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A Note on Oscillating Reactions

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The equations originally set up by Volterra to describe the interaction between two biological species are interpreted as a set of chemical reactions and discussed from a thermodynamic point of view. The equations are solved by the methods of Kryloff and Bogoliuboff, and it is shown that the frequency is lower the farther the system is from the stationary state, decreasing proportional to the square of the average distance from the stationary state.

1. In recent years the possible existence of oscillating chemical reactions and their use in explaining certain biological phenomena have attracted considerable attention [1-5]. Burton [1] discussed it from a biological point of view in connection with "overshoot phenomena", and Christiansen [2] has recently suggested it as an explanation of "spike potentials". Moore [3] has studied a specific model closely related to the one we shall discuss here, where the periodicity is caused by autocatalytic steps. Hearon [4] has considered the possibility of oscillations for several simple reaction mechanisms and concludes that, under certain general conditions, periodicities are not possible for them. Finally Bierman [5] has discussed more complicated mechanisms and shown how autocatalytic steps or reactions at the wall (where the absorption is assumed to be governed by a Langmuir isotherm) can lead to oscillatory behaviour. This paper also contains a discussion of the biological implications of these mechanisms. It must be remarked that in no cases have the differential equations set up by Bierman actually been solved.

By far the simplest example of an oscillating system, however, is that proposed by Volterra [6,7] as a model of interacting biological species. A similar model was discussed by Lotka [8] who gave an interpretation in terms of chemical reactions. Prigogine and Balescu [9] have used the Volterra equations, similarly interpreted, as an example in a discussion of the thermodynamics of irreversible processes.

Although these interpretations in principle are correct, it is exceedingly doubtful whether the Volterra equations represent a set of chemical reactions which actually occur in nature. Even as a model for the study of population dynamics [10] it probably is too simplified. On the other hand it is as realistic as any other model proposed so far, and therefore, because of its simplicity, the one that should be studied first. The interpretation in terms of chemical reactions is convenient, because it easily leads to an expression for the entropy-production.

It is the purpose of this note to show how the Volterra equations can be solved using the methods of Kryloff and Bogoliuboff. We start by giving the equations and deriving expressions for the relevant thermodynamic quantities.

2. It was assumed by Volterra that the interaction between two biological species, 1 and 2, of which 2 feeds on 1, can be described by the equations

$$\dot{A}_1 = w_1A_1 - w_2A_1A_2$$

$$\dot{A}_2 = w_3A_1A_2 - w_4A_2$$

n which A_1 and A_2 are concentrations and w_i (i = 1, 2, 3, 4) are constants. Below we give and interpretation of these equations in four partial reactions. J_i (i = 1, 2, 3, 4) are the corresponding flows and X_i (i = 1, 2, 3, 4) are the thermodynamic forces defined so that $\sigma = \Sigma X_iJ_i$ is the entropy production in units of the gas-constant R per second.

Reaction	Flow	Force
$A_1 \rightarrow 2A_1$	$J_1 = k_1A_1$	$X_1 = \ln \frac{k_1}{k_{-1}A_1}$
$A_1 + A_2 \rightarrow A_2$	$J_2 = k_2A_1A_2$	$X_2 = \ln \frac{k_2A_1}{k_{-2}}$
$A_1 + A_2 \rightarrow 2A_2$	$J_3 = k_3A_1A_2$	$X_3 = \ln \frac{k_3A_1}{k_{-3}A_2}$
$A_2 \rightarrow M$	$J_4 = k_4A_2$	$X_4 = \ln \frac{k_4A_2}{k_{-4}}$

(M is an inert substance)

The four reactions correspond biologically to growth of species 1, species 2 feeding on 1, species 2 propagating the faster the more food there is, species 2 dying.

If the four reactions are considered as chemical reactions it is evident that they do not conserve matter, *i.e.*, other substances, whose concentrations are kept constant, must be involved.

We see that with $k_1 = w_1$, $k_2 + k_3 = w_2$, $k_3 = w_3$, and $k_4 = w_4$ we have $\dot{A}_1 = J_1 - J_2 - J_3$ and $\dot{A}_2 = J_3 - J_4$. We must now eliminate k_{-1}, k_{-2}, k_{-3}, k_{-4} from the expressions for the forces. To do so we observe that the original equations have a stable stationary point $(A_1^s, A_2^s) = (w_4/w_3, w_1/w_2)$. It is known form the investigations of Volterra [6] that the representative point in the A_1, A_2-plane moves in closed curves counter-clockwise around this stationary point. This suggests introducing relative forces $\Delta X_i = X_i - X_i^s$ in which X_i^s is the force at the stationary point.

We find:

$$\Delta X_1 + \Delta X_3 + \Delta X_4 = 0 = \Delta X_1 + \Delta X_2$$

so that

$$\sigma - \sigma^s = \Sigma \Delta X_i J_i = (J_1 - J_2 - J_3)\ \Delta X_1 + (J_3 - J_4)\ (\Delta X_1 + \Delta X_3) = \Sigma j_i x_i$$

with

$$x_1 = \Delta X_1 = \ln \frac{w_4}{w_4 + w_3 \alpha_1} \sim - \frac{w_3}{w_4} \alpha_1$$

$$x_2 = \Delta X_1 + \Delta X_3 = \ln \frac{w_1}{w_1 + w_2 \alpha_2} \sim - \frac{w_2}{w_1} \alpha_2$$

In these equations j_i is the time derivative of A_i (or α_i) and $\alpha_i = A_i - A_i^s$. The approximate values given are valid for $\alpha_i \sim 0$. In terms of the α_i's the original equations read

$$\dot{\alpha}_1 = - \frac{w_2 w_4}{w_3} \alpha_2 - w_2 \alpha_1 \alpha_2$$

$$\dot{\alpha}_2 = \frac{w_1 w_3}{w_2} \alpha_1 + w_3 \alpha_1 \alpha_2$$

and we see that when $\alpha_1 \alpha_2$ can be neglected compared with α_1 or α_2, *i.e.*, when we linearize the equations, the representative point describes an ellipse around the stationary point (0,0) in the α_1, α_2-plane.

We see that near the stationary point $\dot{\alpha}$ and α as well as x and j are connected by matrices with constant coefficients and no diagonal elements. They are, however, not simply antisymmetric matrices as in the simpler case discussed by Prigogine and Balescu [9]. To ensure oscillations the 2 × 2 matrix must have purely imaginary eigenvalues. The conditions for this is that the determinant is positive and the trace vanishes. These conditions are satisfied.

The system so far described has no tendency to approach the stationary state, and this state is therefore, thermodynamically speaking, not a stable state. If $w_1 A_1$ is replaced by a constant as suggested by Lotka [8] or if terms containing A_1^2 and A_2^2 are included in the equations [6], the representative point in the A_1, A_2-plane will spiral in towards the stationary state. This is seen by linearizing the equations. Arbitrarily close to the stationary state there will, however, exist states with $\sigma - \sigma^s < 0$ and therefore the approach to the statinary state does not minimize σ. Nor does it seems possible to construct a physically meaningful function which is minimized. We have, therefore, here a thermodynamically stable state which seemingly is not governed by a minimum principle related to the principle of minimum entropy production.

Finally we should mention the differential form

$$\Sigma j_i dx_i = w_2 \alpha_2 \mathrm{d}\alpha_1 - w_3 \alpha_1 \mathrm{d}\alpha_2$$

which has been shown by Glansdorff and Prigogine [12] to be always negative. Since the rotation is counter-clockwise this is immediately verified, and the theorem of Glansdorff and Prigogine can be said to fix the sense of rotation as pointed out by Prigogine and Balescu [9]. This differential form will not in general possess an integrating multiplier [13] although in this case, with only two independent variables, it does (*i.e.*, $(\alpha_1\alpha_2)^{-1}$).

3. If one tries to solve the non-linear equations of Volterra by usual iteration-methods starting from the solution of the linearized equation one immediately gets terms which diverge strongly as $t \to \infty$. We must therefore use an iterative procedure where, at each step, the occurrence of such terms is prevented. Such a method has been devised by Kryloff and Bogoliuboff [11], and we refer to their book for details.

It is convenient to introduce new variables y_1 and y_2 by $\alpha_1 = w_2\sqrt{w_4}y_1$ and $\alpha_2 = w_3a\sqrt{w_1}y_2$. We then have

$$\dot{y}_1 = -\nu y_2 - a y_1 y_2$$

$$\dot{y}_1 = \quad \nu y_1 + b y_1 y_2$$

with $\nu = \sqrt{w_1w_4}$; $a = w_2w_3\sqrt{w_1}$; $b = w_2w_3\sqrt{w_4}$ or:

$$\ddot{y}_1 + \nu^2 y_1 = b y_1 \dot{y}_1 - a\nu y_1^2 + \frac{a\dot{y}_1^2}{\nu + a y_1}$$

and an analogous equation for y_2.

In the first approximation the representative point in y_1y_2 space now moves on a circle around (0,0). We see that the right-hand side of the last equation contains terms which, when expanded in power series near (0,0), are smaller than the terms on the left-hand side by increasing orders of magnitude. Expanding the fraction on the right-hand side we rewrite the equation as:

$$\ddot{y}_1 + \nu^2 y_1 = \varepsilon(b y_1 \dot{y}_1 - a\nu y_1^2 + \frac{a}{\nu}\dot{y}_1^2) - \varepsilon^2(\frac{a}{\nu})^2 \dot{y}_1^2 y_1 + \ldots$$

$$= -\varepsilon f_1(y_1, \dot{y}_1) - \varepsilon^2 f_2(y_1, \dot{y}_1) - \ldots$$

where the factor ε indicates the smallness of the perturbation. This separation of the right-hand side into terms of increasing order of smallness appears to be necessary for the successful application of the Kryloff-Bogoliuboff method. In the final solution we shall of course put $\varepsilon = 1$.

We want to find a solution of the form $y_1 = z(\tau)$, with $\tau = \omega t + \varphi$, where $z(\tau)$ is a function with period 2π. Substitutiong we get

$$\omega^2 z'' + \nu^2 z = -\varepsilon f_1(z, \omega z') - \varepsilon^2 f_2(z, \omega z') - \ldots$$

and we now assume

$$z = z_0(\tau) + \varepsilon z_1(\tau) + \varepsilon^2 z_2(\tau) + \ldots$$

$$\omega = \omega_0 + \varepsilon\,\omega_1 + \varepsilon^2\omega_2 + \ldots$$

Using the above assumption and collecting powers of a we have the recursive system:

1. $\omega_0^2 z_0'' + \nu^2 z_0 = 0$
2. $\omega_0^2 z_1'' + \nu^2 z_1 = - f_1(z_0, \ \omega_0 z_0') - 2\omega_0\omega_1 z_0''$
3. $\omega_0^2 z_2'' + \nu^2 z_2 = - f_1'(z_0, \ \omega_0 z_0') - f_2(z_0, \ \omega_0 z_0') - (\omega_1^2 + 2\omega_0\omega_2) z_0'' - 2\omega_0\omega_1 z_1$

etc.

These linear differential equations are solved, and at each step in the iterative procedure we adjust ω so that secular terms do not develop, *i.e.*, we adjust ω so that the Fourier-expansion of the right-hand side does not contain terms with sin ωt or cos ωt. We obtain:

1. $y_1 = r \ \cos(\nu t + \varphi) \quad \nu = \sqrt{w_1 w_4}$

   $y_2 = r \ \sin(\nu t + \varphi)$

2. $y_1 = r \ \cos(\nu t + \varphi) + \frac{a}{3\nu} \ r^2 \cos 2(\nu t + \varphi) + \frac{b}{6\nu} \ r^2 \sin 2(\nu t + \varphi)$

   $y_2 = r \sin \ (\nu t + \varphi) - \frac{b}{3\nu} \ r^2 \cos 2(\nu t + \varphi) + \frac{a}{6\nu} \ r^2 \sin 2(\nu t + \varphi)$

   $\omega_1 = 0$, *i. e.*, the frequency is as in the first approximation

3. $\omega_2 = - \frac{r^2}{12} (a^2 + b^2)$, *i. e.*, the frequency is

   $\nu - \frac{r^2}{12} (a^2 + b^2) = \sqrt{w_1 w_4} - \frac{w_2^2 w_3^2 r^2}{12} (w_1 + w_4)$

It is hardly worth while to go on to higher approximations for y_1 and y_2, since the most important result certainly is the expression for the frequency. Experimentally the frequency will be easily accessible even for very fast reactions, and if the chemical reactions leading to the Volterra equations could be realized, it would be easy to check this expression, since at least one rate-constant can be changed at will simply by adding the substance which must serve as "food" for A_1 to conserve matter. It is of course intuitively clear that the frequency will decrease when r increases, since the path length increases towards infinity and at the same time the path approaches the other stationary point (which is unstable). Although the frequency goes down, the actual velocity of the system in its path in a_1, a_2 space increases — in the first approximation proportional to r.

The method we have applied here can be used on most second order non-linear differential equations leading to oscillations and should therefore make it possible to discuss more closely the models for oscillatory behaviour which are found in the literature.

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