Qeios

Peer Review

Review of: "The Steady State Approximation in Enzyme Kinetics: Reflections in Its Centennial Year"

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The aim of this manuscript is to critically reflect on the validity and use of the quasi-steady-state approximation (QSSA) in enzyme kinetics. This assumption leads to the so-called Henri-Michaelis-Menten (HMM) equation, which is widely applied to describe enzymatic and other reactions in physiology, biotechnology, food science, among other fields. A plethora of analyses have been published in the last 4-5 decades, aimed at mathematically demonstrating the conditions under which the QSSA is valid. To mention a few publications that are relevant to me:

Tzafriri, A. R., & Edelman, E. R. (2007). Quasi-steady-state kinetics at enzyme and substrate concentrations in excess of the Michaelis–Menten constant. *Journal of Theoretical Biology*, *245*(4), 737-748.

Srinivasan, B. (2022). A guide to the Michaelis–Menten equation: steady state and beyond. *The FEBS journal*, *289*(20), 6086-6098.

Schnell, S. (2014). Validity of the Michaelis–Menten equation–steady-state or reactant stationary assumption: that is the question. *The FEBS journal*, *281*(2), 464-472.

The studies reported by Professor Schnell and colleagues have gone far in establishing sufficient conditions to support the validity of the HMM equation. The reflection by Eric Barnsley concluded that the Haldane relationship between catalytic constants and the equilibrium constant of the reaction is not generally true. This postulate, although true, has been a topic of interest for researchers interested in the validity of the application of QSSA to the Michaelis-Menten kinetic mechanism. Eric Barnsley's reflection, although not a rigorous analysis, raises the issue of the validity of QSSA as a current and not completely resolved problem. Interestingly, Barnsley highlights the fact that variations in the basic reaction scheme (e.g., reversible steps in chemical reactions) further challenge the application of QSSA.

doi.org/10.32388/B79IK7

The problem, besides being interesting, has practical implications, since estimated parameters of the HMM equation based on experimental data are commonly used to interpret and elucidate kinetic mechanisms for enzymatic reactions in, e.g., physiology studies. Thus, the lack of clarity in the application of QSSA can lead to erroneous interpretations, since in many cases the estimated parameters would have little to do with the actual reaction mechanisms. My conclusion is that Eric Barnsley's reflection contributes to highlighting the importance of verifying the conditions of validity of the HMMM equation in order to avoid erroneous interpretations in terms of enzymatic reaction mechanisms. Given the long tradition of using the HMM equation, the conclusion is that the problem deserves more and better analysis, both from a theoretical-mathematical point of view and from the applications in a large number of fields.

Declarations

Potential competing interests: No potential competing interests to declare.