A short recursive procedure for evaluating effectiveness factors for immobilized enzymes with reversible Michaelis–Menten kinetics

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Abstract

A short recursive procedure for calculating the effectiveness factor for enzymes immobilized in porous spherical particles is presented. The method is mathematically simple and very precise; it is valid for reversible Michaelis–Menten kinetics including, as particular situations, simple Michaelis–Menten and product competitive inhibition kinetics.

The procedure is a modification of the two-parameter model previously published by the authors. The definition of an auxiliary dimensionless concentration leads to a recursive equation which simplifies the resolution of the model by means of elementary numerical methods. The solution algorithm has been transformed into a computer program, whose source code is appended.

The exact values of the effectiveness factors for zero and first order kinetics, as a function of the Thiele module, were compared with those obtained with the numerical procedure proposed in this work. The good agreement between both results demonstrates the validity of the method.
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1. Introduction

The advantage of using immobilized enzymes on a porous support is that the enzyme can be separated easily from the reaction bulk and reused. However, since the reaction takes place inside the particles, the reaction rate can be affected by the external diffusion processes and by diffusion within the particles.

The internal diffusional effects can be quantitatively expressed by the effectiveness factor, η, defined as the ratio of the average rate inside the particle to the rate in the absence of diffusional limitations [1].

Usually, the mathematical models for estimating the effectiveness factor in heterogeneous enzymatic systems are based on the following assumptions:

- The catalytic particle is spherical and its radius is R.

- The enzyme is uniformly distributed throughout the whole catalytic particle.
- The system is in a steady-state and isothermal.

Under these hypotheses, the mass balance differential equations for substrate and product in spherical coordinates, as well as the boundary conditions, are:

$$\frac{D_S}{r^2}\frac{d}{dr}\left(r^2\frac{dC_S}{dr}\right) = v_r; \qquad r = 0 \Rightarrow \frac{dC_S}{dr} = 0;$$
$$r = R \Rightarrow C_S = C_{SR} \tag{1}$$

$$\frac{D_P}{r^2}\frac{d}{dr}\left(r^2\frac{dC_P}{dr}\right) = -v_r; \qquad r = 0 \Rightarrow \frac{dC_P}{dr} = 0;$$
$$r = R \Rightarrow C_P = C_{PR} \tag{2}$$

The type of resolution method used to solve the differential equations and its degree of complexity depends on the mathematical form of v_r.

Most previously published enzymatic kinetic models involve non-reversible Michaelis–Menten kinetics, and are solved by numerical calculus. Among these models, some of the most

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Nomenclature

Area$_{new}$ area under the new profile of C
Area$_{old}$ area under the old profile of C
C dimensionless substrate concentration, defined in Eq. (8)
C_P product concentration inside the spherical particle
C_{PE} equilibrium product concentration
C_{PR} local product concentration at the particle surface
C_S substrate concentration inside the spherical particle
C_{SE} equilibrium substrate concentration
C_{SR} local substrate concentration at the particle surface
D_P effective product diffusivity inside the particle
D_S effective substrate diffusivity inside the particle
K_{eq} equilibrium constant
K_M Michaelis constant
K_P competitive product inhibition constant
m dimensionless module defined in Eq. (34)
N number of subintervals of the spherical particle radius
r particle radial coordinate
R particle radius
S dimensionless substrate concentration, defined as $(C_S-C_{SE})/(C_{SR}-C_{SE})$ in the two-parameter model [8]
v_C dimensionless reaction rate, defined in Eq. (10)
v_r local reaction rate per unit of particle volume
v_S dimensionless reaction rate, defined in Eq. (4)
V_M maximum reaction rate per unit of particle volume

Greek letters
α dimensionless module defined in Table 1, for the two-parameter model [8]
ε convergence limit of the calculation procedure
Φ dimensionless module defined in Table 1, for the two-parameter model [8])
η effectiveness factor
ρ dimensionless particle radial coordinate

Subscripts
i ith node (finite difference method)
new   new calculated value (finite difference method)
old   previous calculated value (finite difference method)

relevant are those proposed by Engasser and Horvath [2], for a simple Michaelis–Menten kinetics, modified by Tuncel [3]; the solution developed by Xiu et al. [4] for product competitive inhibition kinetics; or the two-substrate model formulated by Engasser and Hisland [5].

However, little attention has been paid to more complex kinetics such as reversible reactions [6]. The three-parameter model developed by the present authors [7] and the two-parameter model reformulated by the same authors [8] could be considered the most general mathematical model published to date. The models were solved for reversible Michaelis–Menten kinetics, which also allows the evaluation of simple Michaelis–Menten and product competitive inhibition kinetics. The first model has been successfully applied in the design of heterogeneous enzymatic reactors: fixed bed reactors [9], continuous tank reactors [10] and fluidized bed reactors [11]. Recently the methodology used in these papers has been applied to the simulation of a packed bed immobilized enzyme reactor performing lactose hydrolysis [12,13].

All the above-cited kinetic models were solved by numerical calculus because v_r is a non-linear function of the substrate and product concentrations. However, approximate analytical solutions, valid only in a limited range of the parameters, have also been published [14–16].

Several numerical methods have been used to solve the boundary problems outlined in Eqs. (1) and (2). The most frequently used are finite differences [17] and orthogonal collocation [18], which transform the problem into a system of algebraic equations. When the mass balance equations are non-linear, as in enzymatic kinetics, the result is also a non-linear equations system. The solution obtained by the finite differences method may not be unique and, moreover, convergence problems could appear. On the other hand, since the orthogonal collocation method uses polynomial expressions to approach the concentration profiles, the method is not very reliable when high diffusional limitations occur.

In the light of the above, many authors have used initial value methods such as the Runge–Kutta method. Such methods need to know the substrate concentration value at $r=0$. Since this value is unknown, the concentration profiles must be calculated based on an assumed value which is adjusted by successive calculations (shooting method) [19].

In this work a modification of the two-parameters model of Gómez et al. [8] is presented. A simple variable change leads to a modification in the value of the boundary condition in the particle centre, which becomes a known value of the new dimensionless concentration. The application of the finite differences method results in a recurrence expression, applicable in every radius node, to calculate substrate concentrations, thus avoiding the formulation of a complicated system of algebraic equations.

2. Theory

The diffusion-reaction equation of the two-parameters model [8] is:

$$\frac{1}{\rho^2}\frac{\mathrm{d}}{\mathrm{d}\rho}\left(\rho^2\frac{\mathrm{d}S}{\mathrm{d}\rho}\right) = \Phi v_S \tag{3}$$

The dimensionless reaction rate expression and the boundary conditions are:

$$v_S = \frac{S}{\alpha + S} \tag{4}$$

$$\rho = 0; \quad \frac{\mathrm{d}S}{\mathrm{d}\rho} = 0 \tag{5}$$