Chemical Oscillations in Enzyme Kinetics

KATHERINE L. QUEENEY¹, ETHAN P. MARIN¹, CORY M. CAMPBELL², and ENRIQUE PEACOCK–LÓPEZ³,*

¹ Department of Chemistry, Williams College, Williamstown, MA 01267
² Department of Anesthesiology, San Diego Veteran Administration Medical Center, 3350 La Jolla Village Drive, San Diego, CA 92161
³ Institute of Theoretical Dynamics, University of California, Davis, CA 95616

The Higgins model is a two variable model in enzyme kinetics. In contrast with other popular simple dynamical models like the Lotka–Volterra model, the Higgins model shows steady states, damped oscillations and stable limit cycles. For these three dynamical behaviors, stability analysis yields expressions of the eigenvalues, which are easy to obtain either analytically or with the use of Mathematica. With these expressions we can find the boundaries between the three dynamical regions in parameter space and the bifurcation point. Also, we have compared the Higgins model with the other two variable models and find that the origin of the richer dynamical behavior of the Higgins model is due to the enzymatic step in the mechanism.

* Permanent address: Department of Chemistry, Williams College, Williamstown, MA 01267
Introduction

For the last thirty years sustained oscillations in the concentration of a chemical substance have been the subject of intensive study. In spite of theoretical predictions of damped oscillations and sustained oscillations by Lotka and Hirniakand [1, 2] in 1910 and Lotka [3] in 1920, and the experimental observation of cyclic changes in the iodate catalyzed decomposition of hydrogen peroxide by Bray in 1921 [4], both experimentalists and theorists virtually ignored the field of chemical oscillations for nearly thirty years. Finally, in the early 1950s Belusov [5, 6] observed cyclic color changes in the bromination of citric acid catalyzed by cerium. By 1967 the first paper on the Belusov–Zhabotinsky (B–Z) [7] reaction written in English reached the West. This reaction caused immense interest among so many researchers that the First Symposium on Biological and Biochemical Oscillators was organized in 1968, forty seven years after Bray’s paper appeared in the Journal of the American Chemical Society.

An interesting aspect of the B–Z system centers around the original motivation that led Belusov to the celebrated reaction. Originally, his interest in biochemistry, and in particular in the Krebs cycle [8], motivated Belusov to seek a simple experimental model in which a carbohydrate was oxidized in the presence of a catalyst. In other words, the B–Z reaction was intended as a model of an enzyme catalyzed reaction. This connection between enzyme kinetics and the B–Z reaction is often forgotten and rarely mentioned. Most likely, this omission can be traced to the differences between an enzyme and its model counterpart Ce, the complicated mechanism underlining the chemical oscillations in the B–Z reaction and the mathematical analyses needed to understand some of the reduced models of the B–Z reaction. From the biochemical point of view these differences are difficult to reconcile with a biological model; therefore, the search for a model of chemical oscillation in enzyme kinetics that is both biochemically relevant and mathematically simple enough to present to an undergraduate audience is worthwhile from the pedagogical point of view.

In the present discussion we consider glycolysis emphasizing the allosteric properties of phosphofructokinase (PFK). For nearly thirty years oscillations in the concentration of nucleotides in the glycolitic pathway have been documented in the case of yeast cells and cell-free extract [9]. For example, reduced nicotinadenine dinucleotide (NADH) oscillations in yeast extract have been observed and determined to be flux dependent, and a minimum external flux is required to sustain oscillations in the concentration of NADH. Moreover, Hess and Boiteux [10] observed that phosphofructokinase plays an