weighting data; (3) becoming a prisoner of formulas; and (4) lacking a holistic view of the modeling process. The authors indicate their desire to remedy these issues, and they do a very good job in accomplishing this objective.

The book is divided into two sections. In section one, there are six chapters:(1) general principles; (2) pharmacokinetic concepts; (3) pharmacodynamic concepts; (4) parameter estimation; (5) modeling strategies; and (6) design elements. This is followed in section two with a comprehensive series of discussions of specific PK/PD models, their applications, and an example of their use.

The first section discusses in great depth most PK/PD concepts, ranging from such mundane topics as the trapezoidal rule to more complex topics such as hepatic clearance models, the sigmoidal E_{max} model, etc. The entire book is heavy on mathematics, e.g., Chapter 2 has 426 equations. This mathematical leitmotif is reminiscent of M. Gibaldi and D. Perrier's "Pharmacokinetics," 2nd edition, Marcel Dekker, NY, 1982. However, Gabrielsson and Weiner cover a much broader array of topics in much greater depth, primarily due to the intervening 24 years between their publications.

The second section (supplemented with a CD) covers an astounding 53 PK and 42 PD models, peppered throughout with wonderfully drawn illustrations of relevant concepts. Covered herein are the following elements of each model: (1) problem specification; (2) sample data; (3) WinNonlin® analysis with inputs and outputs; and (4) interpretation of results and conclusions.

Overall, this book raises the stature of PK/PD modeling to its highest level. For

anyone employing PK/PD models, this book is an essential resource.

Finally, I should like to link this book to two of my favorite mathematical/modeling quotations: (1) ... to this day, our confidence in any science is roughly proportional to the amount of mathematics it employs – that is, to its ability to formulate its concepts with enough precision to allow them to be handled mathematically (J. Bronowski & B. Mazlish); and (2) In dealing with any natural phenomenon – especially one of a vital nature, with all the complexity of living organisms in type and habit – the mathematician has to simplify the conditions until they reach the attenuated character which lies within the power of his analysis (Karl Pearson).

Words to the author from a Canadian scientist:

"I have enjoyed your book on Pharmacokinetic & Pharmacodynamic Data Analysis very much. It is one of the best written scientific books I have consulted, the clarity of the text and the useful examples are particularly noteworthy. We consult it regularly.

Best regards, Pierre Leonard Pharm D, V-P Drug development, Enobia Pharma, Montreal, Canada"