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Analytical solution of New NADH Oxidase from Lactobacillus brevis in Enzyme Membrane Reactor

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Abstract
In this paper mathematical modelling of new NADH oxidase from lactobacillus brevis in enzyme membrane reactor. In this model the mass balance equations are solved analytically by using homotopy perturbation method and comparing numerical results (Scilab program). Simple analytical expressions of the concentrations are derived good agreement is noted.
Keywords: NADH oxidase, coenzyme regeneration, enzyme kinetics, enzyme membrane reactor, Mathematical Modelling.

Introduction

Found in every single living cell, NAD is a coenzyme that is a hydrogen transporter in metabolic responses particularly in tissue breath. It exists in two structures, an oxidized one and decreased structure, as NAD^+ and NADH separately. NADH is utilized to produce proton intention power that can drive the blend of ATP. The cofactor is therefore found in two structures in cells NAD^+ is an oxidizing specialist it acknowledges electrons from different atoms and gets diminished. This response structures NADH, which can be utilized as a decreasing specialist to signify electrons. These electron move responses are the principle capacity of NAD.

NADH oxidase is the most encouraging chemical for that reason, despite the fact that it isn't industrially accessible, unlike formate dehydrogenase. It has been used before in two frameworks that include amino acid dehydrogenase [1, 2]. NADH oxidases from different origins (Lactobacillus brevis and Lactobacillus sanfranciscensis) were utilized. They were both quite successful in coenzyme regeneration and equilibrium shifting. Findrik et.al., [3] are developed the mathematical model of the reaction. Most previously published NADH oxidation catalyzed by new NADH oxidase from Lactobacillus brevis in enzyme membrane reactor are solved by numerical methods [4].

Up to the excellence of our knowledge, no general analytical results for the NADH oxidation have been stated. The purpose of this communication is to derive expression for the mass balance equations are solved analytically using Homotopy perturbation method.

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Mathematical formulation of the problem

The Michaelis-Menten model with unviable regarding the production has been used to describe NADH oxidation kinetics Eqn. (1). Mass balance equations were shown in Eqns. (2) and (3) for the continuous mode of enzyme membrane reactor. First order enzyme decomposition was thought to be Eqns. (4) and (5).

$$\frac{dc_{NAD^+}}{dt} = \frac{c_{NAD^+0}}{\tau} - \frac{c_{NAD^+}}{\tau} + r \quad (1)$$

$$\frac{dc_{NADH}}{dt} = \frac{c_{NADH\ 0}}{\tau} - \frac{c_{NADH}}{\tau} - r \quad (2)$$

where

$$r_1 = \frac{V_m \gamma_{NADH\ oxidase} c_{NADH}}{K_m^{NADH} + c_{NADH}\left(1+\left(c_{NAD^+} \Big/ K_i^{NAD^+}\right)\right)} \quad (3)$$

$$V_m = V_{m0}\, e^{-k_d t} \quad (4)$$

Here, HPM was widely used to solve nonlinear boundary and initial value problems since this approach was of great interest to many researchers. Initially, this approach was used to establish JiHuanHe[6-8]. Complicated problems are constantly deformed into simple issues in HPM, that are a simple way to solve and obtain a theoretical or approximate solution [9].Recently, Pavithra et. al., [10] and Iswarya et. al., [11, 12] solving this type of rate equations, Michaelis-Menten kinetics using the new homotopy perturbation method (NHPM). For this continuous process, I solved this problem in the homotopy perturbation method.

Solutions of the above Eqns. (1)- (2) as below:

$$\begin{aligned} c_{NAD^+} &= \left(\frac{b}{f}\right) + \left[\left(c_{NAD^+}\right)_i - \left(\frac{b}{f}\right)\right] e^{-f t} + \frac{m(k_d + f)}{f^2} - \frac{k_d\, m t}{f} \\ &+ \frac{n e^{-g t}\left(k_d + g k_d t - f k_d t - g + f\right)}{(f-g)^2} - \left[\frac{m(k_d + f)}{f^2} + \frac{n\left(k_d + g k_d t - f k_d t - g + f\right)}{(f-g)^2}\right] e^{-f t} \end{aligned} \quad (5)$$

$$c_{NADH} = j + l\, e^{-g t} + \frac{a\, j\, k_d}{g}\left(\frac{1}{g} - t\right) + \frac{a\, k_d\, l t^2 e^{-g t}}{2} + \frac{a\, j\, k_d e^{-g t}}{g^2} \quad (6)$$

Where,

$$a = \frac{V_{m0}\gamma_{NADH\ oxidase}}{K_m^{NADH} + (c_{NADH})_i\left(1+\left((c_{NAD^+})_i \Big/ K_i^{NAD^+}\right)\right)}, b = \frac{(c_{NAD^+})_i}{\tau}, c = \frac{(c_{NADH})_i}{\tau}, \quad (7)$$

$$f = 1/\tau, g = f + a, j = c/g, l = (c_{NADH})_i - (c/g), m = aj, n = al$$

Result and Discussion

From figure 1 and 2 compared the analytical solutions of the concentrations of NAD+ and NADH with the numerical results.

In figure 1, (a) – (c) denotes that the concentration of NAD^+ increases when the values of $\gamma_{NADH\ oxidase}$, V_{m0}, τ increases. In (d) noted that the concentration of NAD^+ decreases when K_m^{NADH} increases. In (e) and (f) signifies that the concentration of NAD^+ has the little extension when the value of k_d and $K_i^{NAD^+}$ increases.

In figure 2, (a) – (c) represents that the concentration of NADH decreases when the values of $\gamma_{NADH\ oxidase}$, V_{m0}, τ increases. In (d) noted that the concentration of NADH increases when K_m^{NADH}

increases. In (e) and (f) indicates that the concentration of NADH has the little changes when the value of k_d and $K_i^{NAD^+}$ increases.

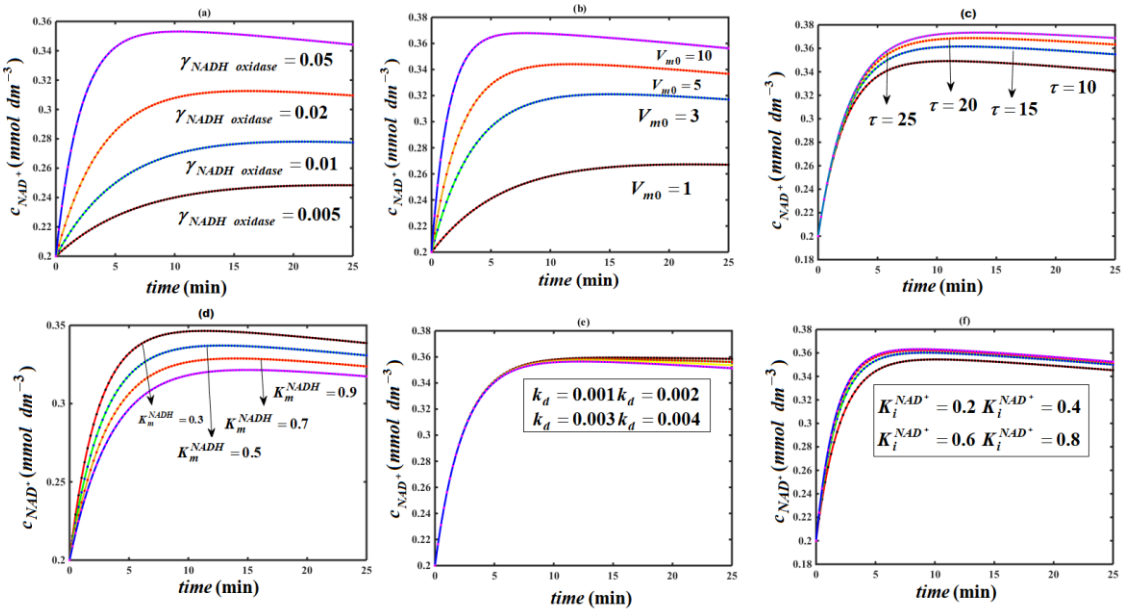

Figure 1: Comparison between the analytical solution of the concentration NAD+ (Eqn. (5)) and the numerical results (Appendix B) by using various values of parameters (Appendix C) where the sprinkled line represents the analytical solution and solid line represents the numerical.

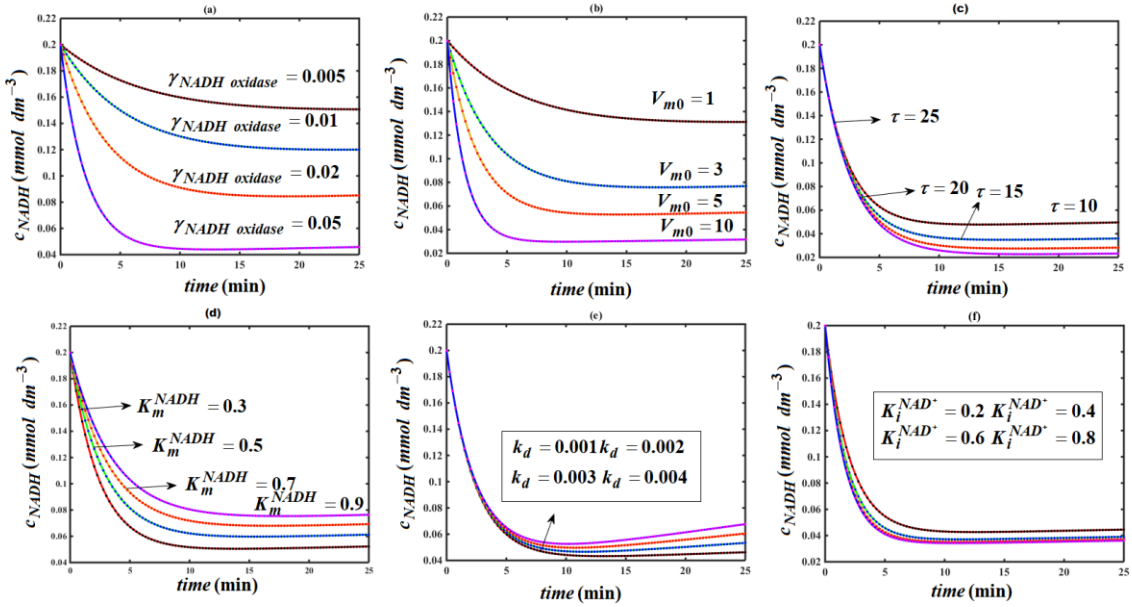

Figure 2: Comparison between the analytical solution of the concentration NADH (Eqn. (6)) and the numerical results (Appendix B) by using various values of parameters (Appendix C) where the sprinkled line represents the analytical solution and solid line represents the numerical.

Conclusion

In this paper,the concentrations of NAD^+ and NADH are solved analytically by using the HPM method. These analytical solutions are compared with the numerical results. Here numerical results are in the Scilab program. The analytical solutions of the concentrations of NAD+ and NADH are compared with the numerical results in figures 1 and 2. A good agreement is noted.

Appendix A: Analytical solutions of the concentrations of NAD+ and NADH by using HPM

Substitute the Eqns. (3), (4) in (1) and (2) we get,

$$\frac{dc_{NAD^+}}{dt} = \frac{c_{NAD^+0}}{\tau} - \frac{c_{NAD^+}}{\tau} + \frac{V_{m0}\, e^{-k_d t}\, \gamma_{NADH\ oxidase}\, c_{NADH}}{K_m^{NADH} + c_{NADH}\left(1+\left(c_{NAD^+} \Big/ K_i^{NAD^+}\right)\right)} \quad \text{(A1)}$$

$$\frac{dc_{NADH}}{dt} = \frac{c_{NADH\ 0}}{\tau} - \frac{c_{NADH}}{\tau} - \frac{V_{m0}\, e^{-k_d t}\, \gamma_{NADH\ oxidase}\, c_{NADH}}{K_m^{NADH} + c_{NADH}\left(1+\left(c_{NAD^+} \Big/ K_i^{NAD^+}\right)\right)} \quad \text{(A2)}$$

Here expand the exponential $e^{-k_d t} = 1 - k_d t + \left(k_d{}^2 t^2 / 2\right) - ....$and substitute the constant values weget,

$$\frac{dc_{NAD^+}}{dt} - b + fc_{NAD^+} - a\, c_{NADH}\ \left(1 - k_d t\right) = 0 \quad \text{(A3)}$$

$$\frac{dc_{NADH}}{dt} - c + fc_{NADH} + ac_{NADH}\ \left(1 - k_d t\right) = 0 \quad \text{(A4)}$$

$$(1-p)\left[\frac{dc_{NAD^+}}{dt} - b + fc_{NAD^+}\right] + p\left[\frac{dc_{NAD^+}}{dt} - b + fc_{NAD^+} - a\, c_{NADH}\ \left(1 - k_d t\right)\right] = 0 \quad \text{(A5)}$$

$$(1-p)\left[\frac{dc_{NADH}}{dt} - c + gc_{NADH}\right] + p\left[\frac{dc_{NADH}}{dt} - c + gc_{NADH} + ac_{NADH}\ k_d t\right] = 0 \quad \text{(A6)}$$

$$c_{NAD^+} = \left(c_{NAD^+}\right)_0 + p\left(c_{NAD^+}\right)_1 + p^2\left(c_{NAD^+}\right)_2 + ... \quad \text{(A7)}$$

$$c_{NADH} = \left(c_{NADH}\right)_0 + p\left(c_{NADH}\right)_1 + p^2\left(c_{NADH}\right)_2 + ... \quad \text{(A8)}$$

Substitute (A7), (A8) in (A5) and (A6) we get,

$$(1-p)\left[\begin{array}{l}\dfrac{d\left[\left(c_{NAD^+}\right)_0+p\left(c_{NAD^+}\right)_1+p^2\left(c_{NAD^+}\right)_2+\ldots\right]}{dt}-b\\+f\left[\left(c_{NAD^+}\right)_0+p\left(c_{NAD^+}\right)_1+p^2\left(c_{NAD^+}\right)_2+\ldots\right]\end{array}\right]$$

$$+p\left[\begin{array}{l}\dfrac{d\left[\left(c_{NAD^+}\right)_0+p\left(c_{NAD^+}\right)_1+p^2\left(c_{NAD^+}\right)_2+\ldots\right]}{dt}-b\\+f\left[\left(c_{NAD^+}\right)_0+p\left(c_{NAD^+}\right)_1+p^2\left(c_{NAD^+}\right)_2+\ldots\right]\\-a\left[\left(c_{NADH}\right)_0+p\left(c_{NADH}\right)_1+p^2\left(c_{NADH}\right)_2+\ldots\right](1-k_d\,t)\end{array}\right]=0 \quad \text{(A9)}$$

$$(1-p)\left[\begin{array}{l}\dfrac{d\left[\left(c_{NADH}\right)_0+p\left(c_{NADH}\right)_1+p^2\left(c_{NADH}\right)_2+\ldots\right]}{dt}-c\\+g\left[\left(c_{NADH}\right)_0+p\left(c_{NADH}\right)_1+p^2\left(c_{NADH}\right)_2+\ldots\right]\end{array}\right]$$

$$+p\left[\begin{array}{l}\dfrac{d\left[\left(c_{NADH}\right)_0+p\left(c_{NADH}\right)_1+p^2\left(c_{NADH}\right)_2+\ldots\right]}{dt}-c\\+g\left[\left(c_{NADH}\right)_0+p\left(c_{NADH}\right)_1+p^2\left(c_{NADH}\right)_2+\ldots\right]\\+ak_d\,t\left[\left(c_{NADH}\right)_0+p\left(c_{NADH}\right)_1+p^2\left(c_{NADH}\right)_2+\ldots\right]\end{array}\right]=0 \quad \text{(A10)}$$

Comparing the coefficients of p we get,

$$p^0:\ \frac{d\left(c_{NAD^+}\right)_0}{dt}-b+f\left(c_{NAD^+}\right)_0=0 \text{ (A11)}$$

$$p^0:\frac{d\left(c_{NADH}\right)_0}{dt}-c+g\left(c_{NADH}\right)_0=0 \text{ (A12)}$$

$$p^1:\frac{d\left(c_{NAD^+}\right)_1}{dt}+f\left(c_{NAD^+}\right)_1+a(1-k_d\,t)\left(c_{NADH}\right)_0=0 \text{ (A13)}$$

$$p^1:\frac{d\left(c_{NADH}\right)_1}{dt}+g\left(c_{NADH}\right)_1-a\,k_d\,t\left(c_{NADH}\right)_0=0 \text{ (A14)}$$

Solutions of the above four equations we get,

$$\left(c_{NAD^+}\right)_0(t)=\left(\frac{b}{f}\right)+\left[\left(c_{NAD^+}\right)_i-\left(\frac{b}{f}\right)\right]e^{-f\,t} \text{ (A15)}$$

$$\left(c_{NADH}\right)_0(t)=j+l\,e^{-g\,t} \text{ (A16)}$$

$$\left(c_{NAD^+}\right)_1(t) = +\frac{m(k_d+f)}{f^2} - \frac{k_d\, m\, t}{f} + \frac{ne^{-g\,t}(k_d + gk_d t - fk_d t - g + f)}{(f-g)^2} - \left[\frac{m(k_d+f)}{f^2} + \frac{n(k_d + gk_d t - fk_d t - g + f)}{(f-g)^2}\right] e^{-f\,t} \quad \text{(A17)}$$

$$\left(c_{NADH}\right)_1(t) = \frac{a\, j\, k_d}{g}\left(\frac{1}{g} - t\right) + \frac{a\, k_d\, l\, t^2\, e^{-g\,t}}{2} + \frac{a\, j\, k_d e^{-g\,t}}{g^2} \quad \text{(A18)}$$

We get the final solutions are,

$$c_{NAD^+}(t) = \left(c_{NAD^+}\right)_0(t) + \left(c_{NAD^+}\right)_1(t) \quad \text{(A19)}$$

$$c_{NADH}(t) = \left(c_{NADH}\right)_0(t) + \left(c_{NADH}\right)_1(t) \quad \text{(A20)}$$

Appendix B: Scilab Program to Find the Numerical Solution of Eqns. (1) and (2).

```
function main1
options= odeset('RelTol',1e-6,'Stats','on');
Xo = [0.2;0.2];
tspan = [0,25];
tic
[t,X] = ode45(@TestFunction,tspan,Xo,options);
toc
figure
holdon
plot(t, X(:,1))
plot(t, X(:,2))
return
function [dx_dt]= TestFunction(t,x)
tow=10,kd=0.0056,g1=0.045,k1=0.247,k2=0.134,vm0=5.68,yi=0.2,xii=0.2,
a=(vm0*g1)/(k1+yi*(1+xii/k2));b=xii/tow;c=yi/tow;f=1/tow;g=f+a;
dx_dt(1)=-(f*x(1))+b+(a*x(2))-(a*kd*t*x(2));
dx_dt(2)=c-(g*x(2))+(a*x(2)*kd*t);
dx_dt = dx_dt';
return
```

Appendix C: Experiment values of the parameters in Eqns. (1) and (2) [5].

Parameter	Value
V_{m1}	3.468 (U cm^{-3}) or 5.68 $\left(mmol\ dm^{-3}\ mg^{-1}\ \min^{-1}\right)$
K_m^{NADH}	0.247 $\left(mmol\ dm^{-3}\right)$
$K_i^{NAD^+}$	0.134 $\left(mmol\ dm^{-3}\right)$
$\gamma_{NADH\ oxidase}$	0.045 $\left(mmol\ dm^{-3}\ mg^{-1}\ \min^{-1}\right)$

k_d	0.055(min^{-1})
τ	12 (min)

Nomenclature

c_{NADPH}	Concentration of nicotinamide adenine dinucleotide phosphate(mmol dm^{-3})
c_{NAD^+}	Concentration of nicotinamide adenine dinucleotide coenzyme(mmol dm^{-3})
$\gamma_{NADH\ oxidase}$	Mass Concentration $\left(mmol\ dm^{-3}\ mg^{-1}\ \min^{-1}\right)$
K_i	inhibition constant(mmol dm^{-3})
K_m	Michaelis–Menten constant (mmol dm^{-3})
r	reaction rate (Umg^{-1}, mmol dm^{-3} min^{-1} mg^{-1})
t	time (min)
V_m	maximal reaction rate (U mg−1, mmol dm^{-3} min^{-1} mg^{-1})
k_d	enzyme deactivation constant (min^{-1})
τ	Residence time (min)

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