

# Dynamics of physicochemical model of selection processes in biomacromolecular systems

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Physicochemical models of selection processes on biomacromolecules — replicators are investigated by making use of simple qualitative theory of differential equations. It is assumed that each replicator is self-reproduced (replicated) with a participation of a substrate (energy-rich molecules). The qualitative features of the studied system are very sensitive to the form of rate functions. It is demonstrated that genuine Darwinian selection is simulated by the model only if the rate functions are determined by the mass-action law. A comparison with the original Eigen theory is presented.

С использованием простой качественной теории дифференциальных уравнений исследованы физико-химические модели селекционных процессов для биомакромолекул — репликаторов. Предполагается, что каждый репликатор самовоспроизводится (реплицируется) с участием субстрата (молекул с высоким содержанием энергии). Качественные характеристики изучаемой системы в сильной степени зависят от вида скоростных функций. Показано, что истинно дарвиновская селекция симулируется данной моделью только в том случае, если скоростные функции определяются законом действия масс. Проводится сравнение с исходной теорией Эйгена.

## I. Introduction

A mathematical modelling of selection processes on molecular level has been initiated by *Eigen* [1, 2] (cf. also [3—10]) at the beginning of seventies. He introduced the notion “information carrier”, which corresponds to a biomacromolecular system capable to reproduce itself (this conceptual notion will be called in the forthcoming part of communication the *replicator*, originally introduced by *Schuster* [11]). The process of self-reproduction of replicators is described by *Eigen's* phenomenological equations with two types of external constraints which would make the reaction system more competitive. The first type of these constraints is called the *constant population*, they require that the

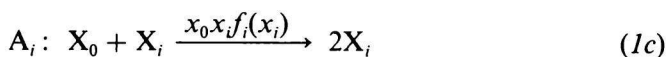
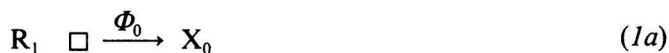
sum of concentrations of replicators is kept fixed in the course of whole time evolution of reaction system. The second type of constraints, called the *constant fluxes*, requires that an inflow of energy-rich molecules (necessary for self-reproduction of replicators) in the reaction system is time invariant. Both these types of external constraints induce a selective pressure among replicators, which gives rise to typical Darwinian selection known up to that time only for biological systems. Eigen has used this physicochemical model as a conceptual tool to abridge a deep gap between information contents of noninstructed synthesis of chemical macromolecules (chemical evolution) and instructed synthesis — self-reproduction of biological macromolecules (a very beginning of biological evolution). Eigen and his successors [4—7] devoted attention mainly to development of the selection model based on the constant-population constraints whereas its, at least, equivalent counterpart involving the constant-fluxes constraints was studied only marginally [1, 4, 8, 12] as a possible and alternative explanation of selection processes on molecular level. This was caused mainly by mathematical difficulties in the stability studies of its stationary states. Ebeling *et al.* [9—10] have shown that this formal “drawback” of the constant-fluxes approach can be surmounted by the standard technique of qualitative theory of differential equations [13], in particular by the so-called linearization method. Furthermore, the constant-fluxes approach has very easy and simple physicochemical interpretation and it can be naturally related to known kinetical and ecological models, which form a main field of interest in the modern formal chemical kinetics [14]. Recently, Krempaský and Květoň [15] have studied an extension of Ebeling’s approach taking into account constant inflows of replicators. They proved that this possibility permits the so-called external regulation of selection processes.

The purpose of this communication is to develop the Ebeling’s approach to selection processes based on constant-fluxes constraints. We shall demonstrate that this unjustly omitted theory represents very fruitful alternative possibility how to explain the selection processes on molecular level. Its theoretical tools are very flexible for further generalization and modification, *i.e.* it permits to develop very deep and exhaustive particular theoretical studies of the selection processes. In our forthcoming communication [16] we shall publish its application to replicator systems with incorrect reduplications and their combination to greater kinetical patterns called the hypercycles [3—5].

## II. General model

We are given a set composed of  $n$  replicators (biomacromolecules)  $X_1, X_2, \dots, X_n$  and a substrate  $X_0$ , confined to a well stirred reactor, which are capable of

replication. It is assumed that each replicator  $X_i$  is self-reproduced (replicated) with a participation of the substrate  $X_0$  and that the reactor walls are permeable to energy-rich compounds (corresponding to the substrate  $X_0$  with constant inflow) and energy deficient compounds (which are allowed to flow out from the reactor) (Fig. 1). These assumptions are formally represented by the following system of chemical reactions



for  $i = 1, 2, \dots, n$ . The square symbol  $\square$  on the r.h.s. of (1b) and (1d) represents those compounds — reaction products ("garbage") that are irrelevant for the kinetics of studied system. The same symbol was used also on the l.h.s. of (1a),

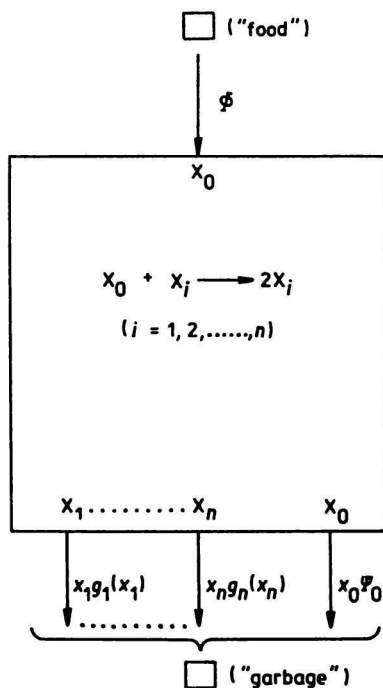


Fig. 1. The evolution reactor composed of a reaction vessel with temperature control. Its walls are impermeable to replicative biomacromolecules. Energy-rich material — substrate ("food") is poured in to the reactor by a constant inflow  $\Phi_0$ . Energy poor material ("garbage") is outflowing from the reactor through reactor walls.

here it means a blank side of chemical reaction. Each arrow (reaction) in (I) is evaluated by the corresponding rate function expressing the velocity of the reaction. The entries  $x_1, x_2, \dots, x_n$  are the concentrations of  $X_1, X_2, \dots, X_n$ , respectively. The reaction  $R_1$ , see (Ia), is a constant inflow  $\Phi_0$  of the substrate  $X_0$ , the reactions  $A_1, A_2, \dots, A_n$ , see (Ic), are replication processes of replicators onto themselves with a participation of the substrate  $X_0$ . The second reaction  $R_2$ , see (Ib), and the last reactions  $B_1, B_2, \dots, B_n$ , see (Id), correspond to a decomposition of the substrate and replicators, respectively, to products that are not appearing in the above replications. The system (I) of chemical reactions may be diagrammatically represented by the so-called *reaction graph* [14, 17, 18] (Fig. 2). In this

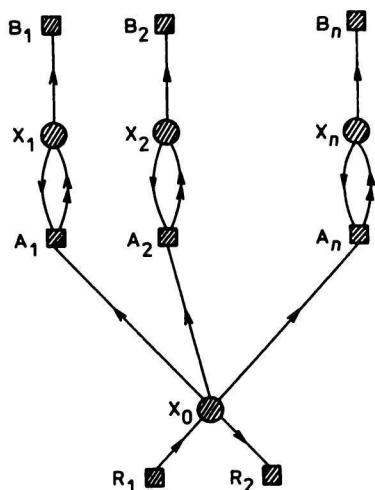


Fig. 2. Reaction graph [17] of the reaction scheme (I). The shaded square vertices are assigned to each individual chemical reaction from (I). The circle shaded vertices are assigned to compounds of kinetic system. The reaction and compound vertices are joined together by oriented lines — edges, the number of arrows on the line corresponds to stoichiometric numbers.

graph each square shaded vertex (assigned to a reaction of (I)) is evaluated by the corresponding rate function already presented in (I). Following very fruitful idea of Volpert [17, 18], the dynamics of the considered chemical reactions is described by the following system of differential equations determined over the reaction graph

$$\dot{x}_0 = \Phi_0 - x_0 \left[ \Psi_0 + \sum_{i=1}^n x_i f_i(x_i) \right] \quad (2a)$$

$$\dot{x}_i = x_i [x_0 f_i(x_i) - g_i(x_i)] \quad (i = 1, 2, \dots, n) \quad (2b)$$

where  $\dot{x}_i = dx_i/dt$  is the time derivative of the concentration  $x_i$  of the compound  $X_i$  and  $\Psi_0$  is the substrate decomposition rate constant. This autonomous system of ordinary differential equations models the kinetics of the physicochemical system of replicating biomacromolecules with a participation of the substrate  $X_0$ . The model contains unspecified functions  $f_i(x_i)$  and  $g_i(x_i)$ , in the forthcom-



ing part of this chapter we shall give their specification and in such a way we arrive at different models of the selection of replicators.

### 1. Ebeling's model of selection

The model of *Ebeling* [9, 10] can be constructed from our general equations (2a, 2b) if the functions  $f_i(x_i)$  and  $g_i(x_i)$  are specified as positive constant functions

$$f_i(x_i) = a_i > 0 \quad g_i(x_i) = b_i > 0 \quad (3)$$

for  $i = 1, 2, \dots, n$ . Then the system (2a, 2b) is

$$\dot{x}_0 = \Phi_0 - x_0 \left[ \Psi_0 + \sum_{i=1}^n a_i x_i \right] \quad (4a)$$

$$\dot{x}_i = x_i(a_i x_0 - b_i) \quad (i = 1, 2, \dots, n) \quad (4b)$$

It corresponds to the fact that the kinetics of (1a—1d) is governed by the mass-action law. We have to emphasize, the present model is a generalization of the original Ebeling's approach, we have introduced very important assumption that the substrate  $X_0$  is monomolecularly decaying, see (1b). It removes an overlooked shortcoming of Ebeling's model, where (if we put  $\Psi_0 = 0$  in our model) exists a "catastrophic" possibility in which all replicators  $X_1, X_2, \dots, X_n$  are becoming extinct whereas the concentration of substrate is linearly increasing to infinity. This inappropriate feature of the Ebeling's model is simply removed postulating the decomposition of  $X_0$ , see (1b).

If the initial concentrations (at  $t = 0$ ) are positive, then for each  $t \geq 0$  the concentration of  $X_0$  is positive and concentrations of  $X_1, X_2, \dots, X_n$  are non-negative, and all are bounded from above

$$0 < x_0(t) < \infty \quad (5a)$$

$$0 \leq x_i(t) < \infty \quad (5b)$$

The vector form of (4a, 4b) is

$$\dot{x}_0 = \Phi_0 - x_0 (\Psi_0 + \mathbf{a}^T \mathbf{x}) \quad (6a)$$

$$\dot{\mathbf{x}} = \text{dg}(x_0 \mathbf{a} - \mathbf{b}) \mathbf{x} \quad (6b)$$

where  $\mathbf{a} = (a_1, a_2, \dots, a_n)^T$  and  $\mathbf{b} = (b_1, b_2, \dots, b_n)^T$  are column vectors of positive rate constants assigned to replication and decomposition processes, respectively, and  $\mathbf{x} = (x_1, x_2, \dots, x_n)^T$  is a column vector of replicator concentrations. The symbol  $\text{dg}(\cdot)$  denotes a diagonal matrix with entries from the vector  $(\cdot)$ .

The stationary states of (4a, 4b) are of the following two kinds:

**1st kind.** The stationary concentration  $\bar{x}_0$  is positive whereas stationary concentrations  $\bar{x}_1, \bar{x}_2, \dots, \bar{x}_n$  are vanishing

$$\bar{x}_0 = \frac{\Phi_0}{\Psi_0} \quad (7a)$$

$$\bar{x}_i = 0 \quad (i = 1, 2, \dots, n) \quad (7b)$$

This stationary state will be denoted by  $S_0$ .

**2nd kind.** The stationary concentrations  $\bar{x}_0$  and  $\bar{x}_p$  (for a preselected index  $1 \leq p \leq n$ ) are positive whereas stationary concentrations  $\bar{x}_1, \dots, \bar{x}_{p-1}, \bar{x}_{p+1}, \dots, \bar{x}_n$  are vanishing

$$\bar{x}_0 = \frac{b_p}{a_p} \quad (8a)$$

$$\bar{x}_i = \delta_{ip} \left( \frac{\Phi_0}{b_p} - \frac{\Psi_0}{a_p} \right) \quad (i = 1, 2, \dots, n) \quad (8b)$$

where  $\delta_{ip}$  is Kronecker's delta symbol,  $\delta_{ip} = 1$  for  $i = p$ , and  $\delta_{ip} = 0$  for  $i \neq p$ . The stationary concentration  $\bar{x}_p$  should be positive, hence

$$\frac{\Psi_0}{\Phi_0} < \frac{a_p}{b_p} \quad (9)$$

This stationary state will be denoted by  $S_p$ . We say that the stationary state  $S_p$  is properly selected if the inequality (9) is satisfied, in the opposite case, we say that the stationary state  $S_p$  does not exist.

In order to study the stability of stationary states  $S_0, S_1, \dots, S_n$  we have to construct the Jacobi matrix of (4a, 4b)

$$\mathbf{J} = \frac{\partial(\dot{x}_0, \dot{\mathbf{x}})}{\partial(x_0, \mathbf{x})} = \begin{pmatrix} -\mathbf{a}^T \mathbf{x} - \Psi_0 & -x_0 \mathbf{a}^T \\ \text{dg}(\mathbf{x}) \mathbf{a} & \text{dg}(x_0 \mathbf{a} - \mathbf{b}) \end{pmatrix} \quad (10)$$

It should be evaluated at the stationary states  $S_0$  and  $S_p$

$$\mathbf{J}(S_0) = \begin{pmatrix} -\Psi_0 & -\frac{\Phi_0}{\Psi_0} \mathbf{a}^T \\ 0 & \text{dg}\left(\frac{\Phi_0}{\Psi_0} \mathbf{a} - \mathbf{b}\right) \end{pmatrix} \quad (11a)$$

$$\mathbf{J}(\mathbf{S}_p) = \begin{pmatrix} -\Phi_0 \frac{a_p}{b_p} & -\frac{\Phi_0}{\Psi_0} \mathbf{a}^T \\ \left( \Phi_0 \frac{a_p}{b_p} - \Psi_0 \right) \mathbf{e}_p & \text{dg} \left( \frac{b_p}{a_p} \mathbf{a} - \mathbf{b} \right) \end{pmatrix} \quad (11b)$$

where  $\mathbf{e}_p = (0, \dots, 1, \dots, 0)^T$  is a column vector with all entries equal to zero except of the  $p$ -th position which is unit.

Since the Jacobi matrix  $\mathbf{J}(\mathbf{S}_0)$  is triangular, its eigenvalues are simply its diagonal elements

$$\lambda_0^{(0)} = -\Psi_0 \quad (12a)$$

$$\lambda_i^{(0)} = a_i \frac{\Phi_0}{\Psi_0} - b_i \quad (i = 1, 2, \dots, n) \quad (12b)$$

The eigenvalue  $\lambda_0^{(0)}$  is automatically negative (the substrate decomposition rate constant  $\Psi_0$  is positive), other eigenvalues  $\lambda_1^{(0)}, \lambda_2^{(0)}, \dots, \lambda_n^{(0)}$  are negative if

$$\frac{\Psi_0}{\Phi_0} > \max_{1 \leq i \leq n} \frac{a_i}{b_i} \quad (13)$$

Hence, the stationary state  $\mathbf{S}_0$  is asymptotically stable if the above condition (13) is satisfied.

The eigenvalues of  $\mathbf{J}(\mathbf{S}_p)$  are determined from its secular equation  $|\mathbf{J}(\mathbf{S}_p) - \lambda \mathbf{E}| = 0$

$$\left( \lambda^2 + \Phi_0 \frac{a_p}{b_p} \lambda + \Phi_0 a_p - \Psi_0 b_p \right) \prod_{\substack{i=1 \\ (i \neq p)}}^n \left( \frac{b_p}{a_p} a_i - b_i - \lambda \right) = 0 \quad (14)$$

From the second term on the l.h.s. of (14) we get  $n - 1$  eigenvalues of  $\mathbf{J}(\mathbf{S}_p)$

$$\lambda_i^{(p)} = \frac{b_p}{a_p} a_i - b_i \quad (i = 1, \dots, p-1, p+1, \dots, n) \quad (15)$$

The remaining two eigenvalues  $\lambda_0^{(p)}$  and  $\lambda_p^{(p)}$  are determined by the quadratic equation (the first term on the l.h.s. of (14)). Its roots (eigenvalues) have negative real part if and only if the coefficients of the quadratic equation are positive

$$\frac{\Psi_0}{\Phi_0} < \frac{a_p}{b_p} \quad (16)$$

The eigenvalues (15) are negative if

$$\frac{a_p}{b_p} = \max_{1 \leq i \leq n} \frac{a_i}{b_i} \quad (17a)$$

Hence, all eigenvalues of  $\mathbf{J}(S_p)$  have negative real part if the conditions (16) and (17a) are simultaneously satisfied

$$\frac{\Psi_0}{\Phi_0} < \frac{a_p}{b_p} = \max_{1 \leq i \leq n} \frac{a_i}{b_i} \quad (17b)$$

This means that among stationary states  $S_0, S_1, \dots, S_p$  is asymptotically stable either  $S_0$ , if the condition (13) is satisfied, or  $S_p$  state ( $1 \leq p \leq n$ ), if the condition (17b) is satisfied; therefore, the only stationary state is asymptotically stable due to the fact that the conditions (13) and (17b) are mutually excluding.

The above results represent only sufficient conditions for a stationary state to be asymptotically stable. Now we would like to demonstrate that the conditions (13) and (17b) are also necessary. The eqns (4a, 4b) can be rewritten as follows

$$\frac{d}{dt'} \left( \frac{1}{y_0} \right) = \Phi_0 y_0 - \sum_{i=1}^n a_i y_i - \Psi_0 \quad (18a)$$

$$\frac{d}{dt'} \ln y_i = a_i - y_0 b_i \quad (i = 1, 2, \dots, n) \quad (18b)$$

where  $y_0 = 1/x_0$ ,  $y_i = x_i$  (for  $i = 1, 2, \dots, n$ ), and  $t'$  is a new time variable determined by  $t' = t'(t) = \int_0^t x_0(\tau) d\tau$ , where  $dt' = x_0(t) dt$ ,  $t'(0) = 0$ ,  $t'(t) \rightarrow \infty$  as  $t \rightarrow \infty$ .

Time average concentrations are defined by

$$z_i(t) = \frac{1}{t} \int_0^t y_i(\tau) d\tau \quad (i = 0, 1, \dots, n) \quad (19)$$

Let us integrate differential equations (18a, 18b) from  $\tau = 0$  to  $\tau = t$ , after dividing by  $t$ , we have

$$\frac{1}{t} \left( \frac{1}{y_0(t)} - \frac{1}{y_0(0)} \right) = \Phi_0 z_0(t) - \sum_{i=1}^n a_i z_i(t) - \Psi_0 \quad (20a)$$

$$\frac{\ln y_i(t) - \ln y_i(0)}{t} = a_i - z_i(t) b_i \quad (i = 1, 2, \dots, n) \quad (20b)$$

We shall assume that the limit values  $z_i(\infty)$  always exist and they are non-negative and bounded from above. Let us assume that the concentration  $y_p(t)$  does not vanish as  $t \rightarrow \infty$ , then from (20b) we get

$$z_0(\infty) = \frac{a_p}{b_p} \quad (21)$$

This means that such index  $p$  of nondecaying replicator is unambiguously determined. If we have two such indices  $p$  and  $q$ , then  $a_p/b_p = a_q/b_q$ , the condition of which is physically highly improbable (it implies that the replicators  $X_p$  and  $X_q$  are kinetically equivalent). For other indices  $i = 1, 2, \dots, p-1, p+1, \dots, n$  the replicator concentrations vanish as  $t \rightarrow \infty$ ; limit values of their time averages are vanishing as  $t \rightarrow \infty$ . Since the variable  $y_0(t)$  is positive and bounded from above, the relation (20a) provides as  $t \rightarrow \infty$

$$z_p(\infty) = \frac{\Phi_0}{b_p} - \frac{\Psi_0}{a_p} \quad (22)$$

The limit values of time averages tend to their stationary values as  $t \rightarrow \infty$

$$\lim_{t \rightarrow \infty} z_i(t) = \bar{y}_i \quad (i = 0, 1, \dots, n) \quad (23)$$

The relation (20b) can be simply rewritten in the form

$$y_i(t) = y_i(0) \exp \{[a_i - z_0(t) b_i] t\} \quad (24)$$

We shall study asymptotical properties of this solution  $y_i(t)$ . For an index  $i = 1, 2, \dots, p-1, p+1, \dots, n$  the concentration  $y_i(t)$  vanishes as  $t \rightarrow \infty$ , this implies that the asymptotical value of exponent in (24) should be negative,  $a_i - z_0(\infty) b_i < 0$ , or by making use of (21) we get  $a_i/b_i < a_p/b_p$ , which is together with a positiveness of (22) equivalent to the condition (17b) for the asymptotical stability of  $S_p$ .

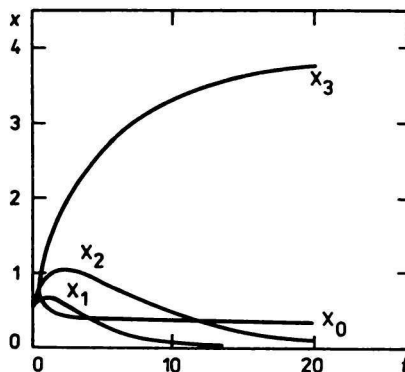


Fig. 3. The results of numerical integration of the system (4a, 4b) consisting of three replicators with the following set of parameters:  $\Phi_0 = 4$ ,  $\Psi_0 = 1$ ,  $a_1 = 2$ ,  $a_2 = 2.5$ ,  $a_3 = 3$ ,  $b_1 = b_2 = b_3 = 1$ , and the initial concentrations are  $x_i(0) = 0.5$  ( $i = 0, 1, 2, 3$ ). The "best-fitted" replicator is  $X_3$ .

Summarizing the above results, for a replicator system determined by (4a, 4b) there exist two mutually excluding alternative possibilities. The first possibility consists in that all replicators are asymptotically becoming extinct (determined by the condition (13)), for the second possibility there exists a molecular selection process which always leads to an unambiguous selection "decision" — to survival of the "best-fitted" replicator (determined by (17)) and to the extinction of all its competitors. An illustrative example of three replicators is shown in Fig. 3.

## 2. Quadratic selection model

The model of quadratic selection is based on the following form of functions  $f_i(x_i)$  and  $g_i(x_i)$  from (2a, 2b)

$$f_i(x_i) = a_i x_i \quad g_i(x_i) = b_i \quad (i = 1, 2, \dots, n) \quad (25)$$

where  $a_i$  and  $b_i$  are positive rate constants. In this approach the velocity of replication processes depends quadratically on concentration of replicators. Introducing (25) into (2a, 2b) we obtain the following system of differential equations

$$\dot{x}_0 = \Phi_0 - x_0 \left( \Psi_0 + \sum_{i=1}^n a_i x_i^2 \right) \quad (26)$$

$$\dot{x}_i = x_i (a_i x_0 x_i - b_i) \quad (i = 1, 2, \dots, n) \quad (27)$$

Let  $\mathcal{J}$  be a subset of  $\mathcal{N} = \{1, 2, \dots, n\}$  composed of the first  $n$  natural integers, we define also  $\mathcal{J}' = \mathcal{N} \setminus \mathcal{J}$  composed of those integers of  $\mathcal{N}$  that are not contained in  $\mathcal{J}$ , then  $\mathcal{N} = \mathcal{J} \cup \mathcal{J}'$  and  $\mathcal{J} \cap \mathcal{J}' = \emptyset$  (empty set). For a preselected set  $\mathcal{J}$  we define a stationary state, denoted by  $S_{\mathcal{J}}$ , as follows

$$\forall i \in \mathcal{J}: \quad \bar{x}_i > 0 \quad \text{and} \quad \forall i \in \mathcal{J}': \quad \bar{x}_i = 0 \quad (28)$$

The stationary concentrations  $\bar{x}_i$ , for  $i \in \mathcal{J}$ , are determined by (27) and we get

$$\bar{x}_i = \frac{b_i}{a_i \bar{x}_0} \quad (29)$$

The stationary concentration  $\bar{x}_0$  is determined by (26), we get

$$\bar{x}_0^2 - \frac{\Phi_0}{\Psi_0} \bar{x}_0 + \frac{c_{\mathcal{J}}}{\Psi_0} = 0 \quad (30a)$$

where the positive constant  $c_{\mathcal{J}}$  is

$$c_{\mathcal{J}} = \sum_{i \in \mathcal{J}} \frac{b_i^2}{a_i} \quad (30b)$$

The roots of the above quadratic equation (30a) have always positive real parts, they are real and positive if the following condition is fulfilled

$$\Phi_0 \geq 2(\Psi_0 c_{\mathcal{J}})^{1/2} \quad (31)$$

It means that for a preselected stationary state  $S_{\mathcal{J}}$ , the corresponding concentration  $\bar{x}_0$  is positive only if the substrate inflow  $\Phi_0$  is greater or, at least, equal to its threshold value  $2(\Psi_0 c_{\mathcal{J}})^{1/2}$ ; if  $\Phi_0$  is smaller than this value, then the stationary concentration  $\bar{x}_0$  is complex. For  $\Phi_0 < 2(\Psi_0 c_{\mathcal{J}})^{1/2}$  we simply say that the stationary state  $S_{\mathcal{J}}$  does not exist, the subset  $\mathcal{J}$  was improperly selected.

In the case  $\mathcal{J} = \emptyset$  (a stationary state for which all replicators are becoming extinct), the stationary concentration  $\bar{x}_0$  is

$$\bar{x}_0 = \frac{\Phi_0}{\Psi_0} \quad (32)$$

For  $\mathcal{J} \neq \emptyset$  the stationary concentration  $\bar{x}_0$  is determined as a root of the quadratic equation (30a). Assuming that the condition (31) is satisfied then we get two positive stationary concentrations denoted by  $(\bar{x}_0)_1$  and  $(\bar{x}_0)_2$ , where  $(\bar{x}_0)_1 < (\bar{x}_0)_2$ ,  $(\bar{x}_0)_1 + (\bar{x}_0)_2 = \Phi_0/\Psi_0$ , and  $0 < (\bar{x}_0)_{1,2} < \Phi_0/\Psi_0$ , their explicit form is

$$(\bar{x}_0)_{1,2} = \frac{\Phi_0}{2\Psi_0} \left( 1 \pm \sqrt{1 - \frac{4\Psi_0 c_{\mathcal{J}}}{\Phi_0^2}} \right) \quad (33)$$

If the substrate inflow  $\Phi_0$  is relatively in a great excess

$$\Phi_0 \gg 2(\Psi_0 c_{\mathcal{J}})^{1/2} \quad (34)$$

then the approximate values of stationary substrate concentrations are

$$(\bar{x}_0)_1 \approx \frac{c_{\mathcal{J}}}{\Phi_0} \quad (35a)$$

$$(\bar{x}_0)_2 \approx \frac{\Phi_0}{\Psi_0} \quad (35b)$$

In order to determine the stability of the stationary state  $S_{\mathcal{J}}$  (this state is determined by (28) for a preselected index subset  $\mathcal{J}$ ) we have to evaluate eigenvalues of the corresponding Jacobi matrix

$$\mathbf{J}(\mathbf{S}_{\mathcal{J}}) = \begin{pmatrix} -\frac{\Phi_0}{\bar{x}_0} & -2b_j & 0 \\ \frac{1}{\bar{x}_0^2} \frac{b_i^2}{a_i} & \delta_{ij} b_j & 0 \\ 0 & 0 & -\delta_{ij} b_i \end{pmatrix} \begin{matrix} i=0 \\ i \in \mathcal{J} \\ i \in \mathcal{J}' \end{matrix} \quad (36)$$

$$j=0 \quad j \in \mathcal{J} \quad j \in \mathcal{J}'$$

We shall separately study the following two special cases:

a)  $\mathcal{J} = \emptyset$ , this stationary state  $\mathbf{S}_0$  contains all replicator concentrations vanishing. The Jacobi matrix (36) is of the diagonal form, where all its diagonal entries are negative. Hence the stationary state  $\mathbf{S}_0$  is asymptotically stable.

b)  $\mathcal{J} = \{p\}$ , the index subset  $\mathcal{J}$  is composed of one element  $p$ . Now, the stability of this stationary state is determined by the eigenvalues of submatrix (cf. eqn (36))

$$\begin{pmatrix} -\frac{\Phi_0}{\bar{x}_0} & 2b_p \\ \frac{1}{\bar{x}_0^2} \frac{b_p^2}{a_p} & b_p \end{pmatrix} \quad (37)$$

Its eigenvalues are determined as roots of the quadratic equation

$$\lambda^2 + \lambda \left( \frac{\Phi_0}{\bar{x}_0} - b_p \right) + 2 \frac{1}{\bar{x}_0^2} \frac{b_p^3}{a_p} - \frac{\Phi_0}{\bar{x}_0} b_p = 0 \quad (38)$$

We know that a quadratic secular equation has roots with negative real parts if and only if its coefficients are positive; hence the submatrix (37) has eigenvalues with negative real part iff the substrate inflow is restricted by

$$\bar{x}_0 b_p < \Phi_0 < \frac{2b_p^2}{\bar{x}_0 a_p} \quad (39)$$

We shall check the above condition (39) for approximate values of  $\bar{x}_0$  (cf. eqns (35a) and (35b)), the constant  $c_{\mathcal{J}}$  for  $\mathcal{J} = \{p\}$  is specified by  $c_{\mathcal{J}} = b_p^2/a_p$ . The substrate inflow excess condition (34) is

$$\Phi_0 \gg 2b_p \left( \frac{\Psi_0}{a_p} \right)^{1/2} \quad (40)$$

The approximate value (35a) of the stationary substrate concentration is

$$(\bar{x}_0)_1 = \frac{1}{\Phi_0} \frac{b_p^2}{a_p} \quad (41)$$



Introducing this value into (39) we get that the right inequality is automatically satisfied and the left inequality gives

$$\Phi_0 > b_p \left( \frac{b_p}{a_p} \right)^{1/2} \quad (42)$$

For the second approximate value of stationary substrate concentration  $(\bar{x}_0)_2$  specified by (35b) we get from the right inequality of (39) the following condition

$$\Phi_0 < b_p \left( \frac{2\Psi_0}{\Phi_0} \right)^{1/2} \quad (43)$$

which is inconsistent with the excess condition (40). Summarizing, the stationary state  $S_{\mathcal{J}}$ , for  $\mathcal{J} = \{p\}$  is properly selected if the substrate inflow satisfies, in general, the condition (31), now specified for the present case as follows

$$\Phi_0 \geq 2b_p \left( \frac{\Psi_0}{a_p} \right)^{1/2} \quad (44)$$

This properly selected stationary state is asymptotically stable if the substrate inflow is, moreover, ranged by the condition (39). The situation is much more simpler for a great excess of substrate inflow  $\Phi_0$ , see eqn (40). Here, the stationary state  $S_{\mathcal{J}}$  with  $(\bar{x}_0)_1$  is asymptotically stable if the substrate inflow satisfies inequality (42) whereas the stationary state  $S_{\mathcal{J}}$  with  $(\bar{x}_0)_2$  is unstable.

c)  $|\mathcal{J}| \geq 2$ , the index subset  $\mathcal{J}$  is composed of two or more indices. We assume that for this index subset the quadratic equation (30a) has positive roots, i.e.  $S_{\mathcal{J}}$  is properly selected. The stability of this state is determined by the eigenvalues of a submatrix of Jacobi matrix (36)

$$\begin{pmatrix} -\frac{\Phi_0}{\bar{x}_0} & -2b_j \\ \frac{1}{\bar{x}_0^2} \frac{b_i^2}{a_i} & \delta_{ij} b_j \end{pmatrix} \begin{matrix} i=0 \\ i \in \mathcal{J} \end{matrix} \quad (45)$$

$$j=0 \quad j \in \mathcal{J}$$

Its eigenvalues are determined as roots of the following equation

$$\frac{2}{\bar{x}_0^2} \sum_{j \in \mathcal{J}} \frac{b_j^3}{a_j(b_j - \lambda)} = \lambda + \frac{\Phi_0}{\bar{x}_0} \quad (46)$$

It is easy to show that it has at least one positive root (Fig. 4), hence the stationary state  $S_{\mathcal{J}}$ , for  $|\mathcal{J}| \geq 2$ , is unstable.

To conclude this section we summarize the obtained main result. **First**, the properly selected stationary states  $S_{\mathcal{J}}$ , where  $|\mathcal{J}| \geq 2$ , are unstable. **Second**, the stationary states  $S_{\mathcal{J}}$ , where  $|\mathcal{J}| = 1$ , may be asymptotically stable as well as unstable, this is fully determined by the inequalities (39). The situation is slightly more transparent assuming the great excess of the substrate inflow  $\Phi_0$ , cf. eqn (40). Here is a greater hope that the condition (42) is satisfied whereas the second one (43) is inconsistent with the assumption of excess of substrate inflow  $\Phi_0$ .

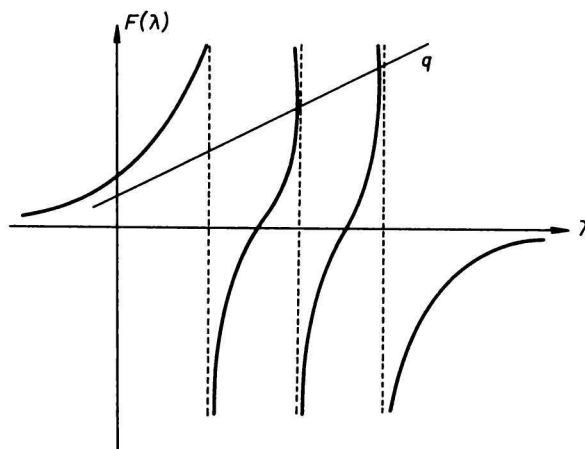


Fig. 4. Graphical solution of the nonlinear eqn (46), the l.h.s. is denoted by  $F(\lambda)$ , its positive singular points are represented by dashed lines. The r.h.s. corresponds to the straight line  $q$ . We can see that for  $|\mathcal{J}| \geq 2$ , the equation has at least one positive root.

**Third**, the stationary state  $S_{\mathcal{J}}$ , for  $\mathcal{J} = \emptyset$ , is asymptotically stable without restriction conditions. The last two items imply that we have a class  $\{S_{\mathcal{J}}; |\mathcal{J}| = 0, 1\}$  of stationary states that are simultaneously asymptotically stable. Which stationary state among them will win in the course of time evolution of the system? This is dependent on the initial state. The whole nonnegative orthant of phase space can be divided into nonoverlapping attractivity domains of single asymptotically stable stationary states  $S_{\mathcal{J}}$ . If an initial state is taken from a given attractivity domain of stationary state  $S_{\mathcal{J}}$ , then the corresponding trajectory is asymptotically ending in this stationary state  $S_{\mathcal{J}}$  as  $t \rightarrow \infty$ , or in other words, this state will win. This selection process is of the “once-for-ever” type, no small concentration fluctuation can produce a transient process of crossing from the given stationary state to another one.

### 3. Michaelis—Menten kinetics model of selection

This model of selection is based on the assumption that the functions  $f_i(x_i)$  from (2a, 2b) are positive, differentiable and monotonously decreasing, and moreover, the products  $x_i f_i(x_i)$  are increasing functions

$$f_i(x_i) > 0 \quad f'_i(x_i) < 0 \quad (x_i f_i(x_i))' > 0 \quad (i = 1, 2, \dots, n) \quad (47a)$$

and the functions  $g_i(x_i)$  are positive and constant

$$g_i(x_i) = b_i > 0 \quad (i = 1, 2, \dots, n) \quad (47b)$$

For instance, in the Michaelis—Menten kinetics the functions  $f_i(x_i)$  look as follows

$$f_i(x_i) = \frac{a_i}{a'_i + x_i} \quad (48)$$

where  $a_i$  and  $a'_i$  are positive constants, this type of functions satisfies general requirements (47a); therefore we shall call the present approach the Michaelis—Menten kinetics model. In the framework of Eigen's "constant population" model [1] the above type of rate functions was initially studied by Epstein [19] and Hofbauer *et al.* [20].

The differential equations (2a, 2b) are

$$\dot{x}_0 = \Phi_0 - x_0 \left( \Psi_0 + \sum_{i=1}^n x_i f_i(x_i) \right) \quad (49a)$$

$$\dot{x}_i = x_i (x_0 f_i(x_i) - b_i) \quad (i = 1, 2, \dots, n) \quad (49b)$$

For a preselected index subset  $\mathcal{J}$  (see Section II. 2) the stationary concentrations  $\bar{x}_i$  fulfil the conditions (28), then from (49b) we get for each  $i \in \mathcal{J}$

$$F_i(\bar{x}_i) = \frac{1}{b_i} f_i(\bar{x}_i) = \frac{1}{\bar{x}_0} \quad (50)$$

where the functions  $F_i(\bar{x}_i)$  are positive and monotonously decreasing. Assuming

$$\frac{1}{\bar{x}_0} < \min_{i \in \mathcal{J}} F_i(0) \quad (51)$$

then the solution of (50) is

$$\bar{x}_i = F_i^{-1} \left( \frac{1}{\bar{x}_0} \right) \quad (\text{for each } i \in \mathcal{J}) \quad (52)$$

where the inverse function  $F_i^{-1}(x)$  is also positive and decreasing in the interval

$[F_i(\infty), F_i(0)]$ ; for simplicity we put  $F_i^{-1}(x) = 0$ , for  $x \geq F_i(0)$ , then such extended function is defined on  $(F_i(\infty), \infty)$  (Fig. 5). The positive stationary concentration  $\bar{x}_0$  is determined by (49a)

$$\Phi_0 - \bar{x}_0 \Psi_0 = H_{\mathcal{J}} \left( \frac{1}{\bar{x}_0} \right) \quad (53a)$$

where

$$H_{\mathcal{J}}(\xi) = \sum_{i \in \mathcal{J}} b_i F_i^{-1}(\xi) \quad (53b)$$

is monotonously decreasing function defined for

$$\xi \geq \max_{i \in \mathcal{J}} F_i(\infty) \quad (54a)$$

and

$$H_{\mathcal{J}}(\xi) = 0 \quad \text{for} \quad \xi \geq \max_{i \in \mathcal{J}} F_i(0) \quad (54b)$$

Let us rewrite eqn (53a) in an equivalent form

$$\Phi_0 - \frac{1}{\xi} \Psi_0 = H_{\mathcal{J}}(\xi) \quad (55)$$

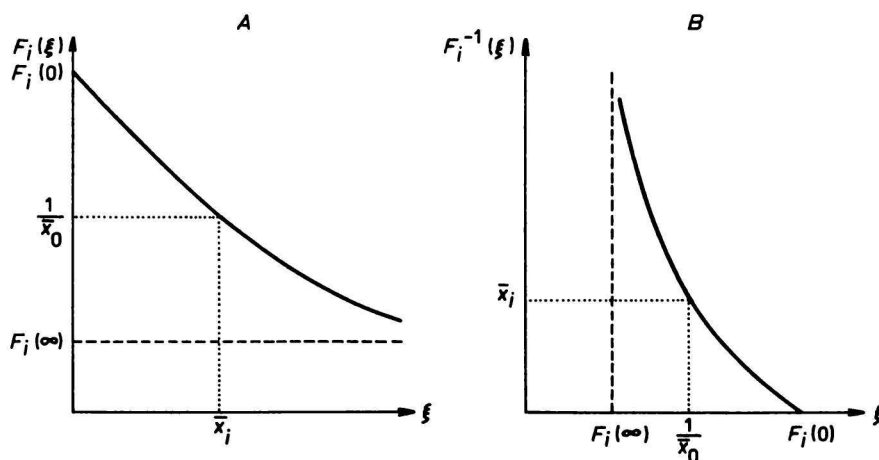


Fig. 5. An illustrative plot of the functions  $F_i(\xi)$  and  $F_i^{-1}(\xi)$  determined by (50) and (52), respectively. From the diagram (A) we can immediately deduce that eqn (50) has a positive solution only if the condition (51) is satisfied.

This equation is graphically illustrated in Fig. 6, we can see that it has a positive solution  $1/\bar{x}_0$  ranged by

$$\frac{\Psi_0}{\Phi_0} < \frac{1}{\bar{x}_0} < \max_{i \in \mathcal{J}} F_i(0) \quad (56)$$

The right inequality is consistent with the condition (51), therefore the relation (56) may be rewritten in the following more sharper form

$$\frac{\Psi_0}{\Phi_0} < \frac{1}{\bar{x}_0} < \min_{i \in \mathcal{J}} F_i(0) \quad (57)$$

Hence, the positive solution  $1/\bar{x}_0$  of (55) exists only if the inequality is satisfied

$$\frac{\Psi_0}{\Phi_0} < \min_{i \in \mathcal{J}} F_i(0) \quad (58)$$

This very important relation (containing only parameters of system) may be taken as a simple criterion whether the index subset  $\mathcal{J}$  was properly selected or not. In the negative case we say simply that the corresponding stationary state does not exist.

The Jacobi matrix of the system (49a, 49b) evaluated for the stationary state  $S_{\mathcal{J}}$  (assuming that the condition (57) is satisfied) is

$$J(S_{\mathcal{J}}) = \begin{pmatrix} -\frac{\Phi_0}{\bar{x}_0} & -\bar{x}_0[f_j(\bar{x}_j) + \bar{x}_j f'_j(x_j)] & -\bar{x}_0 f_j(0) \\ \bar{x}_i f_i(\bar{x}_i) & \delta_{ij} \bar{x}_0 \bar{x}_i f'_i(\bar{x}_i) & 0 \\ 0 & 0 & \delta_{ij} [\bar{x}_0 f_i(0) + b_i] \end{pmatrix} \begin{matrix} i=0 \\ i \in \mathcal{J} \\ i \in \mathcal{J}' \end{matrix} \quad (59)$$

$$\begin{matrix} j=0 & j \in \mathcal{J} & j \in \mathcal{J}' \end{matrix}$$

It has a block-triangular form, therefore the right-down block (for  $i, j \in \mathcal{J}'$ ) should have negative entries

$$\max_{i \in \mathcal{J}'} F_i(0) < \frac{1}{\bar{x}_0} \quad (60)$$

Combining the relation (51) we get the following range for  $1/\bar{x}_0$

$$\max_{i \in \mathcal{J}'} F_i(0) < \frac{1}{\bar{x}_0} < \min_{i \in \mathcal{J}} F_i(0) \quad (61)$$

The eigenvalues of the left-up block (for  $i, j \in \mathcal{J} \cup \{0\}$ ) are determined as roots of the equation

$$\sum_{i \in \mathcal{J}} \frac{\bar{x}_i f_i(\bar{x}_i) \bar{x}_0 [f_i(x_i) + \bar{x}_i f'_i(\bar{x}_i)]}{\bar{x}_0 \bar{x}_i f'_i(\bar{x}_i) - \lambda} = \lambda + \frac{\Phi_0}{\bar{x}_0} \quad (62)$$

Since the terms placed in brackets are always positive (*cf.* assumption (47a)), the above equation has roots with negative real parts (Fig. 7) if the following inequality (obtained from (62) for  $\lambda = 0$ ) is satisfied

$$\sum_{i \in \mathcal{J}} \frac{f_i(\bar{x}_i) [f_i(\bar{x}_i) + \bar{x}_i f'_i(x_i)]}{f'_i(x_i)} < \frac{\Phi_0}{\bar{x}_0} \quad (63)$$

which can be simply verified remembering that  $\sum_{i \in \mathcal{J}} \bar{x}_i f_i(\bar{x}_i) = \Phi_0/\bar{x}_0 - \Psi_0$  and  $f'_i(\bar{x}_i) < 0$ . Hence, the asymptotical stability of the stationary state  $S_{\mathcal{J}}$  is fully determined by the right-down block of the Jacobi matrix (59), *i.e.* the condition (61) should be fulfilled.

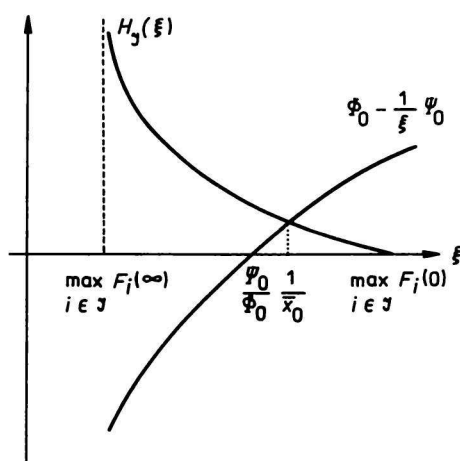


Fig. 6. Graphical solution of the nonlinear eqn (55), we can see that the lines corresponding to the l.h. and r.h. sides have a common point if the condition (56) is satisfied, it corresponds to the solution  $1/\bar{x}_0$ .

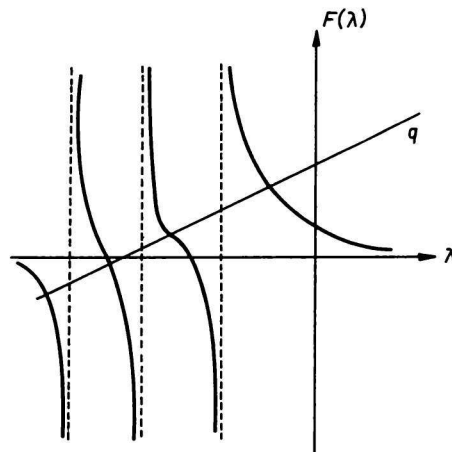


Fig. 7. Graphical solution of the nonlinear eqn (62), its l.h.s. is denoted by  $F(\lambda)$ , the negative singular points of this function are represented by dashed lines. The r.h.s. is represented by the straight line  $q$ . One can see that the roots of (62) are always negative.

Summarizing the obtained results, in the set of all positive stationary states  $\{S_{\mathcal{J}}\}$  are asymptotically stable only those ones which are satisfying the crucial condition (61). It means that the Michaelis—Menten kinetics model of selection does not satisfy the criterion of genuine Darwinian selection, *i.e.* a surviving of the only “best-fitted” replicator. In the present model many replicators may survive simultaneously.

#### 4. Selection model with intrareplicator antagonism

In the original Ebeling's model (see Section II. 1) the replicators are decaying linearly with respect to their concentrations, or kinetically, this process is controlled by the first-order kinetics. Assuming that the replicators are decomposed by another type of kinetics with order higher than of the first one, we have introduced, in fact, an antagonism among replicators of the same type. The above verbal formulations are represented formally as follows: The functions  $f_i(x_i)$  are equal to positive constants, and  $g_i(x_i)$  are positive and monotonously increasing

$$f_i(x_i) = a_i > 0 \quad (64a)$$

$$g_i(x_i) > 0 \quad \text{and} \quad g'_i(x_i) > 0 \quad (64b)$$

for  $i = 1, 2, \dots, n$ . In a more simpler form (in particular, for  $g_i(x_i) = b_i x_i$ ) this type of selection was initially studied by *Ebeling* and *Feistel* [10].

Introducing (64a, 64b) in (2a, 2b) we get the following system of differential equations

$$\dot{x}_0 = \Phi_0 - x_0 \left( \Psi_0 - \sum_{i=1}^n a_i x_i \right) \quad (65a)$$

$$\dot{x}_i = x_i (a_i x_0 - g_i(x_i)) \quad (i = 1, 2, \dots, n) \quad (65b)$$

For a fixed subset of indices  $\mathcal{J}$  the stationary state  $S_{\mathcal{J}}$  is composed of positive stationary replicator concentrations ( $\bar{x}_i > 0$ ,  $i \in \mathcal{J}$ ) determined by (65a) as follows

$$G_i(\bar{x}_i) = \frac{1}{a_i} g_i(\bar{x}_i) = \bar{x}_0 \quad (66)$$

If the stationary substrate concentration  $\bar{x}_0$  is bounded from below by (Fig. 8)

$$\max_{i \in \mathcal{J}} G_i(0) < \bar{x}_0 \quad (67)$$

then eqns (66) are solved as

$$\bar{x}_i = G_i^{-1}(\bar{x}_0) \quad (68)$$

where  $G_i^{-1}(\xi)$  is an inverse function defined in the interval  $0 \leq \xi < G_i(\infty)$ , and

$$G_i^{-1}(\xi) = 0 \quad (\text{for } 0 \leq \xi \leq G_i(0)) \quad (69)$$

The stationary substrate concentration  $\bar{x}_0$  is determined by (65a), we get

$$\frac{\Phi_0}{\bar{x}_0} - \Psi_0 = H_{\mathcal{J}}(\bar{x}_0) \quad (70a)$$

where

$$H_{\mathcal{J}}(\xi) = \sum_{i \in \mathcal{J}} a_i G_i^{-1}(\xi) \quad (70b)$$

This function defined in the interval

$$0 \leq \xi < \min_{i \in \mathcal{J}} G_i(\infty) \quad (71a)$$

is monotonously increasing, and

$$H_{\mathcal{J}}(\xi) = 0 \quad (\text{for } 0 \leq \xi < \min_{i \in \mathcal{J}} G_i(0)) \quad (71b)$$

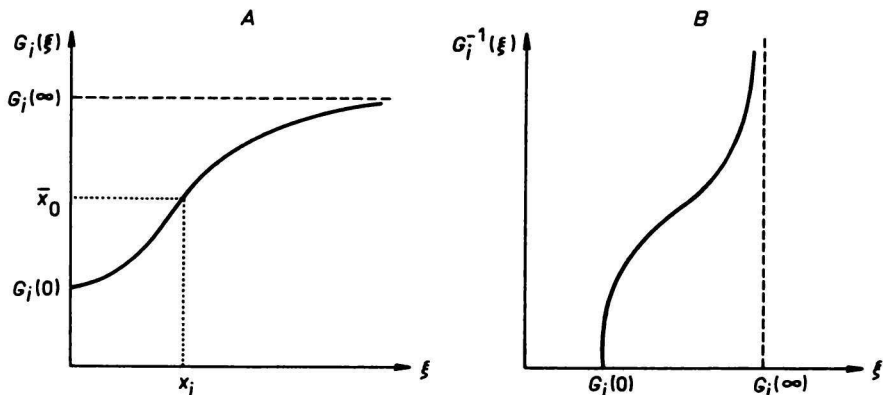


Fig. 8. An illustrative plot of the functions  $G_i(\xi)$  and  $G_i^{-1}(\xi)$  determined by (66) and (68), respectively. From the diagram (A) we can see that a positive solution of (66) exists only if the condition (67) is satisfied.

The relation (70a) has a positive solution  $\bar{x}_0$  (Fig. 9) ranged by

$$\min_{i \in \mathcal{J}} G_i(0) < \bar{x}_0 < \frac{\Phi_0}{\Psi_0} \quad (72)$$

Hence, the positive solution  $\bar{x}_0$  of (70a) exists if the following inequality is satisfied

$$\min_{i \in \mathcal{J}} G_i(0) < \frac{\Phi_0}{\Psi_0} \quad (73)$$



The relation (72) may be combined with (67) in a more sharper form

$$\max_{i \in \mathcal{I}} G_i(0) < \bar{x}_0 < \frac{\Phi_0}{\Psi_0} \quad (74)$$

It can serve as a condition for positive solutions of stationary concentrations  $\bar{x}_i$  (for  $i \in \mathcal{I}$ ) as well as  $\bar{x}_0$ . If this condition is satisfied, then the stationary state  $S_{\mathcal{I}}$  was properly selected, in the opposite case we say that this state does not exist.

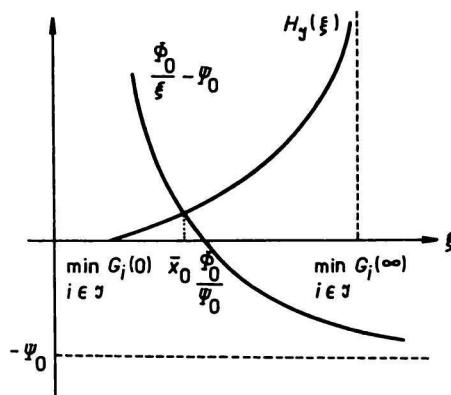


Fig. 9. Graphical solution of the nonlinear eqn (70a), the intersection of the lines determines the positive solution  $\bar{x}_0$  if the condition (72) is satisfied.

The Jacobi matrix of the system (65a, 65b) evaluated at the stationary state  $S_{\mathcal{I}}$  is

$$\mathbf{J}(S_{\mathcal{I}}) = \begin{pmatrix} -\frac{\Phi_0}{\bar{x}_0} & -a_j \bar{x}_0 & -a_j \bar{x}_0 \\ a_i \bar{x}_0 & -\delta_{ij} \bar{x}_i f'_i(\bar{x}_i) & 0 \\ 0 & 0 & \delta_{ij}(a_i \bar{x}_0 - f_i(0)) \end{pmatrix} \begin{matrix} i=0 \\ i \in \mathcal{I} \\ i \in \mathcal{I}' \end{matrix} \quad (75)$$

$j=0 \qquad j \in \mathcal{I} \qquad j \in \mathcal{I}'$

Similarly as in the previous section (II. 3) this matrix is of triangle-block structure. The right-down diagonal block (for  $i, j \in \mathcal{I}'$ ) has negative eigenvalues if its entries are negative

$$\bar{x}_0 < \min_{i \in \mathcal{I}'} G_i(0) \quad (76a)$$

The eigenvalues of the left-up block (for  $i, j \in \mathcal{I} \cup \{0\}$ ) are determined as roots of the equation

$$\sum_{i \in \mathcal{I}} \frac{a_i^2 \bar{x}_i \bar{x}_0}{\bar{x}_i f'_i(\bar{x}_i) + \lambda} = -\frac{\Phi_0}{\bar{x}_0} - \lambda \quad (76b)$$

Recalling that  $f'_i(\bar{x}_i) > 0$ , for each  $i \in \mathcal{J}$ , we can simply demonstrate that the roots of (76b) have always negative real parts. It means that asymptotical stability of the stationary state  $S_{\mathcal{J}}$  is fully determined by the condition (76a), by its combination with the left inequality (74) (for  $S_{\mathcal{J}}$  to be existing) we get

$$\max_{i \in \mathcal{J}} G_i(0) < \bar{x}_0 < \min_{i \in \mathcal{J}'} G_i(0) \quad (77)$$

From the above considerations we have obtained that a stationary state  $S_{\mathcal{J}}$  (where the subset  $\mathcal{J}$  was properly selected) is asymptotically stable only if the stationary substrate concentration  $\bar{x}_0$  is ranged by (77); the question which stationary state will win depends on the initial concentrations, whether they are placed inside of attractivity domain of  $S_{\mathcal{J}}$ .

### 5. Summary of results

We have studied different models of selection process between replicators based on the general equations (2a, 2b). The following three quite distinct behaviours of the replicator system were obtained:

1. The functions  $f_i(x_i)$  and  $g_i(x_i)$  are positively constant (Section II. 1), then we have proved that the replicator system is owned by the only asymptotically stable stationary state  $S_p$ , all remaining stationary states  $\{S_q; q \neq p\}$  are unstable. It means that the replicator system simulates the so-called **Darwinian selection** [21], only that replicator  $X_p$  will survive which is "best-fitted" for the selection process, *i.e.* its ratio  $a_p/b_p$  composed of replicating and decaying rate constants, respectively, is the largest, see eqn (17); all other replicators  $\{X_q; q \neq p\}$  are becoming extinct as  $t \rightarrow \infty$ .

2. The functions  $f_i(x_i)$  linearly depend on the replicator concentrations  $x_i$  and the functions  $g_i(x_i)$  are constant, see eqn (26). It was proved that for this model of selection from the set of stationary states  $\{S_{\mathcal{J}}\}$  those states are asymptotically stable that are containing only one nonvanishing replicator (*i.e.*  $|\mathcal{J}| = 1$ ); all stationary states  $S_{\mathcal{J}}$ , where  $|\mathcal{J}| \geq 2$ , are unstable. The positive orthant of phase space can be divided into nonoverlapping domains of attractivity of individual asymptotically stable stationary states. If an initial state belongs to a given domain, then whole trajectory of the system is situated at the domain and will end at the corresponding stationary state as  $t \rightarrow \infty$ . It means that in this model a Darwinian selection does not exist. The time evolution of the system is fully predetermined by its initial state, or in other words, the only replicator asymptotically surviving as  $t \rightarrow \infty$  is sharply designed by the initial conditions. The obtained solution is of a "once-for-ever" type, there is no chance for other replicators (asymptotically vanishing) owing to small perturbations (or fluctua-

tions) of their concentrations to survive with respect to the former already survived replicator. Such an event needs a "giant" fluctuation of concentrations the fact of which is highly physically improbable.

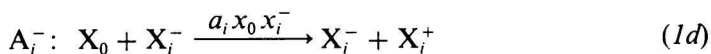
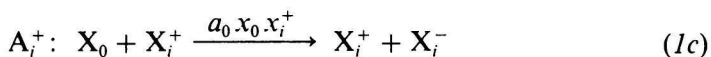
3. The Michaelis—Menten kinetics model (Section II. 3) or the model with intrareplicator antagonism (Section II. 4) give almost the same qualitative features of the studied replicator system. In the present case several replicators may survive simultaneously whereas the remaining ones are becoming extinct as  $t \rightarrow \infty$ . Theoretically, a set  $\{S_s\}$  of simultaneously asymptotically stable stationary states can be composed of more than one state, therefore, that one will win in which attractivity domain of the initial state is placed. The conditions (61) or (77) are usually very sharp, they are fulfilled only for one index subset  $\mathcal{J}$ , hence the system contains only one asymptotically stable stationary state  $S_{\mathcal{J}}$ .

The qualitative features of the studied system are very sensitive to the form of rate functions  $f_i(x_i)$  and  $g_i(x_i)$ . The genuine Darwinian selection is simulated only by the model (Section II. 1) in which the above functions were kept positive and constant.

### III. Selection of complementary replicators

The Ebeling's model of selection (Section II. 1) will be now generalized for a system composed of the so-called complementary replicators (a replicator is replicated to its complementary counterpart, see below). The problem of selection of complementary replicators was studied by *Eigen* [1] in the framework of his "constant population" approach, see also [4, 7].

Let us consider a system of a substrate  $X_0$  and two sets of complementary replicators  $X_1^+, X_2^+, \dots, X_n^+$  and  $X_1^-, X_2^-, \dots, X_n^-$ . The pattern of chemical reactions (II. 1a—1d) is specified as follows



for  $i = 1, 2, \dots, n$ . We have assumed, for simplicity, that the rate constants of replication and decay for couples of complementary replicators are the same. The corresponding system of differential equations is (cf. eqns (II. 4a—4b))

$$\dot{x}_0 = \Phi_0 - x_0 \left[ \Psi_0 + \sum_{i=1}^n a_i (x_i^+ + x_i^-) \right] \quad (2a)$$

$$\dot{x}_i^+ = a_i x_0 x_i^- - b_i x_i^+ \quad (2b)$$

$$\dot{x}_i^- = a_i x_0 x_i^+ - b_i x_i^- \quad (2c)$$

for  $i = 1, 2, \dots, n$ . Let us introduce new dynamical variables for replicators

$$u_i = x_i^+ + x_i^- \quad (3a)$$

$$v_i = x_i^+ - x_i^- \quad (3b)$$

then the differential equations (2a—2c) are

$$\dot{x}_0 = \Phi_0 - x_0 \left( \Psi_0 + \sum_{i=1}^n a_i u_i \right) \quad (4a)$$

$$\dot{u}_i = u_i (a_i x_0 - b_i) \quad (4b)$$

$$\dot{v}_i = v_i (a_i x_0 + b_i) \quad (4c)$$

The stationary states of the system are of the following two kinds:

**1st kind.** The stationary concentration  $\bar{x}_0$  is positive whereas stationary values of  $\bar{u}_1, \bar{u}_2, \dots, \bar{u}_n$  and  $\bar{v}_1, \bar{v}_2, \dots, \bar{v}_n$  are vanishing

$$\bar{x}_0 = \frac{\Phi_0}{\Psi_0} \quad (5a)$$

$$\bar{u}_i = \bar{v}_i = 0 \quad (i = 1, 2, \dots, n) \quad (5b)$$

This stationary state will be denoted by  $S_0$ .

**2nd kind.** For preselected  $1 \leq p \leq n$  stationary concentrations  $\bar{x}_0, \bar{x}_p^+$  and  $\bar{x}_p^-$  are positive whereas all others are vanishing, i.e.

$$\bar{x}_0 = \frac{b_p}{a_p} \quad (6a)$$

$$\bar{u}_i = \delta_{ip} \left( \frac{\Phi_0}{b_p} - \frac{\Psi_0}{a_p} \right) \quad (6b)$$

$$\bar{v}_i = 0 \quad (6c)$$

for  $i = 1, 2, \dots, n$ . The stationary value  $\bar{u}_p$  should be positive, hence an analogue of eqn (II. 9) must be fulfilled

$$\frac{\Psi_0}{\Phi_0} < \frac{a_p}{b_p} \quad (7)$$

This stationary state will be denoted by  $S_p$ .

The Jacobi matrix of (4a—4c) evaluated at stationary states  $S_0$  and  $S_p$  (where  $1 \leq p \leq n$ ) is

$$\mathbf{J}(S_0) = \begin{pmatrix} -\Psi_0 & 0 & 0 \\ 0 & \text{dg}\left(\frac{\Phi_0}{\Psi_0} \mathbf{a} - \mathbf{b}\right) & 0 \\ 0 & 0 & -\text{dg}\left(\frac{\Phi_0}{\Psi_0} \mathbf{a} + \mathbf{b}\right) \end{pmatrix} \quad (8a)$$

$$\mathbf{J}(S_p) = \begin{pmatrix} 0 & -\frac{b_p}{a_p} \mathbf{a}^T & 0 \\ \left(\Phi_0 \frac{a_p}{b_p} - \Psi_0\right) \mathbf{e}_p & \text{dg}\left(\frac{b_p}{a_p} \mathbf{a} - \mathbf{b}\right) & 0 \\ 0 & 0 & -\text{dg}\left(\frac{b_p}{a_p} \mathbf{a} + \mathbf{b}\right) \end{pmatrix} \quad (8b)$$

The Jacobi matrix  $\mathbf{J}(S_0)$  is of a triangular form, its eigenvalues are its diagonal elements, all its eigenvalues are negative if the following condition is satisfied (see eqn (II. 13))

$$\frac{\Psi_0}{\Phi_0} > \max_{1 \leq i \leq n} \frac{a_i}{b_i} \quad (9)$$

The stationary state  $S_0$  is asymptotically stable if the above inequality is fulfilled.

The Jacobi matrix  $\mathbf{J}(S_p)$  has block-diagonal structure, its right-down block is diagonal with negative entries. The left-up block is formally identical with the Jacobi matrix (II. 16), therefore the stationary state  $S_p$  is asymptotically stable if an analogue of eqn (II. 17b) is satisfied

$$\frac{\Phi_0}{\Psi_0} < \frac{a_p}{b_p} = \max_{1 \leq i \leq n} \frac{a_i}{b_i} \quad (10)$$

In an analogous way as was done for Ebeling's model (see Section II. 1) we have proved that among stationary states  $S_0, S_1, \dots, S_n$  either  $S_0$ , if (7) is satisfied, or  $S_p$  state (where  $1 \leq p \leq n$ ), if (10) is satisfied, is asymptotically stable; since these conditions are mutually excluding the system of complementary replica-

tors has the only asymptotically stable stationary state  $S_0$  or  $S_p$ . Returning to the original concentration variables, the stationary concentrations of  $S_p$  are

$$\bar{x}_0 = \frac{b_p}{a_p} \quad (11a)$$

$$\bar{x}_i^+ = \bar{x}_i^- = \frac{1}{2} \delta_{ip} \left( \frac{\Phi_0}{b_p} - \frac{\Psi_0}{a_p} \right) \quad (i = 1, 2, \dots, n) \quad (11b)$$

Hence, we have proved, the generalization of the original Ebeling's model by the concept of complementary replicators did not introduce new qualitative features of the selection process.

#### IV Comparison with Eigen's theory

The *Eigen* phenomenological equations for the selection are [1]

$$\dot{y}_i = y_i(w_i - \Phi) \quad (1a)$$

$$\Phi = \frac{1}{c} \sum_{i=1}^n w_i y_i \quad (1b)$$

where  $y_i$ 's are replicator concentrations constrained by the so-called "constant population" condition

$$\sum_{i=1}^n y_i = c = \text{const} \quad (2)$$

and  $w_i$ 's are decomposition rate constants.

It was demonstrated that in the framework of Eigen's selection model the replicator system manifests typical selection properties, to survival of a replicator  $X_p$  and to the extinction of all its competitors  $X_1, \dots, X_{p-1}, X_{p+1}, \dots, X_n$  if the index  $p$  is determined by

$$w_p = \max_{1 \leq i \leq n} w_i \quad (3)$$

We focus our attention on the problem of the relation between the Eigen approach and the theory presented in this communication. The differential equations (II. 18a—18b) of Ebeling's model can be rewritten in the form

$$\dot{y}_0 = -y_0^2 \left( \Phi_0 y_0 - \sum_{i=1}^n a_i y_i - \Psi_0 \right) \quad (4a)$$

$$\dot{y}_i = y_i(a_i - y_0 b_i) \quad (i = 1, 2, \dots, n) \quad (4b)$$

In order to relate these equations with the Eigen system (1a—1b) we put  $\Psi_0 = 0$  and  $b_i = 1$  (for  $i = 1, 2, \dots, n$ ), we get

$$\dot{y}_0 = -y_0^2 \left( \Phi_0 y_0 - \sum_{i=1}^n a_i y_i \right) \quad (5a)$$

$$\dot{y}_i = y_i (a_i - y_0) \quad (i = 1, 2, \dots, n) \quad (5b)$$

Let us postulate that the concentration  $y_0$  is determined by the condition  $\dot{y}_1 + \dot{y}_2 + \dots + \dot{y}_n = 0$ , then from (5b) we get

$$y_0 = \left( \sum_{i=1}^n y_i \right)^{-1} \sum_{i=1}^n a_i y_i \quad (6)$$

The time derivative of  $y_0$  determined by the above formula is

$$\dot{y}_0 = \left( \sum_{i=1}^n y_i \right)^{-1} \sum_{i=1}^n y_i (a_i - y_0)^2 \geq 0 \quad (7)$$

This time derivative  $\dot{y}_0$  also satisfies the relation (5a), it determines uniquely the inflow  $\Phi_0$  of  $X_0$  (now as a time-dependent function)

$$\Phi_0 = \frac{1}{y_0} + \sum_{i=1}^n y_i - \frac{1}{y_0^3} \frac{\sum_{i=1}^n a_i^2 y_i}{\sum_{i=1}^n y_i} \quad (8)$$

where  $y_0$  is determined by (6). We can see that the present theory reduces to the Eigen approach if (i) all rate constants  $b_i$  are equal and (ii) the inflow  $\Phi_0$  is a time-dependent function controlled by actual concentrations of replicators, see eqn (8).

## V Conclusion

It was demonstrated that in the system of replicators the selection processes are very sensitive to actual form of rate functions. The genuine Darwinian selection among replicators exists if the rate functions are positive and constant. Another type of rate functions gives rise to the processes that are not Darwinian, for example, the resulting asymptotical state is predetermined by initial concentrations. This very serious conclusion considerably increases the potential applicability of Ebeling's approach for theoretical studies of selection processes on molecular level. We have introduced in the standard model a process of the substrate decomposition, it removes the possible "catastrophic" state of original Ebeling's model where all replicators are becoming extinct whereas the substrate

is linearly increasing to infinity. The considered model was compared with the Eigen's model of selection based on the "constant population" constraint; we have demonstrated that if the external inflow of substrate is a time-controlled function, then we have arrived at Eigen's phenomenological equations.

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