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Brusselator: an abstract chemical reaction?

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Contents

Abstract. In this paper we consider the Brusselator and the Sel'kov model, which describes the irreversible reaction of glycolysis in the regime of self-sustained oscillations. We show that these two differently constructed models can be reduced to a single equation — a generalized Rayleigh equation. The physical basis for this generality is investigated. The advantages of this equation as a tool for qualitative and quantitative analyses, as well as the similarities and differences of the solutions realized for each of the two concrete models in the cases of almost harmonic and relaxation self-sustained oscillations, are discussed.

1. Introduction

Just eighty years ago A A Andronov introduced the concept of autooscillating systems [1–3], oscillating processes in which, in contrast to oscillating processes in other dissipative systems, do not require periodic action from outside for their maintenance. In this case, the form of self-sustained oscillations depends on the properties of the system, but it does not depend on the initial conditions. However, it should be noted that Andronov's main merit is the fact that he gave a clear mathematical sense to this concept by connecting this type of oscillations with the Poincaré limit cycles.

By that time such systems had already been known; their basic properties had been formulated and rigorously analyzed at a physical level several decades earlier by Rayleigh [4, 5]. Rayleigh's interest in this topic arose, first and foremost, due to questions associated with the theory of sound, such as vibrations of a string upon a uniform motion of a bow, the motion of air in organ pipes, and the motion of an electromechanical tuning fork, i.e., the systems characterized by the coexistence of various nonlinear processes which are responsible for the dissipation and the maintenance of the energy of vibrations.

Later on, such mechanisms taking the part of a feedback loop, obtained (beginning from the work of van der Pol devoted to a triode generator) wide acceptance in radio engineering and radio physics which were closely related to the boom in the theory of nonlinear oscillations. The survey of the basic results in this field obtained by the scientific school of L I Mandelstam, N D Papaleksi, and A A Andronov can be found in Ref. [6]. It should be noted that it is precisely the Rayleigh equation that was taken as one of the basic models considered in review [6].

However, examples of autooscillating systems are not limited only to purely physical systems. In the last 40 years, undamped oscillations have been revealed in many biophysical and chemical systems, for example, the Belousov–Zhabotinsky reaction [7], periodic phenomena in photosynthesis [8] and other metabolic processes in cells, in particular, in glycolysis, oscillations of calcium concentration [9], neurodynamics [10], and in many other systems.

The simplest classical example of the existence of self-sustained oscillations in chemical reactions is the 'Brusselator' proposed in 1967 by Prigogine and Lefevre [11], announcing this reaction as a model that describes an abstract trimolecular chemical reaction, which, however, makes it possible in a simple and visual way to establish qualitative types of behavior compatible with the fundamental laws of chemical and biological kinetics [12]. The Brusselator standed alongside classical models of autooscillating systems, such as the Rayleigh and van der Pol equations utilized in acoustics and radio engineering. So far, the Brusselator continues to play the role of the basic model used for the examination of more complex situations which include stochastic and synchronizing effects, and the role of a

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test model for constructing mathematical methods of analysis of systems with a strong nonlinearity, which is not however related to concrete chemical processes [13].

In turn, for describing self-sustained oscillations in real chemical and metabolic systems numerous models resting on experimentally established interactions have been developed. In particular, one of the first models was the Sel'kov model [14] developed almost simultaneously with the Brusselator in 1967, which described oscillations of substrates and products of glycolysis — one of the most important biochemical pathways of generating energy for living organisms.

A further development in studies was the change from localized dynamical systems to distributed systems (see, e.g., the results generalized in the reviews issued in *Phys. Usp.* and devoted both to general problems of the application of the theory of traveling waves to biophysical systems [15] and to more specific problems, such as traveling waves in separate cells [16] and cellular populations [17, 18], models of blood coagulation [19], and also in the fundamental monographs [20, 21]). Thus, it can be said, citing the subtitle of Blomberg's monograph [22], that over the past century the ideas of the description of self-sustained oscillations, laid in acoustics and radio physics, have paved a noticeable portion of 'the physicist's road to biology'.

At the same time, it makes sense from the methodological viewpoint to return to two key points from which this 'road' began, i.e., to the Rayleigh equation, which has laid the basis of the theory of self-sustained oscillations in physics, and to the Prigogine–Lefevre model (Brusselator) and the Sel'kov model, which have played the same role in chemistry, biochemistry, and biophysics, and to examine their interconnection from the modern viewpoint.

The aims of this paper are to show that these two basic models of chemical and biochemical kinetics — the Brusselator and the Sel'kov model — can be reduced to a common generalized Rayleigh equation and all the regimes found in the Brusselator model and the Sel'kov model can be easily and clearly explained from the viewpoint of the classical model of the physical oscillator, and to reveal the interconnections between these models in order to understand to what extent the Brusselator represents a model of just an abstract chemical reaction.

2. Models

Let us consider the three models mentioned above. Since their classical form has well been studied and has been described in detail (see, e.g., Refs [5, 9, 13, 23]), below we give only a brief representation of these models, which will elucidate the physical essence and origin of each model.

2.1 Rayleigh oscillator

Rayleigh [5] examined a situation where a system with friction contains an internal energy source, and the force with which this source acts on the oscillating object is assumed to be small, i.e., linear in the variables — displacement ξ and velocity $\dot{\xi}$ — that enter into the equations of motion. Then, the equations of motion are written as

$$m\,\frac{\mathrm{d}^2\xi}{\mathrm{d}t^2} = -k_0\,\frac{\mathrm{d}\xi}{\mathrm{d}t} - k_1\xi + k_2\,\frac{\mathrm{d}\xi}{\mathrm{d}t}\,, \tag{1}$$

where k_0 is the coefficient of linear friction, k_1 is the coefficient of elasticity, and k_2 is the coefficient of the velocity-dependent force component. Physically, the last term on the right-hand side of Eqn (1) corresponds to the force that is transferred to the system by an impact, i.e., by a rapid transfer of additional momentum to it. A similar component arises naturally in some techniques of eliciting sounds from musical instruments or when sustaining operation of a clockwork. The solution to such a linear equation under the condition of $k_2 > k_0$ will exponentially grow with time, and at a certain instant the velocity will cease to be small, i.e., the first term on the right-hand side of Eqn (1) will be added by a term containing the velocity to the next power, which is directed opposite to the velocity, i.e., proportional to $\dot{\xi}^3$.

As a result, the classical Rayleigh equation takes on the form

$$\frac{\mathrm{d}^2\xi}{\mathrm{d}t^2} + \lambda\,\frac{\mathrm{d}\xi}{\mathrm{d}t} + \lambda'\left(\frac{\mathrm{d}\xi}{\mathrm{d}t}\right)^3 + \Omega^2\xi = 0\,, \tag{2}$$

where the following designations were introduced: $\lambda = (k_2 - k_0)/m$, and $\Omega^2 = k_1/m$.

Based on an analysis of Eqn (2), Rayleigh showed that in this system stationary oscillations are possible if λ and λ' have opposite signs. In this case, if λ is negative and λ' is positive, such oscillations are stable. Rayleigh also determined (if we use modern terminology) the radius of the limit cycle of these stable self-sustained oscillations and, for a stationary motion over this cycle, he found an approximate solution to Eqn (2) with an accuracy to the third harmonic.

2.2 Brusselator

The Brusselator describes the simplest chemical reaction of the transformation of the initial substances (substrates) A and B into products C and D, namely

$$\mathrm{A} + \mathrm{B} \to \mathrm{C} + \mathrm{D}\,,$$

as a reaction consisting of the following stages:

$$\mathrm{A} \xrightarrow{k_1} \mathrm{X}\,, \tag{3}$$

$$2\mathrm{X} + \mathrm{Y} \xrightarrow{k_2} 3\mathrm{X}\,, \tag{4}$$

$$\mathrm{B} + \mathrm{Y} \xrightarrow{k_3} \mathrm{Y} + \mathrm{C}\,, \tag{5}$$

$$\mathrm{X} \xrightarrow{k_4} \mathrm{D}\,. \tag{6}$$

The most nontrivial step in the set of equations (3)–(6) is the utilization of intermediate substances X and Y connected with one another via a trimolecular reaction (4), which ensures the existence of an oscillatory regime. Given the products are irreversibly moved away from the sphere of reaction, the substrates prove to be in excess and the values of the reaction rate constants are equal to unity, and the dynamics of the concentrations of the intermediate reagents is described by the following set of equations:

$$\begin{aligned} \frac{\mathrm{d}x}{\mathrm{d}t} &= A + x^2y - (B+1)x\,,\\ \frac{\mathrm{d}y}{\mathrm{d}t} &= Bx - x^2y\,, \end{aligned} \tag{7}$$

where x and y are the dimensionless concentrations of the metabolites of the reaction, and A and B are the dimensionless parameters of the reaction.

Beginning from the original article [11], the authors of the Brusselator model emphasized that the scheme (3)–(6) is physically unrealistic because of the presence of the trimolecular step (4); however, its structure is very convenient for

considering the important problems of nonequilibrium processes if the simple condition that the reaction involve only two intermediate components is fulfilled.

One should, however, note that, in contrast to the usual chemical reactions, in enzyme kinetics the reaction can sometimes be reduced to a cubic form. This is possible if the ferment has at least three catalytic centers capable of simultaneously fixing two molecules of one kind and one molecule of another kind under the condition that the resultant intermediate complexes decompose at a sufficiently high rate and the ferment is present in small amounts. Then, it can easily be shown that the entire sequence of reactions can be reduced to one stage which gives a nonlinear term of the x^2y or xy^2 type. The simplest example of this type is the Sel'kov system.

2.3 Sel'kov model

In contrast to the Brusselator, the Sel'kov model was developed from the very beginning for describing oscillations in a concrete biochemical process, namely, glycolysis. In particular, the Sel'kov model describes the first, key stage of glycolysis, which is catalyzed by an enzyme called phosphofructokinase.

If the substrate X enters into the system at a constant rate v, the product Y is moved away at a rate w, and the free enzyme E (phosphofructokinase) is not active by itself but contributes to the formation of trimolecular complexes, this stage of the reaction of glycolysis can be represented as follows:

$$\begin{aligned}
&\xrightarrow{v} \mathrm{X} + \mathrm{EY}^2 \underset{k_{-1}}{\overset{k_{+1}}{\rightleftharpoons}} \mathrm{XEY}^2\,,\\
&\mathrm{XEY}^2 \xrightarrow{k_{+2}} \mathrm{EY}^2 + \mathrm{Y} \xrightarrow{w},\\
&2\mathrm{Y} + \mathrm{E} \underset{k_{-3}}{\overset{k_{+3}}{\rightleftharpoons}} \mathrm{EY}^2\,.
\end{aligned}$$

In dimensionless variables, the system of equations describing the reaction in terms of concentrations can be written in the following form

$$\begin{aligned}
\frac{\mathrm{d}x}{\mathrm{d}t} &= v - xy^2\,,\\
\frac{\mathrm{d}y}{\mathrm{d}t} &= xy^2 - wy\,.
\end{aligned} \tag{8}$$

It is seen that, similar to Eqn (7), equations (8) contain a cubic nonlinearity formed by the product xy^2 and that this product enters into each of the equations of the system with a different sign but with the same coefficient equal to unity. Furthermore, the right-hand sides of both systems of equations contain a linear term in only one of the variables and a constant term. When taking all this into account, the question arises as to whether there can exist a single equation whose special cases are, at a specific choice of the variables and parameters, Eqns (7) and (8), and if such an equation does exist, what its physical sense is.

3. Reduction of the set of equations describing Brusselator and of the set of Sel'kov equations to a generalized Rayleigh equation

Let us begin from the set of Sel'kov equations (8), which is simpler in form, and rewrite these equations in new variables. As such variables, let us introduce the total concentration of reactants, $z = x + y$, and the total flux of exchange with the environment, $u = v - wy$. Summing up equations (8) and substituting z and u into them, we obtain the following set of equations:

$$\begin{aligned}
\frac{\mathrm{d}z}{\mathrm{d}t} &= u\,,\\
\frac{\mathrm{d}u}{\mathrm{d}t} &= -w(u - v) - w^{-2}(wz + u - v)(u - v)^2\,,
\end{aligned} \tag{9}$$

which describes the dynamics of the total concentration of the reagents and its exchange with the environment.

Set (9) possesses the stationary solution

$$\begin{aligned}
u_0 &= 0\,,\\
z_0 &= \frac{w^2}{v} + \frac{v}{w}\,,
\end{aligned}$$

which has a transparent physical sense: the constancy of the total concentration of reagents corresponds to a zero total flux.

For the convenience of studying nonstationary processes, let us introduce a new variable, namely, the deviation from the equilibrium concentration, $\xi = z - z_0$. Substituting the new variable into Eqn (9) and grouping similar terms, we arrive at the following set of equations:

$$\begin{aligned}
\frac{\mathrm{d}\xi}{\mathrm{d}t} &= u\,,\\
\frac{\mathrm{d}u}{\mathrm{d}t} &= -\lambda u - (\lambda'' + \lambda' u)\,u^2 - \left[\Omega(1 - \kappa u)\right]^2 \xi\,,
\end{aligned}$$

which can be written in the form of a single second-order equation

$$\frac{\mathrm{d}^2\xi}{\mathrm{d}t^2} + \lambda\,\frac{\mathrm{d}\xi}{\mathrm{d}t} + \lambda''\left(\frac{\mathrm{d}\xi}{\mathrm{d}t}\right)^2 + \lambda'\left(\frac{\mathrm{d}\xi}{\mathrm{d}t}\right)^3 + \Omega^2\left(1 - \kappa\,\frac{\mathrm{d}\xi}{\mathrm{d}t}\right)^2 \xi = 0\,. \tag{10}$$

Here, $\lambda = v^2w^{-2} - w$, $\lambda'' = (z_0w - 3v)/w^2$, $\lambda' = w^{-2}$, $\kappa = v^{-1}$, and $\Omega = v/\sqrt{w}$.

Equation (10), if we compare it with equation (2), quite realistically can be called the generalized Rayleigh equation: the nonlinearity in it, just as in the classical Rayleigh equation (2), in contrast, for example, to the nonlinearity in the van der Pol and Duffing equations, is due only to velocities rather than to displacements. Namely, in this case in the 'dissipative' part [second, third, and fourth terms on the left-hand side of Eqn (2)] an expansion in all powers of the velocity appears up to the third one, and its influence on the free oscillation frequency Ω is manifested to an accuracy of the first power. It is necessary to note here that the parameter $\lambda'' > 0$ determines the asymmetry in the position of the center of the limit cycle.

Let us now examine the Brusselator equations (7). We again introduce the total concentration of substances, $z = x + y$, and a variable $u = A - x$. The substitution of the new variables and the summing up of the equations of set (7) gives the following system of equations:

$$\begin{aligned}
\frac{\mathrm{d}z}{\mathrm{d}t} &= u\,,\\
\frac{\mathrm{d}u}{\mathrm{d}t} &= A(B + A^2) - (1 + B + 3A^2)u + 3Au^2 - u^3 - (A - u)^2 z\,.
\end{aligned} \tag{11}$$

The stationary points for Eqn (11) are $z_0 = \left(B + A^2\right)/A$ and $u_0 = 0$. We again shift the stationary point into the origin by introducing a variable $\xi = z - z_0$. Substituting this variable into equation (11) and then grouping and collecting similar terms, we obtain

$$\begin{aligned} \frac{\mathrm{d}\zeta}{\mathrm{d}t} &= u\,, \\ \frac{\mathrm{d}u}{\mathrm{d}t} &= (B - A^2 - 1)u + \left(2A - \frac{B}{A}\right)u^2 - u^3 - (A - u)^2\xi\,. \end{aligned} \tag{12}$$

Representing Eqn (12) in the form of a single second-order differential equation, we again come to the generalized Rayleigh equation (10) whose coefficients now take the form: $\lambda = \left(1 + A^2 - B\right)$, $\lambda' = 1$, $\lambda'' = (B - 2A^2)/A$, $\Omega = A$, and $\kappa = A^{-1}$.

Thus, both models — the originally 'abstract' Brusselator and the set of Sel'kov equations, which describes quite a concrete biochemical process — at an appropriate choice of variables, sufficiently natural and clear from the viewpoint of the physics of the processes, take on a completely identical mathematical form. A similar problem was touched on in Ref. [24]. Therefore, an analysis of the generalized Rayleigh equation (10), which is also sufficiently transparent because of the form of the latter, will give complete information on both the models. The concrete dynamic regimes will be determined by the magnitudes of the constants entering into equation (10), which are characteristic of each concrete problem.

4. Discussion of the generalized Rayleigh equation

Let us carry out a brief analysis of Eqn (10) with the aim to, first of all, show that this form of writing down has large methodological advantages in studying self-sustained oscillations in classical biochemical systems. Let us also emphasize that this form of writing the equation allows the most natural method of linearization in the vicinity of a fixed point $\xi = 0$, $\dot{\xi} = 0$; it is sufficient to simply discard all terms taken to a power higher than first:

$$\frac{\mathrm{d}^2\xi}{\mathrm{d}t^2} + \lambda\,\frac{\mathrm{d}\xi}{\mathrm{d}t} + \Omega^2\xi = 0\,. \tag{13}$$

The solution to Eqn (13), namely

$$\xi(t) = \xi_0 \exp\left(-\frac{\lambda t}{2}\right)\cos\left(\omega t + \phi_0\right)$$

[where $\omega = \left(\Omega^2 - \lambda^2/4\right)^{1/2}$, and ξ_0 and ϕ_0 are the initial amplitude and phase, respectively], makes it possible to vividly determine the condition of loss of the stability of the fixed point (Hopf bifurcation): if $\lambda < 0$, then the oscillations will grow exponentially. Otherwise, the point remains stable and any small deviations from zero will decrease (also exponentially) for $\lambda > 0$. In the case of the Sel'kov model, the bifurcation point is determined by the following relationship between the parameters: $v = w\sqrt{w}$; in the case of the Brusselator, one finds: $A^2 + 1 = B$.

Furthermore, the change of the type of unstable fixed point is introduced just as naturally: for $\Omega^2 \leqslant \lambda^2/4$, it changes from the focus (oscillatory increase) to a node (anharmonic growth).

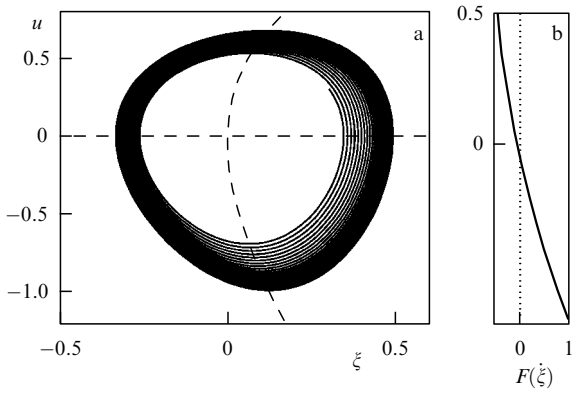

Figure 1. (a) Phase portrait of the solution to the set of Sel'kov equations in the form of a generalized Rayleigh equation at $v = 2.8$ and $w = 2$; the dashed lines are nullclines. (b) Variation of the factor that ensures the existence of self-sustained oscillations at the above parameters; $F(\dot{\xi}) = \lambda + \lambda''\,\mathrm{d}\xi/\mathrm{d}t + \lambda'(\mathrm{d}\xi/\mathrm{d}t)^2$.

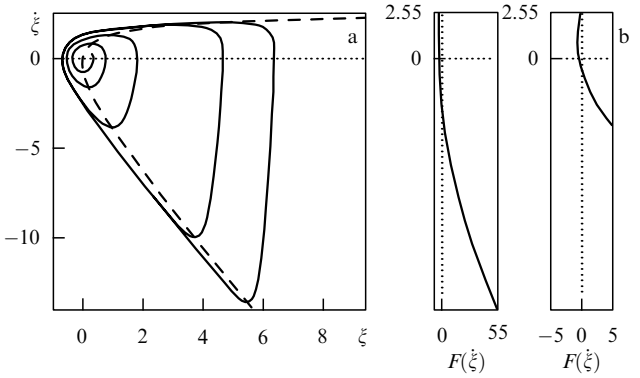

Figure 2. (a) Phase portrait of the solution to the set of Sel'kov equations in the form of a generalized Rayleigh equation at $v = 2.55$ and $w = 2$; the dashed lines are nullclines. (b) Variation of the factor that ensures the existence of self-sustained oscillations at the above parameters.

For demonstrating the principle of existence of self-sustained oscillations in a nonlinear regime, it is convenient to rewrite equation (10) in the typical 'self-oscillatory' form:

$$\frac{\mathrm{d}^2\xi}{\mathrm{d}t^2} + \left[\lambda + \lambda''\,\frac{\mathrm{d}\xi}{\mathrm{d}t} + \lambda'\left(\frac{\mathrm{d}\xi}{\mathrm{d}t}\right)^2\right]\frac{\mathrm{d}\xi}{\mathrm{d}t} + \Omega^2\left(1 - \kappa\,\frac{\mathrm{d}\xi}{\mathrm{d}t}\right)^2\xi = 0\,. \tag{14}$$

Notice that the nonlinear factor of Ω^2 is always non-negative as a result of being squared, so that it has no effect on the existence condition of the limit cycle and this condition will be determined by the behavior of the bracket at $\dot{\xi}$ [second term on the left-hand side of Eqn (14), which in Figs 1–3 is designated as $F(\dot{\xi})$]. Namely, if $\lambda < 0$, then an increase in the velocity can lead to a change of the sign of this term and the excitation of oscillations will merge into damping. As a result, a motion over a stable limit cycle will develop. For the Sel'kov model and for the Brusselator, the illustrations are given in Figs 1–3, from which it is seen that at sufficiently large $u = \dot{\xi}$ the sign of the coefficient of the velocity coincides with the sign of the velocity, i.e., there can exist steady periodic motions which are demonstrated in the phase portraits of the solutions given in the same figures.

The power type dependences also make it possible to sufficiently readily obtain an approximate solution to

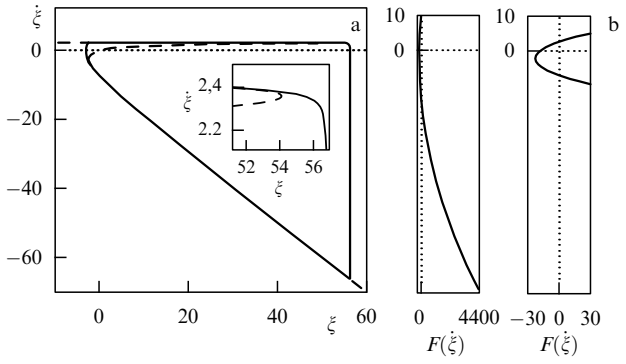

Figure 3. (a) Phase portrait of the Brusselator in the form of a generalized Rayleigh equation at $A = 2.55$ and $B = 25$; in the inset, its section near the point of quenching of relaxation oscillations; the dashed lines are nullclines. (b) Variation of the factor that ensures the existence of self-sustained oscillations at the above parameters.

Eqn (10), for example, using the van der Pol–Krylov–Bogoliubov method, since in this case when substituting harmonic functions their powers can easily be reduced, which leads to a set of harmonics for which each can be investigated separately. In this case, a characteristic feature that distinguishes the motion described by a generalized Rayleigh equation from classical motion is the presence of a term that is quadratic in velocity and, therefore, never changes its sign, thus leading to a shift of the characteristic center of the limit cycle. Notice that such a quadratic nonlinearity effect was first analyzed by Rayleigh for the case of stable dissipativeless oscillations [5]. In particular, such a method yields a high-precision approximation for an analytical description of the passage to a stationary regime for oscillations close to harmonic ones in the solution of the Sel'kov equations [30]. This result can qualitatively easily be explained based on the phase portrait given in Fig. 1, where the limit cycle is close to an ellipse in shape. In the case of the Brusselator, it has an analogous shape near the Hopf bifurcation.

The difference in the behavior of these two concrete models manifests itself when considering relaxation oscillations (see Figs 2 and 3). This difference is related to the fact that the physically realizable values of the parameters lead to a qualitatively different type of isoclines $\dot{\xi} = 0$. In the Sel'kov model, this isocline has only one extremum (see Fig. 2), while the Brusselator can have two extrema (see Fig. 3 and the inset to this figure). The second extremum appears with increasing B, which can be arbitrarily large. In this case, the 'self-oscillatory dissipative' term begins prevailing over the 'oscillatory' term $[\Omega^2(1 - \kappa\dot{\xi})\xi]$ and in the limit $B \to \infty$ the oscillations are described by the classical methods of the analysis of relaxation oscillations as slow movements along a nullcline and rapid disruptions along the perpendiculars dropped to it from the points of the extrema of the nullcline (see inset to Fig. 3, where B, although finite, is already sufficiently large). This is especially useful from the methodological point of view, since it enables an easy explanation of the properties of the Brusselator, when moving to it upon the consideration of relaxation oscillations in the solutions of the classical Rayleigh equation, which were considered in detail in the well-known book [25].

The case of the Sel'kov model is less trivial, since an explicit large parameter is absent in it, and with a decreasing coefficient of the rate v of the substrate intake the relaxation type oscillations are generated upon the simultaneous tending to zero of both terms on the right-hand side of Eqn (14). Therefore, as is seen from Fig. 2, the line of rapid motions in the phase portrait is not vertical and the finding of the point of quenching of relaxation type glycolytic oscillations is a more difficult problem.

5. Conclusions

Thus, both basic models of chemical and biochemical oscillatory kinetics, which were originally proposed completely independently on the basis of different assumptions — the assumption of an abstract minimum scheme that allows the existence of chemical self-sustained oscillations, and the assumption of a scheme that is maximally simplified but realistic according to physical and chemical considerations — from a mathematical point of view represent one and the same equation with an accuracy to the physical interpretation of the change of variables.

Moreover, this equation is closely related to the basic equation that describes self-sustained oscillations in physical systems — to the Rayleigh equation — and generalizes it in a thoroughly natural way. This unification makes it possible to explicitly and physically clearly separate terms that are responsible for excitation, damping, and sustaining of oscillations; moreover, the appropriate linear analysis can be carried out without resorting to any formal expansions, but simply using the fact that the differential equations corresponding to all three models are reduced to the elementary equation of a linear harmonic oscillator.

This also simplifies the analysis of slightly and strongly nonlinear regimes in comparison with the analysis based on standard methods whose application is quite cumbersome, as is evident, in particular, from the example of the Brusselator, for which an analysis of its quasiharmonic and relaxation limit cycles has been carried out in a series of articles [26, 27], as well as in the approximation of strong nonlinearity, although sufficiently far from the regime of ideal relaxation oscillations — a case that was recently investigated [28] by He's method [29]. The last approach, which is a further generalization of the van der Pol method for averaging over the period of arbitrary nonharmonic functions, seems especially promising. This is connected with the fact that the above-derived generalized Rayleigh equation belongs to the class of nonlinear equations that satisfies the condition of the equality of one of the variables (in our case, total flux) averaged over the period to its steady-state value, which assumes a certain specific importance in the simulation of biophysical processes (see Ref. [30]).

Let us examine one fundamental property of systems that can be described by the generalized Rayleigh equation. The basic physical sense of the Rayleigh equation lies in the allowance for the dependence on the highest powers of the velocity in the 'dissipative coefficient' (coefficient of the rate $\mathrm{d}\xi/\mathrm{d}t$) and in the 'frequency' (coefficient of the shift ξ from the equilibrium position) for a classical oscillator written down in the standard form (14). Therefore, upon a change of the variables which linearize one of two equations, it is necessary that the new rate $\mathrm{d}\xi/\mathrm{d}t$ be a linear function of only one of the initial variables (x, y), for example,

$$\frac{\mathrm{d}\xi}{\mathrm{d}t} = k_1 x + b_1 ,$$

where k_1 and b_1 are some constants with respect to u. In this case, the shift ξ from the equilibrium position is a linear function of another variable: $\xi = k_2 y + b_2$ (which also coincides with the condition that generates the equality of the average and stationary values [30]). Here, the need for the existence of precisely this condition is connected with the fact that the reaction term in models of the type in question has the form $x^2 y$ or x^3, and the dependence $\mathrm{d}\xi/\mathrm{d}t$ on two variables should not lead to the appearance of terms nonlinear in ξ in Eqn (14).

One should also say in conclusion that the representation in the form of a generalized Rayleigh equation is an efficient theoretical method [31] which permits one to reveal a new-type mechanism of traveling waves in the distributed reaction of glycolysis, which occurs in a dense medium with an extremely low diffusion, traveling waves which are actively being investigated experimentally at present [32].

Finally, one curious fact can be noted, namely, that the approach connecting the equations of biochemical kinetics with the Rayleigh equation also has an interesting gateway to radio physics; indeed, the authors of patent [33] developed a generator of nonlinear self-sustained oscillations whose basic innovation involves a rearrangement of the limit cycle of the Rayleigh equation into the limit cycle of the Brusselator owing to the introduction of specific synchronization circuits. This article shows that a similar empirical approach is mathematically substantiated and allows the possibility of assigning the required additive terms explicitly.

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