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New Theoretical Schemes of the Simplest Chemical Oscillators

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Abstract—Based on the sufficient conditions for existence of concentration oscillations of the components of bicomponent reaction, all possible chemical reactions with two, three, or four intermediate stages proceeding via the mass-action expression are considered. About forty new schemes of chemical/biochemical oscillators are developed.

Key words: chemical/biochemical oscillations, oscillator

It is known that many biochemical systems are able to function in an oscillatory mode. However, the role of such oscillations is not completely elucidated. Oscillator types not yet studied may exist in living cell. That is why it is necessary to reveal simple theoretical reaction schemes in complex networks of various biological processes that may result in concentration oscillations of reagents and to estimate under what conditions oscillations arise and are maintained.

In mathematical modeling of biochemical oscillators, terms taken from technical sciences (regulation, negative/positive feedback) are used. The concepts of feedback and direct relation suggest participation of an inhibitor in regulation of some enzyme. However, oscillations may be induced by other mechanisms. Empirical dependences of steady-state activity of enzyme on various ligands (activators/inhibitors) are often used in modeling enzymatic reactions. Besides this, the standard formulae and analogies with the technical concepts often do not allow revealing a true mechanism of initiation and maintenance of oscillations.

The goal of this study was to describe the simplest kinetic models (critical fragments), which can be responsible for critical phenomena in a network of biochemical reactions, and to analyze conditions under which these critical fragments induce concentration oscillations of the system participants.

METHODS OF INVESTIGATION

To study critical phenomena in chemical/biochemical system, we used Lyapunov's stability theory. In order to use the theory of steady-state stability in a dynamic chemical system, let us consider the main terms of chemical kinetics.

Main terms. Equations of chemical kinetics. Let us designate participants of a complex chemical/biochemical reaction consisting of R elementary reactions as X_1, X_2, ..., X_n (reagents, intermediates, and products). Hereafter we shall consider a reversible complex reaction as two elementary reactions: direct v_i and reverse v_{-i}. In this case, the stoichiometric equation of a complex reaction is as follows:

$$\sum_{i=1}^{n} \alpha_{ri} x_i \xrightarrow{v_r} \sum_{j=1}^{n} \beta_{rj} x_j \qquad (r = 1, 2, ..., R), \quad (1)$$

where v_r is the rate of rth elementary stage and α_{ri} and β_{rj} are stoichiometric coefficients—non-negative integer values indicating how many molecules of reagent X_i and the product X_j, respectively, are consumed and formed as a result of one reaction stage v_n. According to the mass-action expression, for mechanism (1), the rate of rth reaction can be written as follows:

$$v_r = k_r x_1^{\alpha_{r1}} \cdot x_2^{\alpha_{r2}} \cdot ... \cdot x_i^{\alpha_{ri}}, \qquad (2)$$

where k_r, x_i, and α_{ri} are the reaction rate constant, concentration, and stoichiometric coefficient of the substance X_i, respectively.

By definition, the reaction rate for component X_i is an algebraic sum of the rates of consumption (l reactions) and formation (p reactions) of substance X_i in all elementary reactions v_r ($r = 1, 2, ..., S$, where $S = l + p$) with participation of X_i, multiplied by the corresponding stoichiometric coefficient:

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$$\frac{dx_i}{dt} \equiv x'_i = \sum_{r=1}^{S} (\beta_{ir} - \alpha_{ir}) \cdot \nu_r \quad (i = 1, 2, ..., m). \qquad (3)$$

Thus, when a number of physicochemical conditions (homogeneous medium, the absence of flows, etc.) are fulfilled, any complex chemical/biochemical reaction with participation of substance X_i ($i = 1, 2, ..., n$) uniquely corresponds with a system of ordinary differential equations of m order ($m < n$) provided that n variables are not all independent and there exist ($n - m$) balance ratios.

It is known that from a minor disturbance of system (3) around the steady state $\bar{x}_1, \bar{x}_2, ..., \bar{x}_n$, its behavior in time is defined by the values of $\lambda_1, \lambda_2, ..., \lambda_m$ roots of characteristic polynomial

$$p(\lambda) = \lambda^m + \lambda^{m-1}a_1 + ... + \lambda^{m-k}a_k + ... + a_m = 0 \qquad (4)$$

of matrix B (the Jacobian), whose elements by definition are given by equation:

$$b_{ij} = \frac{\partial x'_i}{\partial x_j}{}_i\bigg|_{\bar{x}_1....\bar{x}_n} \quad (i, j = 1, 2, ..., m). \qquad (5)$$

Substituting expression (3) for derivative x_i with the rate v_r written according to definition (2) into Eq. (5), we obtained the equation for calculation of the values of the Jacobian elements in an explicit form:

$$b_{ij} = \sum_{r=1}^{S} (\beta_{ir} - \alpha_{ir})\alpha_{jr} \frac{\nu_r}{x_j} = \sum_{r=1}^{S} \gamma_{ir}\alpha_{jr} \frac{\nu_r}{x_j}, \qquad (6)$$

where $\gamma_{ir} = \beta_{ir} - \alpha_{ir}$ ($i, j = 1, 2, ..., m$).

As known from linear algebra, coefficient a_1 of the characteristic polynomial (4) is equal to the sum of all diagonal elements of matrix B, but with the opposite sign:

$$a_1 = (-1)^1 \sum_{i=1}^{m} b_{ii}. \qquad (7)$$

Coefficients $a_2, a_3, ..., a_{m-1}$ with corresponding sign are equal to the sums of determinants of all diagonal minors of the second order ($M_i = M^{i_1, i_2}_{i_1, i_2}$), third order ($M_i = M^{i_1, i_2, i_3}_{i_1, i_2, i_3}$), ..., ($m - 1$) order of the Jacobian ($m \times m$):

$$a_k = (-1)^k \sum_{i=1}^{l} M_i \quad (k = 2, 3, ..., m-1), \qquad (8)$$

where l is the number of all diagonal minors of k order in the Jacobian and is equal to the number of combinations k of m. Coefficient a_m is equal to the determinant of matrix B with the corresponding sign:

$$a_m = (-1)^m \, det \, B. \qquad (9)$$

Equations (6)-(9) are the main relationships for search for the necessary and sufficient conditions for existence of critical phenomena in complex chemical or biochemical systems.

Criteria for existence of periodic solutions (oscillations) in mathematical models of biochemical systems. A number of criteria and indications of the absence or existence of periodic solutions of a system of differential equations were obtained in the context of qualitative theory of differential equations. Criteria are based on studies of either the properties of coefficients a_i ($i = 1, 2, ..., m$) of characteristic polynomial (the Rauss–Gurvits criterion, Clark method [1]), or the properties of matrix elements of the Jacobian [2, 3], or the properties and topology of phase space (the Poincare–Bendickson–Dulakue criteria [4] and others). As shown in [5, 6], the positive value of the senior coefficient a_m and the negative value of any of a_k ($k = 1, 2, ..., m - 1$) coefficients of characteristic polynomial of m order, that is, conditions $a_k < 0$ and $a_m > 0$ are the sufficient conditions for the existence of a periodic solution of a corresponding system of differential equations. And to the contrary, if all coefficients a_i ($i = 1, 2, ..., m$) are strictly positive at any values of the system parameters and variables, that is, are a sign-determining function, then the single steady-state point is stable, and this excludes periodic solutions.

As proved in [7], if a system of inequalities

$$L_i(s) = \sum_{k=1}^{m} \gamma_{ik} s_k \le 0 \quad (i = 1, 2, ..., n) \qquad (10)$$

has non-negative solutions $s \geqslant 0$ ($i = 1, 2, ..., n$), solutions of system (3) are limited at $t \to \infty$. A requirement for existence of a positive solution of system (10) has a simple physical meaning. In chemical kinetics, it means material balance in the reaction system (1).

In correct mathematical models of real chemical reactions, stable steady-state solutions should be limited, that is, a system of inequalities (10) should have a non-negative solution. A break of this condition means that a model is incorrect and further improvements are needed.

RESULTS AND DISCUSSION

Since there is a great interest in the simplest schemes of chemical/biochemical oscillators, in this work we consider a possibility for initiation of oscillations in a bicomponent system.

Strictly speaking, "oscillator" means a system of reactions giving rise to oscillation independently of the internal parameters (the rate constants). Such systems will be further named *non-parametric oscillators*.

There are systems of reactions initiating oscillations in a certain interval of internal parameters. Such systems will be further named *parametric oscillators*.

Only a few schemes of the simplest bicomponent oscillators are described in literature. Study of all possible bicomponent reaction schemes revealed several schemes of chemical oscillators not described earlier.

A search for simple schemes of chemical oscillators was performed so that they should suffice the following conditions:

– for each scheme inequality (10) is fulfilled;

– there are two reagents;

– in each elementary reaction act, stoichiometric coefficients of reagents cannot bee more than three, that is, the maximal number of molecules of reagents is three; in other words, the maximal reaction order of an elementary stage is trimolecular;

– each elementary stage obeys the mass-action expression (2).

This search was performed using the Generator program developed by us; generating all possible matrices of stoichiometric coefficients, this program chooses schemes corresponding to chemical oscillators.

It is convenient to classify the results by the number of elementary stages and thus consider them.

Two-stage reaction schemes. All possible 600 reaction schemes were considered in the framework of the abovementioned conditions. As a result, only one scheme appeared to be a parametric oscillator. This reaction scheme consists of the following stages:

$$X_1 + 2X_2 \rightarrow 3X_2$$

$$X_2 \rightarrow . \qquad (11)$$

This system corresponds with a system of differential equations:

$$\begin{aligned} x_1' &= \upsilon_{01} - k_1 x_1 x_2^2 \\ x_2' &= k_1 x_1 x_2^2 - k_2 x_2 \end{aligned} , \qquad (12)$$

where x_1 and x_2 are concentration variables and v_{01} is the inflow rate of component X_1. In this system, there is a single steady-state point with coordinates $x_1 = k_2^2/(k_1 v_{01})$, $x_2 = v_{01}/k_2$.

The following quadratic equation is a characteristic equation of system (12):

$$\lambda^2 + a_1\lambda + a_2 = 0 . \qquad (13)$$

In the steady state, coefficients a_1 and a_2 for this scheme are as follows:

$$a_1 = \frac{k_1\upsilon_0^2}{k_2^2} - k_2; \qquad a_2 = \frac{k_1\upsilon_0^2}{k_2}.$$

It follows hereafter that for chemical oscillations in system (11) it is sufficient that $a_1 \leqslant 0$. As follows from the expression for coefficient a_1 that this is true when parameters k_1 and k_2 are related as follows:

$$k_2^3 > k_1\upsilon_0^2 .$$

However, the only steady state will be unstable, the concentration values cannot go to infinity (inequality (10) is satisfied), and a stable limiting cycle will be established in the system, that is, auto-oscillations will arise. Numerical solution of system (12) at parameter values sufficing conditions for initiation of oscillations in this system is presented in Fig. 1. As is obvious from the aforesaid, chemical oscillator (11) is parametric, because existence of oscillation depends on the choice of internal parameters k_1 and k_2.

So, *there is only one parametric oscillator (11) in a two-stage bicomponent chemical system.*

Three-stage systems. In the framework of aforesaid general conditions, the number of various reaction schemes in a three-stage bicomponent system is equal to 20,529. Bifurcation analysis of stability of the steady state in all these schemes revealed several new theoretical schemes of the chemical oscillator. There are both para-

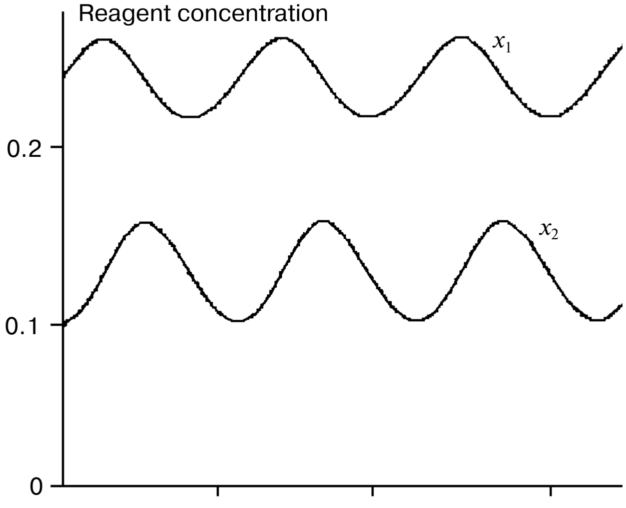

Fig. 1. Concentration oscillations of components of reaction system (11). Results are obtained at the following values of parameters: $k_1 = 100$, $k_2 = 1$, $v_{01} = 0.1$.

metric and non-parametric oscillators. Let us consider these schemes separately.

The first chemical oscillator of this type was suggested by Lotka [8]. This scheme is known as the simplest chemical non-parametric oscillator and is widely used in oscillatory kinetics in many chemical and biological processes. Search for other non-parametric oscillators revealed the following schemes of chemical oscillators unknown until now.

The schemes presented in Table 1 have not been reported earlier. These models have much in common: they are the simplest models describing behavior of nonlinear systems, and at the same time, they are important for certain chemical and biological problems. All these schemes are characterized by a special center-like point and have infinite numbers of possible periodic solutions; transfers between these solutions are performed by change in the initial conditions and parameters. As an example, let us consider behavior of one of the schemes (for instance, the second) far from the equilibrium point.

This system corresponds with a system of differential equations:

$$\begin{aligned} x_1' &= -k_1 x_1 + k_3 x_1 x_2^2 \\ x_2' &= -k_3 x_1 x_2^2 + k_2 x_2^2 \end{aligned}, \tag{14}$$

where x_1 and x_2 are concentration variables. In this system, there is a single steady-state point with coordinates $x_1 = k_2/k_3$ and $x_2 = (k_1/k_3)^{1/2}$.

In the steady state, coefficients a_1 and a_2 are as follows:

$$a_1 = 0; \quad a_2 = 2k_1k_2\sqrt{\frac{k_1}{k_3}}\,.$$

Consequently, the characteristic equation for this system looks rather simple:

$$\lambda^2 + 2k_1k_2\sqrt{\frac{k_1}{k_3}} = 0\,.$$

Decisions of the characteristic equation are completely imaginary; its roots define the frequency of arising harmonic oscillations. Numerical solution of differential equations of the considered reaction scheme is presented in Fig. 2.

All given schemes of non-parametric oscillator characterize conservative systems. However, real systems are nonconservative, and that is why the schemes of nonconservative chemical processes with periodic behavior are of particular interest. Search for such schemes gave tens of schemes with oscillatory behavior. In many of them, oscillations occur under "severe conditions", that is, in a rather narrow range of internal parameters. We considered the schemes with oscillatory behavior in a very broad range of varying internal parameters. The obtained schemes of parametric oscillators are presented below. (Earlier obtained and studied schemes, for example, the Prigozhin–Lefeuvre model (brusselator) and so on, are not presented in Table 2.)

Table 1. Non-parametric oscillators

	Reaction schemes	Coefficients of characteristic polynomial (13)	Oscillation frequency*
1.	$x_2 \rightarrow$ $x_1 + 2x_2 \rightarrow 2x_2$ $x_1 + x_2 \rightarrow 2x_1 + 2x_2$	$a_1 = 0$ $a_2 = \frac{k_1k_3^2}{k_2}$	$k_3\sqrt{\frac{k_1}{k_2}}$
2.	$x_1 \rightarrow$ $2x_1 \rightarrow 3x_2$ $2x_2 + x_1 \rightarrow 2x_1 + 2x_2$	$a_1 = 0$ $a_2 = 2k_1k_2\sqrt{\frac{k_1}{k_3}}$	$\sqrt{2k_1k_2\sqrt{\frac{k_1}{k_3}}}$
3.	$2x_2 \rightarrow x_2$ $x_1 + 2x_2 \rightarrow 3x_2$ $x_1 + x_2 \rightarrow 2x_1 + x_2$	$a_1 = 0$ $a_2 = \frac{2k_1k_3^3}{k_2^2}$	$\frac{1}{k_2}\sqrt{2k_1k_3^3}$
4.	$2x_2 + x_1 \rightarrow 2x_2$ $x_1 + x_2 \rightarrow 2x_1$ $2x_1 + x_2 \rightarrow 2x_1 + 2x_2$	$a_1 = 0$ $a_2 = \frac{k_2^4}{k_1k_3}$	$k_2^2\sqrt{\frac{1}{k_1k_3}}$

* Numeration of parameters corresponds with the stage sequence.

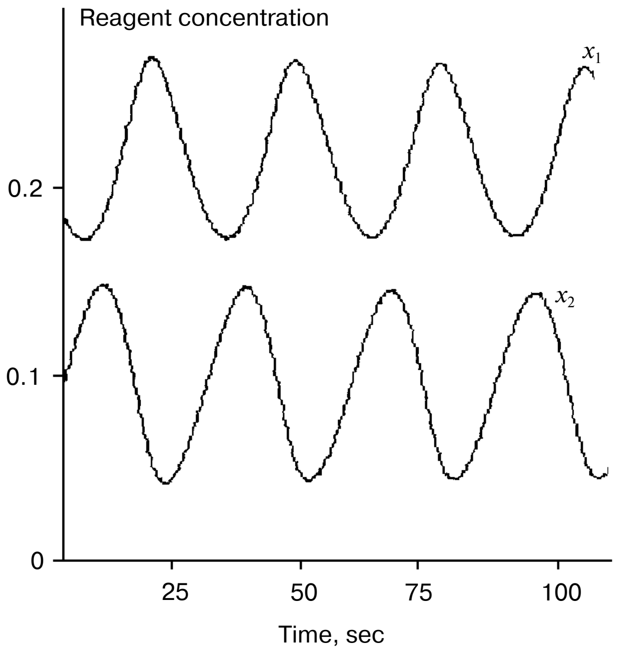

Fig. 2. Concentration oscillations of the components of reaction scheme (14). Results are obtained at the following values of parameters: $k_1 = 30$, $k_2 = 50$, $k_3 = 100$.

Let us study behavior of any model from Table 2 (for example, the first one) far from the equilibrium point. As can be seen, the maximal order of the stages is two. Behavior of the corresponding reaction is described by a system of differential equations:

$$x_1' = -k_2 x_1 x_2 + k_3 x_1^2$$
$$x_2' = -k_1 x_2 + k_3 x_1^2 \, . \tag{15}$$

Coordinates of the single steady-state point are:

$$x_1 = \frac{k_1}{k_2}; \quad x_2 = \frac{k_1 k_3}{k_2^2} \, .$$

In this case, coefficients of characteristic polynomial (13) are as follows:

$$a_1 = k_1 \left(1 - \frac{k_3}{k_2}\right); \quad a_2 = \frac{k_1^2 k_3}{k_2} \, .$$

As follows from the expression for coefficients of characteristic polynomial, $a_2 > 0$ at any parameter values. If together with this $k_2 = k_3$, then $a_1 = 0$. The steady-state point is center-like, that is, harmonic oscillations with a frequency $\omega = k_1$ will be observed. If $k_2 < k_3$, then $a_1 < 0$, the single steady state becomes unstable, and since concentration values cannot go to infinity, a stable limiting cycle will be established in the system, that is, auto-oscillation will arise. Numerical solution of dynamic equations of the considered kinetic scheme is presented in Fig. 3.

Four-stage reactions. Analysis of all possible four-stage reaction schemes in a bicomponent system (more than 120,000 schemes) showed that there are hundreds of schemes that can induce periodic behavior. However, in the overwhelming majority of these reactions oscillations begin at a very narrow range of internal parameters. For this reason, we do not consider these schemes. Bifurcation analysis resulted in choosing schemes that induce oscillations under “milder” conditions. Only those schemes where the oscillation conditions are not presented, because each scheme can be analyzed separately if needed, are given in Table 3. Analogously to the abovementioned schemes, both parametric and non-parametric oscillators can exist here. For example, Scheme 9 is a non-parametric oscillator:

$$x_1 \rightarrow$$
$$x_2 \rightarrow 2x_2$$
$$x_1 + x_2 \rightarrow x_1$$
$$x_1 + 2x_2 \rightarrow 2x_1 + 2x_2 \, .$$

In fact, for this scheme coefficients of the characteristic polynomial of the system of differential equations are the following:

$$a_1 = 0, \quad a_2 = 2k_1 k_2 \sqrt{\frac{1}{k_4}} \, .$$

Consequently, the roots of characteristic polynomial are completely imaginary and define the frequency of harmonic oscillations.

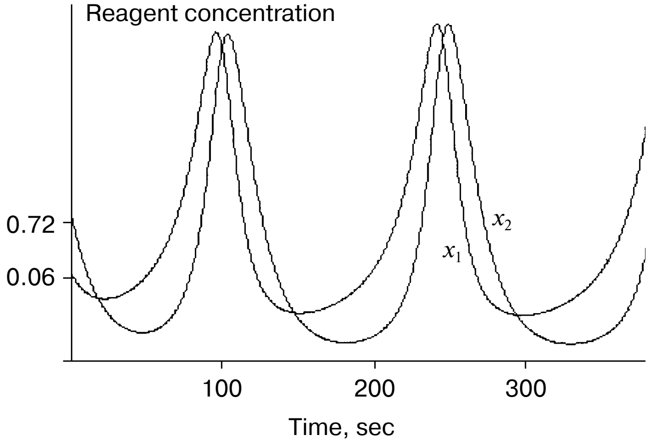

Fig. 3. Concentration oscillations of the components of reaction scheme (15). Results are obtained at the following values of parameters: $k_1 = 30$, $k_2 = 500$, $k_3 = 600$.

Table 2. Parametric oscillators

	Reaction schemes	Coefficient a_1 of characteristic polynomial (13)	Condition for initiation of oscillations*
	1	2	3
1.	$x_2 \rightarrow$ $x_1 + x_2 \rightarrow x_2$ $2x_1 \rightarrow 3x_1 + x_2$	$a_1 = k_1 - \frac{k_1 k_3}{k_2}$	$k_3 \geqslant k_2$
2.	$3x_2 \rightarrow 2x_2$ $2x_2 + x_1 \rightarrow 3x_2$ $2x_1 \rightarrow 3x_1$	$a_1 = \frac{k_1^2 k_3^2}{k_2^3}\left(\frac{k_1}{k_2} - 1\right)$	$k_1 \geqslant k_2$
3.	$2x_2 \rightarrow$ $2x_2 + x_1 \rightarrow 3x_2$ $2x_1 + x_2 \rightarrow 3x_1 + 2x_2$	$a_1 = \frac{k_1^2 k_3}{k_2^2}(2 - k_3)$	$k_3 \geqslant 2$
4.	$x_2 \rightarrow$ $x_1 + x_2 \rightarrow$ $2x_2 \rightarrow x_1 + 3x_2$	$a_1 = k_1 + \frac{\upsilon_0}{k_1}\left(\frac{1}{k_2} - k_3\right)$	$k_1^2 \leqslant \upsilon_{02}\left(k_3 - \frac{1}{k_2}\right)$
5.	$2x_2 \rightarrow x_2$ $x_1 + 2x_2 \rightarrow 2x_2$ $2x_1 + x_2 \rightarrow 3x_1 + 2x_2$	$a_1 = \frac{k_1^2 k_3}{k_2^2}(1 - \frac{k_3}{k_2})$	$k_3 \geqslant k_2$
6.	$x_2 \rightarrow$ $x_1 + x_2 \rightarrow$ $2x_1 + x_2 \rightarrow 3x_2 + 2x_1$	$a_1 = \frac{-k_2 k_3 + k_1^2 + k_2^2}{k_1}$	$k_2 k_3 \leqslant k_1^2 + k_2^2$
7.	$x_2 \rightarrow$ $x_1 + 2x_2 \rightarrow x_2$ $2x_1 + x_2 \rightarrow 3x_1 + 3x_2$	$a_1 = k_1 - \frac{k_3^3}{k_1 k_2}$	$k_1^2 \leqslant \frac{k_3^3}{k_2}$ $k_1, k_2, k_3 > 1$
8.	$x_1 + x_2 \rightarrow$ $x_1 + x_2 \rightarrow x_2$ $2x_1 + x_2 \rightarrow 3x_1 + 2x_2$	$a_1 = \frac{1}{k_3} - \frac{1}{k_2}$	$k_2 \leqslant k_3$
9.	$x_1 + x_2 \rightarrow$ $2x_2 + x_1 \rightarrow 2x_2$ $2x_1 \rightarrow 3x_1 + x_2$	$a_1 = k_2 + \upsilon_0 k_1 - \frac{\upsilon_0 k_3}{k_2}$	$\upsilon_0 k_3 \geqslant k_2 (k_2 + \upsilon_0 k_1)$
10.	$x_1 + x_2 \rightarrow$ $x_1 + 2x_2 \rightarrow 2x_2$ $2x_1 + x_2 \rightarrow 3x_1 + 2x_2$	$a_1 = \sqrt{\frac{\upsilon_0 k_1 k_3}{k_2}} - \frac{\upsilon_0 k_3}{k_1}$	$k_1^3 \leqslant \upsilon_0 k_2 k_3$
11.	$2x_2 \rightarrow 3x_2$ $2x_1 + x_2 \rightarrow x_1$ $3x_2 \rightarrow 3x_2 + x_1$	$a_1 = \frac{k_1^2}{k_3}\left(2\sqrt{\frac{k_2}{k_3}} - 1\right)$	$4k_2 \geqslant k_3$

Table 2. (Contd.)

1		2	3
12.	$x_1 + x_2 \to$ $2x_2 \to 3x_2$ $3x_2 \to 3x_2 + x_1$	$a_1 = (k_1 - k_2)\frac{k_2}{k_3}$	$k_1 \leqslant k_2$
13.	$x_1 + x_2 \to x_2$ $2x_2 \to 3x_2 + x_1$ $2x_1 + x_2 \to 2x_1$	$a_1 = (k_1 - k_2)\frac{k_1^1}{k_2 k_3}$	$k_2 \geqslant k_1$

* Numeration of parameters corresponds with the stage sequence.

Analysis of possible initiation of periodic behavior in bicomponent systems shows that there are tens of multistage chemical reactions—candidates for a "chemical watch". Mechanisms of these reactions have much in common. First of all, these mechanisms contain autocatalytic stages. The impossibility of other oscillatory mechanisms in bicomponent system is obvious, because for existence of oscillations in a bicomponent system it is necessary that the first coefficient a_1 of the characteristic polynomial (13) would contain a negative term. However, coefficient a_1 can have a negative term when (and only when) at least one of the stages is autocatalytic. In all other cases, coefficient a_1 is positive. In fact, as seen from expression (7), coefficient a_1 of characteristic polynomial (4) is equal to the sum of all diagonal elements of the Jacobian taken with the opposite sign. Diagonal elements

Table 3. Kinetic schemes of four-stage oscillators

1. $x_1 + x_2 \to 2x_1$ $x_2 \to 3x_2$ $x_2 \to$ $x_1 \to$	2. $x_1 + x_2 \to 2x_2$ $2x_2 \to 3x_2$ $x_2 \to$ $x_1 \to$	3. $x_1 + x_2 \to$ $2x_2 \to 3x_2$ $2x_2 + x_1 \to 2x_2 + 2x_1$ $x_2 \to$	4. $x_1 + x_2 \to x_2$ $2x_2 + x_1 \to 3x_2$ $x_1 \to 2x_1$ $x_2 \to$
5. $x_2 \to$ $2x_2 \to x_2$ $2x_2 + x_1 \to 3x_2$ $x_1 + x_2 \to 2x_1 + 2x_2$	6. $x_2 \to$ $x_1 + x_2 \to$ $x_1 + 2x_2 \to 3x_2 + x_1$ $x_1 \to 2x_1 + x_2$	7. $x_2 \to$ $x_1 + x_2 \to$ $x_1 + 2x_2 \to x_1 + 3x_2$ $2x_1 + x_2 \to 2x_1 + 2x_2$	8. $x_1 \to$ $x_1 + x_2 \to$ $2x_2 \to 3x_2 + x_1$ $2x_2 + x_1 \to$
9. $x_1 \to$ $x_2 \to 2x_2$ $x_1 + x_2 \to x_1$ $x_1 + 2x_2 \to 2x_1 + 2x_2$	10. $2x_2 \to x_2$ $x_1 + x_2 \to x_2$ $x_1 + 2x_2 \to 3x_2 + 1$ $x_1 \to 2x_1$	11. $x_2 \to$ $x_1 + x_2 \to$ $x_1 \to 2x_1$ $2x_1 + x_2 \to 2x_1 + 3x_2$	12. $x_2 \to$ $x_1 \to$ $2x_1 + x_2 \to 2x_1$ $x_1 + 2x_2 \to 3x_2 + 2x_1$
13. $x_2 \to$ $x_1 + x_2 \to x_2$ $2x_1 + x_2 \to 2x_1$ $x_1 + 2x_2 \to 2x_1 + 3x_2$	14. $x_2 \to$ $x_1 + 2x_2 \to 2x_2$ $x_1 \to 2x_1$ $2x_1 + x_2 \to 2x_1 + 2x_2$	15. $x_2 \to$ $x_1 + 2x_2 \to 2x_2$ $x_1 + x_2 \to 2x_1$ $2x_1 + x_2 \to 2x_1 + 3x_2$	16. $x_2 \to$ $x_1 + 2x_2 \to 2x_2$ $x_1 + x_2 \to 2x_1 + x_2$ $2x_1 + x_2 \to 2x_1 + 2x_2$
17. $x_2 \to$ $x_1 + x_2 \to x_1$ $x_1 + 2x_2 \to 3x_2$ $x_1 \to 2x_1 + x_2$	18. $x_2 \to$ $x_1 + x_2 \to x_1$ $x_1 + 2x_2 \to 3x_2$ $2x_1 + x_2 \to 2x_1 + 2x_2$	19. $x_1 \to$ $2x_2 \to 2x_2 + x_1$ $x_1 + 2x_2 \to x_1 + 3x_2$ $2x_1 + x_2 \to 2x_1$	20. $x_1 \to$ $x_1 + x_2 \to x_1$ $2x_1 + x_2 \to 2x_1$ $x_1 + 2x_2 \to 2x_1 + 3x_2$
21. $x_1 \to x_2$ $x_1 + x_2 \to x_1$ $2x_1 + x_2 \to 2x_1$ $x_1 + 2x_2 \to 2x_1 + 3x_2$	22. $x_1 \to$ $x_1 + x_2 \to 2x_1$ $2x_2 \to 3x_2$ $2x_1 + x_2 \to 2x_1$	23. $x_2 \to$ $x_1 + x_2 \to 2x_1$ $x_1 + 2x_2 \to 3x_2$ $2x_1 \to 2x_1 + x_2$	24. $x_1 + x_2 \to$ $2x_1 + x_2 \to 2x_1$ $x_2 \to 3x_2$ $x_1 + 2x_2 \to 2x_1 + 2x_2$
25. $x_1 + x_2 \to$ $2x_1 + x_2 \to 2x_1$ $2x_2 \to 3x_2$ $x_1 + 2x_2 \to 2x_1 + 2x_2$	26. $2x_2 \to x_2$ $x_1 + x_2 \to 2x_1$ $x_1 + 2x_2 \to 3x_2$ $2x_1 + x_2 \to 2x_1 + 2x_2$		

of the Jacobian corresponding to autocatalytic stages have a positive sign and those corresponding to non-catalytic stages—negative. Consequently, a negative term of coefficient a_1 arises when (and only when) at least one of the stages is autocatalytic.

The second common feature of these reactions is so-called "zero" loop. A loop is a kinetic reaction scheme in which one and the same substance participates as a reagent and as a product:

$$\alpha_{ir} x_i + \alpha_{jr} x_j \rightarrow \beta_{ir} x_i ,$$

where $\alpha_{ir} \neq 0$, $\beta_{ir} \neq 0$. However, if $\beta_{ir} > \alpha_{ir}$, then $\gamma_{ir} > 0$, and a loop is characterized as positive. A positive loop arises at autocatalytic stages. If $\gamma_{ir} = 0$, reagent is not consumed at this stage, although it participates in it. As obvious, all enzymatic reaction schemes contain a zero loop. If $\gamma_{ir} < 0$, a loop is characterized as negative; in this case the *i*th reagent is consumed.

So, all the obtained reaction schemes contain a loop as a kinetic element; schemes which do not contain a loop will not have periodic behavior at any parameter values.

The obtained schemes are hypothetical reaction models with several intermediate stages. Existence of real chemical systems corresponding to these schemes is proved by Korzukhin's theorem [9], according to which it is always possible to develop a chemical system of kinetic equations with behavior as closely as is wished coinciding with behavior of the given system of kinetic equations:

$$d\psi_i / dt = \psi_i (x_1 x_2 \ldots x_n),$$

where $\psi_i(x_1 x_2 \ldots x_n)$ are polynomials with integer non-negative powers.

The developed schemes allow expansion of the theoretical base on modeling of oscillatory phenomena in chemistry, biology, sociology, ecology, etc. It is well known that autocatalytic stages describe auto-reproduction of biological system in population kinetics. From this viewpoint, these schemes give a good possibility for theoretical justification of oscillatory auto-reproduction of living systems.

REFERENCES

1. Clark, B. L. (1974) *J. Chem. Phys.*, **60**, 1481-1492.
2. Quik, J., and Ruppert, R. (1965) *Rev. Econ. Studies*, **32**, 311-319.
3. Tyson, J. J. (1975) *J. Chem. Phys.*, **62**, 1010-1015.
4. Andronov, A. A., Witt, A. A., and Khaikin, S. E. (1959) *Theory of Oscillations* [in Russian], USSR Academy of Sciences, Moscow.
5. Ivanova, A. N. (1979) *Kinet. Katal.*, **20**, 1019-1023.
6. Ivanova, A. N. (1979) *Kinet. Katal.*, **20**, 1024-1028.
7. Wol'pert, A. I. (1972) *Mat. Sbornik*, **88**, 578-588.
8. Lotka, A. J. (1920) *J. Amer. Chem. Soc.*, **42**, 1595-1599.
9. Korzukhin, M. D., and Zhabotinskii, A. M. (1965) in *Molecular Biophysics* (Frank, G. M., ed.) [in Russian], Nauka, Moscow, p. 52.