

Citation Classics

Cleland, William W. The kinetics of enzyme-catalyzed reactions with two or more substrates or products. I. Nomenclature and rate equations.
Biochimica et Biophysica Acta **67**:104-37, 1963.

A nomenclature is proposed to facilitate discussion of possible mechanisms for enzyme-catalyzed reactions with more than one substrate or product. A general method for expressing the full steady-state rate equations for these mechanisms in terms of measurable kinetic constants is explained, and the resulting rate equations are given for a number of mechanisms with two or three substrates or products. [The SC[®] indicates that this paper was cited 819 times in the period 1961-1975.]

William W. Cleland
Department of Biochemistry
University of Wisconsin
Madison, Wisconsin 53706

January 31, 1977

"Enzyme kinetics has clearly come of age when a theoretical paper published in 1963 makes the 'most cited' list. The article is probably cited as much for its definition of nomenclature as for the theory and equations themselves, and it is gratifying that both the nomenclature and equations seem to have stood the test of time and are used as widely as they are today. I am pleased that there is so little of what I said in 1963 that I would change today. We certainly understand the fundamental reasons behind the observed kinetic patterns today, while in 1963 we could only predict them by empirical rules. Many new types of kinetic experiments have been devised, but all of our new knowledge supplements, rather than replaces, what was said then.

"The story of how this work came to be published in *BBA* is amusing in retrospect, although it was traumatic at the time. When the work was in preprint form as three long articles, I sent it to *Biochemistry* early in 1962 and asked whether they would consider publishing such material. Dr. Neurath replied that with their bimonthly publication schedule, they really could not publish material of such length.

I then wrote to three other journals, enclosing preprints and asking them whether they'd be interested. 'If so,' I wrote, 'I will put them in the proper format, make some small revisions, and submit them formally.' Both the *Journal of Theoretical Biology* and *Journal of Biological Chemistry* replied favorably to this letter within two weeks, but I did not hear from *BBA*. On July 5, therefore, I formally submitted the papers to the *Journal of Biological Chemistry*. I then received a letter from *BBA* dated July 12, saying, 'I take pleasure to inform you that we have accepted your papers... Please send the corrections you wrote about in your letter of May 18.' This letter caused real panic, but I decided to play dead and imagine I was on vacation and not receiving my mail. It was not until a month later that I finally received a very detailed 5-page letter from John Edsall expressing interest, but requesting considerable revision and changes in nomenclature. It closed with, 'We recognize that the above rather drastic revisions may be disheartening after your efforts in writing three articles. We have taken this trouble, however, because we believe you have developed a system of substantial value which is well worthy of publication in the *Journal of Biological Chemistry*.' I felt unhappy that Dr. Edsall had spent so much time on the manuscript, but with an ace in the hole I sat down and wrote him that I wished to withdraw the papers, rather than revise them as drastically as he suggested, and I then sent the final corrected copies to *BBA*.

"It is interesting to speculate what might have happened if I had not also sent the preprints originally to *BBA* or they had not misunderstood my letter. Such now familiar terms as ping pong' might never have seen the light of day! It is gratifying that Dr. Edsall recognized the value of the theory, but in retrospect I think I was right and he was wrong about the nomenclature. This should perhaps be a lesson to all of us; brash youth is probably a better judge of nomenclature in a new field than established authority!"