Analytic Solution of a Time Fractional Enzyme Kinetics Model Using Differential Transformation Method and Pade Approximant

S.T. Akinyemi[1,2,*], S.A.Salami [2], I.B.Akinyemi[3], & S.Sahabi[4]
[1]Department of Mathematics,
University of Ilorin,
Kwara State,
Nigeria.
[2]Global Kids Academy,
Marmaro Layout, Arkilla,
Sokoto State
[3]Department of Physics,
Kebbi State University of Science and Technology,
Aliero
[4]Department of Sciences,
Kebbi State Polytechnic,
Dakingari
[*]Sammysalt047@gmail.com

Abstract
This work is interested in finding the analytic solution of a time fractional enzymes kinetics model. Instead of using traditional method that requires perturbation, discretization or linearization, we used a method that is made up of the differential transformation method and Pade approximant called DTM-Pade. It is established that the proposed method avoids large computational work, is reliable and efficient when compared with fourth order Runge Kutta solution for enzyme kinetics model of integer derivatives.

1.0 Introduction

Enzymes are organic catalysts produced by living organism. They are proteins made up of tens or hundreds of amino acids. Enzymes are central to every biochemical process, acting in organised sequences; they catalyse the hundreds of stepwise reactions that degrade nutrient molecules (Robert, 1977).

The catalytic activities of enzymes depend on the sequence of amino acids in the chain and the functional groups present on the amino acids. Enzyme have a complex 3-D structure which is responsible for the high catalytic specificity, only substrates with a precise shape and size fit into the enzyme surface and bind with the functional groups at the active site of the enzyme (Fersht, 1990).

The reactant in an enzyme-catalysed reaction is called the substrate. The active site of an enzyme is that small portion of the molecule which is responsible for the catalytic action of the enzyme. Enzymes provide a chemical pathway that has lower activation energy than the same reaction uncatalysed (Bugg, 2004).

The study of enzymes has immense practical importance in some diseases especially inheritable genetic disorders; there may be a deficiency or even a total absence of one or more enzymes. For other disease conditions, excessive activity of an enzyme may be the cause. Measurements of activities of enzymes in blood plasma, or tissue samples are important in diagnosing certain illnesses. Many drugs exert their biological effects through

interactions with enzymes (Williams, 1975). Thus, it is important to study enzymes kinetics which provides better understanding on the temporal behaviour of various reactants, conditions influencing reactant and rates of reactant (Murray, 1989).

The Michaelis-Menten model is one of the simplest and best-known approaches to enzyme kinetics. It takes the form of an equation relating velocity to substrate concentration for a system where a substrate S binds reversibly to an enzyme E to form an enzyme-substrate complex ES, which then reacts irreversibly to generate the free enzyme E. (Briggs and Haldane, 1925). Several biochemical reaction models with integer derivatives are presented in Meena et al., 2009; Malik et al., 2014 (and other references cited there in).

In recent times, several studies carried out in the area of mathematical modelling of physical phenomena involving nonlinear dynamics has continue to gained popularity and success by applying fractional calculus. This is due to the advantages it has over integer calculus in modelling, which include

1. Reduction of errors from neglected parameters (Sofuoglu and Ozalp, 2014).
2. Consideration of memory loss or after effect (Zeb, 2014)
3. Greater degree of freedom (Alawneh, 2012**)**

The purpose of this work is to study the effectiveness and reliability of DTM-PADE to solve the MichealisMenten biochemical model of fractional order.

The rest of the paper is organized as follows. The basic idea of DTM-Pade Approximant is discussed in section 2. Application to a time fractional enzyme kinetics model is presented in section 3, while section 4 presents numerical simulation and discussion of results. Section 5 concludes the paper.

2.0 Basic Idea of DTM-Pade Approximant

A well-known semi analytic numerical method, suitable for solving linear and nonlinear differential equations, differential algebraic equations, integro- differential equation is the Differential Transformation Method (DTM) which was first proposed by Zhou (Peker et al., 2011; Akinboro et al., 2014; Adio, 2015). This method provides a highly accurate results or exact solution without linearization, discretization or perturbation.

Table 1: Fundamental Operations of Differential Transformation Method

Original function $f(t)$	**Transformed function** $F(p)$
$u(t)\pm v(t)$	$U(p)\pm V(p)$
$c\dfrac{du(t)}{dt}$	$\dfrac{c(p+n)!}{p!}U(p+n)$
t^n	$\delta(p-n)=\begin{cases}p=n\\p\neq n\end{cases}$
$u(t)v(t)$	$\sum_{l=0}^{p}U(l)V(p-l)$
$(1+t)^n$	$\dfrac{n(n-1)...(n-p+1)!}{p!}$
$\int_0^t u(t)\,dt$	$\dfrac{U(p-1)}{p}$
e^{ct}	$\dfrac{c^p}{p!}$

The use of polynomials to approximate truncated power series is common but not always advisable due to the singularities of polynomials which are caused by inadequate radius of convergence. Hence Pade approximants are extensively used to overcome these shortcomings. The Pade approximation of a function $f(t)$ of order $[m/n]$ is defined by (Vazquez-Leal et al., 2014; Mohamed and Torky, 2013)

$$[m/n]_{f(t)} = \frac{a_0 + a_1 t + \ldots + a_m t^m}{1 + b_1 t + \ldots + b_n t^n} \quad (1)$$

Where we consider $b_0 = 1$, the numerator and denominator have no common factors. It is important to note that the Pade approximant can be obtain with ease through the help of the in-built utilities of symbolic computational software such as Maple, Matlab and Mathematica (Oturanc, 2009). Thus the procedure of the aforementioned method to solve fractional order differential equation is summarized as:

1. Apply the differential transformation method to any given system of fractional order differential equations.
2. Perform several desirable numbers of iterations (i.e. of p times) and get the solution in power series form, let say $f(t) = \sum_{n=o}^{p+1} f(n) t^{\alpha n}$.
3. Replace the powers of the independent variable with another (that is t^{α} with x) to have the power series solution as $f\left(x^{\frac{1}{\alpha}}\right) = \sum_{n=o}^{p+1} f(n) x^n$.
4. Find the Pade approximation $[m/n]_{f\left(x^{\frac{1}{\alpha}}\right)}$ of the new series solution obtained from step 3
5. Substitute back the independent variable to finally have the solution in the powers of fractions

3.0 Application to Time Fractional Enzyme Kinetics

In this section, DTM-Pade technique is applied to solve an enzymekinetic model of nonlinear fractional derivatives. The model presented in Alawneh (2012), is governed by the following system of nonlinear fractional differential equation.

$$D_t^{\alpha_1} u = -u\varepsilon + \varepsilon(u + k - \lambda)v \quad (2)$$

$$D_t^{\alpha_2} v = u - (u + k)v \quad (3)$$

$$D_t^{\alpha_3} w = \lambda v \quad (4)$$

Subject to the following initial conditions

$$u(0) = 1, \qquad v(0) = 0, \qquad w(0) = 0 \quad (5)$$

Where ε, k and λ are dimensionless parameters.Here $D_t^{\alpha_i}$ for all $i = 1,2,3$ is the fractional derivatives in the Caputo sense, and α_i is the parameter describing the order of fractional time derivatives with $0 < \alpha_i < 1 \; \forall \; i = 1,2,3$. For $\alpha_1 = \alpha_2 = \alpha_3 = 1$, system (2)-(4) reduces to system of ordinary differential of (10a)-(10c) presented in Meena et al., 2010. Thus, system (1)-(3) is the generalized form of the system of equations in Meena et al., 2010. We refer

readers to Zeb et al., 2014 (and other references cited there in) for the details of basic idea and notation of fractional calculus.

Applying the differential transformation method to (1)-(3) we have

$$U(p+1)=\frac{\Gamma(\alpha_1 p+1)}{\Gamma(\alpha_1(p+1)+1)}\left[-\varepsilon U(p)+\varepsilon\left(\sum_{l=0}^{p}U(l)V(p-l)+(k-\lambda)V(p)\right)\right] \quad (6)$$

$$V(p+1)=\frac{\Gamma(\alpha_2 p+1)}{\Gamma(\alpha_2(p+1)+1)}\left[U(p)-\sum_{l=0}^{p}U(l)V(p-l)(p)-kV(p)\right] \quad (7)$$

$$W(p+1)=\frac{\Gamma(\alpha_3 p+1)}{\Gamma(\alpha_3(p+1)+1)}\lambda W(p) \quad (8)$$

$$U(0)=1, \qquad V(0)=0, \qquad W(0)=0 \quad (9)$$

The differential inverse transform of system (6)-(8) is gotten as

$$u=\sum_{n=0}^{p}U(n)t^{\alpha_1 n} \quad (10)$$

$$v=\sum_{n=0}^{p}V(n)t^{\alpha_2 n} \quad (11)$$

$$w=\sum_{n=0}^{p}W(n)t^{\alpha_3 n} \quad (12)$$

4.0 Numerical Simulation

In this section, several cases study was presented to show the reliability and validity of DTM-Pade Approximant approach to solve a time fractional enzyme kinetics model. To do this, we compare the proposed method with the fourth order Runge– Kutta method.

For different values of dimensionless parameters, ε, k and λ when $\alpha_1=\alpha_2=\alpha_3=1$, figure 1and 2 clearly depicts that the solution obtained by the proposed method and fourth order Runge– Kutta method are in excellent agreement. Thus DTM-Pade is very effective and accurate to obtain analytic solutions for an integer order enzyme kinetic model.

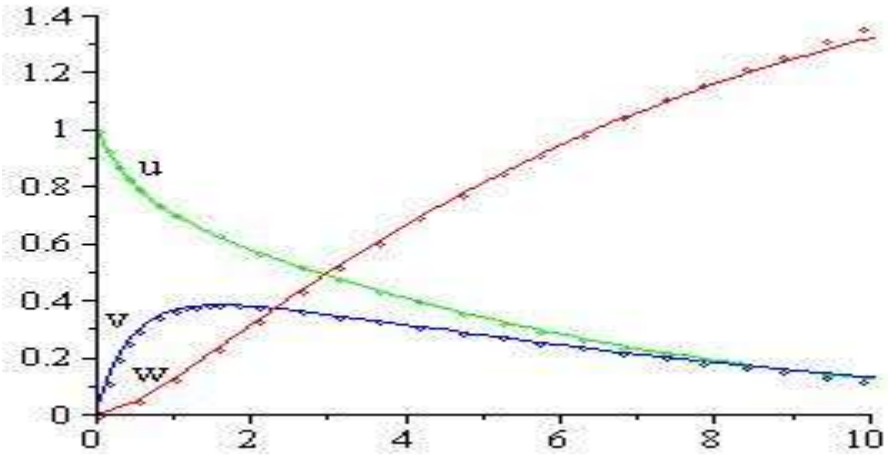

Figure 1: Comparison of the solutions obtained by DTM-Pade (dotted line) and Runge-Kutta method (solid line) for the normalized concentrations of the substrate u, enzyme-substrate complex v, and product w for $\lambda=0.5, k=1, \varepsilon=0.6$ and $\alpha_1=\alpha_2=\alpha_3=1$.

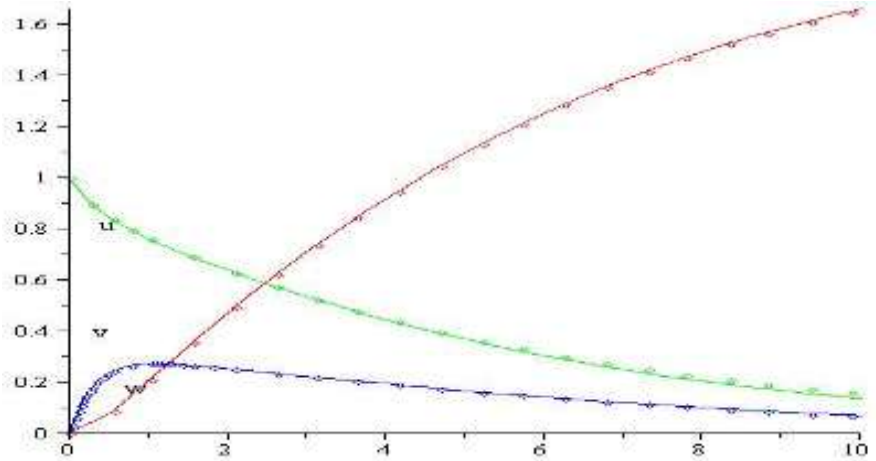

Figure 2: Comparison of the solutions obtained by DTM-Pade (dotted line) and Runge-Kutta method (solid line) for the normalized concentrations of the substrate u, enzyme-substrate complex v, and product w for $\lambda = 1, k = 2, \varepsilon = 0.5$ and $\alpha_1 = \alpha_2 = \alpha_3 = 1$.

Figure 3-6 shows the effect of fractional derivatives on the concentrations of the substrate u, enzyme-substrate complex v, and product w by fixing the value of the dimensionless parameters $\lambda = 0.5, k = 1, \varepsilon = 0.6$ while varying the magnitude of the order of fractional derivatives.

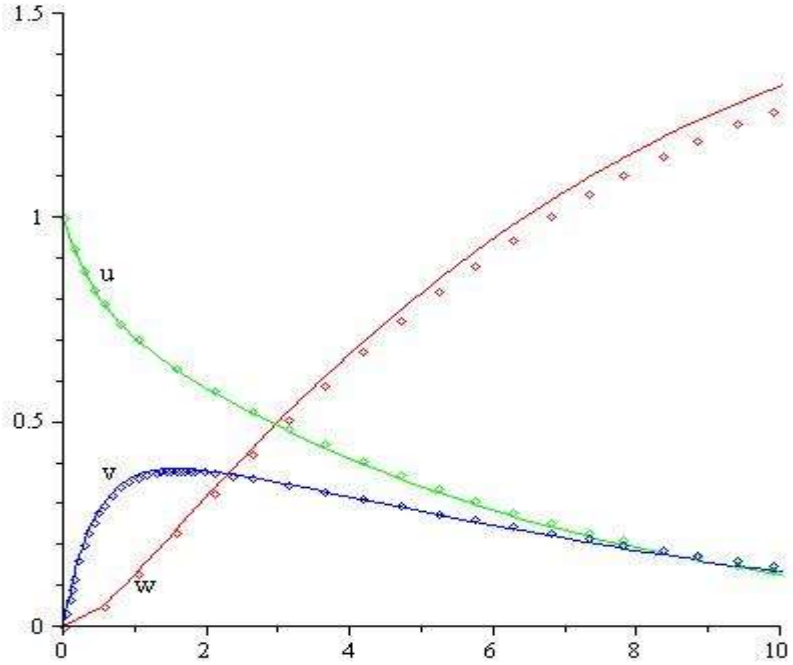

Figure 3: Profile of normalized concentrations of the substrate u, enzyme-substrate complex v, and product w for $\lambda = 0.5, k = 1, \varepsilon = 0.6$ and $\alpha_1 = \alpha_2 = \alpha_3 = 0.98$ (dotted line); $\alpha_1 = \alpha_2 = \alpha_3 = 1$ (solid line).

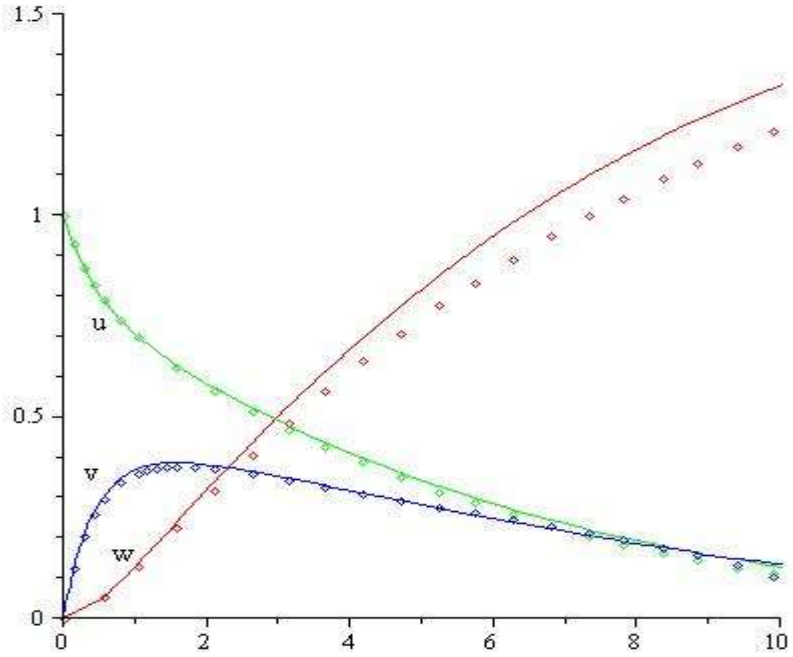

Figure 4: Profile of normalized concentrations of the substrate u, enzyme-substrate complex v, and product w for $\lambda = 0.5, k = 1, \varepsilon = 0.6$ and $\alpha_1 = 1, \alpha_2 = 0.95, \alpha_3 = 0.95$ (dotted line); $\alpha_1 = \alpha_2 = \alpha_3 = 1$ (solid line).

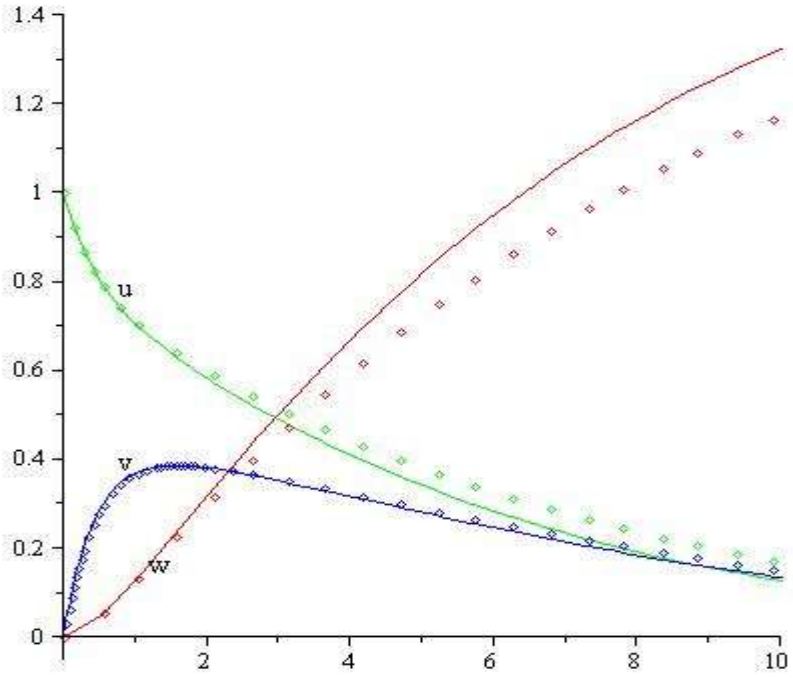

Figure 5: Profile of normalized concentrations of the substrate u, enzyme-substrate complex v, and product w for $\lambda = 0.5, k = 1, \varepsilon = 0.6$ and $\alpha_1 = 0.95, \alpha_2 = 1, \alpha_3 = 0.9$ (dotted line); $\alpha_1 = \alpha_2 = \alpha_3 = 1$ (solid line).

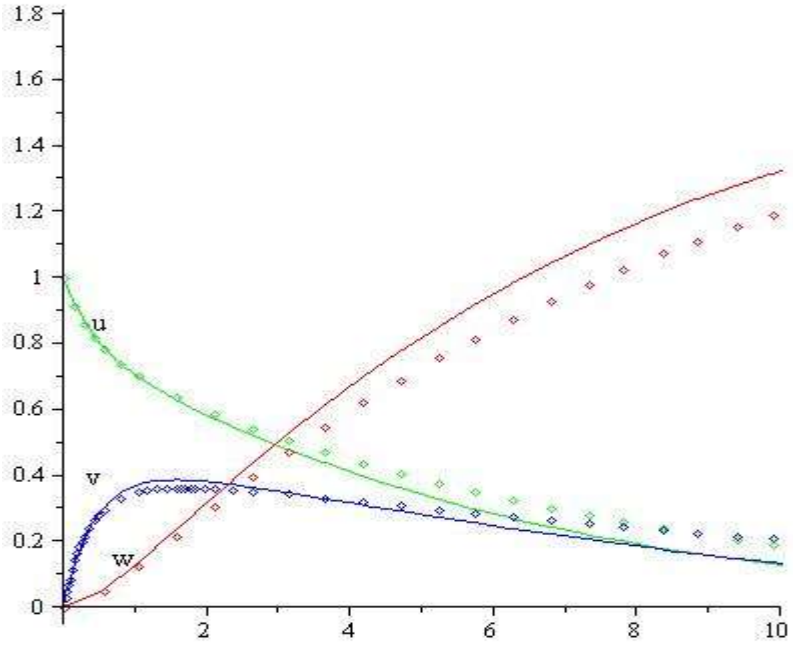

Figure 6: Profile of normalized concentrations of the substrate u, enzyme-substrate complex v, and product w for $\lambda = 0.5, k = 1, \varepsilon = 0.6$ and $\alpha_1 = 0.9, \alpha_2 = 0.85, \alpha_3 = 0.95$ (dotted line); $\alpha_1 = \alpha_2 = \alpha_3 = 1$ (solid line).

It is obvious to note that the concentration of the product w strictly increases from its initial value, the concentration of enzyme-substrate complex v increases at first and later decreases and concentration of the substrate u, gradually decreases.

5.0 Conclusion

In this paper, we were able to show that the proposed method is effective, powerful and accurate to solve a time fractional enzyme kinetics model. DTM-Pade works well for obtaining analytical solution not only for system of nonlinear differential equations with fractional derivatives but also for integers when compared with existing method(s). The direct application of this method requires no perturbation, linearization or discretization thus stressing the point that DTM-Pade should be applied for various nonlinear models.

References

Adio, A.K. (2015).Differential Transform Technique for Second Order Differential Equations: A Comparative Approach.International Research Journal of Engineering and Technology,2(7): 128-132.

Akinboro, F.S., Alao, S. and Akinpelu, F.O. (2014). Numerical Solution of SIR Model using Differential Transformation Method and Variational Iteration Method. Gen. Math. Notes, 22(2): 82-92.

Alawneh, A. (2013). Application of the Multistep Generalized Differential Transform Method to Solve a Time-Fractional Enzyme Kinetics. Discrete Dynamics in Nature and Society,Volume 2013, Article ID 592938, 7 pages.

Briggs, G.E. and Haldane, J.B. (1925). Anote on the kinetics of enzymes action. Biochem J,19:338-339.

Bugg, T. (2004). Introduction to enzyme and co-enzyme chemistry. University of Warwick.

Fersht, A. (1990). Structure and Mechanism in Protein Science. A Guide to Enzyme and

Catalysis and Protein Folding, W.H. Freeman and Company, New York.

Meena, A., Eswari, A. and Rajendran, L. (2010). Mathematical modelling of enzyme kinetics reaction mechanisms and analytical solutions of non-linear reaction equations. J. Math Chem,48: 179-186.

Mohamed, M.A. and Torky, M.Sh. (2013). Numerical Solution of Nonlinear System of Partial Differential Equations by the Laplace Decomposition Method and the Pade Approximation. American Journal of Computational Mathematics, 3: 175 184.http://dx.doi.org/10.4236/ajcm.2013.33026.

Murray, J.D. (1989). Mathematical Biology Springer, Berlin. p.109.

Oturanc, G. (2009). A New Approach to the Thomas-Fermi Equation. Selçuk Journal of Applied Mathematics, 10 (2): 67-74.

Peker, H.A., Karaoğlu, O. and Oturanç, G. (2011).The Differential Transformation Method and Pade Approximation for a Form of Blasius Equation. Mathematical and Computational Applications, 16(2): 507-513.

Robert,D.V. (1997).Cambridge University Press,Cambridge.

Sofuoglu, Y. Ozalp, N. (2014). A Fractional Order Model on Bilingualism. Commun. Fac. Sci . Univ. Ank .Series A1 63(2):81-89.

William P. J. (1975). Article in advances in enzymology.

Vazquez-Leal H.,Benhammouda B.,Filobello-Nino U.,Sarmiento-ReyesA.Jimenez-Fernandez V.M., …and Gonzalez-Lee M. (2014). Direct application of Padé approximant for solving nonlinear differential equations.Springer Plus, 3:563.

Zeb,A., Khan,M.,Zaman, G., Momani, S. and Ertürk, V.S. (2014). Comparison of Numerical Methods of the SEIR Epidemic Model of Fractional Order. Z. Naturforsch. 69a:81 – 89.