

# Analytical solution of non-linear equations in chemical reaction systems using homotopy perturbation method

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**Abstract:** A mathematical method is a powerful tool for the study of chemical reactions. This model is based on reaction-diffusion equations that contain a non-linear term analogous to the enzymatic kinetics of response of Michaelis-Menten and the hill binding. In this paper, an approximate analytical solution of the non-linear differential equations that describe the concentrations in mass-action kinetics has been derived for all values of parameter using the new homotopy perturbation method. These results are compared with the numerical result, and satisfactory agreement is noted.

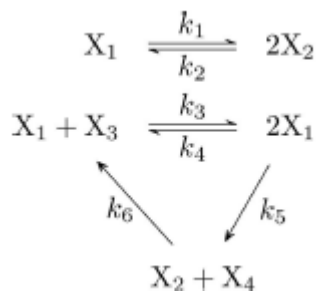
**Keywords:** Non-linear Equations, Mathematical models; Mass-action kinetics; Hill binding kinetics; New homotopy perturbation method; Numerical Simulation.

## 1. INTRODUCTION:

The rate of reaction is directly proportional to the concentrations of reactant species in normal deterministic mass-action kinetics. For example, according to mass-action kinetics, the rate of the reaction  $X_1 + X_2 \rightarrow X_3$  is of the form  $k x_1 x_2$ , where  $x_i$  the concentration of species is  $X_i$  and  $k$  is a positive constant.

Guldberg and Waage[1] first proposed the rule of mass action and recently recorded its 150th anniversary[2]. Kinetics derived from the law of mass-action are inevitable in chemistry and biology, are Michaelis-Menten kinetics or Hill kinetics [3-12]. The possible behaviours of mass-action systems also vary wildly; some systems have a single steady-state for all choices of rate constants, systems that have multiple steady states, systems that oscillate, and systems that admit chaotic behaviour [13].

This paper presents new theoretical methods for the analysis of the non-linear differential equation in chemical reaction systems. In this communication, unique and simple approximate analytical expressions for the concentration of Mass-action kinetics, concentration of Michaelis-Menten enzyme kinetics and Mass action system at chemical reaction systems are obtained using homotopy perturbation method for various values of parameters.



**Fig.1.** Schematics diagram of reaction [16].

## 2. The mathematical formulation of the problem

### 2.1. Mass-action kinetics

The network (Fig.1) contains the following system of differential equations according to mass-action kinetics[16]:

$$\frac{dx_1}{dt} = -k_1 x_1 + k_2 x_2^2 + k_3 x_1 x_3 - k_4 x_1^2 - 2k_5 x_1^2 + k_6 x_2 x_4 \quad (1)$$

$$\frac{dx_2}{dt} = 2k_1 x_1 - 2k_2 x_2^2 + k_5 x_1^2 - k_6 x_2 x_4 \quad (2)$$

$$\frac{dx_3}{dt} = -k_3 x_1 x_3 + k_4 x_1^2 + k_6 x_2 x_4 \quad (3)$$

$$\frac{dx_4}{dt} = k_5 x_1^2 - k_6 x_2 x_4 \quad (4)$$

where  $x_i = [X_i]$  is the concentration of species  $X_i$ . At any given time, the concentration vector  $x(t) = (x_1(t), x_2(t), \dots, x_n(t))^T$  is a point in  $\mathbb{R}^4 > 0$ . The initial conditions are  $x_1 = x_1^*, x_2 = x_2^*, x_3 = x_3^*, x_4 = x_4^*$  at  $t = 0$  (5)

### 2.2. Approximation analytical expression of concentrations in mass-action kinetics using the new approach of the homotopy perturbation method

Recently, the new approach of the homotopy perturbation method (NHPM) has been employed to solve the non-linear differential equations [17-19]. In this method, one or two iterations lead to highly accurate solutions of non-linear problems in physical and chemical sciences [20-21]. Solving the non-linear Eqs. (1-5) using the new approach of the homotopy perturbation method (Appendix A), the analytical expressions of concentration of mass-action kinetics can be obtained as follows:

$$\begin{aligned}
 x_1(t) &= x_1^* \exp(-k_1 t) + \frac{(1 - \exp(-k_1 t))}{k_1} (k_6 x_2^* x_4^* + k_2 (x_2^*)^2 + k_3 x_1^* x_3^* - 2k_5 (x_1^*)^2 + k_4 (x_1^*)^2) \\
 x_2(t) &= x_2^* \exp(-(2k_2 x_2^* + k_6 x_4^*)t) \\
 &\quad + \frac{(2k_1 + k_5 x_1^*) x_1^*}{2k_2 x_2^* + k_6 x_4^* - k_1 + k_3 x_3^* - k_4 x_1^* - 2k_5 x_1^* + k_6 x_2^*} \\
 &\quad \left[ \exp(-(k_1 - k_3 x_3^* + k_4 x_1^* + 2k_5 x_1^*)t) - \exp(-(2k_2 x_2^* + k_6 x_4^*)t) \right] \quad (7)
 \end{aligned}$$

$$\begin{aligned}
 x_3(t) = & x_3^* \exp(-(k_3 x_1^*)t) \\
 & + \frac{k_4 (x_1^*)^2}{k_3 x_1^* - k_1 + k_3 x_3^* - k_4 x_1^* - 2k_5 x_1^* + k_6 x_2^*} \left[ \exp(-(k_1 - k_3 x_3^* + k_4 x_1^* + 2k_5 x_1^*)t) - \exp(-(k_3 x_1^*)t) \right] \\
 & + \frac{k_6 x_4^* x_2^*}{k_3 x_1^* - 2k_2 x_2^* - k_6 x_4^*} \left[ \exp(-(2k_2 x_2^* + k_6 x_4^*)t) - \exp(-(k_3 x_1^*)t) \right]
 \end{aligned}
 \tag{8}$$

$$\begin{aligned}
 x_4(t) = & x_4^* \exp(-k_6 x_2^* t) \\
 & + \frac{k_5 (x_1^*)^2}{k_6 x_2^* - k_1 + k_3 x_3^* - k_4 x_1^* - 2k_5 x_1^*} \left[ \exp(-(k_1 - k_3 x_3^* + k_4 x_1^* + 2k_5 x_1^*)t) - \exp(-k_6 x_2^* t) \right]
 \end{aligned}
 \tag{9}$$

### 2.3. Michaelis-Menten enzyme kinetics or the Hill binding kinetics

It is usual in biochemistry to see the kinetics of the Michaelis-Menten enzyme or the kinetics of Hill binding. These are obtained by quasi-steady-state approximation from mass-action kinetics, which is a method of model reduction based on the removal of fast intermediates [5,9,14].

The Michaelis-Menten and Hill kinetics mathematically give rise to functions of the reaction rate that are rational functions. By using time-rescaling to delete all denominators [15], the analysis of these systems can be simplified to the study of dynamical analogous mass-action systems.

Consider the reversible reaction  $X_1 + X_2 \rightleftharpoons 2 X_1$  where the forward reaction  $X_1 + X_2 \rightarrow 2 X_1$  is modelled with a Michaelis-Menten reaction rate function  $\frac{k_1 x_1 x_2}{k_2 + x_1}$ , and the backward reaction  $2 X_1 \rightarrow X_1 + X_2$  is modelled using standard mass-action kinetics with reaction rate function  $k_3 x_1^2$ . Then the system of differential equations corresponding to these two reactions are described as follows [16]:

$$\frac{dx_1}{dt} = \frac{k_1 x_1 x_2}{k_2 + x_1} - k_3 x_1^2
 \tag{10}$$

$$\frac{dx_2}{dt} = -\frac{k_1 x_1 x_2}{k_2 + x_1} + k_3 x_1^2
 \tag{11}$$

The initial conditions are

$$x_1 = x_1^*, \quad x_2 = x_2^* \quad \text{at } t = 0
 \tag{12}$$

By instead using the above equations, one can study the mass-action method as follows [16]:

$$\frac{dx_1}{dt} = k_1 x_1 x_2 - k_2 k_3 x_1^2 - k_3 x_1^3
 \tag{13}$$

$$\frac{dx_2}{dt} = -k_1 x_1 x_2 + k_2 k_3 x_1^2 + k_3 x_1^3
 \tag{14}$$

The initial conditions are

$$x_1 = x_1^*, \quad x_2 = x_2^*, \quad \text{at } t = 0
 \tag{15}$$

corresponding to the reaction network  $X_1 + X_2 \rightleftharpoons 2X_1$  and  $3X_1 \rightarrow 2X_1 + X_2$ . To get from the original system to the mass action system, we have multiplied the vector field by the nonzero scalar field  $k_2 + x_1$ ; this preserves the trajectory curves of the system and corresponds to a time-rescaling along the trajectories [15].

#### 2.4. Approximation analytical expression of concentrations in Michaelis-Menten enzyme kinetics or the hill binding kinetics using the new approach of the homotopy perturbation method

Solving the non-linear Eqs. (10-12) using the new approach of the homotopy perturbation method (Appendix A), the analytical expressions of concentration in Michaelis-Menten enzyme kinetics can be obtained as follows:

$$x_1(t) = x_1^* \exp\left(\left(\frac{k_1 x_2^*}{k_2 + x_1^*}\right) t\right) - \frac{k_3 (x_1^*)^2 (x_1^* + k_2)}{k_1 x_2^*} \left(1 - \exp\left(\left(\frac{k_1 x_2^*}{k_2 + x_1^*}\right) t\right)\right) \quad (16)$$

$$x_1(t) = x_2^* \exp\left(\left(-\frac{k_1 x_1^*}{k_2 + x_1^*}\right) t\right) - \frac{k_3 (x_1^*)^2 (x_1^* + k_2)}{k_1} \left(1 - \exp\left(\left(-\frac{k_1 x_1^*}{k_2 + x_1^*}\right) t\right)\right) \quad (17)$$

The analytical expressions of concentration in the mass-action system can be obtained as follows:

$$x_1(t) = x_1^* \exp(k_1 x_2^* t) - \frac{k_3 (x_1^*)^2 (1 - \exp(k_1 x_2^* t))}{k_1 x_2^*} (k_2 + x_1^*) \quad (18)$$

$$x_1(t) = x_2^* \exp(-k_1 x_2^* t) - \frac{k_3 x_1^* (1 - \exp(-k_1 x_1^* t))}{k_1} (k_2 + x_1^*) \quad (19)$$

### 3. Numerical Simulation

The non-linear differential Eqs. (1-5) for Mass-action kinetics, Eqs. (10-15) for Michaelis-Menten enzyme kinetics and Mass action system are also solved using numerical methods. The function `pdx4` in MATLAB software which is the function of solving the initial value problems for ordinary differential is used to solve this equation. The Matlab program is also given in Appendix B. The concentrations which are derived from the NHPM are compared with the simulation results in Fig. 2-9. Satisfactory agreement is found for all values of time  $t$ .

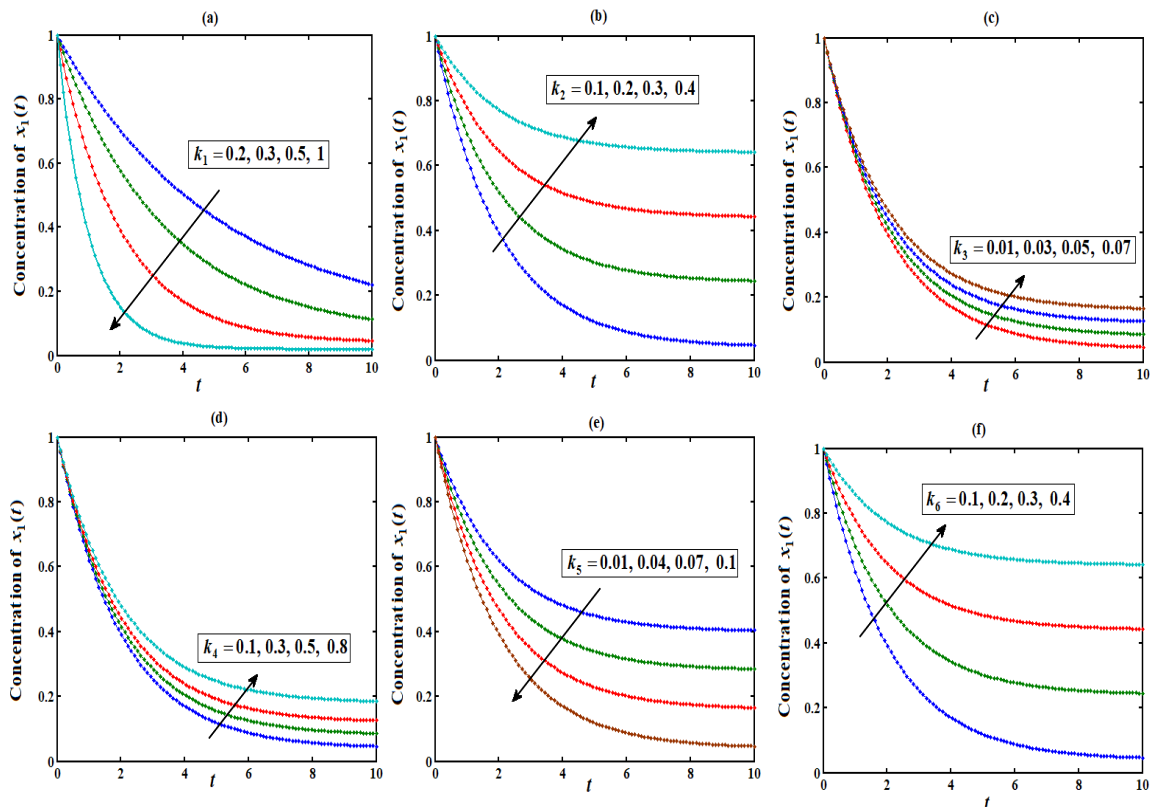
### 4. Result and discussion

#### 4.1 Mass-action kinetics

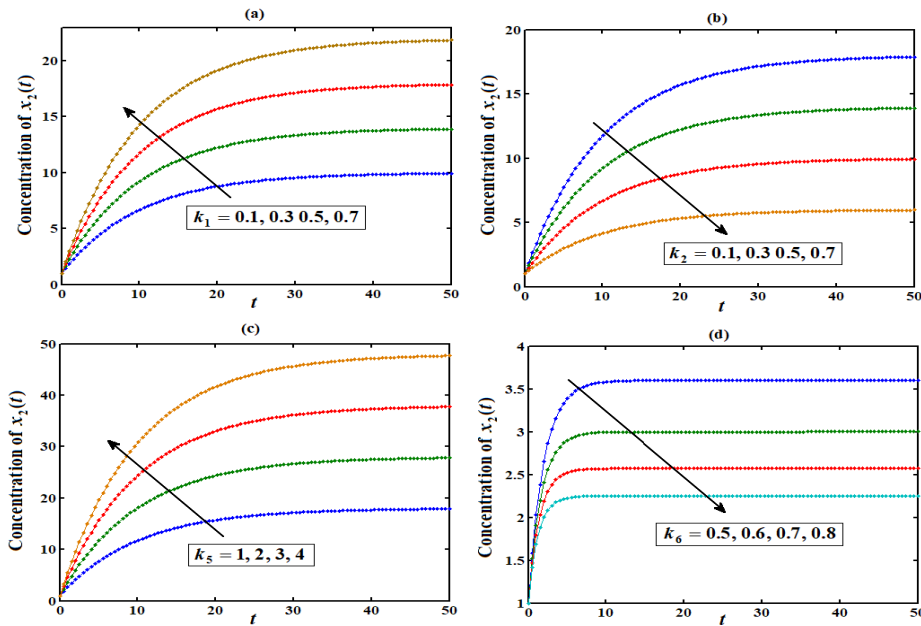
Eqs. (6-9) represent the new and simple analytical expressions of the concentrations of species in Mass-action kinetics for all possible values of parameters.

Figures 2 and 3 illustrates the behavior of the concentration profiles of  $x_1$ ,  $x_2$ ,  $x_3$ , and  $x_4$  for different values rate constant. The values parameters are taken as follows  $k_1 = 0.5$ ,  $k_2 = 0.1$ ,  $k_3 = 0.01$ ,  $k_4 = 0.01$ ,  $k_5 = 0.1$  and  $k_6 = 0.1$ . The effect of all the parameter on the concentration are illustrated in Figs. 2,3. From Figure 2, it is inferred

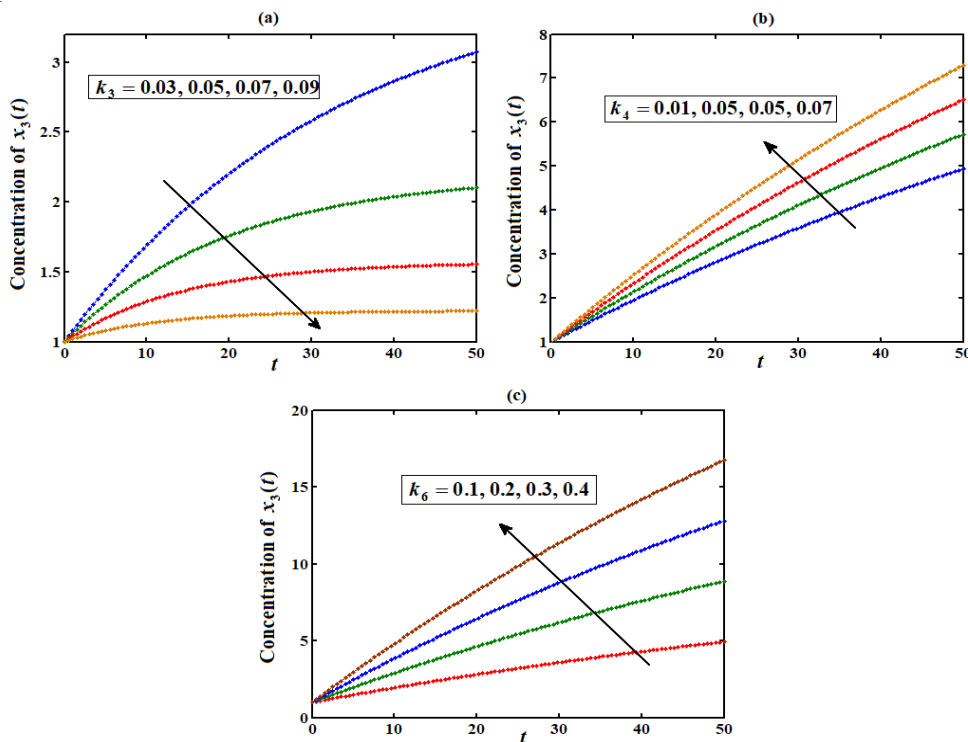
that the concentration of  $x_1$  increases when  $k_2, k_3, k_4, k_6$  and  $k_7$  increases or  $k_1$  and  $k_5$  decreases. From Figure 3, it is observed that the concentration of  $x_2$  increases when  $k_1$  and  $k_5$  increases or  $k_2, k_6$  decreases. From Figure 4, it is inferred that the concentration of  $x_3$  increases when  $k_4$  and  $k_6$  increases or  $k_3$  decreases. From Figure 5, it is observed that the concentration of  $x_4$  increases when  $k_5$  increases or  $k_6$  decreases.



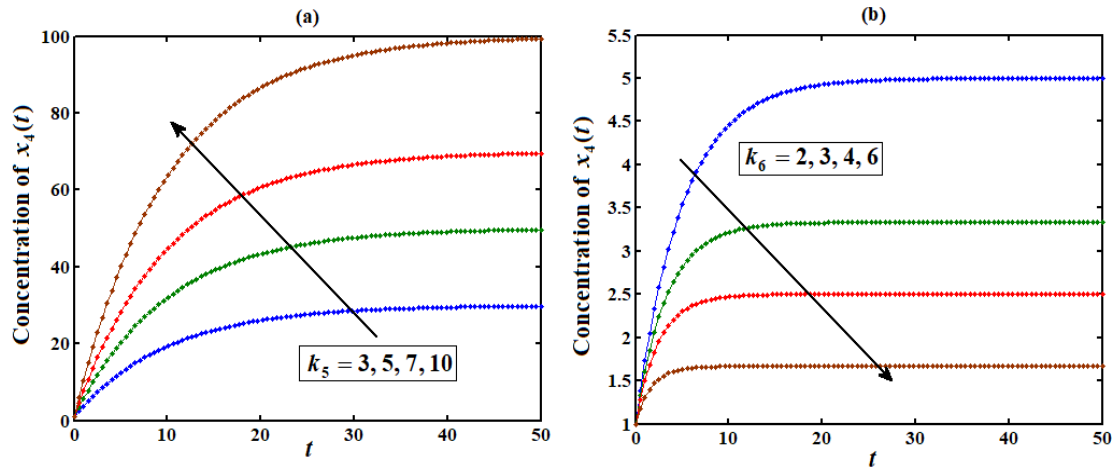
**Fig.2.** Comparison of analytical expression of the concentration of  $x_1$  (Eq.6) with simulation results for the initial conditions  $(x_1^* = 1, x_2^* = 1, x_3^* = 1, x_4^* = 1)$  for the Mass-action kinetics. The bold line “—” represent the analytical result and dotted line “\*\*\*\*” represent the numerical result.



**Fig. 3.** Comparison of analytical expression of the concentration of  $x_2$  (Eq.7) with simulation results for the initial conditions  $(x_1^* = 1, x_2^* = 1, x_3^* = 1, x_4^* = 1)$  in Mass-action kinetics. The bold line “—” represent the analytical result and dotted line “\*\*\*\*” represent the numerical result.



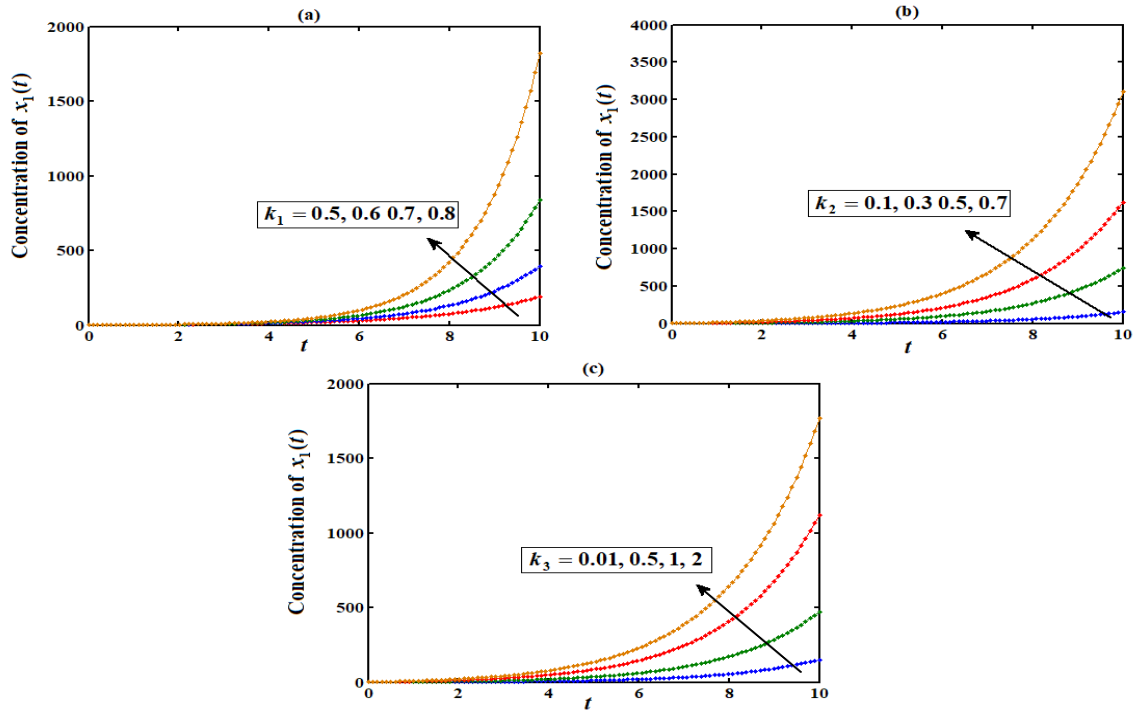
**Fig.4.** Comparison of analytical expression of the concentration of  $x_3$  (Eq.8) with simulation results for the initial conditions  $(x_1^* = 1, x_2^* = 1, x_3^* = 1, x_4^* = 1)$  in the Mass-action kinetics for various values of the parameters. The bold line “—” represent the analytical result and dotted line “\*\*\*\*” represent the numerical result.



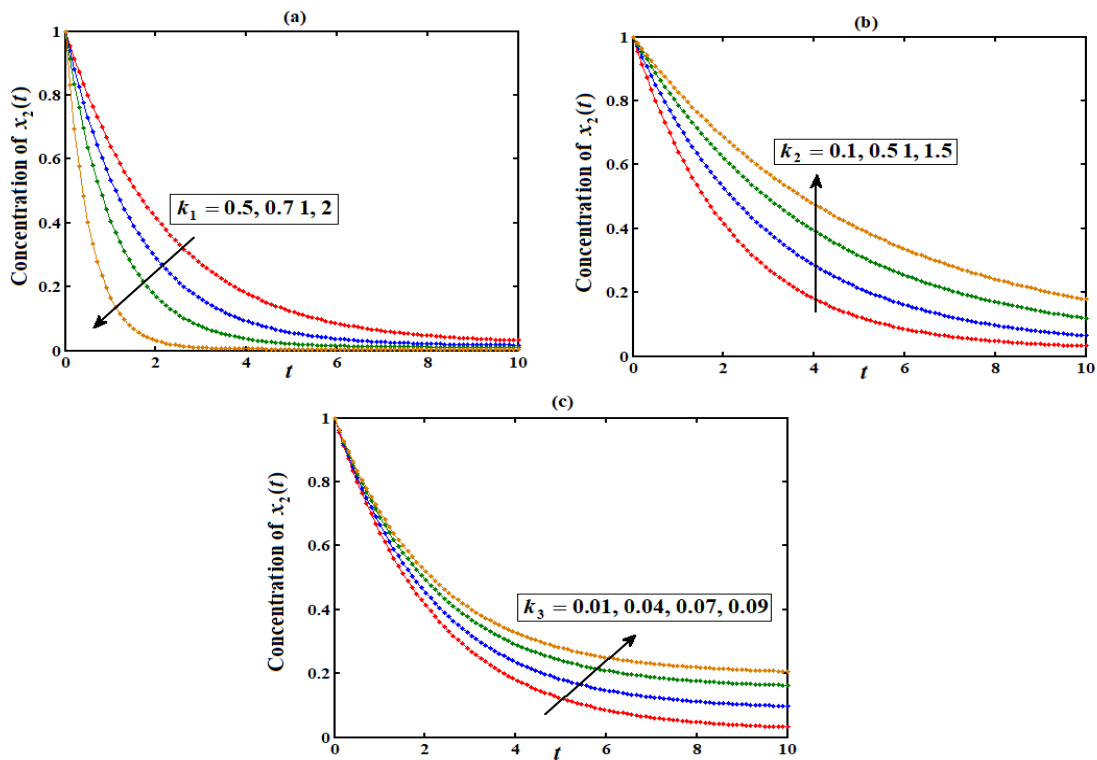
**Fig.5.** Comparison of analytical expression of the concentration of  $x_4$  (Eq.9) with simulation results for the initial conditions ( $x_1^* = 1, x_2^* = 1, x_3^* = 1, x_4^* = 1$ ) in the Mass-action kinetics for various values of the parameter. The bold line “—” represent the analytical result and dotted line “\*\*\*” represent the numerical result.

#### 4.2 Michaelis-Menten enzyme kinetics

Eqs. (16-19) represent the new and simple approximate analytical expressions of the concentration of species in Michaelis-Menten enzyme kinetics for all possible values of parameters. In Figs. 6 and 7, represents the concentration of the Michaelis-Menten enzyme kinetics for the concentration of  $x_1$  and  $x_2$ . The parameters value is  $k_1 = 0.5, k_2 = 0.1$ , and  $k_3 = 0.01$ . From the Figure-6, it is observed that the concentration  $x_1$  increases as the increasing value of a parameter  $k_1, k_3$  or decreasing the value of a parameter  $k_2$ . From the Figure-7, it is concluded that the concentration of  $x_2$  increases as the increasing value of a parameter,  $k_2, k_3$  or decreasing the value of a parameter  $k_1$ .



**Fig.6.** Comparison of analytical expression of the concentration of  $x_1$  (Eq.16) with simulation results for the initial conditions ( $x_1^* = 1, x_2^* = 1$ ) in of the Michaelis-Menten enzyme kinetics. The bold line “—” represent the analytical result and dotted line “\*\*\*\*” represent the numerical result.



**Fig.7.** Comparison of analytical expression of the concentration of  $x_2$  (Eq.17) with simulation results for the initial conditions ( $x_1^* = 1, x_2^* = 1$ ) In Michaelis-Menten enzyme

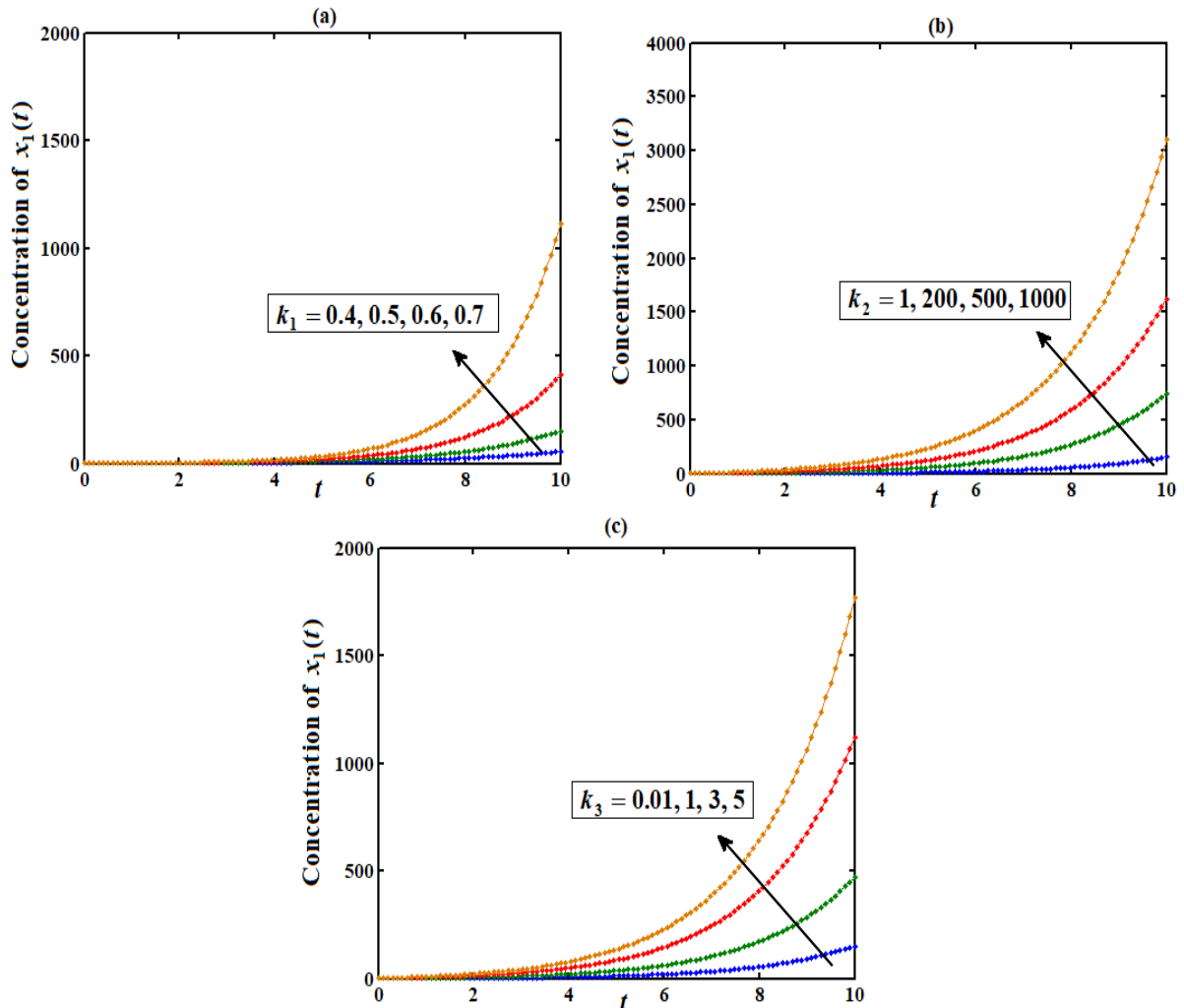


kinetics. The bold line “—” represent the analytical result and dotted line “\*\*\*\*” represent the numerical result.

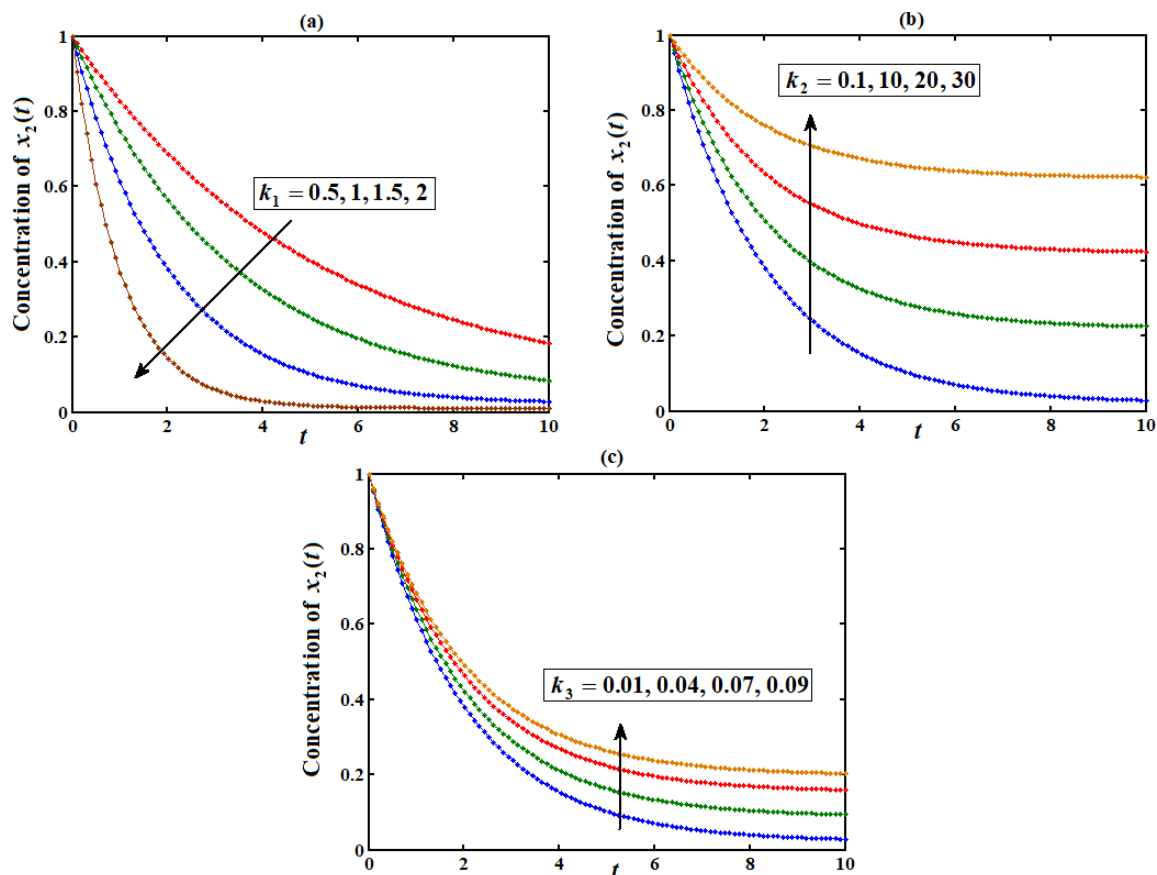
Equations (18-19) describe, for all possible parameter values, new and simple estimated analytical expressions of species concentration  $x_1$  and  $x_2$  in the mass action system.

Figs. 8 and 9, represents the concentration of  $x_1$  and  $x_2$  in the mass-action system for different values of parameters. The value of rate constant are  $k_1 = 0.5, k_2 = 0.1$ , and  $k_3 = 0.01$ . Figs.8 shows the effect of parameters  $k_1, k_2$  and  $k_3$ , on concentration profile. It is notice that an increase in  $k_1, k_2$  and  $k_3$  leads to increase in the values of concentration  $x_1$ .

Figs. 9, illustrate the behavior of the concentration profiles  $x_2$  for different values of the rate constant. From Figure9, it is observed that an increase in the rate constant  $k_1$  results in a decreasing in concentration  $x_2$ . An increase in rate constant  $k_2$  and  $k_3$  leads to increase in concentration  $x_2$ .



**Fig.8.** Comparison of analytical expression of the concentration of  $x_1$  (Eq.18) with simulation results for the initial conditions ( $x_1^* = 1, x_2^* = 1$ ) in Hill kinetics. The bold line “—” represent the analytical result and dotted line “\*\*\*\*” represent the numerical result.



**Fig.9.** Comparison of analytical expression of the mass-action system for the concentration of  $x_2$  (Eq.19) with simulation results and initial condition with various values of parameters ( $x_1^* = 1, x_2^* = 1$ ). The bold line “\_” represent the analytical result and dotted line “\*\*\*” represent the numerical result.

## 5. Conclusion

The system of differential equations describes a chemical reaction solved analytically using the new homotopy perturbation method for various values of parameters. This work is mainly derived for the concentration of Mass-action kinetics, the concentration of Michaelis-Menten enzyme kinetics and Mass action system. The effects of various parameters on concentration profiles are discussed. The obtained results have a satisfactory agreement with simulation results.

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## Appendix - A

### Analytical solution of Eqs. (10) - (12) using the new homotopy perturbation method.

Eqs. (10) - (12) can be written as follows:

$$\frac{dx_1}{dt} = \frac{k_1 x_1 x_2}{k_2 + x_1} - k_3 x_1^2 \quad (A1)$$

$$\frac{dx_2}{dt} = -\frac{k_1 x_1 x_2}{k_2 + x_1} + k_3 x_1^2 \quad (A2)$$

The initial conditions are

$$x_1 = x_1^*, \quad x_2 = x_2^* \quad \text{at } t = 0 \quad (A3)$$

Homotopy for the above eqs. (A1) - (A3) can be constructed as follows:

$$(1-p) \left[ \frac{dx_1}{dt} - \frac{k_1 x_1 x_2}{k_2 + x_1} + k_3 x_1^2 \right] + p \left[ \frac{dx_1}{dt} - \frac{k_1 x_1 x_2}{k_2 + x_1} + k_3 x_1^2 \right] = 0 \quad (A4)$$

$$(1-p) \left[ \frac{dx_2}{dt} + \frac{k_1 x_1 x_2}{k_2 + x_1} - k_3 x_1^2 \right] + p \left[ \frac{dx_2}{dt} + \frac{k_1 x_1 x_2}{k_2 + x_1} - k_3 x_1^2 \right] = 0 \quad (A5)$$

The approximate solution of the eqs. (A4) - (A5) are

$$x_1 = x_{1_0} + p x_{1_1} + p^2 x_{1_2} + p^3 x_{1_3} + \dots \quad (A6)$$

$$x_2 = x_{2_0} + p x_{2_1} + p^2 x_{2_2} + p^3 x_{2_3} + \dots \quad (A7)$$

Substituting eqs. (A6) and (A7) into eqs. (A4) and (A5) and comparing the coefficients of like powers  $p'$

$$p^0 : \frac{dx_{1_0}}{dt} - \frac{k_1 x_1 x_{2_{in}}}{k_2 + x_{1_{in}}} + k_3 x_1^2 = 0 \quad (A8)$$

$$p^0 : \frac{dx_2}{dt} + \frac{k_1 x_{1_{in}} x_2}{k_2 + x_{1_{in}}} - k_3 x_{1_{in}}^2 = 0 \quad (A9)$$

Solving eqs. (A8) and (A9) with initial condition (A3), yields

$$x_{1_0}(t) = x_1^* \exp\left(\left(\frac{k_1 x_2^*}{k_2 + x_1^*}\right)t\right) - \frac{k_3 (x_1^*)^2 (x_1^* + k_2)}{k_1 x_2^*} \left(1 - \exp\left(\left(\frac{k_1 x_2^*}{k_2 + x_1^*}\right)t\right)\right) \quad (A10)$$

$$x_{2_0}(t) = x_2^* \exp\left(\left(-\frac{k_1 x_1^*}{k_2 + x_1^*}\right)t\right) - \frac{k_3 (x_1^*)^2 (x_1^* + k_2)}{k_1} \left(1 - \exp\left(\left(-\frac{k_1 x_1^*}{k_2 + x_1^*}\right)t\right)\right) \quad (A11)$$

The solution of the above equations as,

$$x_1(t) = x_1^*(t), \quad x_2(t) = x_2^*(t)$$

$$x_1(t) = x_1^* \exp\left(\left(\frac{k_1 x_2^*}{k_2 + x_1^*}\right)t\right) - \frac{k_3 (x_1^*)^2 (x_1^* + k_2)}{k_1 x_2^*} \left(1 - \exp\left(\left(\frac{k_1 x_2^*}{k_2 + x_1^*}\right)t\right)\right) \quad (A12)$$

$$x_1(t) = x_2^* \exp\left(\left(-\frac{k_1 x_1^*}{k_2 + x_1^*}\right)t\right) - \frac{k_3 (x_1^*)^2 (x_1^* + k_2)}{k_1} \left(1 - \exp\left(\left(-\frac{k_1 x_1^*}{k_2 + x_1^*}\right)t\right)\right) \quad (A13)$$

### Appendix B. Matlab code for numerical solution of eqns.(10) and (11)

```
function matrix1
options=odeset('RelTol',1e-6,'Stats','on');
% initial conditions
Xo = [1;1];
tspan = [0,10];
tic
[t,X] = ode45(@TestFunction,tspan,Xo,options);
toc
figure
hold on
% plot(t, X(:,1),'-')
plot(t, X(:,2),'-')
legend('x1','x2')
xlabel('t')
return
function [dx_dt]= TestFunction(t,x)
k1=0.5;k2=0.1;k3=0.01;x1=1;x2=1;
dx_dt(1) = ((k1*x1*x(1))/(k2+x1))-(k3*x1*x1);
dx_dt(2) = -((k1*x1*x(2))/(k2+x1))+k3*x1*x1;
dx_dt = dx_dt';
return
```