This Week's Citation Classic

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Dalziel K. Initial steady state velocities in the evaluation of enzyme-coenzymesubstrate reaction mechanisms. *Acta Chem. Scand.* **11**:1706-23, 1957. [Dept. Biochemistry, Nobel Medical Inst., Stockholm, Sweden]

Initial rate equations derived for several plausible mechanisms are particular cases of a common equation involving four kinetic coefficients, which can be estimated experimentally. Mechanisms are more easily distinguished by relations between these coefficients than by Haldane relations. Complex mechanisms that account for nonlinear Lineweaver-Burk plots and substrate inhibition and activation are considered. [The *SCI*® indicates that this paper has been cited over 315 times since 1961.]

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"I went to the Nobel Institute on a Rockefeller Fellowship in 1955, to work for a year with Hugo Theorell. My visit was remarkably well-timed. Two-substrate enzyme kinetics was in its infancy —and Theorell received the Nobel prize that year.

"I had already spent a few weeks at the Nobel Institute in the previous year, making some magnetic susceptibility measurements with their uniquely sensitive balance (with Anders Ehrenberg) on a supposed haemoglobin-H_2O_2 complex I had come across in kinetic studies of oxyhaemoglobin dissociation. I enjoyed that brief visit enormously, and was delighted when K.G. Paul suggested that I should try to go again for a longer period.

"Haemoglobin kinetics and the development of a constant-flow rapid reaction apparatus had been my life till then. That was changed when I got to Stockholm in 1955. Theo suggested that I might spend 'a few weeks' looking at the effects of pH change and NaCl in the kinetics of liver alcohol dehydrogenase, before continuing with my haemoglobin project. I had the advantage of complete ignorance of enzyme kinetics, and of the few good papers on two-substrate kinetics that had appeared at that time.[1] So I could look at the design and interpretation of our experiments without preconceived notions about the fundamental significance of a Michaelis constant, or that two-substrate kinetics are a simple extension of one-substrate kinetics. As it happened, I spent a lot of time, guided by Åke Åkeson, on further purification of alcohol dehydrogenase and separating a minor active component that turned out later to be the sterol isoenzyme. Then I ruined my first kinetic studies by forgetting about the effects of 0.5 M NaCl on the pH of phosphate buffer.

"This paper was written as the basis for interpreting our kinetic data, mostly obtained during a five-month extension of the original year. This enabled me to meet Robert Alberty, whose 1953 paper[2] was the starting point of mine. I suppose that my paper happened to appear at just the right time, and offered a simple, direct method for evaluating kinetic coefficients(Φ's) that have the dimensions of reciprocal rate constants, are independent of enzyme concentration, and describe the initial rate behaviour of two-substrate reactions in the simplest way. Compared with K_m's, the Φ's for most mechanisms are less complex functions of the rate constants, which simplifies the representation and manipulation of rate equations, especially for three-substrate reactions.[3] They also vary independently of one another with inhibitor concentration and pH. The representation of k_m/k_{cat} for a single substrate reaction as Φ never caught on, however, despite the fundamental significance of this ratio. I suspect that the frequency of citation of the paper simply reflects the need for authors to refer to some source for their rate equations and their method for estimating parameters—and the benefit of advertisement of the paper in the 1964 edition of Dixon and Webb![4]

"Were there any obstacles to the research or its publication? No. Under Theorell, the Nobel Institute was the ideal place for work and fun."

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1. **Schwert G W & Hakala M T.** Lactic dehydrogenase. I. Kinetics. *Arch. Biochem. Biophys.* **38**:55-65, 1952.
2. **Alberty R A.** The relationship between Michaelis constants, maximum velocities and the equilibrium constant for an enzyme-catalyzed reaction. *J. Amer. Chem. Soc.* **75**:1928-32, 1953.
3. **Dalziel K.** The interpretation of kinetic data for enzyme-catalysed reactions involving three substrates. *Biochemical J.* **114**:547-56, 1969.
4. **Dixon M & Webb E C.** *Enzymes.* London: Longmans Green, 1964. 950 p.