## This Week's Citation Classic<sup>®</sup>\_

Segel I H. Enzyme kinetics: behavior and analysis of rapid equilibrium and steady-state enzyme systems. New York: Wiley-Interscience, 1975. 957 p. [Department of Biochemistry and Biophysics, University of California, Davis, CA]

This book is a comprehensive reference text on the basic principles and applications of enzyme kinetics. [The  $SCI^{\textcircled{o}}$  indicates that this book has been cited in over 1,735 publications.]

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Unlike the events that lead to the publication of a research paper, the reasons for writing a book are often more personal than scientific and, thus, harder to document objectively. I wish that I could say that "I saw a need for a comprehensive yet understandable text on enzyme kinetics and, feeling quite confident and fully qualified for the task, I wrote such a text." But the actual sequence of events was quite different.

In 1970 I submitted my first "kinetics" paper for publication. The reviews came back saying, in effect, that the author didn't understand kinetics and "has completely misinterpreted Cleland's rules." Seeking help, I brought some of my confusing kinetic data to a well-known enzymologist who was visiting our department at the time. He diagnosed the problem immediately: "Obviously, your enzyme is repelling the substrate." Clearly, I needed to know more about kinetics if I intended to continue studying enzymes.

The texts on enzyme kinetics available at the time were of no help. They were either superficial in their treatment of bireactant and terreactant enzymes or completely incomprehensible (to me at least; I'm sure that the authors considered their books to be models of clarity and enlightenment). Cleland's classic *Biochimica et Biophysica Acta* papers<sup>1-3</sup> were an obvious starting point, except that I didn't even recognize equation 1. Someone, I thought, should write a text on enzyme kinetics that started at ground zero and progressed to research-level material while remaining "user friendly" to mathematically unsophisticated readers.

The idea of writing such a text myself was inconceivable; the discovery of a substrate-repelling enzyme was not sufficient qualification. However, I did feel qualified to write about the more elementary aspects of enzyme kinetics, i.e., those topics usually covered in the introductory biochemistry courses that I teach. So, in 1971 I started to revise my first book, *Biochemical Calculations*.<sup>4</sup>

I began with the chapter on enzyme kinetics. By 1972 this chapter had grown to several hundred pages. It was obvious that I was no longer writing the second edition of Biochemical Calculations but, rather, something else. My first idea was to make that "something else" a text on general enzymology. But that year my colleague, John R. Whitaker, published his Principles of Enzymology for the Food Sciences,5 which, in spite of its title, is a general enzymology text. I didn't think that the world needed two new general texts from the same campus. This left me with only one course of action: continue writing about kinetics and produce the text I wished I had had available two years earlier. With the indispensable help of my wife, Dr. Leigh D. Segel, Enzyme Kinetics: Behavior and Analysis of Rapid Equilibrium and Steady-State Enzyme Systems was completed in 1974 and published in May 1975.

The first review (quite favorable) appeared in late 1975.<sup>6</sup> Other reviews, ranging from complimentary to hatchet jobs, appeared over the next several years. But by then, the comments of many enzyme researchers (often included as notes accompanying reprints I had requested) convinced me that I was on target. *Enzyme Kinetics* was cited in three research papers in 1976 and in 54 papers published in 1977. Since 1978 the book has been cited in more than 100 papers each year. I am gratified that the book continues to be useful to researchers in both basic and applied areas. (The citing papers have appeared in more than 50 different journals.) And, at about five cents per page, the book is still affordable to students.

While cumulative or annual citation counts are informative, I would like to propose a different method for evaluating books in specialized areas (where the total number of practitioners may be small): the Usefulness Index, U.I. = C/S, where C = total citations and S = total copies sold. Thus, a U.I. of 0.1 would mean that, on the average, 1 out of every 10 owners of the book has found it useful enough to cite it as a reference. To be meaningful, U.I. should be applied only when S is greater than some minimal value, e.g., 500. If anyone is interested, I'd be happy to divulge the U.I. of *Enzyme Kinetics*.

4. Segel I H. Biochemical calculations. New York: Wiley, 1976. 441 p. (Cited 30 times.)

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Cleland W W. The kinetics of enzyme-catalyzed reactions with two or more substrates or products. I. Nomenclature and rate equations. Biochim. Biophys. Acta 67:104-37, 1963. (Cited 1,635 times.) [See also Citation Classic. Commentary on Biochim. Biophys. Acta 67:104-37, 1963. (Cited 1,635 times.) [See also Citation Classic. Volume 2: the molecules of life. Philadelphia: ISI Press, 1986. p. 195.]

The kinetics of enzyme-catalyzed reactions with two or more substrates or products. II. Inhibition: nomenclature and theory. Biochim. Biophys. Acta 67:173-87, 1963. (Cited 795 times.)

The kinetics of enzyme-catalyzed reactions with two or more substrates or products. III. Prediction of initial velocity and inhibition patterns by inspection. Biochim. Biophys. Acta 67:188-96, 1963. (Cited 470 times.)

Whitaker J R. Principles of enzymology for the food sciences. New York: Dekker, 1972. 636 p. (Cited 130 times.)
Phillips A T. Review of "Enzyme kinetics" by I.H. Segel, "Enzymes: physical principles" by H. Gutfreund, and
Underschaft and the science for the science of the science area. Seg. Microphyl. Neurol. 2016, 1975.

<sup>&</sup>quot;Handbook of enzyme biotechnology" by A. Wiseman. Amer. Soc. Microbiol. News 41:795-6, 1975.