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Approximation of intra-particle reaction/diffusion effects of immobilized enzyme system following reverse Michaelis–Menten (*rMM*) mechanism: third degree polynomial and Akbari–Ganji methods

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Abstract

Two approximate analytical expressions based on third degree polynomial and Akbari–Ganji's method (AGM) were derived for the reaction/diffusion controlled kinetics of an immobilized enzyme (*IE*) systems. The approximation methods predict substrate concentration profile and effectiveness factor (η) in a porous spherical particle. The reaction is assumed to follow reverse Michaelis–Menten (*rMM*) kinetics. The approximate methods predictions were comparable to that of numerical solution (using the Matlab finite difference function, *bvp*4*c*) at wide range of ϕ^2 and y_o especially at low ϕ^2 and high y_o (polynomial equation) and low ϕ^2 and low y_o (AGM equation). Although the approximate solution was derived for *rMM* kinetics, the results can be used to describe other important enzymatic reaction kinetics such as simple Michaelis–Menten (*MM*) kinetics and *MM* with competitive product inhibition kinetics. A necessary design equation should be satisfied when using polynomial or AGM approximation for different enzyme kinetic equations. In this work, two examples of enzymatic reactions of industrial interest were studied, namely glucose-fructose isomerization follows *rMM* kinetics and hydrolysis of lactose follows Michaelis–Menten (*MM*) equation with competitive product (galactose) inhibition. Predictions of the developed third degree polynomial and AGM approximation equations agree with that of numerical solution, the percentage relative error for the effectiveness factor was less than 11 in comparison with the numerical solution. Good agreement between approximate and numerical estimations demonstrates the validity of these approximation methods.

Keywords Reverse Michaelis–Menten · Enzyme immobilization · Third degree polynomial · Akbari–Ganji's method · Effectiveness factor · Intra-particle diffusion

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List of symbols

a_0, a_1, a_2, a_3, b, c	Constants given in Eqs. (3.1–3.7)
D_e [m^2/s]	Effective diffusivity
k' [h^{-1}]	Reaction rate constant for pseudo first order reaction (V_s /k_s)
k_e [–]	Equilibrium constant
k_p [mol/l]	*MM* Constant for product
k_s [mol/l]	*MM* Constant for substrate
P [mol/l]	Concentration of product
R [m]	Radius of particle
r [m]	Radial length of particle
S [mol/l]	Substrate concentration
S_o [mol/l]	Substrate concentration outside the particle
S_e [mol/l]	Substrate concentration at equilibrium
V [mol/l h]	Rate of reaction
V_s [mol/l h]	The max. reaction rate for substrate
V_p [mol/l h]	The max. reaction rate for product
y_o [–]	Substrate concentration outside the particle in dimensionless form (S_o/k_s)
y [–]	Substrate concentration in dimensionless form (S/k_s)

Greek symbols

η [–]	Effectiveness factor
ζ [–]	$\zeta = k_s/k_p$
ψ [–]	$S_o/k_p = y_o\,\zeta$
ρ [–]	r/R
ϕ [–]	Thiele modulus $\phi = \frac{R}{3}\sqrt{\frac{V_s}{k_s D_e}}$ (Thiele modulus for *MM*, *rMM* kinetics and *MM* with product competitive inhibition). $\phi_1 = \frac{R}{3}\sqrt{\frac{k\prime}{D_e}}$ (Thiele modulus for first order kinetics)

Abbreviations

HFCS	High fructose corn syrup
IE	Immobilized enzyme
GI	Glucose isomerase
MM	Michalis–Menten
rMM	Reverse Michaelis–Menten

Introduction

Several advantages are achieved by enzyme immobilization compared to enzymes in suspension such as the enzyme reuse and improved catalytic activity. The kinetics of immobilized enzyme (*IE*) is different from enzyme in suspension due to mass transfer (external and internal) limitations. Increasing the level of agitation in reactor reduces the external mass transfer resistance. For porous particle, the internal diffusional resistance is more important and is difficult to eliminate.

Conducting substrate material balance on spherical particle at steady state resulted in a differential equation of second order (nonlinear) and two boundary conditions. Analytical solution is not available for these equations. The two-point boundary value problem is normally solved by numerical procedures such as finite difference, shooting method [1] and orthogonal collocation procedure [2]. The effectiveness factor (η) is used to determine the effect of inter-particle diffusional limitation on the overall reaction.

In general, using numerical techniques for solving differential equations is not easy and slow and also may have stability problem or difficulty of adjusting the variable to match numerical data. Although there are many numerical methods used to solve nonlinear differential equations with boundary conditions, to find approximate analytical method is still a goal to determine the effect of various parameters on the system. In the literature, several approximate methods are used for solution of the system controlled by diffusion and reaction kinetics [3]. Some of the widely used analytical method are homotopy perturbation method [4], adomain decomposition method [5], green function method [6], Taylor series method [7] and Akbari–Ganji method [8].

In the last decade, several publications were devoted for solving the reaction–diffusion problem for nonlinear kinetics such as: Babolian et al. [9] who used Sinc-Galerkin method, Azimi and Azimi [10] used differential transformation method, Lee and Kim [11] used global approximation method, Rani and Rajendran [12] and Ananthaswamy et al. [13] used Homotopy perturbation method, Praveen et al. [14] used modified Adomain decomposition method. Good agreements were found between approximate and numerical methods in all these approximation methods of solution. Also for solving the reaction–diffusion problem, Li et al. [15] derived an approximate third order polynomial equation for an *IE* catalyst performing *MM* kinetic equation. Good agreement with numerical solution was achieved at high substrate concentration in the bulk and at low Thiele modulus.

An approximate analytical method based on modified Adomain decomposition was used by Meena et al. [16] for solution of non-linear reaction–diffusion process based on *MM* kinetics. Analytical results showed good agreement with the third order approximation methods used. Saadatmandi et al. [17] solved the nonlinear boundary value problem using Chebyshev finite difference and differential transform method with Pad'e approximations. Results are compared with that reported using Homotopy analysis method. Rani et al. [12] developed analytical expression for the estimation of the η and substrate concentration for the nonlinear reaction–diffusion system. Using the new homotopy perturbation method, results showed good agreement compared to simulation predictions. Shanthi et al. [18] used AGM method to approximate the mathematical model for steady state reaction of pH-based potentiometric biosensor. Manimegalad et al. [19] used AGM method to approximate the diffusion and kinetics model of immobilized enzyme at different shapes of electrode. Good agreement was found between the analytical and numerical results, Also Mirgolbabaee et al. [20] used AGM method to approximate the nonlinear equation of the circular sector oscillation system. Results agree with Rung-Kutta numerical method for different values of the system parameters.

Most of the enzymatic reactions are capable of reversing (reversible) even the ones that are complete reactions. In the literature, most of the reported work on *IE* consider simple *MM* kinetics. Very little is published about complex enzyme reactions such as kinetics described by *rMM* [21] or *MM* with product inhibition term [22, 23]. Many of the industrially important enzymes these days are represented by complex kinetics. Isomerization of glucose and hydrolysis of lactose are described respectively by *rMM* kinetics and *MM* with competitive product inhibition kinetics. Extension of the calculations of η besides the simple *MM* equation is necessary to have clear knowledge of these complex enzymatic systems. Our present work is an attempt to expand the η calculations to *rMM* kinetics and *MM* kinetics with product competitive inhibition. The aim of this paper is to derive two analytical approximate solution of the reaction–diffusion controlled kinetics of *IE* system in spherical porous particle considering *rMM* kinetics. The approximation equations are based on polynomial of third order and Akbari–Ganji's methods. The approximation equation predictions were compared to that of numerical solution using the Matlab finite difference function "*bvp4c*" in terms of concentration of substrate variation in the solid particle and values of the effectiveness factor, η.

Theory

Approximation based on third degree polynomial

Assume an enzyme immobilized in a porous solid spherical particles (Radius = R). The kinetics of the enzyme reaction is represented by *rMM* equation. Substrate balance at steady state resulted in the following nonlinear differential equation with boundary conditions.

$$D_e\left(\frac{d^2S}{dr^2}+\frac{2}{r}\frac{dS}{dr}\right)=\frac{V_s\left(S-\frac{P}{K_e}\right)}{K_s\left(1+\frac{P}{K_p}\right)+S} \tag{1}$$

The boundary conditions are given by:

$$\text{A}\quad \text{t}\, r=0\quad \frac{dS}{dr}=0 \tag{1.1}$$

$$\text{A}\quad \text{t}\, r=R\quad S=S_o \tag{1.2}$$

In the derivation of the approximate equation, the assumptions below are assumed:

1. Negligible deactivation of enzyme.
2. Uniform activity of the enzyme within the particle.
3. The substrate internal particle diffusion is described by Fick's first law.
4. Substrate and product have similar diffusion coefficients (D_e).

5. Uniform distribution of enzyme in the particle.
6. Negligible external mass transfer resistance, S=S_o at the surface.
7. Constant reactor temperature.
8. Unity partition coefficient.

Making use of dimensionless parameters, the three equations above reduced to:

$$\frac{d^2y}{d\rho^2} + \frac{2}{\rho}\frac{dy}{d\rho} = 9\phi^2 \frac{y - \left[\frac{y_o - y}{k_e}\right]}{1 + \zeta y_o + (1-\zeta)y} \tag{2}$$

The boundary conditions are given by:

$$\rho = 0 \quad \frac{dy}{d\rho} = 0 \quad \text{B.C.1} \tag{2.1}$$

$$\rho = 1 \quad y = y_o \quad \text{B.C.2} \tag{2.2}$$

The dimensionless variables are

$$y = \frac{S}{k_s},\ y_o = \frac{S_o}{k_s},\ \rho = \frac{r}{R},\ \zeta = \frac{k_s}{k_p},\ \phi = \frac{R}{3}\sqrt{\frac{V_s}{k_s D_e}}$$

The Eqs. 2, 2.1, 2.2 are usually solved by numerical methods [2, 24]; ϕ describes the relation between reaction to diffusion rate in porous particle (Thiele modulus). High ϕ indicates diffusion controlled process, while low ϕ indicates reaction controlled process.

In this method, derivation of analytical approximate equation for the reaction/diffusion system assumed third degree polynomial for the profile of substrate concentration in the particles.

$$\rho = a_o + a_1\rho + a_2\rho^2 + a_3\rho^3 \tag{3}$$

Substituting Eq. 3 into Eqs. 2, 2.1 and 2.2, the polynomial coefficients can be determined:

$$a_o = \frac{-b + \sqrt{b^2 - 4c}}{2} \quad \zeta < 1 \tag{3.1}$$

$$a_o = \frac{-b - \sqrt{b^2 - 4c}}{2} \quad \zeta > 1 \tag{3.2}$$

$$a_1 = 0 \tag{3.3.}$$

$$a_2 = 2\left(y_o - a_o\right) - \frac{\frac{3}{2}\phi^2 y_o}{1 + \zeta y_o + (1-\zeta)y_o} \tag{3.4}$$

$$a_3 = y_o - a_o - a_2 \tag{3.5}$$

here

$$b = \frac{1}{1-\zeta}\left[1 + (2\zeta - 1)y_o + \frac{\frac{3}{4}\phi^2 y_o(1-\zeta)}{1 + \zeta y_o + (1-\zeta)y_o} + \frac{\frac{3}{4}\phi^2\left(k_e + 1\right)}{k_e}\right] \tag{3.6}$$

$$c = \frac{1}{1-\zeta}\left[\frac{\frac{3}{4}\phi^2 y_o\left(1 + \zeta y_o\right)}{1 + \zeta y_o + (1-\zeta)y_o} - \frac{\frac{3}{4}\phi^2 y_o}{k_e} - y_o\left(1 + \zeta y_o\right)\right] \tag{3.7}$$

The approximate equation is used also to determine the effectiveness factor, η that is defined as:

$$\eta_{approx.} = \frac{\frac{3}{R}D_e \left.\frac{dS}{dr}\right|_{r=R}}{\frac{V_s\left(S_o - \frac{P_o}{K_e}\right)}{K_s\left(1 + \frac{P_o}{K_p}\right) + S_o}} \tag{4}$$

Considering dimensionless parameters, η is given by the following equation:

$$\eta_{poly.approx.} = \frac{1}{3\phi^2}\frac{y_o + 1}{y_o}\left(2a_2 + 3a_3\right) \tag{5}$$

Equation 5 is used to determine the approximate value of the effectiveness factor (η). In addition, the concentration of product can be determined by the equation, $P = k_s(y_o - y)$.

Akbari–Ganji's method (AGM)

AGM approximation method is a powerful, fast and efficient semi-analytical approach for solving nonlinear reaction diffusion equation resulted from material balance in immobilized enzyme system using porous spherical particle. This method was developed in 2014 by [25, 26]. It is simple and accurate technique that converged fast and predict approximate solution in different fields of science and engineering [5, 8, 18–20, 27, 28]. In this work, there is good agreement between AGM and numerical solution based on the Matlab finite deference function, bvp4c. AGM assume the solution of Eq. 2 in the form of the following hyperbolic equation:

$$y(\rho) = A_0\, cosh(b\rho) + B_0\, sinh(b\rho) \tag{6}$$

here A_o and B_o are constants that can be found from boundary conditions of Eq. 2 ($B_o = 0, A_o = \frac{y_o}{\cosh b}$).

Equation 6 reduced to the following equation, which satisfies the boundary conditions (Eqs. 2.1 and 2.2).

$$y(\rho) = y_0 \frac{\cosh(b\rho)}{\cosh b} \tag{7}$$

This dimensionless substrate concentration equation represent a new approximate analytical expression at all values of ϕ^2 and y_o. The value of b can be determined by inserting Eq. 7 into Eq. 2. The resulted equation for the case of *rMM* equation is given by:

$$b^2 + 2b\tanh b = 9\phi^2 \frac{1}{(1 + 1/K_e) + y_o} \tag{8}$$

For the case of *MM* kinetics and *MM* kinetics with competitive product inhibition the above equation reduced to:

$$b^2 + 2b\tanh b = 9\phi^2 \frac{1}{1 + y_o} \tag{9}$$

Using AGM, the dimensionless effectiveness factor parameters, η is given by the following equation:

$$\eta_{AGMapprox.} = \frac{1}{3\phi^2} \frac{y_o + 1}{y_o} \frac{dy}{dx}\bigg|_{\rho=1} \tag{10}$$

This equation is reduced to the following

$$\eta_{AGMapprox} = \frac{1}{3\phi^2} \left(y_o + 1\right)(b\tanh b) \tag{11}$$

The accuracy of the AGM method is determined at different ϕ^2 and y_o, by comparing the result of substrate concentration profile and effectiveness factor with that obtained from numerical solution method.

Numerical solution

Numerical solution of the above second order differential equation (Eq. 2) with boundary conditions (Eqs. 2.1 and 2.2) can be achieved using the commercially available Matlab function *bvp4c* [29]. The *bvp4c* solver uses finite difference. The solution starts with an initial guess that is provided. The "bvp4c" function syntax command line is written in the form: sol = bvp4c (@odefun, @bcfun, solinit, options). Here odefun: a function that determines the differential equations. bcfun: a function determines the boundary conditions residual. solinit: containing the initial guess of the solution. Options: optional parameters that change the default integration properties. The Matlab function, bvp4c showed to be very efficient in solving second order differential equations with boundary conditions. Once the profile of substrate concentration is determined, η can be estimated numerically using Eq. 4 that reduces to the following:

Table 1 Reaction rate equations

Kinetic model	Rate equation
(1) Reverse Michaelis–Menten (*rMM*)	$V = \frac{V_s k_p S - V_p k_s P}{k_s k_p + k_p S + k_s P} = \frac{V_s (S - \frac{P}{k_e})}{k_s \left(1 + \frac{P}{k_p}\right) + S}$
(2) *MM* with competitive product inhibition	$V = \frac{V_s S}{k_s \left(1 + \frac{P}{k_p}\right) + S}$
(3) *MM*	$V = \frac{V_s S}{k_s + S}$
(4) Reversible first order	$V = k' \left(S - \frac{S_o}{k_e + 1}\right) = k'(S - S_o)$
(5) Irreversible first order	$V = k' S$

Table 2 Material balance equations for different kinetic models in dimensionless form

Kinetic equation	Material balance equation	Condition
(1) *rMM*	$\frac{d^2y}{d\rho^2} + \frac{2}{\rho}\frac{dy}{d\rho} = 9\phi^2 \frac{y - [\frac{y_o - y}{k_e}]}{1 + \zeta y_o + (1-\zeta)y}$	
(2) *MM* with competitive product inhibition	$\frac{d^2y}{d\rho^2} + \frac{2}{\rho}\frac{dy}{d\rho} = 9\phi^2 \frac{y}{1 + \zeta y_o + (1-\zeta)y}$	$\frac{1}{k_e} = 0$
(3) *MM*	$\frac{d^2y}{d\rho^2} + \frac{2}{\rho}\frac{dy}{d\rho} = 9\phi^2 \frac{y}{1+y}$	$\frac{1}{k_e} = 0, \zeta = 0$
(4) Reversible first order	$\frac{d^2y}{d\rho^2} + \frac{2}{\rho}\frac{dy}{d\rho} = 9\phi_1^2 (y - y_o/k_e + 1)$	$\zeta = 1$
(5) Irreversible first order	$\frac{d^2y}{d\rho^2} + \frac{2}{\rho}\frac{dy}{d\rho} = 9\phi_1^2 y$	$\frac{1}{k_e} = 0, \zeta = 1$

$$\eta_{num.} = \frac{1}{3\phi^2} \frac{y_o + 1}{y_o} \left.\frac{dy}{dx}\right|_{\rho=1} \tag{12}$$

The developed approximation model is based on the *rMM* kinetics. This general kinetic model is reduced to other simpler kinetic models at certain conditions such as *MM* and *MM* with competitive product inhibition and first order reaction kinetics. Table 1 shows all these kinetic models. Substrate balance using dimensionless parameters for the kinetic equations are shown in Table 2. The last column in this table shows the conditions for reduction of *rMM* equation to other kinetic equations.

The dimensionless mass balance equations for the different kinetic equations are shown in Table 2. At $k_e \rightarrow \infty$ (i.e. $1/k_e \rightarrow 0$), the *rMM* kinetic equation reduces to *MM* with competitive type product inhibition. At $k_s = k_p$ or $\zeta = 1$, Eqs. 2, 2.1 and 2.2 reduces to 1st—order reversible kinetics. The *MM* kinetic equation with competitive type product inhibition reduces to *MM* kinetics with no inhibition by product (i.e. $\zeta = 0$). At low concentration of substrate (i.e. $y << 1$), the *MM* equation can be further simplified to 1st—order kinetics. Table 2 also shows the conditions to obtain the different kinetic models from the general *rMM* equation.

Results and discussions

Profile of the dimensionless substrate concentration (y) in the spherical particle using approximation methods

It can be seen from the Eqs. 3–3.7 that the profile of dimensionless substrate concentration depends on: (i) The Thiele modulus, ϕ. (ii) The dimensionless concentration of the bulk substrate,y_o. (iii) $\zeta = k_s/k_p$ and iv) the equilibrium constant, k_e. The substrate concentration profile is estimated using a third order polynomial approximation and is compared with the results of numerical solution (Matlab bvp4c function) at the same conditions. Fig. 1a presents the dimensionless substrate concentration profile (y/yo) vs the dimensionless particle radius distance (r/R) using polynomial approximation (dotted line) and numerical solution (solid line) at $\phi^2 = 2$ and using four values of$y_o(2, 5, 10, 20)$.

Fig. 1b shows the same relation predicted by the AGM approximate method vs numerical solution method at the same conditions in Fig. 1a. It is clear from Fig. 1a, b ($\phi^2 = 2$) that for each y_o, the substrate concentration reaches the maximum value at the surface of the particle while it reaches the minimum value at the center of the particle. The concentration of substrate drops rapidly at lowy_o. (i.e. the substrate concentration in the center of the particle decrease with decreasing y_o). Large y_o indicates zero order, while $y_o \rightarrow 0$ indicate that the reaction approached first order.

Fig. 2 below is similar to Fig. 1 using constant value of $y_o = 5$ and using four different values of ϕ^2(0.2, 1, 2, 4). As shown in Fig. 2, The substrate concentration drops rapidly at high value of ϕ^2 (i.e. the substrate concentration in the center of the particle decrease with increasing ϕ^2). Large ϕ^2 indicates that the reaction is fast and the substrate is consumed near the exterior surface of the particle (diffusion controlled) and not penetrates to the center. Small ϕ^2 indicates reaction

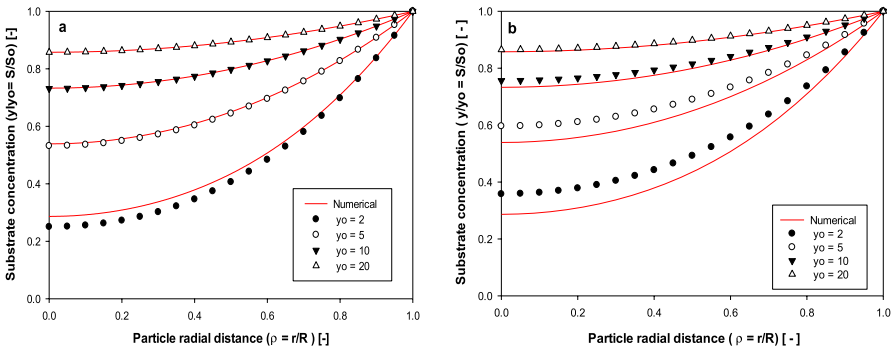

Fig. 1 Plot of the dimensionless substrate concentration (y/y_o) versus the dimensionless distance (r/R) in the spherical particle predicted by numerical method (solid line) for polynomial approximate solution (**a**) and AGM method (**b**) for $y_o = 2, 5, 10, 20, \phi^2 = 2$ (Michaelis–Menten kinetics,$\frac{1}{k_e} = 0, \zeta = 0$)

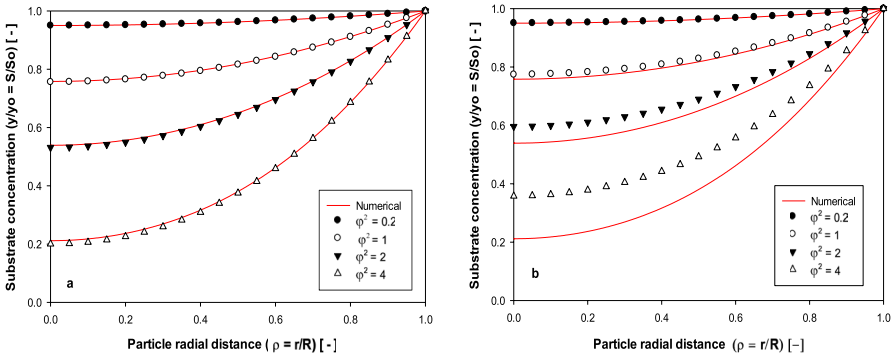

Fig. 2 Plot of the dimensionless substrate concentration (y/y_o) versus the dimensionless distance (r/R) in the spherical particle predicted by numerical method (solid line) for polynomial approximate solution (**a**) and AGM method (**b**) for $y_o = 5$ and $\phi^2 = 0.2, 1, 2, 4$ (Michaelis–Menten kinetics, $\frac{1}{k_e} = 0, \zeta = 0$)

controlled process and a significant amount of substrate penetrate to the interior of the particle without being consumed.

It is clear from the figures above that there is good agreement between the prediction of polynomial approximation and numerical solution especially at high y_o (Fig. 1a) and low ϕ^2(Fig. 2a). Also there is good agreement between the prediction of AGM approximation and numerical solution especially at high y_o (Fig. 1b) and low ϕ^2(Fig. 2b).

To determine the percentage error using the approximate solution in comparison to numerical solution method, the percentage relative error was calculated:

$$\%relative\ error(\%RE) = 100\,(y_{approx.} - y_{num.})/y_{num.} \tag{13}$$

Fig. 3 shows the percentage relative error $(\%RE)$ in substrate concentration across the spherical particle at different y_o and ϕ^2 imported from using the approximate polynomial method (Fig. 3a) and the AGM method (Fig. 3b) compared to numerical method using *MM* kinetics. It is clear from Fig. 3 that the two methods of solution agree at large range of y_o and ϕ^2 values especially at low ϕ^2 and high y_o (polynomial approximation) and at low ϕ^2 and low y_o (AGM approximation). Very large error was obtained at very high ϕ^2 and low y_o (polynomial approximation) and at very high ϕ^2 and y_o (AGM approximation). In these cases significant deviations from numerical solution were observed. It is also clear from Figs. 1 and 2 that the approximate polynomial solution predicted higher substrate conversion while the AGM approximate method predicted lower conversion compared to the numerical solution.

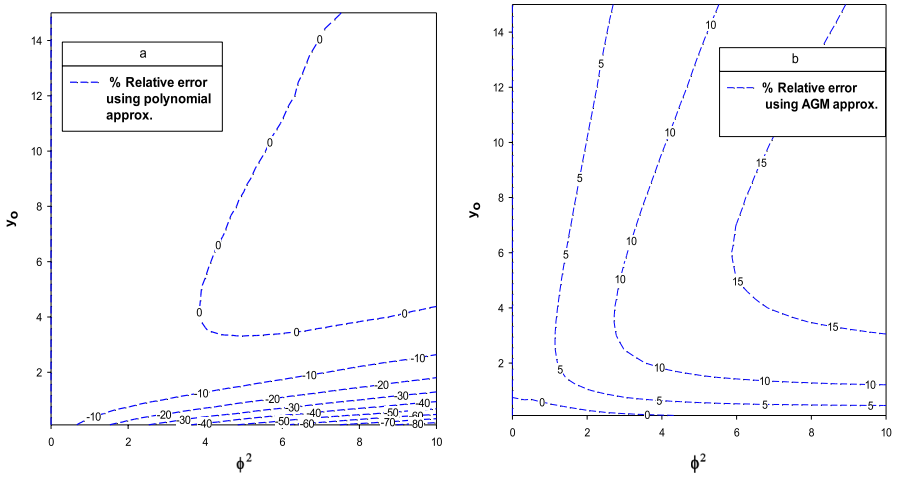

Fig. 3 The percentage relative error (*%RE*) in substrate concentration across the spherical particle at different y_o and ϕ^2 imported from using the approximate polynomial method (**b**) and the AGM method (**b**) compared to numerical method (*MM* kinetics, $\frac{1}{k_e} = 0, \zeta = 0$)

Conditions for the use of analytical polynomial approximate solution method

The constant a_o in Eq. 3 should be equal to or larger than 0 ($y_o = a_o$ at $\rho = 0$). This resulted in ($c \leq 0$ for $\zeta < 1$ according to Eq. 3.1). Therefore, the following condition should be satisfied for $\zeta < 1$:

$$y_o \geq \frac{{}^{3}\!/_{3}\phi^2(1+\Psi)k_e}{{}^{3}\!/_{3}\phi^2 + k_e(1+\Psi)} - 1 \tag{14}$$

$\psi = (S_o/k_p) = y_o\,\zeta$ (product inhibition modulus). Equation 3.2 is used when $\zeta > 1$ that leads to $c \geq 0$. Equation 14 can be derived at this condition for the case $\zeta > 1$ in addition to $\zeta < 1$. Equations 2, 2.1 and 2.2 reduced to 1st—order rate equation with analytical solution for the case of $\zeta = 1$. Equation 14 is reduces to Eq. 15 for *MM* kinetics and *MM* with competitive product inhibition kinetics.

$$y_o \geq {}^{3}\!/_{3}\phi^2 - 1 \tag{15}$$

Using simple *MM* kinetics, Eq. 15 was obtained by Li et al. [15].

Effect of the degree of product inhibition

Fig. 4 shows the effect of degree of product inhibition represented by ζ on the substrate concentration profile estimated by the polynomial approximation and numerical solution method at $\phi^2 = 2$, $y_o = 10$ (Fig. 4a), $y_o = 5$ (Fig. 4b). The case of $\zeta = 0$, represents simple *MM* kinetics with no product inhibition. Increasing ζ increases the

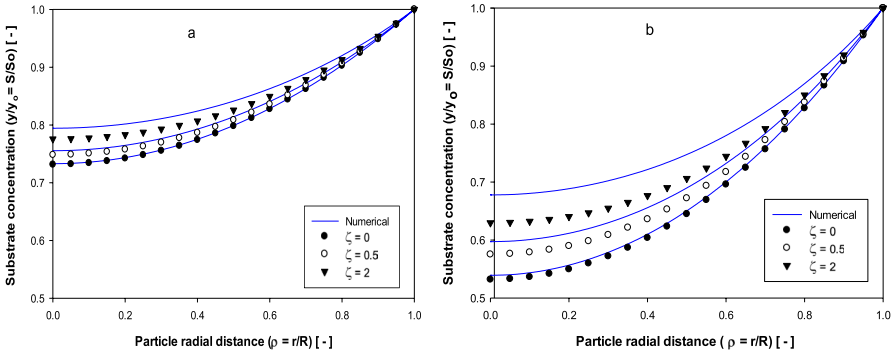

Fig. 4 Substrate concentration profiles across the spherical particles as a function of the degree of product inhibition ($\zeta = 0, 0.5, 2$) at $y_o = 10$ and $\phi^2 = 2$ (**a**) and at $y_o = 5$ and $\phi^2 = 2$ (**b**) using polynomial approximate method in comparison to numerical method (*MM* kinetics with competitive product inhibition, $\frac{1}{k_e} = 0$)

degree of product inhibition. It is seen in Fig. 4 that lower conversion is achieved at high ζ. The maximum conversion (The lowest concentration) is achieved at no product inhibition (*MM* kinetics). As shown in Fig. 4, the two solution methods give almost the same results for *MM* kinetics ($\zeta = 0$). The difference between them increases with increasing the degree of product inhibition with the approximate equation gives more conversion compared to the numerical solution method. Comparison between Fig. 4a, b shows that decreases y_o increases the substrate conversion.

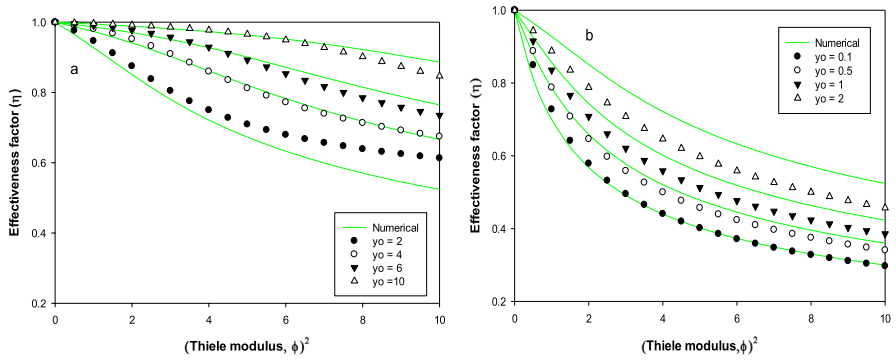

Fig. 5 Effect of the bulk substrate concentration,y_o and Thiele modulus, ϕ^2 on the effectiveness factor (η) estimated by polynomial approximation and numerical method (**a**), AGM approximation and numerical method (**b**) (*MM* kinetics, $\frac{1}{k_e} = 0, \zeta = 0$)

The effectiveness factor (η)

Equations 5, 10 and 11 are used to determine the η using the polynomial, AGM approximation and numerical solution method respectively. Fig. 5 shows the effect of the dimensionless bulk substrate concentration, y_o and the square of ϕ (ϕ^2) on the effectiveness factor (η) using polynomial approximation and the numerical solution (Fig. 5a), the AGM approximation and numerical solution (Fig. 5b). From Fig. 5, it can be seen that effectiveness factor decreases with increasing ϕ^2 and decreasing y_o. Deviation from numerical solution is higher for low y_o in polynomial approximation (Fig. 5a) while the opposite was noticed in the AGM approximation method (Fig. 5b). This deviation is shown to be significant at high ϕ^2.

Fig. 6 shows the effect of y_o, ϕ^2 on the effectiveness factor (η) estimated by numerical solution (Fig. 6a), polynomial approximation (Fig. 6b) and AGM approximation (Fig. 6c) for the case of *MM* kinetics.

First order kinetics

The Eqs. 2, 2.1 and 2.2 reduced to kinetics of reversible 1st—order when ζ=1 as shown in Eq. 4, Table 2. This equation is reduced to irreversible 1st—order when $1/k_e \rightarrow 0$ (Eq. 5 in Table 2). Analytical solution is available for first order kinetics as given by [30].

$$y = y_o \frac{\sinh 3\phi_1 \rho}{\rho \sinh 3\phi_1} \tag{16}$$

Here ϕ_1 is the first order Thiele modulus given by $\phi_1 = \frac{R}{3}\sqrt{\frac{kf}{D_e}}$

Using the definition of the effectiveness factor, analytical expression can be derived for η [30].

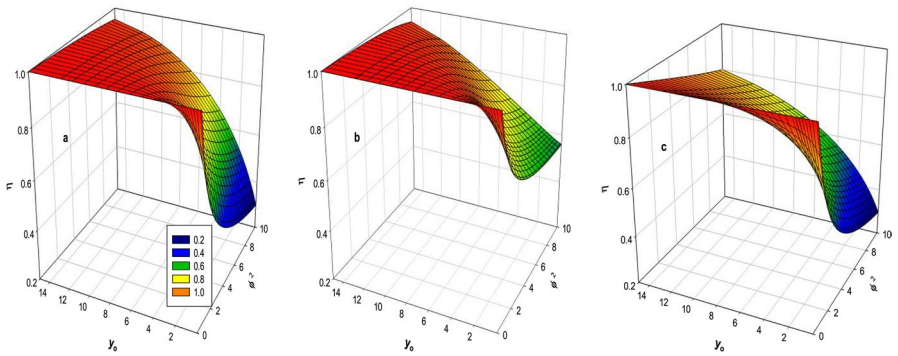

Fig. 6 Effect of the bulk substrate concentration, y_o (dimensionless) and Thiele modulus (ϕ^2) on the effectiveness factor (η) estimated by numerical solution (**a**) and polynomial approximation (**b**) and AGM approximation (**c**) (*MM* kinetics, $\frac{1}{k_e} = 0, \zeta = 0$)

$$\eta = \frac{1}{\phi_1}\left[\frac{1}{\tanh 3\phi_1} - \frac{1}{3\phi_1}\right] \tag{17}$$

The effectiveness factor depends solely on ϕ_1.

Industrial practical examples

The approximate methods predictions were tested and compared with that of the numerical solution using the Matlab function, bvp4c for two examples of enzymatic reactions with practical interest.

Glucose isomerization

The conversion of glucose to fructose is carried out using glucose isomerase (*GI*) enzyme. This is the last step in the production of high fructose corn syrup (HFCS). Enzymatic glucose—fructose isomerization is the most important process in industry. It is widely used process in food industry. Fructose is 75% sweeter than sucrose and absorbed slowly compared to glucose. Traditionally, this enzymatic reaction process used packed bed reactor with the immobilized enzyme*GI*. Usually the *GI* reactor operates at 60 °C [31].The concentration of glucose used is about 2.8 mol/L that is typical concentration of the product from the enzymatic saccharification and liquefaction of starch [32]. The kinetics of this enzymatic reaction usually described by *rMM* equation. Table 3 shows the *GI* reactor conditions from the literature [31, 32]. The first case in this table is at temperature of 60 °C. Using the kinetic and operation conditions available in the literature at this temperature, the polynomial and AGM approximation methods predicted 0.94 and 0.97 for the effectiveness factor compared to 0.94 predicted using the numerical method. The second case in Table 3 is at temperature of 70 °C [33, 34]. At this temperature, k_s=k_p (i.e. ζ=1), the *rMM* kinetics reduced to 1st—order reversible reaction kinetics with available analytical solution as given by Eqs. 16 and 17 [30]. Using Eq. 17 an η of 0.9215 was obtained. As shown in Table 3, the values of ζ and y_o decline with temperature, the decline of y_o is very small in low bulk concentration of glucose [35], therefore, the effectiveness factor can be considered constant at the temperature range from 60 to 80 °C which is typical for practical operation of *GI* reactor. From above, one can

Table 3 Practical example 1: production of HFCS using the enzyme glucose isomerase (GI)

GI reactor	pH	S_o (mole/l)	R (cm)	ϕ^2	y_o	ζ	$\eta_{Numerical.}$	$\eta_{polynom.}$ % relative error	$\eta_{AGM.}$ % relative error
T = 60 °C	7.5	2.805	0.06	0.3748	3.889	1.5	0.94 23	0.9406 − 0.18	0.9742 3.38
T = 70 °C	7.5	2.805	0.06	0.4071	3.334	1.0	0.9478	0.9417 − 0.64	0.9684 2.17

Table 4 Practical example 2: hydrolysis of lactose using the enzyme β-galactosidase on silica-alumina

Lactose hydrolysis reactor	ϕ^2	y_o	ζ	$\eta_{num.}$	$\eta_{polynom.}$ % relative error	$\eta_{AGM.}$ % relative error	$\eta_{exper.}$
$R(m)10^4 = 0.75$	0.36	13.291	0.423	0.993	0.9956 0.262	0.9916 − 0.141	1.0
$R(m)10^4 = 3.25$	6.587	13.291	0.423	0.8735	0.9067 3.8	0.8475 − 2.976	0.95
$R(m)10^4 = 6.5$	26	13.291	0.423	0.6282	0.6989 11.25	0.5789 − 7.85	0.89

T = 40 °C; pH = 6.5; $S_o = 50$ kg/m^3

conclude that use of the approximate equations to estimate the effectiveness factor is reasonable with the *%RE* less than 10 in the temperature range of operation for *GI* reactor.

Lactose hydrolysis

Lactose is a disaccharide present in milk (2–8% of the solid in milk). Lactose hydrolysis to glucose and galactose is important for production of milk with low lactose that is suitable for people who suffers from lactose intolerance. Hydrolysis of milk or whey is necessary for physiological, nutritional, technological and environmental purposes. The conversion step is important to prevent crystallization of lactose in the frozen dairy products such as ice cream. Lactose hydrolysis process is usually executed in packed bed reactor using the enzyme lactase (β –galactosidase). This enzymatic reaction is usually exhibited *MM* kinetics with competitive product (galactose) inhibition [22, 36, 37]. The kinetic constants and operating parameters for the hydrolysis of lactose by lactase is available in the literature [36]. Table 4 shows an example from the literature for hydrolysis of lactose [38]. From the table, it is clear that the calculated η using the numerical Matlab function, bvp4c, polynomial approximation, AGM approximation and from experimental results decrease with an increase in solid particle radius. The polynomial and AGM approximate equation predictions are higher in comparison with that of numerical solution method. The *%RE* using the approximate equation in comparison with numerical method increases with an increase in the solid particle radius. It can be concluded that the two approximate solutions are more suitable for estimation of the effectiveness factor (η) for particle with small radius.

Conclusions

Two approximate analytical methods were used to solve reaction–diffusion controlled problem in an immobilized enzyme reactor system using *rMM* kinetics. The analytical methods are based on the third degree polynomial equation and the AGM approximation. The developed approximation methods estimated the concentration

of the substrate in the spherical particle and the effect of internal diffusion resistance measured by the effectiveness factor, the results were compared with numerical solution determined by the Matlab finite difference function, bvp 4*c*. The following is a summary of specific conclusions drawn from the present work:

1. Predictions of the two analytical approximate methods agree well with that of the numerical solution for substrate concentration profile and effectiveness factor (η) at wide range of ϕ^2 and y_o especially at low ϕ^2 and high y_o (polynomial equation) and low ϕ^2 and low y_o (AGM equation), where the approximation method has almost the same predictions as numerical solution.
2. Using a third-order polynomial approximation, Eqs. 14 and 15 should be satisfied for *rMM* kinetics and *MM* kinetics with competitive product inhibition or simple *MM* kinetics respectively. While using AGM approximation, Eqs. 8 and 9 should be satisfied for *rMM* kinetics and *MM* kinetics with competitive product inhibition or simple *MM* kinetics respectively.
3. The third polynomial approximate method is not a good choice at high ϕ^2 and low y_o, while the AGM approximation method is not a good choice at high ϕ^2 and high y_o. The percentage relative error compared with numerical solution can be very high.
4. Although the approximate equations were derived with the assumption of *rMM* kinetics, this equation describes other simpler kinetics such as simple *MM* and *MM* with competitive product inhibition kinetics.
5. The developed third degree polynomial and AGM approximation equations were used to estimate the concentration profile for substrate and the effectiveness factor for two industrially important enzymatic reactions (i.e. hydrolysis of lactose and isomerization of glucose). The percentage relative error for the effectiveness factor was less than 11 in comparison with that of numerical solution.

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Data availability The data presented in this study are available in the article.

Declarations

Conflict of interest The author declares no competing interests.

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