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# Selection in Regulated Autocatalytic Systems

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**Abstract.** The paper deals with problems involved in the formation of stable structures in a system, in which processes typical of bimolecular autocatalytical reactions occur when the respective components are directly influenced from the outside. Such systems can arise in biochemical, biological and ecological sphere (see, e.g. Glansdorff and Prigogine 1971; Nicolis and Prigogine 1977; Haken 1977; 1980). It has been shown that a regions of so-called subcritical and supercritical regulation exist, manifested by the fact that the given system component would either persist or disappear. The selection of processes consists in the fact that generally only one solution can be realized from $N$ alternatives as a stable state having the nature of a stable node, or a stable focus. When one of the components is supplied to the system from the exterior in a supercritical amount, the system can be "forced" to produce only that single substance. Thus, the system studied can be considered as a model of a biological filter. The results can also be applied in ecology and biotechnology.

**Key words:** Direct regulation — Selective processes — Autocatalytic systems

## Introduction

It is well known that various spatial, temporal and spatio-temporal structures can develop in autocatalytic systems. This is based on the fact that the dynamics of such systems is described by means of nonlinear evolution equations. In case of competitive autocatalytic reactions where several substances (with concentrations $C_i$) are synthetized from one basic substance (raw material or food with a concentration $C_A$) with a reaction rate $k_i$, and disintegrate with a rate constant $k_i'$, the evolution equations get the form (Ebeling 1976)

$$\frac{\mathrm{d}C_A}{\mathrm{d}t} = J_A - C_A \sum_i k_i C_i \tag{1a}$$

$$\frac{dC_i}{dt} = J_i + C_i(k_i C_A - k_i') \qquad i = 1, 2, 3, \ldots \tag{1b}$$

Here, $J_A$ and $J_i$ stand for the input substance flow and for flows of the respective components.

If several kinds of animals or other living systems need the same type of food for their existence (e.g. several kinds of predators need the same type of preys) then the evolution of the system as a whole is described (in the "first approximation") by the equations

$$\frac{dN}{dt} = J_N - N \sum_i k_i M_i \tag{2a}$$

$$\frac{dM_i}{dt} = J_{M_i} + M_i(k_i N - k_i') \qquad i = 1, 2, 3, \ldots \tag{2b}$$

where $N$ and $M$ are characteristic numbers of predators and preys, $J_N$ and $J_{Mi}$ are changes in these numbers per unit time due to external influence (e.g. shooting). An analogical situation can also occur for systems on the cellular level. We can thus say that a large variety of living and non-living systems can be described by the systems of equations (1).

In any system of this type selection can become operative, i.e. the priority formation of only one possible structure, namely of that one with the most favourable parameters with regard to synthesis and decomposition.

If $J_i = 0$, $J_A = \text{constant}$, or $J_i = 0$ and $\Sigma C_i = \text{constant}$, the system of equations (1) has only one stable solution corresponding to nonzero concentration of the input substance and to one of $n$ components, for which the ratio $k_i / k_i'$ is the highest. This process has been solved in papers (Ebeling 1976; Ebeling et al. 1977) mathematically for bimolecular autocatalytic reactions under variable limiting conditions.

The situation radically changes if $J_i \neq 0$ is supposed, i.e. if there is a direct external interference into the concentrations of substances synthetized. Such a direct supply of a synthetized substance was postulated e.g., in the theoretical explanation of the presence of a limit cycle-state in glycolysis (Volkenshtein 1978). Such a system would be considered as a directly regulated system.

A relatively great number of papers in the last years have dealt with the problem of the regulation of biochemical, biological and ecological systems (see, e.g. Boltynsky 1966; Kaiser 1980; Hess et al. 1978; Tyson and Kaufmann 1975; Goodwin 1965; Tomita and Kai 1977; Svirezhev and Elizarov 1971). The present paper is aimed at the mathematical analysis of the dynamics of regulated systems described by equations (1). Similar special biochemical systems may obviously not only concern biochemical processes in biological systems, but actual ecological and biotechnological problems as well. Results obtained in the present paper allow to find a regulation pattern which would generate a desired structure in an actual system type.

**Stationary States in Directly Regulated Systems**

In nonregulated systems ($J_i = 0$) the stationary states are characterized by concentrations of the input substance and one of the components, which can be formed in the system, different from zero, while concentrations of other components are zero. It follows from the stability theory of respective solutions that the only stable solution is that which corresponds to the non-zero component with the highest value of the ratio $k_i/k_i'$. Let this component have a concentration $C_1$. Other components may be arranged according to the decreasing magnitude of the ratio $k_i/k_i'$, so that a series is obtained

$$\frac{k_1}{k_1'} > \frac{k_2}{k_2'} > \frac{k_3}{k_3'} > \ldots > \frac{k_n}{k_n'} \tag{3}$$

We shall study the effect of external regulation on a system, present without external regulation in the stationary state, i.e. in a state in which, according to (3), only substance $X_1$ has been left over. It is, therefore, sufficient to examine the effect of non-negative regulations only ($J_i \geqslant 0$, $i = 2, 3, \ldots$). It is not purposeful to consider direct non-negative regulation of the first component, since this would not result in the development of a new quality; it is, however, purposeful to consider negative regulation of this component (i.e. direct extraction of the component from the system), since this would allow another substance to dominate in the competition.

Stationary solutions of the system of equations (2) with direct regulation are the solutions of the equations

$$J_A - C_{As} \sum_{i=1}^{n} k_i C_{is} = 0,$$

$$J_i + C_{is}(k_i C_{As} - k_i') = 0, \qquad i = 1, 2, 3, \ldots, n \tag{4}$$

where the subscript $s$ denotes stationary concentration values of the substances. In solving the system (4), the equation describing the concentration $C_{js}$ is chosen as the leading equation, and solutions for other equations of this non-linear system would be derived from the solution of this equation.

The equation for the concentration $C_{js}$ can be solved in three various ways in dependence on the regulation $J_j$

1. $J_j = 0, \qquad C_{js} = 0$

2. $J_j = 0, \qquad C_{As} = \dfrac{k_j'}{k_j}, \quad C_{js} = \dfrac{J_A}{k_j'} - \sum_{i \neq j} \dfrac{k_i J_i}{k_i' k_j - k_i k_j'}$ (5)

3. $J_j \neq 0, \qquad C_{js} = \dfrac{J_j}{k'_j - k_j C_{As}}$

The first solution is trivial, decreassing the degree of the non-linear equation sytem (4). The second solution is non-trivial and the solution derived for $i \neq j$ has the following form

$$C_{is} = \frac{k_j J_i}{k'_i k_j - k_i k'_j} \tag{6}$$

The third solution assumes regulation and converts the system of equations (4) to a non-linear equation for the concentration

$$C_{As} = \frac{J_A}{\sum_i \dfrac{k_i J_i}{k'_i - k_i C_{As}}} \tag{7}$$

Let us assume that from $n$ substances no other than $m$ is regulated. Then equation (7) will be of the $m + 1$-th degree and shall generally have $m + 1$ complex roots. From the concentration of the input substance $C_{As}$, the other concentrations can be computed using relationship

$$C_{is} = \frac{J_i}{k'_i - k_i C_{As}} \tag{8}$$

It can be seen that this third solution encompasses all the equations having non-zero regulation. Relationship (8) puts several assumptions allowing the solution of non-linear equation (7) for positive regulations

$$C_{As} < \frac{k'_i}{k_i} \tag{9}$$

Equation (7) can be rewritten into the form

$$J_A + \sum_i J_i = \sum_i \frac{J_i}{1 - (k_i/k'_i) C_{As}} \tag{10}$$

Assuming (9), solving equation (10) we can use the known development ($q < 1$)

$$\frac{1}{1-q} = \sum_{n=0}^{\infty} q^n$$

$$J_A = C_{As} \sum_i J_i (k_i/k'_i) + C_{As}^2 \sum_i J_i (k_i/k'_i)^2 + \ldots \tag{11}$$

According to the Descartes theorem, this equation has just one real positive root, its value being determined in the linear approach by the relationship

$$C_{As} = \frac{J_A}{\sum_i J_i(k_i/k'_i)}$$

Thus, the number of solutions to the system of equations (4) gets reduced from $n$ to $n-m+1$, while the system of equations (4) would have $n-m$ solutions of the second type and one solution of the third type. An analysis of the stability of the respective solutions will show which one of the solutions will be realized.

**Stability of Solutions**

The stability of the solutions of the equation system (2) was analysed using the method of small perturbations ($c_i$) from stationary values

$$C_A = C_{As} + c_A$$
$$C_i = C_{is} + c_i, \qquad i = 1, 2, 3, \ldots, n \tag{12}$$

Substituting the above expressions into equations (2) and neglecting the quadratic members we obtain the following equations:

$$\frac{dc_A}{dt} = -c_A \sum_i k_i C_{is} - C_{As} \sum_i k_i c_i \tag{13}$$

$$\frac{dc_i}{dt} = k_i C_{is} c_A + (k_i C_{As} - k'_i) c_i, \qquad i = 1, 2, \ldots, n$$

Their solution can be found in the form

$$c_i = \text{const. } e^{p_i t}, \qquad i = A, 1, 2, 3, \ldots, n$$

Thus, we obtain a system of linear homogenous equations with a characteristic matrix

$$\begin{Vmatrix} -\sum_i k_i C_{is} - p, & -k_1 C_{As} & , \ldots, & -k_n C_{As} \\ k_1 C_{1s}, & k_1 C_{As} - k'_1 - p & , \ldots, & 0 \\ k_2 C_{2s}, & 0 & , \ldots, & 0 \\ \vdots & \vdots & \vdots & \vdots \\ k_n C_{ns}, & 0 & , \ldots, & k_n C_{As} - k'_n - p \end{Vmatrix} \tag{14}$$

Developing this characteristics matrix according to the first line (see Appendix I.), and by its annulment we obtain the characteristic equation in the form

$$\prod_{i=1}^{n} (k'_i - k_i C_{As} + p) \cdot \left( p + \sum_{i=1}^{n} k_i C_{is} \frac{k'_i + p}{k'_i - k_i C_{As} + p} \right) = 0 \tag{15}$$

Analysing this later equation it can be generally demonstrated that system studied has, when the condition $k'_i - k_i C_{As} > 0$ (16) is met, always a single stable solution, either of the stable node, or stable focus type (see Appendix II.).

It follows from equation (15) that the system stability requires that $k'_i - k_i C_{As} > 0$ (i.e. all the coefficients of the characteristic polynom, obtained after the multiplication of equation (15), have to be positive).

For system with positive regulation this condition is identical with condition (9), required for the solution of the third type. As will be seen, this condition is necessary but not sufficient. For this purpose, the effect of stationary solutions (5) on the solution to the characteristic equation (15) should be investigated. After introducing the stationary solution into the first type of equation (15), we obtain one root of the stationary equation

$$p_j = -k'_j \left( 1 - \frac{k_j}{k'_j} C_{As} \right) \tag{17}$$

With regard to solution stability, it is necessary that $Re(p_j) > 0$. This, however, is equivalent to condition (16).

From the stationary solution type 2 for $m$ regulations we obtain $n - m - 1$ roots of the characteristic equation

$$p_i = -k'_i \left( 1 - \frac{k_i}{k'_i} \frac{k'_j}{k_j} \right) \tag{18}$$

$i \neq j$ and $J_i = 0$. According to this relationship the stationary solution type 2 can only be stable when the subscript $j$ has the lowest value of all the values $i$ meeting the condition $J_i = 0$. We shall denote it $j^*$. This is a result of indication (3), and the number type 2 solutions is reduced from $n - m$ to one. Condition (16) would be thus fulfiled for positive regulation except for the component $j^*$, for which it holds

$$C_{As} = \frac{k'_{j^*}}{k_{j^*}}$$

and

$$C_{j^*s} = \frac{J_A}{k'_{j^*}} - \sum_{i \neq j^*} \frac{k_i J_i}{k'_i k_{j^*} - k_i k'_{j^*}} \tag{19}$$

For physical reasons, the inequality $C_{js} \geqslant 0$ must hold, in addition to condition (16).

Considering this inequality, we obtain from relationship (19) the condition for the stability of the type 2 solution in the form

$$\sum_{i \neq j^*} \frac{J_i}{\frac{k_i' k_{j^*}}{k_i k_{j^*}'} - 1} \leq J_A \tag{20}$$

It can be seen that the stability of the type 2 solution depends on the extent of external regulations.

Let us investigate the type 3 solution. Introducing condition (16) for $j = j^*$ into equation (10), we obtain the condition for the validity of the type 3 solution in the form

$$\sum_{i \neq j} \frac{J_i}{\frac{k_i' k_j}{k_i k_j'} - 1} > J_A \tag{21}$$

From inequalities (20) and (21) it follows that solution types 2 and 3 replace each other as soon as, at solution type 2, $X_{j^*}$ would attain physically improbable negative concentration values $C_{j^*s}$. Solution types 2 and 3 represent a complementary system.

With respect to the existence of substance $X_{j^*}$ we can introduce the terms of subcritical regulation (condition 20) and supercritical regulation (condition 21), resulting in the destruction of substance $X_{j^*}$ in the system. Substance $X_{j^*}$ is removed in the competition with other substances, which become their parameters "improved" through external regulation.

### The Case of One Positive Regulation

Let us assume substance $X_j$ becomes regulated with $j \neq 1$. The stationary solution type 2 has, according to relationship (6), the following form

$$C_{As} = \frac{k_1'}{k_1}$$

$$C_{1s} = \frac{J_A}{k_1'} - \frac{k_j J_j}{k_j' k_1 - k_j k_1'} \qquad C_{js} = \frac{k_1 J_j}{k_j' k_1 - k_j k_1'}$$

$$C_{is} = 0 \qquad \text{for } i \neq 1 \quad \text{and} \quad i \neq j.$$

The validity of the solution type 2 is limited by the critical regulation determined by condition (20)

$$J_j \leq J_A \left( \frac{k_j' k_1}{k_j k_1'} - 1 \right)$$

After surpassing critical regulation, solution type 3 is obtained as determined by relationships (7) and (8)

$$C_{As} = \frac{k_j'}{k_j}\frac{J_A}{J_j + J_A}, \qquad C_{js} = \frac{J_j + J_A}{k_j'}$$

$$C_{is} = 0 \quad \text{for} \quad i \neq j$$

According to the results shown in previous sections, all the results presented are stable. Figs. 1—5 illustrate the situation for a system consisting of four components at various degrees of regulation. Curve 5 represents the concentration of the input substance, curve 3 that of the regulated substance and curve 1 that of the nonregulated substance with optimum parameters in the system. For all the cases shown $J_A = J_5 = 1$, $J_3 = 0$ (Fig. 1), $J_3 = 0.1$ (Fig. 2), $J_3 = 0.2$ (Fig. 3), $J_3 = 0.4$ (Fig. 4) and $J_3 = 0.8$ (Fig. 5).

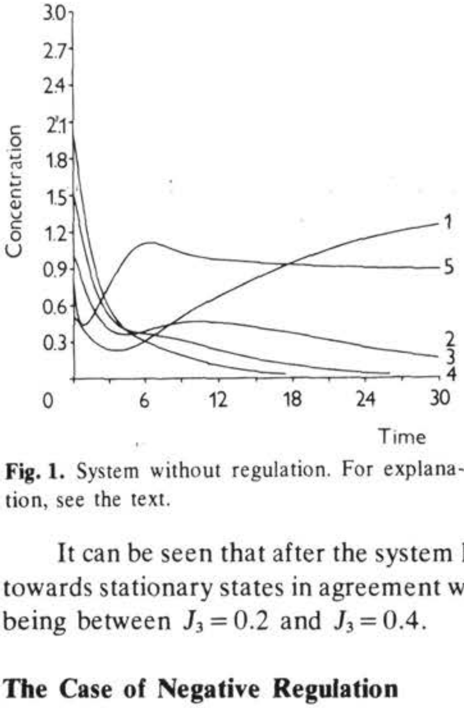


**Fig. 1.** System without regulation. For explanation, see the text.

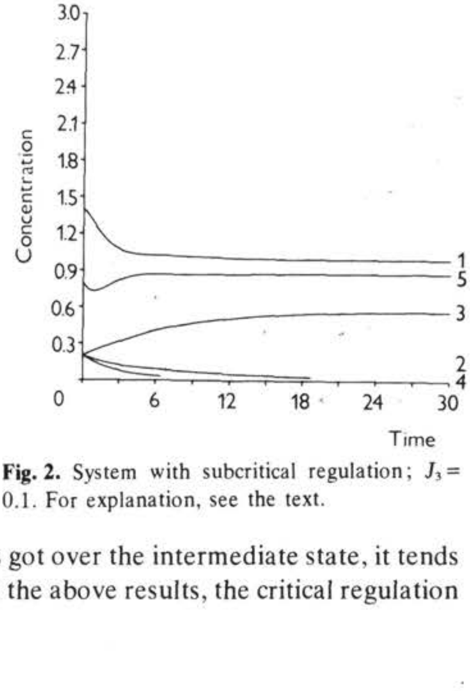


**Fig. 2.** System with subcritical regulation; $J_3 = 0.1$. For explanation, see the text.

It can be seen that after the system has got over the intermediate state, it tends towards stationary states in agreement with the above results, the critical regulation being between $J_3 = 0.2$ and $J_3 = 0.4$.

## The Case of Negative Regulation

Let us now suppose negative regulation of substance $X_1$, i.e. a substance present alone in a system without external regulation. Contrary to the case of positive regulation, we obtain for subcritical regulation determined by the condition

$$J_1 > J_A\left(\frac{k_1' k_2}{k_1 k_2'} - 1\right)$$

the solution type 3

$$C_{As} = \frac{k_1'}{k_1}\frac{J_A}{J_1 + J_A}, \qquad C_{1s} = \frac{J_1 + J_A}{k_1'}$$

$$C_{is} = 0 \quad \text{for} \quad i \neq 1$$

For supercritical regulation, solution types 3 and 2 are unstable according to the condition $C_{1s} \geq 0$. The above two situations are illustrated in Figs. 6 and 7. In the first case $J_1 = -0.05$, in the other one $J_1 = -0.15$.

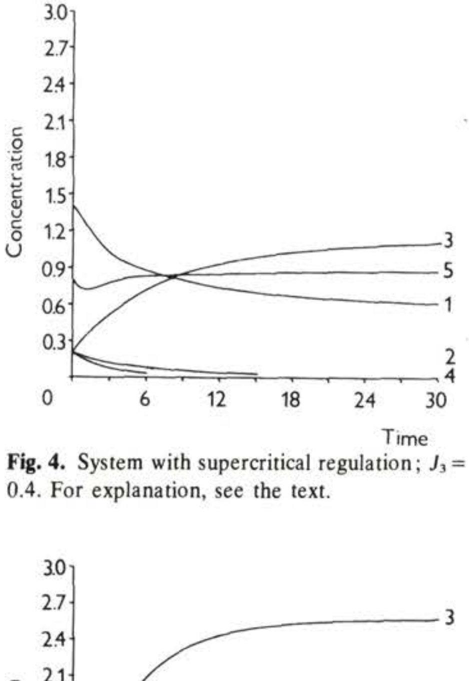


**Fig. 4.** System with supercritical regulation; $J_3 = 0.4$. For explanation, see the text.

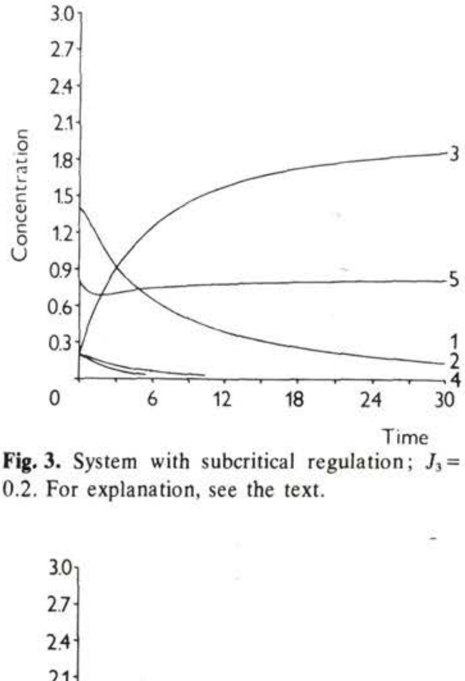


**Fig. 3.** System with subcritical regulation; $J_3 = 0.2$. For explanation, see the text.

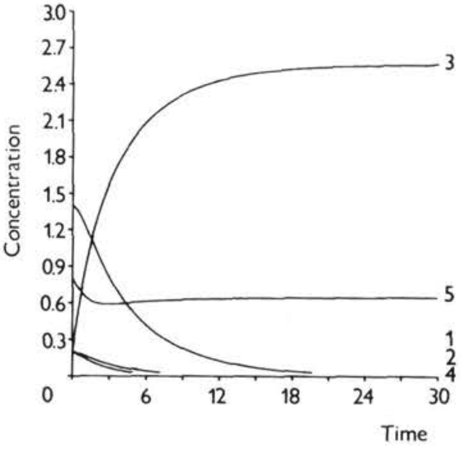


**Fig. 5.** System with supercritical regulation; $J_3 = 0.8$. For explanation, see the text.

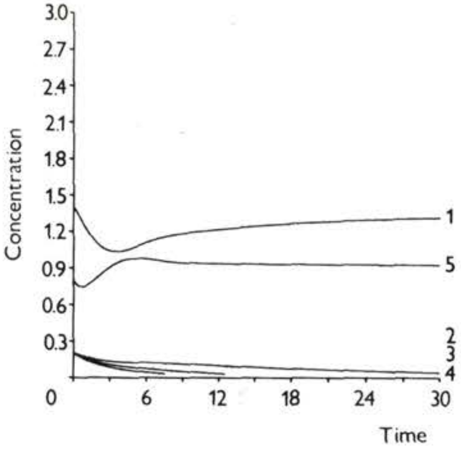


**Fig. 6.** System with subcritical regulation; $J_1 = -0.05$. For explanation, see the text.

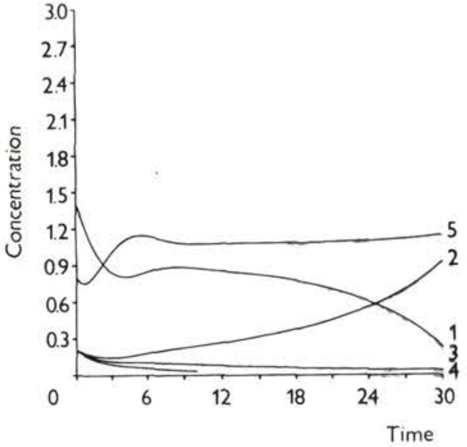


**Fig. 7.** System with supercritical regulation; $J_1 = -0.15$. For explanation, see the text.

## Conclusions

It was demonstrated that in a system, in which new substances are synthetized by autocatalytic competition, substantial changes in chemical structure occur, due to direct regulation. Intensification of direct regulation brings the system to a bifurcation point in which the stable solution undergoes qualitative changes. Over the range of supercritical regulations, the unregulated substance even disappears. This means that an adequately intensive "Feedback" realized by direct supply into the system of the substance required can bring the whole system to produce only that single substance. On the contract, by intensive extraction of a substance, which alone of all the substances was able to „survive" in the unregulated system, its total extinction can be achieved.

We believe that the results obtained are interesting and useful both, for a better understanding of peculiar autocatalytic processes and with regard to their potential applications in the field of biotechnology.

## Appendix I.

Let us rewrite the characteristic matrix in a conciser form

$$\left\| \begin{array}{cccccc} u_0 & a_1 & a_2 & a_3 & \dots & a_n \\ b_1 & u_1 & 0 & 0 & \dots & 0 \\ b_2 & 0 & u_2 & 0 & \dots & 0 \\ b_3 & 0 & 0 & u_3 & \dots & 0 \\ \hline b_n & 0 & 0 & 0 & \dots & u_n \end{array} \right\| = M$$

After developing this characteristic matrix according to the first line, we obtain it in the form

$$M = u_0 u_1 u_2 \dots u_n - a_1 \cdot \begin{vmatrix} b_1 & 0 & 0 & \dots & 0 \\ b_2 & u_2 & 0 & \dots & 0 \\ b_3 & 0 & u_3 & \dots & 0 \\ \\ b_n & 0 & 0 & & u_n \end{vmatrix} +$$

$$+ a_2 \cdot \begin{vmatrix} b_1 & u_1 & 0 & \dots & 0 \\ b_2 & 0 & 0 & \dots & 0 \\ b_3 & 0 & u_3 & \dots & 0 \\ \\ b_n & 0 & 0 & \dots & u_n \end{vmatrix} - a_3 \cdot \begin{vmatrix} b_1 & u_1 & 0 & \dots & 0 \\ b_2 & 0 & u_2 & \dots & 0 \\ b_3 & 0 & 0 & \dots & 0 \\ \\ b_n & 0 & 0 & \dots & u_n \end{vmatrix} + \dots$$

The single determinants in this order have values $b_1 u_2 u_3 \dots u_n$, $-b_2 u_1 u_3 u_4 \dots u_n$, $b_3 u_1 u_2 u_4 \dots u_n$, etc.; we can write thus the value of the determinant $M$ in the form

$$M = \sum_{i=1}^{n} u_i \cdot \left( u_0 - \sum_{i=1}^{n} \frac{a_i b_i}{u_i} \right)$$

With regard to the meaning of the respective symbols, we can write equation for the determinant (14) in form

$$M = \prod_{i=1}^{n} (k_i' - k_i C_{As} + p) \left( \sum_{i=1}^{n} k_i C_{is} + p + \sum_{i=1}^{n} \frac{k_i^2 C_{is} C_{As}}{k_i' - k_i C_{As} + p} \right)$$

After arrangement and annulment we obtain eq. (15).

## Appendix II.

A detailed analysis of the characteristic eq. (15) shows that for any indexes $j$ for which holds

$$k_j' - k_j C_{As} + p \neq 0$$

we can write a separate equation

$$\sum_j k_j C_{js} + p = - \sum_j \frac{k_j^2 C_{js} C_{As}}{k_j' - k_j C_{As} + p} \tag{II.1}$$

Let us assume the solution in a form of a complex number $p = a + i \cdot b$, and let us develop separate eqs. (II.1) for real and imagined parts. We obtain two equations

$$a + \sum_j k_j C_{js} = - \sum_j C_{As} k_j^2 C_{js} \frac{a + k_j' - k_j C_{As}}{(a + k_j' - k_j C_{As})^2 + b^2} \tag{II.2}$$

$$b = \sum_j C_{As} k_j^2 C_{js} \frac{b}{(a + k_j' - k_j C_{As})^2 + b^2} \tag{II.3}$$

Using conditon (16) and after multiplication, we obtain from eq. (II.2) a polynom with non-negative coefficients, and therefore

$$Re(p) = a < 0$$

We can thus confirm that solutions which fulfil condition (16) (all systems with positive regulation) always are stable stationary solutions. Eq. (II.3) provides information about the nature of the solution to eq. (II.1).

Eq. (II.3) has two solutions, one trivial ($b = 0$) when

$$\sum_j \frac{C_{As} k_j^2 C_{js}}{(a + k_j' - k_j C_{As})^2} \leq 1$$

and one non-trivial ($b \neq 0$) when

$$\sum_j \frac{C_{As} k_j^2 C_{js}}{(a + k_j' - k_j C_{As})^2} > 1$$

the first solution presents a stable node, the other one is a stable focus.

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