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VALIDITY OF THE QUASI STEADY STATE ASSUMPTION FOR ENZYME-CATALYSED REACTIONS WITH COMPETITIVE INHIBITION AND SUBSTRATE INPUT *

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Dedicated to Dr. Dan Tiba on the occasion of his 70^{th} anniversary

Abstract

Enzyme-catalysed reactions are chemical reactions within cells in which the rate of the reaction is significantly increased through the action of enzymes. They are usually part of large and complex biochemical networks, which form the central processing units of the living cell. Enzymatic reactions often operate on multiple time scales, which can be characterized as being either fast or slow. The quasi steady-state approximation (QSSA) utilizes time scale separation to project

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these complex models onto lower-dimensional slow manifolds. In this paper, we investigate the validity of a quasi steady-state assumption for enzyme-catalysed biochemical reactions with competitive inhibition that are subject to a constant substrate input. Necessary and sufficient conditions for the validity of these assumptions were derived and were shown to be dependent, among others, on the substrate input. The validity conditions are numerically verified using the classical Runge-Kutta method.

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keywords: enzyme kinetics; inhibition; quasi steady-state; open system; multiple time scales; validity conditions.

1 Introduction

A biochemical reaction is a chemical transformation of one molecule into a different molecule inside a living cell. These reactions are mediated by enzymes, which are biological catalysts (in general, proteins) that help to convert specific molecules (which are called substrates) into products, without being themselves consumed in the process. The main functions of an enzyme are to speed-up and regulate the conversion of substrates into products by lowering the activation free energy of the reaction. An example of enzymatic reaction is the first reaction of the glycolysis (the conversion of glucose into pyruvate), which is catalysed by an enzyme called hexokinase.

Enzyme kinetics is the study of the binding affinities of other molecules (substrates or inhibitors) to enzymes, and the maximal catalytic rates that can be achieved. By understanding the kinetics of an enzyme, one can get insights into the catalytic mechanism of this enzyme, how its activity is controlled in the cell, and how specific drugs and poisons can inhibit its activity.

The kinetics of the enzymes do not follows the mass action kinetics directly, as also observed and studied by Michaelis and Menten in [8]. Their research on enzyme-catalysed reactions led them to propose that the formation of enzyme-substrate complex is a general mechanism of enzyme reactions, which is now known as the Michaelis-Menten formalism. The Michaelis-Menten model (represented in Figure 1) is the one of the simplest and best-known approaches to enzyme kinetics. This formulation considers that a substrate S binds reversibly to an enzyme E to form a complex C. The complex can decay irreversibly to form a product P and the en-