

## Note on a Model of a Biochemical Reaction\*

PETER J. PONZO

*Department of Applied Mathematics, University of Waterloo, Waterloo, Ontario, Canada*

AND

NELSON WAX

*Department of Electrical Engineering, University of Illinois,  
Urbana-Champaign, Illinois 61801**Submitted by G. Leitmann*

## 1. INTRODUCTION

The autonomous system

$$\begin{aligned}\frac{dX}{dt} &= A - (B + 1)X + X^2Y, \\ \frac{dY}{dt} &= BX - X^2Y\end{aligned}\tag{1}$$

proposed as the chemical kinetic description of a model biochemical reaction, has been the subject of several recent studies [1, 2, 3, 4; see 3 and 5 for a derivation and discussion of these equations];  $X$ ,  $Y$  represent the concentrations of two intermediate product reactants,  $A$ ,  $B$  constant (initial) concentrations, and  $t$  the time.

The only singular point of (1) is at  $X_0 = A$ ,  $Y_0 = B/A$ . One finds, after a standard calculation, that the singular point is unstable, but not a saddle point when  $B > A^2 + 1$ . We thus consider only the first quadrant  $Q \stackrel{\text{def}}{=} \{X \geq 0, Y \geq 0\}$  in the  $X$ - $Y$  plane, and take  $A > 0$ ,  $B > A^2 + 1$  throughout.

We transform (1) to a system that has been investigated in considerable detail [6, 7]. We show, for the first time to our knowledge, and as an immediate consequence of this earlier work, that (1) has a unique stable limit cycle, when  $B > A^2 + 1$ . Furthermore, the amplitude, period, and "wave shape" can also be given readily when  $B \gg 1$  [7], thereby circumventing the elaborate asymptotic calculations of previous studies [2, 4].

\* This research was supported in part by a grant from the National Research Council of Canada, and in part by The Joint Services Electronics Program, (U. S. Army, U. S. Navy, and U. S. Air Force) under Contract DAAB-07-72-C-0259.

## 2. THE TRANSFORMED SYSTEM

Let

$$X = \frac{A}{1 + (B - 1)x}$$

and

$$t = \frac{(B - 1)^{1/2}}{A} \tau,$$

then (1) becomes, on eliminating  $Y$ ,

$$\ddot{x} + \mu \left[ 2x - 1 + \frac{1}{\mu^2(x + \lambda)^2} \right] \dot{x} + \frac{x}{x + \lambda} = 0, \quad (2)$$

where  $\mu = (B - 1)^{3/2}/A$ ,  $\lambda = 1/(B - 1)$  and the dot indicates differentiation with respect to  $\tau$ .

Equation (2) is a special case of

$$\ddot{x} + \mu f(x)\dot{x} + g(x) = 0 \quad (3)$$

which, in turn, is equivalent to the first order Lienard system

$$\begin{aligned} \dot{x} &= \mu[y - F(x)], \\ \dot{y} &= -g(x)/\mu \end{aligned} \quad (4)$$

with

$$F(x) = x^2 - x + \frac{1}{\mu^2} \left[ \frac{1}{\lambda} - \frac{1}{x + \lambda} \right] = \int_0^x f(s) ds$$

and

$$g(x) = \frac{x}{x + \lambda}$$

for (2).

The above functions satisfy the conditions listed in [6]; thus the proof given there of uniqueness and stability of the periodic orbit applies. One concludes that (1) has a unique stable periodic solution when  $B > A^2 + 1$ .

The values  $A = 8.2$ ,  $B = 77$  have been used in previous numerical calculations [2, 4] and we adopt them. One gets that  $\mu = 80.8$  and  $\lambda = 0.01316$ . A phase portrait of (4) using these values, is sketched in Fig. 1, which also portrays the limit cycle.

Let the zeros of  $F'(x) = f(x)$  be denoted by  $a$  and  $b$ , as shown in Fig. 1, and let  $\alpha$ ,  $\beta$  be defined by  $F(\alpha) = F(b)$ ,  $F(\beta) = F(a)$ , respectively.

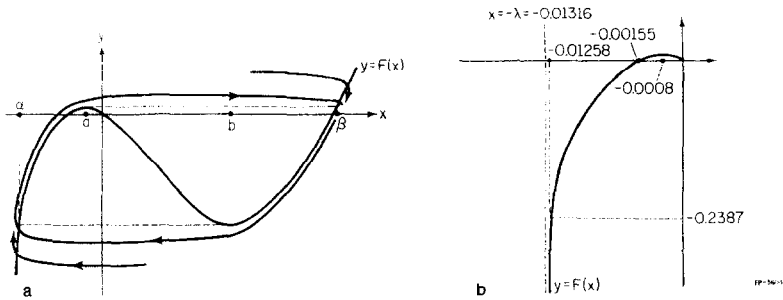


FIG. 1. (a) A phase portrait of the solutions of Eq. (4) is given in the  $x$ - $y$  plane. The unique stable limit cycle is shown. The quantities  $a$ ,  $\alpha$ ,  $b$ ,  $\beta$  are defined in the text. The drawing is not to scale. (b) A plot of  $y = F(x)$  in the second and third quadrants of the  $x$ - $y$  plane is shown. The drawing is not to scale.

Expressions for the amplitude and period are, when  $\mu \gg 1$ , [7]:

$$\text{Negative amplitude} = \alpha + \frac{2.33811}{f(\alpha)} \left[ -\frac{2g^2(b)}{f'(b)} \right]^{1/3} \mu^{-4/3} + \dots,$$

$$\begin{aligned} \text{Period} = & -\mu \int_{\alpha}^a \frac{f(x)}{g(x)} dx - \mu \int_b^{\beta} \frac{f(x)}{g(x)} dx \\ & + 2.33811 \left\{ \left[ \frac{2}{g(a)f'(a)} \right]^{1/3} + \left[ \frac{2}{g(b)f'(b)} \right]^{1/3} \right. \\ & \left. + \frac{1}{g(\beta)} \left[ -\frac{2g^2(a)}{f'(a)} \right]^{1/3} + \frac{1}{g(\alpha)} \left[ -\frac{2g^2(b)}{f'(b)} \right]^{1/3} \right\} \mu^{-1/3} + \dots \end{aligned}$$

Using the above functions and numerical values one finds that  $a = -0.0008$ ,  $\alpha = -0.01258$ ,  $b = 0.4997$ , and  $\beta = 0.9884$ .

Thus

$$\begin{aligned} x_{\min} &= \text{Negative amplitude} \doteq -0.01258 \\ \text{Period} &\doteq 24.00. \end{aligned}$$

Converting to the original variables, one has

$$X_{\max} = \frac{A}{1 + (B-1)x_{\min}} \quad \text{and} \quad \Delta T = \frac{(B-1)^{1/2}}{A} \Delta \tau$$

or

$$X_{\max} \doteq 186.7, \quad \Delta T = 25.5,$$

in excellent agreement with the estimates given in [2, 4].

We observe, finally, that other biochemical models, or any autonomous system transformable to (4) and satisfying the conditions on  $F$  and  $g$  given in [6], may be treated similarly. A sketch of one such possibility is depicted in Fig. 2.

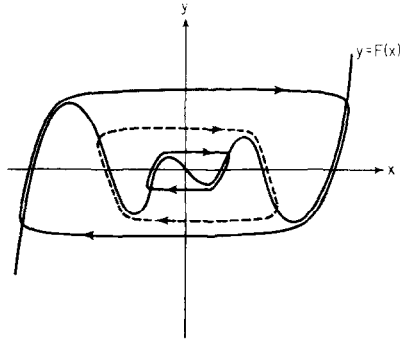


FIG. 2. A possible set of nested limit cycles, the solid curves stable, and the dotted curve unstable, is shown in the  $x$ - $y$  plane.

#### REFERENCES

1. R. LEFEVER AND G. NICOLIS, Chemical instabilities and sustained oscillations, *J. Theoret. Biol.* **30** (1971), 267-284.
2. B. LAVENDA, G. NICOLIS, AND M. HERSCHKOWITZ-KAUFMAN, Chemical instabilities and relaxation oscillations, *J. Theoret. Biol.* **32** (1971), 283-292.
3. J. A. BOA AND D. S. COHEN, Bifurcation of localized disturbances in a model biochemical reaction, *SIAM J. Appl. Math.* **30** (1976), 123-135.
4. J. A. BOA, Asymptotic calculation of a limit cycle, *J. Math. Anal. Appl.* **54** (1976), 115-137.
5. C. C. LIN AND L. A. SEGEL, "Mathematics Applied to Deterministic Problems in the Natural Sciences," pp. 537-539, Macmillan, New York, 1974.
6. P. J. PONZO AND N. WAX, On certain relaxation oscillations: Confining regions, *Quart. Appl. Math.* **23** (1965), 215-234.
7. P. J. PONZO AND N. WAX, On certain relaxation oscillations: Asymptotic solutions, *J. Soc. Indust. Appl. Math.* **13** (1965), 740-766.