MODELING BIOLOGICAL KINETICS BY EULER'S METHOD: SOLVING MEDIATOR STABILITY PROBLEM

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INTRODUCTION

Biological kinetics – evolution of biological processes at time is described by differential equations. Analytical solutions of such equations often cause large problems. For example, even in the simplest Michaelis–Menten scheme reaction components change are characterized by nonlinear differential equations and require individually tailored, usually approximate solution.

High speed computation permits to use different numerical solution of complex biological schemes. Euler's method of numerical integration implies component y_{i+1} calculation by using expression:

$$y_{i+1} = y_i + \Delta y_i. \tag{1}$$

Replacing the differential term by the ratio of two small increments in the differential equation of biological kinetics opens possibility to calculate all components at the time t.

$$\frac{dy_i}{dt} = \frac{\Delta y_i}{\Delta t}. \tag{2}$$

The aim of this work is application of Euler's method to the solving mediator stability problem. The mediators, that are shuttling between different enzymes, are taking part in many biological transformations [1]. Some of them are very unstable. For example, life–time of cation radical of veratryl alcohol, the main lignin transforming mediator, is 50 ms. Still now it is not clear how these unstable mediators are acting. Here we suggest scheme that shows increased stability of functioning mediator.

MATHEMATICAL SIMULATION

Kinetic scheme includes enzyme interaction with mediator following reduced enzyme and oxidized mediator formation (3), oxidized mediator interaction with substrate with product formation and mediator regeneration (4), reduced mediator regeneration in auxiliary (not specified) reaction (5) and oxidized mediator splitting (6):

$$e + m \rightarrow er + mo, \qquad k_1, \tag{3}$$

$$mo + s \rightarrow p + m, \qquad k_2, \tag{4}$$

$$er \rightarrow e, \qquad k_3, \tag{5}$$

$$mo \rightarrow in, \qquad k_4. \tag{6}$$

The rate of corresponding reactions is characterized by reaction constants $k_1 - -k_4$.

Kinetic differential equations expressing reaction rate may be written:

$$\frac{de}{dt} = -k_1 e\, m + k_3 e, \tag{7}$$

$$\frac{der}{dt} = k_1 e\, m - k_3 er, \tag{8}$$

$$\frac{dm}{dt} = -k_1 e\, m + k_2 mo\, s, \tag{9}$$

$$\frac{dmo}{dt} = k_1 e\, m - k_2 mo\, s - k_4 mo, \tag{10}$$

$$\frac{ds}{dt} = -k_2 mo\, s, \tag{11}$$

$$\frac{dp}{dt} = k_2 mo\, s, \tag{12}$$

$$\frac{din}{dt} = k_4 mo. \tag{13}$$

Calculations were performed by using following initial conditions, which corresponded to some real experimental values: $e(0) = 0.001\, mM$, $m(0) = 0.1\, mM$, $s(0) = 0.4\, mM$, $er(0) = mo(0) = p(0) = in(0) = 0$. Constants were applied: $k_1 = 4 mM^{-1} s^{-1}$, $k_3 = 0.9\, s^{-1}$, $k_4 = 0.08\, s^{-1}$.

RESULTS AND EXPLANATION

A typical kinetic curve of concentration of mediator and product change at moderate k_2 value is depicted in Fig. 1. The decrease of mediator concentration is a result of m ding of reaction (hich corresponded

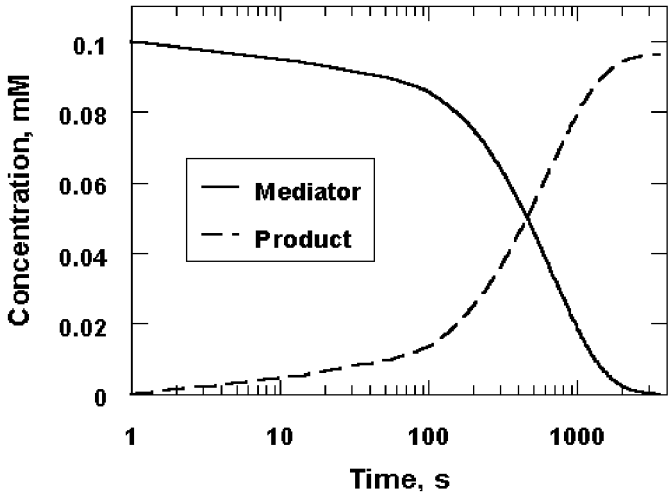

Fig. 1: Kinetics of mediator and product concentration change. Calculations were performed by using $k2 = 0.22\, mM^{-1} s^{-1}$ and other parameters described in the text.

To simulate life–time dependence on functional activity of mediator, k_2 changed from $0.04\, mM^{-1} s^{-1}$ to $4.1\, mM^{-1} s^{-1}$. The results presented in Fig. 2 demonstrate

that when k_2 increased then an apparent mediator life–time change from 250 to $1780\,s$.

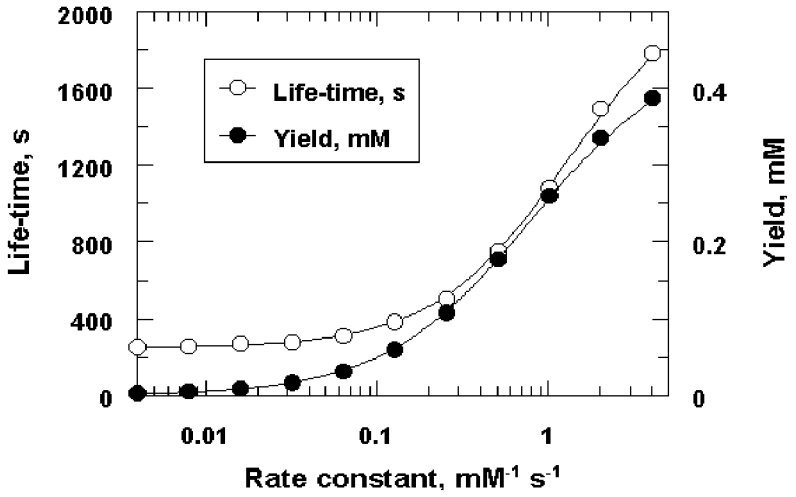

Fig. 2: Life–time and yield dependence on functional activity of mediator. Calculations by using parameters described in the text.

The simulations also show that the product yield (14) increased when activity of system increased. It reaches saturated level due to fixed ($0.4\,mM$) initial substrate concentration.

$$yield = \sum_i k_2 mo_i s_i. \tag{14}$$

In summary, the simulations performed demonstrate mediator life–time increase under functioning conditions. By keeping constant (or infinitive) initial substrate concentration life–time approaches infinitive value, too.

References

1. T. Danhus, J. Kulys, P. Schneider, *Synergism in Peroxidase–catalyzed Oxidation of Substrates. In: Abstracts "Eurobic II. Metal Ions in Biological Systems.* Florence, Italy, August 30–September 3, 1994", p. 101.