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POSITIVITY PRESERVING DISCRETE MODEL FOR THE COUPLED ODE'S MODELING GLYCOLYSIS

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Abstract. We construct a nonstandard finite difference scheme for the two coupled ODE's that model glycolysis. The primary emphasis is having the scheme satisfy a positivity condition and also retain the limit-cycle behavior for certain values of the parameters. We show that this is possible and give a full discussion of the scheme along with some of its numerical properties.

1. Introduction. A basic biochemical reaction occurring in living cells is glycolysis. An elementary model was given by Sel'kov [1] and is represented by the following two coupled first-order differential equations [2]

$$\frac{dx}{dt} = -x + ay + x^2 y$$
$$\frac{dy}{dt} = b - ay - x^2 y.$$
(1.1)

These equations are in dimensionless form with the parameters (a, b) being nonnegative. The two dependent variables, x and y, can only be non-negative since they stand for (dimensionless) chemical concentrations. Consequently, the physically relevant solutions to Eqs. (1) have the property

$$\begin{aligned} x_0 &= x(0) > 0, \quad y_0 &= y(0) > 0 \\ \implies & x(t) > 0, \quad y(t) > 0. \end{aligned}$$
 (1.2)

This condition of positivity [3] must also be satisfied by any scheme used to provide accurate numerical solutions for Eqs. (1). Another important feature of Eqs. (1) is that under a certain restriction on the parameter values, a and b, a stable limit-cycle can exist. Again, any viable numerical integration scheme should also have a stable limit-cycle solution for suitable values of the time step-size.

Our major purpose in this paper is to construct a nonstandard finite difference scheme [4] for Eqs. (1) which satisfies a positivity condition on its numerical solutions. Further, we show, using numerical experiments, that a stable limit-cycle exists under the appropriate limits on the parameters (a, b). A brief discussion is given of the bifurcation which occurs as the time step-size is increased with (a, b) held fixed at values for which the differential equations have a stable limit-cycle and an unstable fixed-point.

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The main advantage of a nonstandard finite difference scheme construction procedure is that it easily allows the enforcement of important dynamical properties of the exact solutions [4] for the numerical solutions. Consequently, the elementary numerical instabilities, such as the violation of positivity [3] for the numerical results when the actual solutions do satisfy this condition, cannot occur. While this method is currently not entirely rigorous, it is at a stage of development such that very usefully new discrete schemes can be constructed and applied to many important dynamical systems [2, 3, 4].

In the next section, we construct the nonstandard finite difference scheme (NSFDS) and examine in detail the reasons for its particular structure. We also illustrate the quality of its numerical solutions by providing figures for the case where a = 0.08 and b = 0.6. Also provided is a sequence of figures showing what happens as $\Delta t = h$ is increased. The paper concludes with a brief discussion of future research issues to be studied.

2. A Nonstandard Discrete Model. A complete discussion of the general method and philosophy of nonstandard finite difference schemes (NSFDS) is given in Mickens [4]. For Eqs. (1), the following NSFDS is constructed:

$$\frac{x_{k+1} - x_k}{\phi} = -x_{k+1} + ay_k + 2x_k^2 y_k - (x_k y_k) x_{k+1},$$
(2.1a)

$$\frac{y_{k+1} - y_k}{\phi} = b - ay_{k+1} - (x_{k+1})^2 y_{k+1},$$
(2.1b)

where $t_k = (\Delta t)k = hk$, h = time step-size; x_k and y_k are, respectively, approximations to $x(t_k)$ and $y(t_k)$; and ϕ is any function having the property

$$\phi = h + O(h^2). \tag{2.1c}$$

A particularly useful form for ϕ is [3, 4]

$$\phi = \left(\frac{1 - e^{-\lambda h}}{\lambda}\right),\tag{2.1d}$$

where λ^{-1} is the smallest time-scale occurring in the equations. In dimensionless time units for Eqs. (1), the three relevant time scales are [4]

$$T_1 = \frac{1}{a}, \quad T_2 = 1, \quad T_3 = \frac{1}{b^{2/3}},$$
 (2.2)

and λ is defined to be

$$\lambda \equiv \operatorname{Min}(T_1^{-1}, T_2^{-1}, T_3^{-1}) = \operatorname{Min}(a, 1, b^{2/3}).$$
(2.3)

The discrete scheme for Eqs. (1) given by Eqs. (2.1) have the following significant features:

(i) The discrete first-derivatives have the structure

$$\frac{dx}{dt} \longrightarrow \frac{x_{k+1} - x_k}{\phi}$$

$$\frac{dy}{dt} \longrightarrow \frac{y_{k+1} - y_k}{\phi},$$
(2.4)

as compared to the simple forward-Euler replacements where $\phi = h$.

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(ii) The first and third terms, on the right-side of the dx/dt equation, have the discrete forms

$$-x \to -x_{k+1}$$

$$x^2 y = 2x^2 y - x^2 y \to 2x_k^2 y_k - (x_k y_k) x_{k+1}.$$
 (2.5)

(iii) Similar replacements are made for the second and third terms on the rightside of the dy/dt equation, i.e.,

$$-ay \to -ay_{k+1}$$

 $-x^2y \to -(x_{k+1})^2y_{k+1},$ (2.6)

where, it should be noted x is replaced by x_{k+1} and not x_k .

(iv) Eqs. (2.1a) and (2.1b) are, respectively, linear in x_{k+1} and y_{k+1} . Consequently, solving for these variables gives

$$x_{k+1} = \frac{x_k + (a\phi)y_k + (2\phi)x_k^2 y_k}{1 + \phi + \phi x_k y_k},$$
(2.7a)

$$y_{k+1} = \frac{b\phi + y_k}{1 + a\phi + \phi(x_{k+1})^2} \,. \tag{2.7b}$$

For numerical evaluation, one proceeds as follows: First, select (x_k, y_k) . Second, calculate x_{k+1} using Eq. (2.7a). Third, using this value for x_{k+1} and the values for (x_k, y_k) , calculate y_{k+1} .

(v) Inspection of Eqs. (2.7) clearly shows that this NSFDS satisfies the positivity condition, i.e.,

$$x_0 > 0, \quad y_0 > 0$$

$$\implies x_k > 0, \quad y_k > 0.$$
(2.8)

We have calculated numerical solutions to Eqs. (1), using the NSFDS given by Eqs. (2.7) for a broad range of parameter values (a, b) and initial values (x_0, y_0) . Figures 1 and 2 show typical results; they were obtained for

$$a = 0.008, \quad b = 0.6, \quad \lambda = 0.08, \quad x_0 = 1, \quad y_0 = 1.$$
 (2.9)

The following is a brief summary of what was found:

(i) The above indicated values of (a, b) allow the existence of a stable limit-cycle [2]. For time step-size values satisfying the constraint

$$0 < h < 0.248, \tag{2.10}$$

a stable limit-cycle was obtained. Thus, the fixed-point interior to the limit-cycle was unstable.

(ii) For h > 0.248, the numerical solutions were oscillatory, but converged to the fixed-point.

(iii) The results from (i) and (ii) imply that the stability of the fixed-point is influenced by the value of the step-size.

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(iv) The general expectation is, for parameters (a, b) selected such that a stable limit-cycle exists for the differential equations, the NSFDS will only have a numerically derived stable limit-cycle if the step-size is smaller than a critical value h_c .

(v) The numerical calculations also indicate that the amplitude and frequency are dependent on the step-size.

All of these results are expected for any general numerical integration scheme and have been discussed in the paper by Mickens and Gumel [6]. The advantage of the NSFDS given here is that it always maintains the important positivity condition. Moreover, for accurate simulations of Eqs. (1), the requirement of Eq. (2.3) must be satisfied along with the additional condition

$$\lambda h \ll 1. \tag{2.11}$$

3. Discussion. The major reason for this study of a NSFDS for the equations modeling glycolysis is to demonstrate that this scheme preserves the important positivity condition which is an essential feature of the solutions to the original differential equations. General methods for calculating numerical solutions to differential equations [7] do not have this property. With this issue in mind, it becomes clear that any scheme that does not possess the positivity condition can allow the possibility for numerical instabilities to exist [3, 4]. Since Eqs. (1) also have a limit-cycle solution for certain values of the parameter (a, b), our NSFDS can be put to a very strong test, i.e., does the imposition of the positivity condition lead to the destruction of the limit-cycle. Our numerical experiments demonstrate that the answer is no, it does not.

It is rather easy to show that Eqs. (1) and (2.7) both have the same fixed-point,

$$x^* = b, \qquad y^* = \frac{b}{a+b^2}.$$
 (3.1)

Defining τ as

$$\tau \equiv -\frac{b^4 + (2a-1)b^2 + (a+a^2)}{a+b^2}, \qquad (3.2)$$

Strogatz [2] shows that the fixed-point has the following stability properties:

$$\tau > 0$$
: unstable, (3.3a)

$$\tau < 0$$
: stable. (3.3b)

The corresponding stability condition for the NSFDS of Eqs. (2.1) will in general be a more complex relation since the function $\phi(h, a, b)$ will also appear in the equation determining the eigenvalues at the fixed-point. An investigation of possible bifurcation behavior as the step-size is varied, for fixed (a, b), may provide interesting results on the mathematical properties of our NSFDS. Another study might consider leaving $\phi(h, a, b)$ unspecified and determine its functional form by the requirement that the NSFDS have exactly the same stability condition as given by Eq. (3.2).

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Figure 1. For these plots h = 0.01, $x_0 = 1$, and $y_0 = 1$. A stable limit-cycle exists.



Figure 2. For these plots h = 0.249, $x_0 = 1$, and $y_0 = 1$. A stable fixed-point exists.

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