Rajendran and Deena, J Material Sci Eng 2015, 4:3
DOI: 10.4172/2169-0022.1000167

Journal of Material Sciences & Engineering

Research Article Open Access

Simulating Plant Metabolic Pathways with Enzyme-Kinetic Models Using a New Approach to Homotopy Perturbation Method

Rajendran L* and Deena N

Department of Mathematics, Sethu Institute of Technology , Kariapatti- 626115, Tamilnadu , India

Abstract

The mathematical models of plant metabolic pathways is discussed. Kinetic modeling is the most detailed mathematical description of a metabolic network and constitutes an important branch in the growing fields of systems biology. This model is based on non-stationary diffusion equations containing a nonlinear term related to the Michaelics-Menten kinetics. An analytical expression of metabolic concentration was obtained for all values of parameters using new approach to Homotopy perturbation method. Our analytical results were compared with simulation results. Satisfactory agreement with simulation data is noted.

Keywords: Nonlinear equations; New homotopy perturbation method; Mathematical modeling; Michaelis-menten kinetics

Introduction

A Mathematical model is a description of a system using mathematical concepts and language. The process of developing a mathematical model is termed mathematical modeling. Mathematical models are used not only in the natural sciences, but also in the social science (such as economics, psychology, sociology, and political science). Mathematical models can take many forms, including but not limited to dynamical systems, statistical models, differential equations, or game theoretic models. Mathematical modeling of metabolism is usually closely associated with changes in compound concentrations that are described in terms of rates of biochemical reactions [1].

Various aspects of plant physiology have been analyzed extensively with kinetic models, and the field has a history going back for more than two decades. Detailed surveys of these models, the pathways they are addressing, and the techniques used can be found in [2,3]. A recent review was devoted to a quantitative comparison and ranking of all the kinetic models that have been published on the Calvin–Benson cycle [4]. This information will not be repeated here; instead, the purpose of this section is 2-fold. First, a summary of recent plant kinetic models that have been published since the last comprehensive review by is presented [3].

Kinetic modeling is the most detailed and complex mathematical description of a metabolic network and constitutes an important branch in the growing fields of systems biology. Kinetics modelling is to express the stoichiometries and regulatory interactions in quantitative terms. The dynamics of metabolic networks are predominated by the activity of enzymes – proteins that have evolved to catalyze specific biochemical transformations. The activity and specificity of all enzymes determines the specific paths in which metabolites are broken down and utilized within a cell or compartment. Note that enzymes do not affect the position of equilibrium between substrates and products [5].

A detailed kinetic description of enzyme catalyzed reactions is paramount to kinetic modeling of metabolic networks-and one of the most challenging steps in the construction of large-scale models of metabolism Elaborate descriptions of the fundamentals of enzyme kinetics are found in a variety of monographs, most notably the book of among many other works on the subject [6].

A metabolic network can be translated in mathematical terms by relatively easy means: the concentration of a metabolite is described by a variable s_i. The rate of each enzymatic step can be described by enzyme kinetic rate laws, such as the Michaelis-Menten equation, as a function depending on metabolite concentration and parameters such as the maximal velocity of a reaction, or binding constants. A metabolic network that consists of m metabolic reactants (metabolites) interacting via a set of r-biochemical reactions or interconversions. Mathematical modeling of metabolism is usually closely associated with changes in compound concentrations that are described in terms of rates of biochemical reactions. More details on different methods for metabolic modelling are given in the recent comprehensive overview of computational models of metabolism [7]. As a result, in this communication we have arrived at an analytical expression corresponding to the concentration of substrate and product using Homotopy perturbation methods for all values of reaction/diffusion parameters.

Mathematical Formulation of Problems and Analysis

During an enzyme-kinetic models [8]

$$D_S \frac{d^2S_1}{dX^2} + R_1 - 2R_2 = D_S \frac{d^2S_1}{dX^2} + k_1 - 2\left(V_{\max}\frac{S_2}{K_M + S_2}\right) = 0 \quad (1)$$

$$D_P \frac{d^2S_2}{dX^2} + 2R_2 - R_3 = D_P \frac{d^2S_2}{dX^2} + 2\left(V_{\max}\frac{S_2}{K_M + S_2}\right) - k_2S_2 = 0 \quad (2)$$

Where S is imported into the modeled system by R_1, converted to P by R_2, and finally taken out of the system by R_3 where K_i are parameters indicating the velocities of the reactions, S and P are the concentrations of the two metabolites. R_1 Carries a constant flux, while R_2 and R_3 follow mass action kinetics; In case of R_2 the product P is acting as an activator of the reaction. At this point it is important to account for reversibility as well as inhibition or activation of an enzyme, since omitting these effects is a common cause of unrealistic behavior [6].

***Corresponding author:** Rajendran L, Department of Mathematics, Sethu Institute of Technology, Kariapatti-626115, Tamilnadu, India Tel: 0452-2673354; E-mail: raj_sms@rediffmail.com

Received April 16, 2015; **Accepted** April 28, 2015; **Published** May 08, 2015

Citation: Rajendran L, Deena N (2015) Simulating Plant Metabolic Pathways with Enzyme-Kinetic Models Using a New Approach to Homotopy Perturbation Method. J Material Sci Eng 4: 167. doi:10.4172/2169-0022.1000167

A general scheme (Figure 1) that represents the change in metabolite concentration is shown below: The differential equations for the metabolites can be established from Eq. (1) and Eq. (2) respectively

$$D_s \frac{d^2S}{dX^2} + k_1 - 2\,V_{\max}\frac{P}{K_m + P} = 0 \tag{3}$$

$$D_p \frac{d^2P}{dX^2} + 2\,V_{\max}\frac{P}{K_m + P} - k_2 P = 0 \tag{4}$$

where S and P are the concentrations of the two metabolites, D_s and D_p are the diffusion coefficients, V_{max} are the maximal velocity of the enzymatic reaction, K_m are the Michaelis- menten constant, K_1, K_2 are parameters indicating the velocities of the reactions. In the above equations the initial and boundary conditions are given by

$$X = 0: \quad S = 0, \frac{dP}{dX} = 0 \tag{5}$$

$$X = L: S = 0, P = P_0 \tag{6}$$

We introduce the following set of dimensionless variables:

$$x = \frac{X}{L}, u = \frac{S}{P_0}, v = \frac{P}{P_0}, \alpha = \frac{2V_{\max}L^2}{D_s K_m}, \beta = \frac{P_0}{K_m}, \alpha_1 = \frac{2V_{\max}L^2}{D_p K_m}, m_1 = \frac{k_2 L^2}{D_p}, m = \frac{k_1 L^2}{P_0 D_s} \tag{7}$$

The above non-linear differential equations are expressed in the following dimensionless form:

$$\frac{d^2u}{dx^2} + m - \frac{\alpha v}{1+\beta v} = 0 \tag{8}$$

$$\frac{d^2v}{dx^2} - m_1 v + \frac{\alpha_1 v}{1+\beta v} = 0 \tag{9}$$

Where α, α_1 and β are the saturation parameters, x is the dimensionless distance, m_1 and m are diffusion parameters, u and v are the dimensionless concentration. The boundary conditions in non-dimensional form for the studied cases are:

$$x = 0: u = 0, \frac{dv}{dx} = 0 \tag{10}$$

$$x = 1: u = 0, v = 1 \tag{11}$$

Analytical Expression of the Concentration Using the New Homotopyperturbation Method

Recently, many authors have applied the Homotopy perturbation method to various problems and demonstrated the efficiency of the Homotopy perturbation method for handling non-linear structures and solving various physics and engineering problems [9-12]. This method is a combination of Homotopy in topology and classic perturbation techniques. Ji-Huan He used the HPM to solve the Lighthill equation, the duffing equation and Blasius equation [13-15]. The idea has been used to solve nonlinear boundary value problems, integral equations and many other problems [16,17]. The HPM is unique in its applicability, accuracy and efficiency. The HPM uses the imbedding parameter P as a small parameter and only a few iterations are needed to search for an asymptotic solution. Using this method (Appendix A), we can obtain the following solution to Eqs. 8 and 9 (Appendix B).

$$u(x) = -\frac{1}{2(m_1 + m_1\beta - \alpha_1)\left(\cosh\sqrt{\left(m_1 - \frac{\alpha_1}{1+\beta}\right)}\right)}\left((1+\beta)\,m\,m_1 x^2 - m\,\alpha_1 x^2\left(\cosh\sqrt{\left(m_1 - \frac{\alpha_1}{1+\beta}\right)}\right) - 2\alpha\left(\cosh\sqrt{\frac{m_1 + m_1\beta x - \alpha_1}{1+\beta}}\right)x - \left((1-x)\alpha\right)\right)$$
$$+\frac{x}{2(m_1 + m_1\beta - \alpha_1)\left(\cosh\sqrt{\left(m_1 - \frac{\alpha_1}{1+\beta}\right)}\right)}\left((1+\beta)\,m\,m_1 - m\,\alpha_1\left(\cosh\sqrt{\left(m_1 - \frac{\alpha_1}{1+\beta}\right)}\right) - 2\alpha\left(\cosh\sqrt{\frac{m_1 + m_1\beta\,x - \alpha_1}{1+\beta}}\right)\right) \tag{12}$$

$$v(x) = \operatorname{sech}\left(\sqrt{\left(m_1 - \frac{\alpha_1}{1+\beta}\right)}\right)\cosh\left(\sqrt{\left(m_1 - \frac{\alpha_1}{1+\beta}\right)}\,x\right) \tag{13}$$

Eq. (12) and Eq. (13) represent the new simple analytical expression of the concentrations for all values of parameters m, α, α_1, β.

Discussion

Eqs. (3) and (4) represents the approximation analytical expression of concentrations of substrate S and product P. The non linear Eqs. (8)-(9) are also solved by numerical methods. Our analytical results for the numerical concentration of substrate is compared with simulation results in Figure 2. (a)-(c) for various values parameter m, α, α_1, β. Also the value of concentration of substrate u(x) is equal to zero when x=0 and 1. From the Figure 2a, it is observed that the substrate concentration of $u(x)$ is slowly increases when m increases for small value of other parameters and then it reaches the maximum values at $x=0.5$. Similarly, in Figure 2b, the value of concentration of substrate $u(x)$ is slowly decreases when β decrease for large value of other parameters. Also

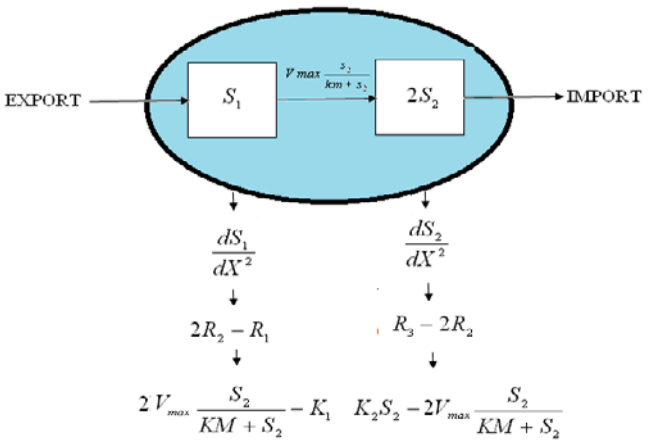

Figure 1: Schematic diagram of the change in metabolite concentrations.

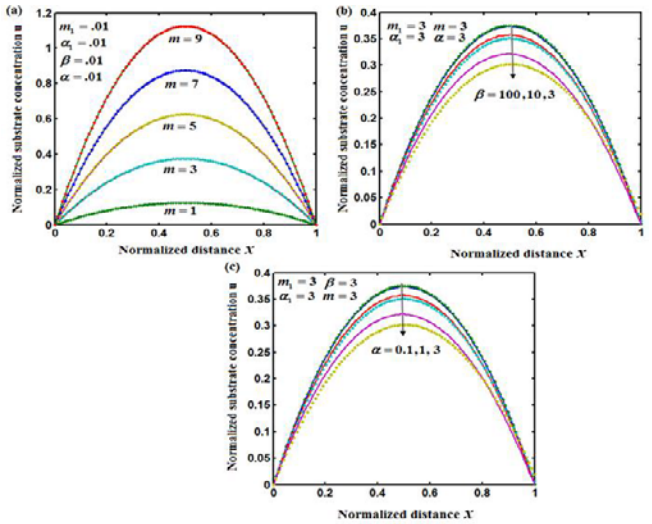

Figure 2: Normalized concentration profiles of substrate $u(x)$ from Eq. (12), for different values of m, α, α_1 and β when (a) $\alpha_1 = .01$, $\alpha = .01$, $\beta = .01$, $m_1 = .01$ (b) $\alpha_1 = 3$, $\alpha = 3$, $m_1 = 3$, $m = 3$ (c) $\alpha_1 = 3$, $\beta = 3$, $\beta = 3$, $m = 3$. Solid lines represent the analytical solution obtained in this work; dotted lines represent the numerical solution.

value of concentration substrate $u(x)$ increases when α decreases for large value of other parameters (Figure 2c).

Figure 3(a)-(c) represents the comparison of analytical expression of concentration of product with simulation results from the Figure 3a it is inferred that the concentration of product $v(x)$ is slowly increases when small values of m_1. In Figure 3b the product concentration $v(x)$ is increases when β decreases for large value of α_1 and m_1. Also value of concentration of product $v(x)$ increases when α_1 increases for different value of saturation parameter β and diffusion parameter m_1 (Figure 3c).

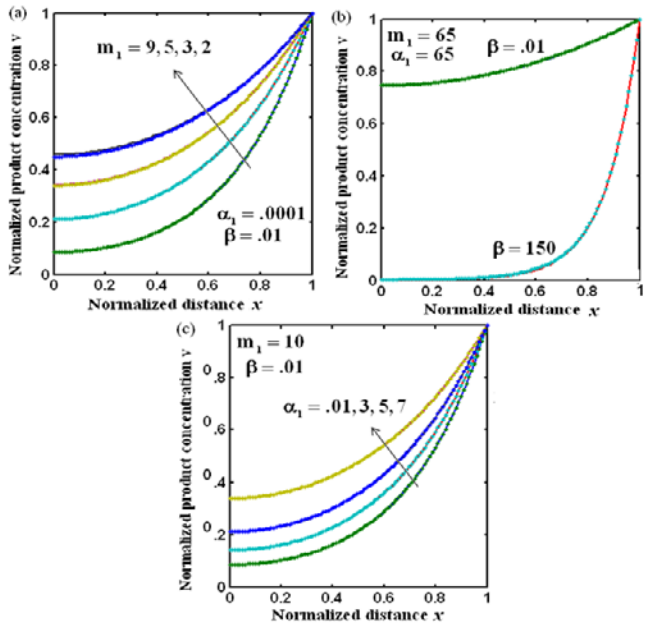

Figure 3: Normalized concentration profiles of product $v(x)$ from Eq. (13), for different values of m_1, α_1 and β when (a) $\alpha_1 = .0001, \beta = .01$ (b) $\alpha_1 = 65$, $m_1 = 65$ (c) $\beta = .01, m_1 = 65$. Solid lines represent the analytical solution obtained in this work; dotted lines represent the numerical solution.

Conclusion

The time independent, non- linear reaction/diffusion equation has been formulated and solved analytically. An approximate analytical expression for the concentration of substrate and product are obtained by using the Homotopy perturbation method. The primary result of this work is simple approximate calculation of concentration for all possible values of parameters. This method can be easily extended to find the solution of all other non-linear reaction diffusion equations in metabolic modeling for various complex boundary conditions.

References

1. Keshet LE (1988) Mathematical modelling in Biology. SIAM pub, New York, NY.
2. Morgan JA, Rhodes D (2002) Mathematical modeling of plant metabolic pathways. Metabolic Engineering 4: 80-89.
3. Rios-Estepa R, Lange BM (2007) Experimental and mathematical approaches to metabolic networks. Phytochemistry 68: 2351-2374.
4. Arnold A, Nikoloski Z (2011) A quantitative comparison of Calvin–Benson cycle models. Trends in Plant Science 16: 676-683.
5. Rohwer JM (2012) Kinetic modelling of plant metabolic pathways. Oxford University Press, Oxford.
6. Segel IH (1975) Enzyme Kinetics: Behaviour and analysis of Rapid Equilibrium and Steady-State Enzyme- Systems. Wiley-Interscience, Malden, MA.
7. Steuer R, Junker BH (2009) Computational models of metabolism: stability and regulation in metabolic networks. Adv Chem Phys 142: 105-251.
8. Schallau K, Junker BH (2010) Simulating Plant Metabolic Pathways with Enzyme-Kinetic Models. Plant Physiology 152: 1763-1771.
9. Li SJ, Liu YX (2006) An important approach to non-linear dynamical system identification using the PID neural networks. International Journal of Nonlinear-Science and Numerical Simulation 7: 177-182.
10. Mousa MM, Ragab SF (2008) Application of the Homotopy perturbation method to linear and nonlinear schrodinger equations. zeitschrift fur naturforschung 63: 140-144.
11. He JH (1999) Homotopy perturbation technique. Computer Methods in Applied Mechanics and Engineering 178: 257-262.
12. He JH (2003) Homotopy perturbation method: a new nonlinear analytical technique. Applied Mathematics and Computations 135: 73-79.
13. He JH (2003) A Simple perturbation approach to Blasius equation. Applied Mathematics and Computations 140: 217-222.
14. He JH (2006) Some asymptotic methods for strongly non-linearequations. International of modern Physics B 20: 1141-1199.
15. He JH, Wu GC, Austin F (2010) The variational iteration method which should be followed. Non-linear Science Letters A 1: 1-30.
16. He JH (2000) A Coupling Method of a Homotopy Technique and Perturbation Technique For Non- Linear Problems. International journal of Non-linear Mechanics 35: 37-43.
17. Ganji DD, Amini M, Kolahdooz A (2008) Analytical Investigation Of Hyperbolic Equations Via He's Methods. American journal of Engineering and Applied Science 1: 399-407.

Appendix A

Approximate analytical solution of the concentration of the substrate and concentration of the product using new Homotopy perturbation method**.** In this appendix, solution of non-linear system of equations Eq. (8) and Eq. (9) Is derived using the new Homotopy perturbation method.

$$(1-p)\left\{\frac{d^2u}{dx^2}+m-\frac{\alpha v}{1+\beta v(x=1)}\right\}+p\left\{(1+\beta v)(\frac{d^2u}{dx^2}+m)-\alpha v\right\}=0 \qquad \text{(A.1)}$$

$$(1-p)\left\{\frac{d^2v}{dx^2}-m_1+\frac{\alpha_1 v}{1+\beta v(x=1)}\right\}+p\left\{(1+\beta v)(\frac{d^2v}{dx^2}-m_1)+\alpha_1 v\right\}=0 \qquad \text{(A.2)}$$

Supposing the approximate solutions of Eq.(A.1)and Eq.(A.2)have the form

$$\begin{cases} u = u_0 + pu_1 + p^2u_2 + ... \\ v = v + pv_1 + p^2v_2 + ... \end{cases} \qquad \text{(A.3)}$$

Substituting Eq. (A.3) into Eq. (A.1) and Eq. (A.3) into Eq. (A.2) (respectively), and equate the terms with the identical powers of *p*, we obtain

$$p^0 = \frac{d^2u_0}{dx^2}+m-\frac{\alpha v_0}{1+\beta} \qquad \text{(A.4)}$$

$$p^1 : \frac{d^2u_1}{dx^2}+\frac{\alpha v_1}{1+\beta v1}-\alpha\alpha_1(v_0+\beta {v_0}^2)=0 \qquad \text{(A.5)}$$

and

$$p^0 : \frac{d^2v_0}{dx^2}-m_1+\frac{\alpha_1 v_0}{1+\beta}=0 \qquad \text{(A.6)}$$

$$p^1 : \frac{d^2v_1}{dx^2}+\frac{\alpha_1 v_1}{1+\beta}-m_1+\alpha_1 v_0(\frac{2+\beta+\beta v_0}{1+\beta})=0 \qquad \text{(A.7)}$$

The initial conditions are as follows:

$$u_0(x=0)=0; u_0(x=1)=0 \qquad \text{(A.8)}$$

$$dv_0(x=0)/dx=0; v_0(x=1)=1 \qquad \text{(A.9)}$$

and

$$u_i(x=0)=0; u_i(x=1)=0 \quad \text{forall } i=1,2,3... \qquad \text{(A.10)}$$

$$dv_i(x=0)/dx=0;\ v_i(x=1)=1 \quad \text{for all } i=1,2,3... \qquad \text{(A.11)}$$

Solving the Eq.(A.4) and Eq.(A.6) and using the boundary conditions Eq.(A.8) and Eq.(A.9), we get

$$u_0(x) = -\frac{1}{2\left(m_1+m_1\beta-\alpha_1\right)\left(\cosh\sqrt{\left(m_1-\frac{\alpha_1}{1+\beta}\right)}\right)}\left(\left((1+\beta)mm_1x^2-m\alpha_1x^2\right)\left(\cosh\sqrt{\left(m_1-\frac{\alpha_1}{1+\beta}\right)}\right)-2\alpha\left(\cosh\sqrt{\left(\frac{m_1+m_1\beta x-\alpha_1}{1+\beta}\right)}x\right)-\left((1-x)\alpha\right)\right) \qquad \text{(A.12)}$$

$$+\frac{x}{2\left(m_1+m_1\beta-\alpha_1\right)\left(\cosh\sqrt{\left(m_1-\frac{\alpha_1}{1+\beta}\right)}\right)}\left(\left((1+\beta)mm_1-m\alpha_1\right)\left(\cosh\sqrt{\left(m_1-\frac{\alpha_1}{1+\beta}\right)}\right)-2\alpha\left(\cosh\sqrt{\left(\frac{m_1+m_1\beta x-\alpha_1}{1+\beta}\right)}\right)\right)$$

$$v_0(\mathrm{x}) = sec\,h\left(\sqrt{\left(m_1 - \frac{\alpha_1}{1+\beta}\right)}\right) cosh\left(\sqrt{\left(m_1 - \frac{\alpha_1}{1+\beta}\right)}\, x\right) \quad \text{(A.13)}$$

Substituting the values of$u_o(x)$ in the Eq. (A.5) and solving the equations, using the boundary conditions Eq. (A.10) and Eq. (A.11), we can obtain the value of$u(x)$. Similarly we can get the value of $v_1(x)$ by solving the Eq. (A.7). When p=1, the approximate solution Eq. (A.3) becomes

$$u_0(x) = u_0 + u_1 \approx u_0 \text{ (A.14)}$$

$$v_0(x) = v_0 + v_1 \approx v_0 \text{ (A.15)}$$

Using the above equations, we get Eq. (12) and Eq. (13) in the next.

Appendix B

Matlab/Scilab program to find the numerical solution of equations (8)-(9).

```
function pdex4
m = 0;
x =linspace(0,1);
t=linspace(0,1);
sol = pdepe(m,@pdex4pde,@pdex4ic,@pdex4bc,x,t);
u1 = sol(:,:,1);
u2 = sol(:,:,2);
figure
plot(x,u1(end,:))
title('u1(x,t)')
xlabel('Distance x')
ylabel('u1(x,2)')
% ------------------------------------------------------------
figure
plot(x,u2(end,:))
title('u2(x,t)')
xlabel('Distance x')
ylabel('u2(x,2)')
% ------------------------------------------------------------
function [c,f,s] = pdex4pde(x,t,u,DuDx);
c = [1;1];
f = [1;1] .* DuDx;
m2=3;
m1=3;
alpha=3;
beta=.01;
alpha1=.0001;
F1=m2-((alpha*u(2))/(1+beta*u(2)));
```

```
F2=-m1*u(2)+((alpha1*u(2))/(1+beta*u(2)));
s=[F1;F2];
% --------------------------------------------------------------
function u0 = pdex4ic(x);
u0 = [0;0];
% --------------------------------------------------------------
function [pl,ql,pr,qr]=pdex4bc(xl,ul,xr,ur,t)
pl=[ul(1)-0;0];
ql=[0;1];
pr=[ur(1)-0;ur(2)-1];
qr =[0;0];
```