

A SIMULATION STUDY ON THE CHEMOTON

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In this paper properties and dynamical behaviour of a theoretical biological model, the chemoton are discussed. The chemoton features the general, common properties of the unicellular living beings. Since the reaction-kinetical function of the chemoton is governed by a set of nonlinear differential equations, the study of its dynamical behaviour required computer simulation. This was carried out by using CSMP programs. The results proved that the model is capable of stable functioning, growing and multiplication.

1. INTRODUCTION

The chemoton is a chemical supersystem which is set up by coupled subsystems fulfilling the criteria characteristic of life. Its abstract model was given by Gánti^{1,2} and he gave its stoichiometric description by a recently elaborated, so called cycle-stoichiometry³⁻⁵. The kinetic description was developed by Békés and his colleagues⁶⁻⁸.

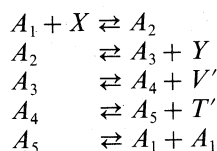
In this paper we examined whether the abstract model of the chemoton can work on an abstract level; under what kind of kinetic conditions is it active; furthermore, whether it fulfils the criteria of a living system, namely that of inherent stability and metabolism. The capacity for adaptation was studied in case of changing environment. Finally, possible variations of inner organisation of the chemoton were considered from the point of view of survival.

2. THE CHEMOTON MODEL

The chemoton works consuming high energy nutrient taken up from its environment and producing low energy waste material. Its functioning is realised in chemical and physical reactions by changing the quantity of its inner materials. Here we assume that there is enough solvent (e.g. water) available, and that the membrane of the chemoton is permeable for the solvent, the nutrient, and for the waste material, but not for the inner materials. The chemoton consists of three functionally dependent, self-reproducing subsystems: The autocatalytic chemical cycle, the template polymerisation and the membrane subsystem enclosing the other two subsystems.

2.1. The Autocatalytic Chemical Cycle

This subsystem performs controlled production of its inner materials by transforming the external materials. The cycle consumes high energy nutrient (X), produces precursors of the template and the membrane (V' and T' , respectively) and gives down low energy waste material (Y). Let us denote the inner materials of the chemical cycle with A_1, \dots, A_5 . During a single cycle for any inner material molecule, A_2 , one X is consumed and one of each Y, V', T', A_1 molecule is produced. The notation of the chemical reactions is as follows:

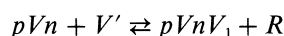


The chemical reactions are assumed to be reversible, i.e. they might be carried out in both directions. Let the reaction rate constants be $k_1, k'_1, \dots, k_5, k'_5$, respectively (the prime marks the reaction rate constants for the backward reactions). Let us transform the assumption that the energy content of X is greater than that of the materials originating from it, into an assumption concerning the reaction rate constants: $k_i \geq k'_i$. Namely, the constants k_i meaning the consumption of X should be greater than the constants k'_i meaning the production of X . The materials V' and T' are produced by the autocatalytic cycle for the template subsystem and the membrane subsystem, respectively. We assume that as large amount of nutrient X is available, and as large amount of waste material Y can be absorbed by the environment of the chemoton that their concentration (mole per volume) can be regarded as constant.

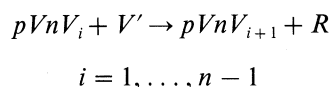
2.2. Template Subsystem

Here, analogously to the nucleic acids, there are polymer fibres denoted by pVn , i.e. homopolymers consisting of n pieces of monomers V . Their replication in the chemoton takes place by a polycondensation process in the course of which the condensation product R is decomposed from V' , and the molecules V form polymer fibres on the sample pVn 's. However,² the process can start only at a certain threshold concentration of V' , denoted by $[V']^*$. The notation of the process as chemical reactions is:

chain initiation step:



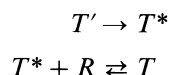
chain propagation step:



Let the reaction rate constants of the chain initiation be k_6 , k'_6 , and that of the chain propagation k_7 . The latter reaction is irreversible. k_6 and k'_6 are equal to zero as long as $[V'] < [V']^*$ (square brackets denote the concentration of the given molecule). This assumption is necessary, since high $[V']$ is needed for the polymerizing process.

2.3. Membrane Subsystem

This subsystem consists of a membrane separating the other two subsystems from the environment, and a short reaction path producing the membrane monomer molecule, T . This subsystem is given molecules T' and R by the other two subsystems. Molecule T' is transformed irreversibly to such a T^* that, reacting with R , it gives T :



Let the reaction rate constants be k_8 , k_9 , k'_9 , respectively. The reaction $T' \rightarrow T$ should be assumed here, since otherwise in the case of certain k_i and k'_i the accumulated T' might make the autocatalytic cycle slow down still before R , originated from the pVn synthesis, might extract it. According to Singer and Nicolson⁹ the monomers forming the membrane can be built into the bimolecular membrane spontaneously, and at a given monomer concentration the speed of this process is proportional to the surface area. Let the proportionality factor be k_{10} . The membrane is permeable for X , Y , and the solvent, as

it was mentioned above. The membrane is spherical in its normal position, but due to changes in the osmotic pressure it may be elongated. We define the surface of the chemoton (S) as the surface of the membrane, and the volume of the chemoton (Q) as the volume enclosed by the membrane. The concentrations are calculated from this volume.

2.4. The Supersystem

The functioning of the chemoton, as a supersystem consisting of the three subsystems mentioned above (Fig. 1) can be realised as follows: In the beginning there are no T and R molecules in the chemoton. As $[T]$ and $[R]$ are zero, the membrane, and in this way the volume of the chemoton, cannot grow. The autocatalytic cycle consuming the nutrient of constant concentration produces its inner materials and the molecules Y , V' , and T' in a controlled way. The concentration of V' , initially less than $[V']^*$, grows gradually. The inner materials keep increasing with accompanying elevation of the osmotic pressure. Hence the chemoton retains its spherical shape, at least until $[V'] < [V']^*$. Thus the concentrations can be computed from the volume Q_0 belonging to the initial time t_0 . When $[V'] \geq [V']^*$ the chain initiation step and the subsequent chain propagation step take place. The molecule R being released during this process react with the accumulated T^* and produces T that is built then into the membrane. This assures that exactly as many T are generated as many V are built into the pVn 's. The initial membrane consists of as many molecules T , as many V are needed to replicate the pVn 's. Therefore, after the replication of the templates the membrane surface area will be doubled too. In the case of spheres a volume of $2^{3/2} Q_0$ belongs to the doubled surface area. Since the number of inner material molecules have been doubled, the osmotic pressure sinks under the initial pressure. Assuming an equilibrium of the initial pressure, the membrane invaginates and the chemoton bipartitions.¹⁰ During modelling it was supposed that both descendants share the inner materials equally. In all cases we followed the behaviour of one descendant only.

METHODS

The dynamic behaviour of the chemoton was studied by kinetical differential equations. The set of differential equations used in our simulations is as follows:

$$\begin{aligned}
 d[A_1]/dt &= 2(k_5[A_5] - k'_5[A_1][A_1]) - k_1[A_1][X] + k'_1[A_2] \\
 d[A_2]/dt &= k_1[A_1][X] - k'_1[A_2] - k_2[A_2] + k'_2[A_3][Y] \\
 d[A_3]/dt &= k_2[A_2] - k'_2[A_3][Y] - k_3[A_3] + k'_3[A_4][V'] \\
 d[A_4]/dt &= k_3[A_3] - k'_3[A_4][V'] - k_4[A_4] + k'_4[A_5][T'] \\
 d[A_5]/dt &= k_4[A_4] - k'_4[A_5][T'] - k_5[A_5] + k'_5[A_1][A_1] \\
 d[V']/dt &= k_3[A_3] - k'_3[A_4][V'] + k'_6[V^+][R] - k_6[V'](pVn - [V^+]) - k_7[V']pVn \\
 d[T']/dt &= k_4[A_4] - k'_4[A_5][T'] - k_8[T'] \\
 d[T]/dt &= k_9[T^*][R] - k'_9[T] - k_{10}[T]S/Q \\
 d[R]/dt &= k_6[V'](pVn - [V^+]) + k_7[V']pVn - k_6[V^+][R] - k_9[T^*][R] + k'_9[T] \\
 d[V^+]/dt &= k_6[V'](pVn - [V^+]) + k_7[V']pVn - k'_6[V^+][R] \\
 d[T^*]/dt &= k_8[T'] - k_9[T^*][R] + k'_9[T] \\
 dS/dt &= k_{10}[T]S/n
 \end{aligned}$$

Here n denotes the length of the templates (the number of V in a pVn) and V^+ is an auxiliary variable used to model the quantity of V' consumed to build new pVn molecules. This set of differential equations is non-linear, e.g. the equation determining the derivative of A_1 contains a quadratic

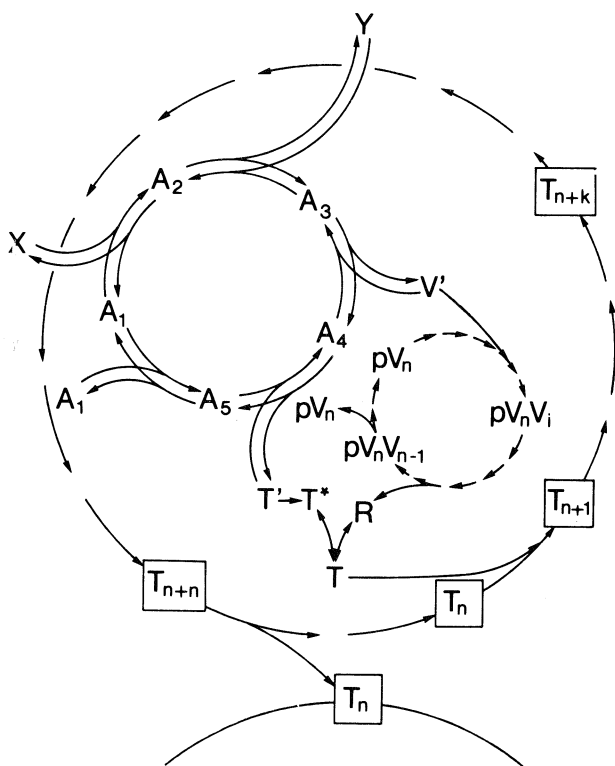


FIGURE 1 The reaction-network of the chemoton. A_1, A_2, \dots, A_5 form the autocatalytic cycle that consumes X and gives down Y . The cycle produces the row-materials for the template and the membrane subsystem, V' and T' , respectively. The duplication of the templates are denoted by $pV_n V_{n-1} + V' \rightarrow pV_n + pV_n + R$ and the duplication of the membrane by $T_{n+n} \rightarrow T_n + T_n$.

coefficient, $k'_5 [A_1][A_1]$. Since the analytical solution of this system is unknown, numerical procedures were used. Concentrations were computed from the actual volume determined for each integration step.

The template synthesis was modelled in the following way: The reactions of chain initiation and chain propagation were interpreted by the corresponding differential equations. The reaction rate constants of the chain initiation were equal to zero for $[V'] < [V']^*$, and also after initiation. In the same way, $k_7 = 0$ until the initiation terminated, and after the templates were replicated. The current volume was constant for $[V'] < [V']^*$, then it was calculated with the value of volume determined by the equilibrium osmotic pressure. Its value should not have been greater than the volume of the sphere belonging to the current surface. We assumed that when the surface area doubles itself, the membrane invaginates and the chemoton is divided automatically.^{1,2} This process was interpreted by halving the quantity of all inner materials. Then the integration of the set of differential equations was resumed with the received new initial values. The reaction rate constants, chosen to possibly speed up cycle functioning, were as in the Table I, except in study 4.2, where just the effect of varying reaction rate constants was investigated.

The computer programs were written in CSMP computer language, and the fourth-order fixed-step Runge-Kutta method was used to integrate the differential equations.

4. RESULTS

4.1. The Basic Model

The basic model of the chemoton is that interpreted by the assumptions and reaction rate constants mentioned above, using the initial values given in the

TABLE I
Reaction rate constants of the basic model

$k_1 = 2.0$	$k'_1 = 0.1$
$k_2 = 100.0$	$k'_2 = 0.1$
$k_3 = 100.0$	$k'_3 = 0.1$
$k_4 = 100.0$	$k'_4 = 0.1$
$k_5 = 10.0$	$k'_5 = 0.1$
$k_6 = 10.0$	$k'_6 = 1.0$
$k_7 = 10.0$	
$k_8 = 10.0$	
$k_9 = 10.0$	$k'_9 = 0.1$
$k_{10} = 10.0$	

Table II. The length of the templates is uniformly $n = 25$. These values are slightly different from the initial concentrations belonging to the stable functioning, and should be understood as attomoles. The dynamic behaviour of the basic model is illustrated in Fig. 2, where the time course of concentrations of inner materials are represented. The chemoton increases the quantity of its inner materials in such a way that the rates of A_i 's are nearly constant [Fig. 2n]. The concentrations of inner materials grow evenly until $[V'] < [V']^*$. Then the concentrations generally decrease, because the membrane and thus the volume of the chemoton increases. Finally, the concentrations increase for a short time, as the increase of volume is slower than that of the quantity of inner materials. The multiplication is indicated by a fall of concentrations. Six perfected divisions can be seen on the Figs. 2a–2r; their generation times, defined by the time passed between two consecutive divisions, are in this case 0.33, 0.31, 0.29, 0.29, 0.29, 0.29.

The generation time of the other models were stabilised similarly. The generation time of the stabilised functioning of the basic model is $t^* = 0.29$. The molecules R and T exist only temporarily, since they are consumed up quickly by the membrane. One-third of the generation time is needed to replicate the templates and the membrane. It can be stated that the model of this chemical supersystem can function in a stable way, and it stimulates metabolism as well.

4.2. Non-functioning Chemoton

This model differs from the basic one only in that $k_i = k'_i = 1.0$ ($i = 1, \dots, 5$). Here $[V']$ can never reach $[V']^*$, and a chemical equilibrium has developed itself [Fig. 3]. This non-functioning could take place since our basic assumption, namely that the energy content of X is greater than that of the products originated from it, is not fulfilled.

4.3. Model without V' , T' and T^*

When the initial concentrations of V' , T' , and T^* are

TABLE II
Initial values of concentrations of the basic model

$[A_1] = 0.32$	$[T^*] = 160.7$
$[A_2] = 2.49$	$[T] = 0.0$
$[A_3] = 4.93$	$[R] = 0.0$
$[A_4] = 1.94$	$[X] = 100.0/Q_0$
$[A_5] = 34.34$	$[Y] = 0.1/Q_0$
$[V'] = 48.77$	$[V']^* = 35.0/Q_0$
$[T'] = 18.68$	$S = 1.0$
$[V^+] = 0.0$	$[pVn] = 1.0/Q_0$

zero, the transient phase of the model becomes longer than that of the basic one, but the same stable functioning is retained. The generation times are: 0.37, 0.28, 0.29, 0.29, 0.28, 0.29 (Fig. 4).

4.4. Chemoton Containing Only A_1

This model differs from the previous one (4.3.) only in the following: $[A_i] = 0$, $i = 2, \dots, 5$. The transient phase is even longer, but the stable functioning belonging to the basic model is reached again. The generation times are: 1.12, 0.31, 0.29 (Fig. 5). These results show that the composition and functioning of the chemoton is independent of the initial state, and after a transient phase a functioning which was characteristic of the chemoton model 4.1. is reached.

4.5. Models with Different Values of $[V']^*$

The following relationship between $[V']^*$ and t^* , the generation time of the stable functioning, was attained:

$[V']^*$	t^*
0.	0.28
20.	0.28
40.	0.30
60.	0.30
80.	0.31
100.	0.33

Since high concentration of V' makes the chemical cycle functioning slower, longer generation times are needed to reach higher $[V']^*$.

4.6. Modified Reaction Networks

We investigated how the sequence of the molecules Y , V' , and T' joined to the chemical cycle of the basic model influences t^* . The reaction rate constants were the same: $k_2 = k_3 = k_4$, and $k'_2 = k'_3 = k'_4$. In contrast to the basic model, here the following autocatalytic cycle belongs to the V' , T' , and Y sequence:

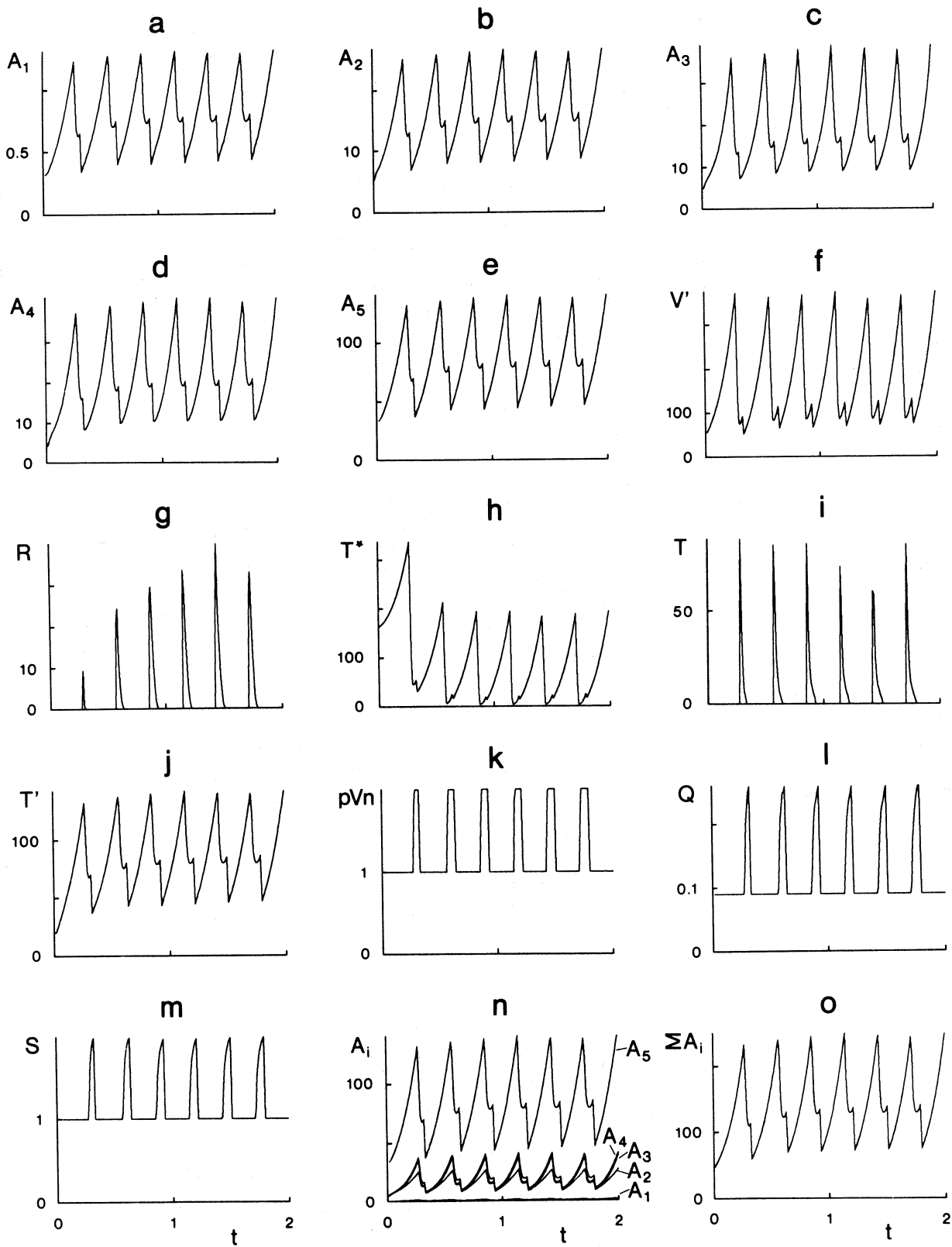


FIGURE 2 Changes of concentrations of the inner materials of the basic model against time. See the initial concentrations in the Table II.

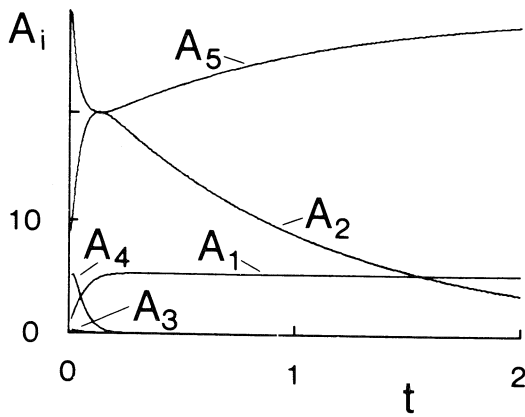
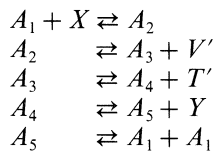


FIGURE 3 The concentration of the inner materials of the autocatalytic cycle for the non-functioning case.



The relationship between the sequence and t^* is the following:

sequence	t^*
V', T', Y	0.27
T', V', Y	0.27
V', Y, T'	0.28
Y, V', T'	0.29
Y, T', V'	0.30
T', Y, V'	0.30

It can be seen that when Y is the last in the sequence, t^* is the least; and when V' is the last, t^* is the greatest. This can be explained by that in the case when V' is the last, the $[V'] \geq [V']^*$ concentration could be formed later. On the other hand, when Y

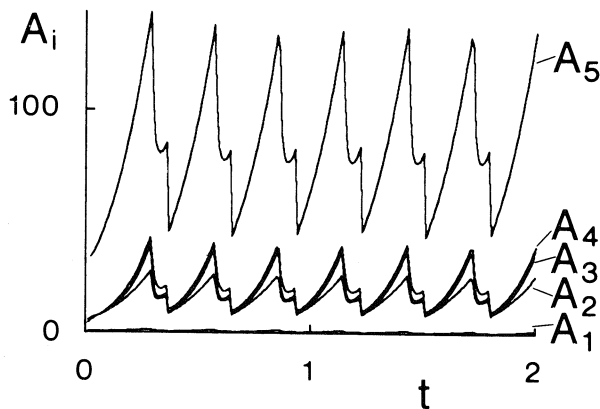


FIGURE 4 The basic model in the case of $V' = T' = T^* = 0$. Note that the transient phase is longer, but the stable functioning reached is identical with the one on the figure 2.n.

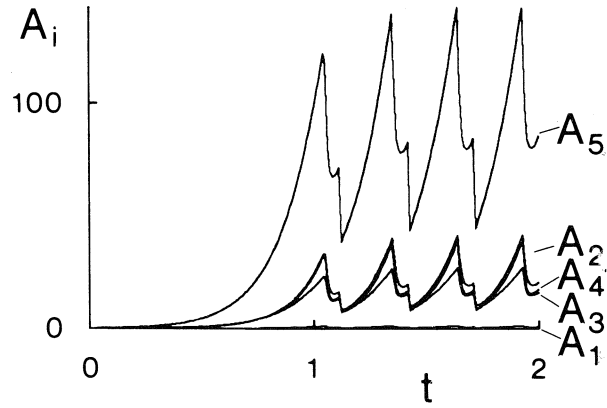


FIGURE 5 The transient phase of the chemoton containing only A_1 .

is the last a relatively quick reaction can take place preceding the autocatalytic reaction step, and this makes the cycle functioning faster.

4.7. Effect of Decreased Concentration of Nutrient

The model considered now is the basic one, with initial values belonging to the state of stable functioning immediately after division. The concentration of the nutrient is decreased from $100/Q_0$ to $1/Q_0$. The generation time of the stable functioning is $t^* = 0.47$, in contrast with the value of 0.29 of the basic model. This study is to disclose the capacity of adaptation of the chemoton to its environment. Since the rate of reaction is proportional to the product of concentrations ($k_1[A_1][X]$), one expects that the decrease in the concentration of the nutrient by two order of magnitude would result in a similar increase of the generation time. However, the generation time increased only by fifty per cent. The concentration relations of the chemoton were transformed so that the concentration of A_1 , the inner material of the critical reaction step, increased fifty

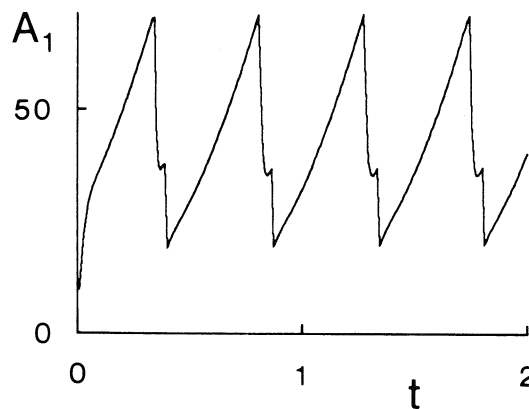


FIGURE 6 The effect of decreasing in nutrient concentration.

times (Fig. 6), thus the product of concentrations of the two partners changed just a little.

4.8. Decrease in Nutrient Concentration in Chemotons Containing Templates of Different Length

The experiment described in 4.7. was repeated in chemotons containing templates of different length. The following values were obtained for the generation times evolved:

the length of the templates	t_1	t_2
10.	0.27	0.80
20.	0.28	0.54
30.	0.30	0.44
40.	0.32	0.43
50.	0.35	0.43

Here t_1 and t_2 denote the generation times of stable functioning before and after the decrease in nutrient concentration. It can be stated that the chemoton containing longer templates can more effectively compensate for the decrease in nutrient concentration. This could indicate a selection factor that could have helped the chemotons containing longer templates in surviving during prebiological evolution.

5. CONCLUSION

The model of chemoton studied in this paper was shown to be capable of stable functioning between wide limits of concentration: under given conditions it produces inner materials in a controlled way, consuming the nutritive material; it grows and multiplies itself. On the other hand, with certain values of the reaction rate constants the model reached chemical equilibrium, and so it was not able to grow and multiply.

The basic model starting with any initial concentration reached the state of stable functioning after

a transient phase. The generation time of the stable functioning was proportional to the threshold concentration of the template polymerisation of the model—when the other parameters were kept constant. The chemoton was also capable of compensating a harmful environmental effect (the decrease in the concentration of the nutrient) the more the longer templates were supposed in the system. On the basis of these simulation studies it can be stated that the chemoton fulfills the following criteria of life: metabolism and inherent stability.

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