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A simple model to predict mass transfer rates and kinetics of biochemical and biomedical Michaelis–Menten surface reactions

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ABSTRACT

In this paper we propose a simple algebraic equation to compute the steady and laminar mass transfer rate produced by a surface chemical reaction that follows the Michaelis–Menten kinetic equation. This kinetic model characterizes the chemical rates of many catalytic biochemical reactions and many enzymatic reactions and, consequently, the equation can be used in experiments to predict the mass transfer rate or to determine the kinetics of reactions occurring on functionalized surfaces. The proposed correlation has been obtained by fitting results of numerical simulations and it relates the surface averaged Sherwood number, or the non-dimensional mass transfer rate, with the Péclet number based on the shear rate, the Damkhöler number (Da) based on the maximal velocity and the non-dimensional Michaelis constant (K_M^*). The validity of the correlation has been analyzed in the range of the non-dimensional parameters that can be found in physically realizable conditions. A procedure to determine experimentally the kinetic constants of the surface reaction is outlined and applied to experimental data.

1. Introduction

Enzymes are biological catalysts that participate in nearly all biochemical reactions occurring in living organisms. They have selective catalytic active sites that act on specific molecules or substrates. Enzymes are responsible, for example, for the metabolic reactions in the cells or the synthesis of DNA. The kinetics of many enzymatic reactions and many catalyzed biochemical transformations can be modeled using the Michaelins–Menten equation (see for example Voet et al. [1]). Examples can be found in some of the reactions of the coagulation cascade [2]. Molecularly engineered surfaces have been developed to obtain a desired biochemical transformation on the surface and have been used in enzymatic microreactors and in vascular prosthesis to control thrombus formation [3].

The use of enzymes for synthesis, diagnostics and screening of *in vitro* production of biomolecules has been possible thanks to the development of the microreactor technology. Miniaturized reactors have a high surface-to-volume ratio and allow an efficient use of small amounts of enzyme and a more precise control of the flow and the heat and mass transfer processes than large scale reactors. The applications of enzymatic microreactors range from the analysis and production of chemicals, such as proteins, to the monitoring and characterization of enzymes kinetics. Extensive reviews on the topic, as well as in immobilization techniques and materials, can be found elsewhere [4–6].

Enzymatic microreactors can be divided into two categories depending on if the enzyme is carried by the flow or if it is immobilized on a surface which is exposed to the flowing substrate. The later approach can be advantageous in some cases because there is no need to separate the enzyme from the outlet stream containing the products of the reaction. Alternatively the enzyme in solution can react with a substrate immobilized on a surface leaving the required product attached to the solid support [7].

Enzymes can be immobilized in the interior of monolith microreactors [8], on the surface of small particles or beads [9], that can be used as packing material to conform the bed of the microreactor, on membranes or on the walls of microchannels [10,11].

In this study we propose simple algebraic equations that relate the reaction rate of a surface reaction, which follows the Michaelis–Menten kinetic law, as a function of the flow parameters, the characteristic length of the surface and the kinetic constants. The application of the proposed equations is illustrated in the determination of the Michaelis constant of the activation of protein C on a surface functionalized with thrombomodulin [12].

These equations, which have been obtained by fitting results of numerical simulations, can be used to easily predict the production rate of the surface biochemical reaction, with known kinetic parameters, under simple and well controlled flow conditions or

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Nomenclature

A	area (m^2)
C	concentration (mol m^{-3})
D	mass diffusion coefficient (m s^{-2})
Da	Damkhöler number, Da = $V_{max}\ \delta/(D\ C_o)$
E''	surface concentration of enzymes (mol m^{-2})
H	height (m)
k	convective mass transfer coefficient, $k = N''/C_o$ (m s^{-1})
k_{cat}	catalytic constant or turnover number (s^{-1})
K_M	Michaelis constant (mol m^{-3})
L	length (m)
N''	molar flux at the wall (mol m^{-2} s^{-1})
Pe	Péclet number, Pe = $Re^2_{\tau\delta}\ Sc = \delta^2\ S/D$
Q	flow rate (m^3 s^{-1})
R	surface reaction rate (mol m^{-2} s^{-1})
$Re_{\tau\delta}$	Reynolds number, $Re_{\tau\delta} = u_\tau\ \delta/\nu = \delta\ (S/\nu)^{1/2}$
S	velocity gradient (s^{-1})
Sc	Schmidt number, $Sc = \nu/D$
Sh	Sherwood number, $Sh = k\ \delta/D = N''\delta/(D\ C_o)$
t	time (s)
u_τ	friction velocity, $u_\tau = (\tau_w/\rho)^{1/2} = (S/\nu)^{1/2}$ (m s^{-1})
V_{max}	maximal velocity, $V_{max} = k_{cat}\ E''$ (mol m^{-2} s^{-1})
V_o	volumetric reaction rate (mol m^{-3} s^{-1})
x, y	Cartesian coordinates (m)

Greek letters

δ	length of the active portion of the wall (m)
ν	kinematic viscosity (m^2 s^{-1})
τ	shear stress (N m^{-2})

Superscripts and subscripts

*	non-dimensional quantity
c	diffusion limited
k	kinetically limited
o	reference value
v	volumetric
w	wall

to straightforwardly determine the kinetic parameters of the surface reaction using the measured production rates. In this case, the use of these equations has evident advantages in the determination of the kinetic constants in comparison with the procedure based on numerical simulations in which the kinetic constants, that are input parameters of the simulations, are adjusted by trial and error until the numerically predicted production rate matches the measured one [11]. Note that this trial and error procedure may require the realization of a great number of simulations to adjust the two kinetic parameters in order to reproduce numerically the experimental measurements.

2. Model

Fig. 1 shows a sketch of the two dimensional physical model and the coordinate system adopted. It is assumed that the fluid has constant physical properties. The flow is incompressible, steady and fully developed. The mass transfer boundary layer is much thinner than the momentum boundary layer ($Sc = (\nu/D) \gg 1$) to, reasonably, assume that the velocity profile within the mass transfer boundary layer is linear ($S = du/dy$ = constant). The validity of this assumption is analyzed in detail in Section 3.2. The chemical reaction that follows the Michaelis–Menten kinetic law occurs on an active portion of the wall with length δ. The concentration of the reacting chemical outside the mass transfer boundary layer is constant, C_o.

Under these hypotheses, the steady-state concentration distribution is governed by Eq. (1).

$$Sy\frac{\partial C}{\partial x} = D\left(\frac{\partial^2 C}{\partial x^2} + \frac{\partial^2 C}{\partial y^2}\right) \tag{1}$$

Note that (Sy) on the left hand side of Eq. (1) corresponds to the streamwise velocity component that varies linearly along the vertical direction within the mass transfer boundary layer.

The non-dimensional version of Eq. (1) can be written as,

$$Re^2_{\tau\delta} Sc\ y^*\frac{\partial C^*}{\partial x^*} = \left(\frac{\partial^2 C^*}{\partial x^{*2}} + \frac{\partial^2 C^*}{\partial y^{*2}}\right) \tag{2}$$

The concentration, length and velocity scales used to obtain the non-dimensional variables are C_o, δ and the friction velocity u_τ, which is related to the shear rate as, $u_\tau = (\nu S)^{1/2}$. In Eq. (2), $Re_{\tau\delta} = u_\tau\delta/\nu$ and $Sc = \nu/D$ are the Reynolds and Schmidt numbers.

On the active part of the wall a chemical or biochemical transformation occurs with a kinetic rate R that can be modeled with the Michaelis–Menten equation. According to this kinetic model,

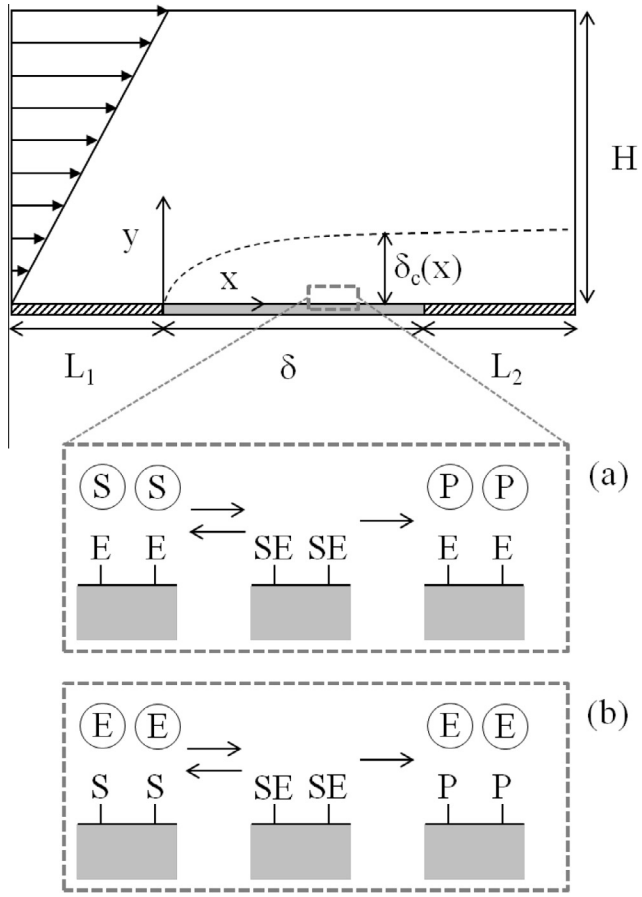

Fig. 1. Physical model, coordinate system and sketches of the Michaelis–Menten mechanism. E = enzyme. S = substrate. ES = enzyme-substrate complex. P = product. (a) Immobilized enzyme. (b) Immobilized substrate.