Dynamical Systems under Constant Organization. III. Cooperative and Competitive Behavior of Hypercycles

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Qualitative analysis for a system of differential equations playing an important role in a theory of molecular self-organization.

1. INTRODUCTION

This note deals with the ordinary differential equation

$$\dot{x}_i = x_i(k_i x_{i-1} - \Phi) \qquad i = 1,...,n, \tag{1.1}$$

where $k_i > 0$ are constants, indices are counted mod n and

$$\Phi = \sum_{j=1}^{n} k_j x_j x_{j-1} \tag{1.2}$$

More precisely, it considers the restriction of (1.1) to the (invariant) simplex S_n defined by

$$x_i \geqslant 0 \qquad \text{and} \qquad \sum_{i=1}^{n} x_i = 1. \tag{1.3}$$

Equation (1.1) plays a central role in the recent theory of self-organization of biological macromolecules which focuses on the notion of the catalytic hypercycle ([1], [2]). We interpret x_i as (relative) concentration of the species i. These species form a cycle: the growth of species i is catalysed by its "predecessor" $i - 1$ through reactions of Michaelis–Menten type. Φ acts as "selection pressure" by keeping the total concentration fixed.

There exists a unique fixed point C in int S_n, given by the relations $k_i x_{i-1} = k_j x_{j-1}$ together with (1.3). It is shown in [3] that if all k_i are equal, then C is a sink for $n = 2$ and 3, no longer a sink but still asymptotically stable for $n = 4$ and unstable for $n \geqslant 5$.

In Section 2 of this paper we show that (1.1) is cooperative in the sense that no species goes extinct, or more precisely that bd S_n is a repeller. The ω-limits of points in int S_n may be limit cycles or perhaps strange attractors. But as we show in Section 3, the only attractor for a "short hypercycle" ($n \leqslant 3$) is the fixed point C. Actually, we prove a more general result on internal equilibration which allows us to show that if several short hypercycles compete (under the constraint of constant total concentration), then all but one of them will vanish. In Section 4, we discuss the biological relevance of this model for the formation and selection of hypercycles and show how it can account for the "once for ever" decisions which occured at many steps of the evolution of selfreproductive biopolymers.

2. The Hypercycle is Cooperative

For $1 \leqslant i, j \leqslant n$ and $x_j > 0$ we have

$$\left(\frac{x_i}{x_j}\right)^{\cdot} = \left(\frac{x_i}{x_j}\right)(k_i x_{i-1} - k_j x_{j-1}) \tag{2.1}$$

The boundary of S_n is invariant, and contains subfaces of fixed points. Let F denote this set of fixed points.

LEMMA 1. *If* $\mathbf{x} \in \mathrm{bd}\, S_n$, *the ω-limit of $\mathbf{x}$ is a subset of F.*

Proof. Let $\mathbf{x}$ be on the boundary, that is, on some face of S_n. Thus assume $x_{i-1} = 0$, $x_i > 0$, $x_{i+1} > 0,..., x_{i+k} > 0$ and $x_{i+k+1} = 0$. We shall show by induction that $x_i \to 0$, $x_{i+1} \to 0,..., x_{i+k-1} \to 0$.

(1) $x_i \to 0$ and x_i/x_{i+1} converges monotonically to some limit v_i. Indeed, since $x_{i-1} = 0$, one has $\dot{x}_i \leqslant 0$, and so $x_i \downarrow h$ for some $h \geqslant 0$. Also, by (2.1)

$$\left(\frac{x_i}{x_{i+1}}\right)^{\cdot} = -k_{i+1}x_i \left(\frac{x_i}{x_{i+1}}\right) < 0$$

and hence $x_i/x_{i+1} \downarrow v_i$. If h were strictly positive, x_i/x_{i+1} would decrease at least exponentially with factor $-k_{i+1}h$, which implies $v_i = 0$, which in turn implies $h = 0$.

(2) $x_{i+1} \to 0$ and x_{i+1}/x_{i+2} converges to some limit v_{i+1} (which may be $+\infty$). For sufficiently large t, x_{i+1}/x_{i+2} is monotone. Indeed, by (2.1)

$$\left(\frac{x_{i+1}}{x_{i+2}}\right)^{\cdot} = k_{i+1}x_{i+1}\left(\frac{x_{i+1}}{x_{i+2}}\right)\left(\frac{x_i}{x_{i+1}} - \frac{k_{i+2}}{k_{i+1}}\right). \tag{2.2}$$

If $v_i \geqslant k_{i+2}/k_{i+1}$, then x_{i+1}/x_{i+2} is increasing, otherwise it is ultimately

decreasing. In any case the limit v_{i+1} is approached monotonically. If $v_i > 0$, then $x_i \to 0$ obviously implies $x_{i+1} \to 0$.

Assume now $v_i = 0$, which according to (2.2) implies $v_{i+1} < \infty$. If $v_{i+1} = 0$, then clearly $x_{i+1} \to 0$. There remains the case that $v_{i+1} > 0$. Suppose x_{i+1} does not converge to 0. There exists, then, a $\delta > 0$ and a sequence $t_k \to +\infty$ with $x_{i+1}(t_k) > \delta$ for $k = 1, 2, \ldots$. Set $T = (k_{i+1})^{-1} \log 2$. Since $\dot{x}_{i+1} \leqslant k_{i+1} x_{i+1}$ and $x_{i+1}(t_k) \geqslant \delta$, one has

$$x_{i+1}(t) \geqslant \frac{\delta}{2} \quad \text{for} \quad t_k - T \leqslant t \leqslant t_k .$$

Let $r = \frac{1}{2} k_{i+2}$ and choose $\epsilon > 0$ such that

$$\epsilon[1 + \exp(rT\delta/2)] < v_{i+1}[\exp(rT\delta/2) - 1].$$

Now choose k so large that

$$\left(\frac{x_i}{x_{i+1}} - \frac{k_{i+2}}{k_{i+1}} \right) k_{i+1} \leqslant -r$$

and

$$\left| \frac{x_{i+1}}{x_{i+2}} - v_{i+1} \right| < \epsilon \tag{2.3}$$

for $t \geqslant t_k - T$. This implies by (2.2) that for $t_k - T \leqslant t \leqslant t_k$

$$\left(\frac{x_{i+1}}{x_{i+2}} \right)^{\cdot} \leqslant \left(\frac{x_{i+1}}{x_{i+2}} \right) (-r\delta/2)$$

and thus

$$\frac{x_{i+1}(t_k)}{x_{i+2}(t_k)} \leqslant \frac{x_{i+1}(t_k - T)}{x_{i+2}(t_k - T)} \cdot \exp(-rT\delta/2)$$

$$\leqslant (v_{i+1} + \epsilon) \exp(-rT\delta/2) < v_{i+1} - \epsilon$$

which is a contradiction to (2.3). Thus $x_{i+1} \to 0$.

The proof that $x_{i+2} \to 0, \ldots, x_{i+k-1} \to 0$ is analogous. Hence $x(t)$ converges to some subface of the boundary with the property that whenever $x_j > 0$ then $x_{j+1} = 0$. On such a subface $\Phi(x) = 0$ and hence $\dot{x}_i = 0$ for $i = 1, \ldots, n$. Thus Lemma 1 is proved.

LEMMA 2. $x \in F$ *implies* $\Phi(x) = 0$.

Proof. Suppose $x_j = 0$ for some j, and $\dot{x}_i = 0$ for $i = 1, \ldots, n$. Since $\dot{x}_{j+1} = 0$ one has either $k_{j+1} x_j - \Phi(x) = 0$ (and hence $\Phi(x) = 0$) or else $x_{j+1} = 0$. In the latter case one repeats this. Since some x_{j+k} has to be strictly positive, one gets finally $\Phi(x) = 0$.

An ODE on S_n will be called cooperative if bd S_n is a repeller, i.e. if there exists an $\epsilon > 0$ such that with

$$I(\epsilon) = \{\mathbf{x} \in S_n : 0 < d(\mathbf{x}, \text{bd } S_n) < \epsilon\}$$

(where d is Euclidean metric), the initial condition $\mathbf{x}(0) \in \text{int } S_n$ implies that $\mathbf{x}(t) \notin I(\epsilon)$ for all sufficiently large t.

THEOREM. *The system* (1.1) *is cooperative.*

Proof. Let $P(\mathbf{x}) = x_1 x_2 \cdots x_n$. One has

$$\dot{P} = P(s - n\Phi)$$

with $s = s(\mathbf{x}) \doteq \sum_{i=1}^{n} k_i x_{i-1}$. Let $m \doteq \min\{s(\mathbf{x}) - n\Phi(\mathbf{x}) : \mathbf{x} \in S_n\}$. Note that, in general, $m < 0$. But $\min\{s(\mathbf{x}) : \mathbf{x} \in S_n\} > 0$, and hence one may choose an $M > 0$ with

$$m < M < \min\{s(\mathbf{x}) : x \in S_n\}$$

and set $L = m/M$. We define

$$A \doteq \{\mathbf{x} \in S_n : s(\mathbf{x}) - n\Phi(\mathbf{x}) > M\}$$

and

$$B \doteq S_n \backslash A$$

A is an open neighbourhood of F. Since by Lemmas 1 and 2 $\mathbf{x} \in$ bd S_n implies $\mathbf{x}(t) \in A$ for all sufficiently large t, the set

$$D(\mathbf{x}) \doteq \{T > 0 : \mathbf{x}(t) \in A \text{ for all } t \in [T, (L+1)T]\}$$

is nonempty and hence we may define

$$T(\mathbf{x}) \doteq \inf D(\mathbf{x})$$

for $\mathbf{x} \in$ bd S_n .

We show now that the map T is upper semicontinuous, and that $T(\mathbf{x})$ and $T(\mathbf{x})$ can be defined for all $x \in S_n$ which are sufficiently close to bd S_n. Indeed, given $\mathbf{x} \in$ bd S_n and $\alpha > 0$, there is a T' with $T(\mathbf{x}) \leqslant T' < T(\mathbf{x}) + \alpha$ such that $\mathbf{x}(t) \in A$ for $t \in [T', (L+1)T' + 1]$.

Since A is open, there is a $\delta(x) > 0$ such that $d(\mathbf{x}, \mathbf{y}) < \delta(\mathbf{x})$ implies $y(t) \in A$ for $t \in [T', (L+1)T' + 1]$ and hence $T(\mathbf{y}) \leqslant T(\mathbf{x}) + \alpha$. In particular for $\alpha = 1$ there are finitely many $\mathbf{x}^{(1)}, \ldots, \mathbf{x}^{(l)} \in$ bd S_n such that the open sets

$$K_j \doteq \{\mathbf{y} \in S_n : d(\mathbf{y}, \mathbf{x}^{(j)}) < \delta(\mathbf{x}^{(j)})\}$$

cover bd S_n . Put

$$I \doteq \bigcup_{j=1}^{l} K_j$$

and

$$T \doteq \max_{1 \leqslant j \leqslant l} \; T(\mathbf{x}^{(j)}) + 1.$$

For any $\mathbf{x} \in I$ there is a $T \leqslant \bar{T}$ such that $\mathbf{x}(t) \in A$ for $t \in [T, (L+1)T + 1]$. Define

$$\bar{P} \doteq \sup\{P(\mathbf{x}): \mathbf{x} \in I\}.$$

Suppose now $\mathbf{x} \in I$ bd S_n. We claim that there is a $t > 0$ such that $\mathbf{x}(t) \notin I$.
Indeed, assume that $\mathbf{x}(t) \in I$ for all $t > 0$ and let

$$t_1 \doteq \inf\{t \geqslant 0: \mathbf{x}(t) \in B\}.$$

t_1 exists since otherwise $\mathbf{x}(t) \in A$ and

$$P(\mathbf{x}(t)) \geqslant P(\mathbf{x}(0)) \exp(Mt)$$

for all $t \geqslant 0$, which is impossible since P is bounded. There is a $T_1 \leqslant \bar{T}$ such that $\mathbf{x}(t) \in A$ for $t - t_1 \in [T_1, (L+1) T_1 + 1]$. Putting

$$t_1' \doteq t_1 + (L+1)T_1 + 1$$

and noting that during the time $[t_1, t_1']$ the orbit of $\mathbf{x}$ spends a time less than T_1 in B and more than $LT_1 + 1$ in A, one sees that

$$P(\mathbf{x}(t_1')) \geqslant P(\mathbf{x}(t_1)) \exp(- m \mid T_1 + LMT_1 + M)$$
$$\geqslant P(\mathbf{x}(t_1))e^M$$
$$\geqslant P(\mathbf{x}(0))e^M.$$

Similarly,

$$t_2 \doteq \inf\{t \geqslant t_1' : \mathbf{x}(t) \in B\}$$

exists and there is a $T_2 \leqslant \bar{T}$ with $\mathbf{x}(t) \in A$ for $t - t_2 \in [T_2, (L+1) T_2 + 1]$. With

$$t_2' = t_2 + (L+1)T_2 + 1,$$

one gets

$$P(\mathbf{x}(t_2')) \geqslant P(\mathbf{x}(t_2))e^M \geqslant P(\mathbf{x}(0))e^{2M}.$$

Proceeding inductively one obtains a sequence t_k', $k = 1, 2, \ldots$ with

$$P(\mathbf{x}(t_k')) \geqslant P(\mathbf{x}(0))e^{kM},$$

which is a contradiction to $P(\mathbf{x}(t)) \leqslant \bar{P}$ for all $t > 0$. Thus $\mathbf{x}(t)$ has to leave

I at some time. Note also that for any $t \geqslant 0$ smaller than the first exit time one has $t \in [t'_k, t'_{k+1}]$ for some k (with $t'_0 = 0$),

$$P(\mathbf{x}(t)) \geqslant P(\mathbf{x}(t'_k)) \exp(-\mid m \mid \bar{T}) \geqslant P(\mathbf{x}(0)) \exp(-\mid m \mid \bar{T} + M)$$

and hence

$$P(\mathbf{x}(t)) \geqslant P(\mathbf{x}(0)) \exp(-\mid m \mid \bar{T})$$

Let

$$\bar{p} = \min\{P(x): x \in S_n \backslash I\}.$$

Clearly $\bar{p} > 0$. Choose $\epsilon > 0$ so small that $I(\epsilon) \subset I$ and that

$$P(\mathbf{x}) < \bar{p} \exp(-\mid m \mid \bar{T}) \qquad \text{for all } \mathbf{x} \in I(\epsilon).$$

The orbit of a point $\mathbf{x} \in S_n \backslash I$ may possible enter I, but never $I(\epsilon)$, since

$$P(\mathbf{x}(t)) \geqslant \bar{p} \exp(-\mid m \mid \bar{T})$$

Any orbit starting in $I(\epsilon)$ leaves I after a finite time and never returns to $I(\epsilon)$. Thus the theorem is proved.

3. Internal Equilibration and Competition of Short Hypercycles

As framework we shall use the ODE on S_n:

$$\dot{x}_i = x_i(G_i - \Phi) \tag{3.1}$$

where the G_i are functions on S_n and $\Phi = \sum_{i=1}^n x_i G_i$.

3.a. *Internal Equilibration for 2-Hypercycles*

Suppose that in (3.1) one has $G_1 = k_1 x_2$ and $G_2 = k_2 x_1$, where k_1 and k_2 are constants >0. Equation (3.1) then describes a system having a 2-hypercycle as subsystem. For x_1 and $x_2 > 0$ one has

$$\left(\frac{x_1}{x_2} - \frac{k_1}{k_2} \right)^{\cdot} = -k_2 x_1 \left(\frac{x_1}{x_2} - \frac{k_1}{k_2} \right)$$

and hence

$$\frac{x_1}{x_2} \to \frac{k_1}{k_2}. \tag{3.2}$$

In particular, all orbits of (1.1) in int S_2 converge to the fixed point C.

3.b. *Internal Equilibration for 3-Hypercycles*

Suppose now that in (3.1) one has $G_1 = k_1 x_3$, $G_2 = k_2 x_1$ and $G_3 = k_3 x_2$. This means we have a 3-hypercycle as subsystem. Note that $x_1 + x_2 + x_3 \leqslant 1$ ($=1$ in case $n = 3$). We shall prove

$$\frac{x_1}{x_2} \to \frac{k_3}{k_2}, \qquad \frac{x_2}{x_3} \to \frac{k_1}{k_3}, \qquad \frac{x_3}{x_1} \to \frac{k_2}{k_1} \qquad (3.3)$$

(In particular, all orbits of (1.1) in int S_3 converge to C).

Let l be the line through the origin (in (x_1, x_2, x_3)-space) given by $k_1 x_3 = k_2 x_1 = k_3 x_2$, and let p_1, p_2 and p_3 be the planes through l and the x_1-, x_2- and x_3-axes respectively. Note that (2.1) is valid for $i = 1$ and $j = 2$. Hence p_2 divides $\mathbb{R}^3$ in such a way that in the half space containing the unit vector $\mathbf{e}_1$, the ratio (x_1/x_2) is decreasing, and in the other one it is increasing.

Let l_1, l_2 and l_3 be the lines obtained as intersection of p_1, p_2 and p_3 with S_3 and consider the following Fig. 1: let P_1 be an arbitrary point between $\mathbf{e}_1$ and C.
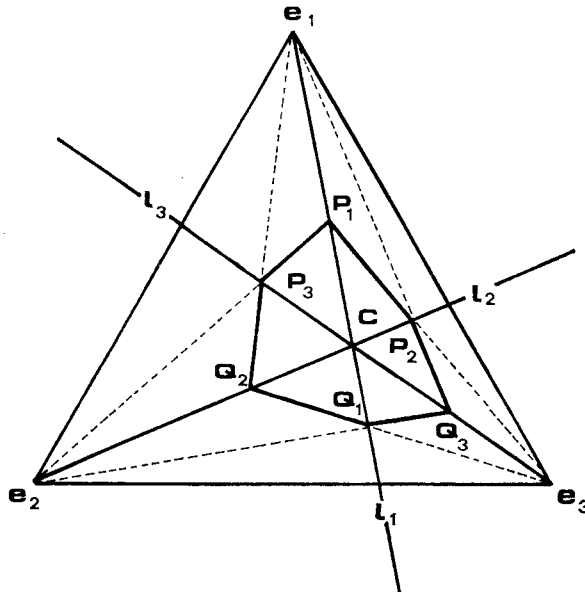

FIGURE 1

Let P_2 (resp. P_3) be the intersection of $P_1 \mathbf{e}_3$ (resp. $P_1 \mathbf{e}_2$) with l_2 (resp. l_3). Let Q_3 (resp. Q_2) be the intersection of $P_2 \mathbf{e}_1$ (resp. $P_3 \mathbf{e}_1$) with l_3 (resp. l_2). We claim that the intersection Q_1 of $Q_3 \mathbf{e}_2$ and $Q_2 \mathbf{e}_3$ lies on l_1.

Indeed, this statement is easily seen by a projective change of coordinates which sends the four points e_1, e_2, e_3 and C into the points e_1', e_2', e_3' and C' with coordinates $(+\infty, 0)$, $(0, 1)$, $(0, 0)$ and $(1, \frac{1}{2})$ (see Fig. 2).
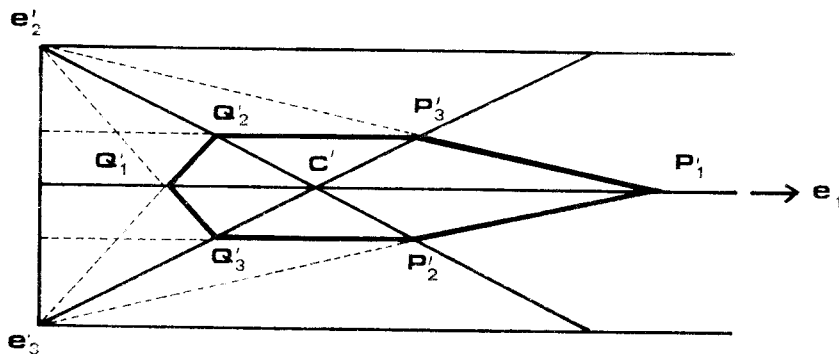

FIGURE 2

Let H denote the hexagon $P_1 P_3 Q_2 Q_1 Q_3 P_2$ lying in S_3 and π the pyramid with base H and summit O (the origin of (x_1, x_2, x_3)-space). Consider one of the faces of π, $OP_1 P_2$ for example. Since P_1, P_2 and e_3 are colinear, $OP_1 P_2$ lies on a plane through the x_3-axis which is therefore of the form $x_1/x_2 = $ const. On the other hand, since $OP_1 P_2$ is not on the same side as e_1 with respect to the plane p_2, the ratio (x_1/x_2) must increase. Thus any orbit through $OP_1 P_2$ must enter the pyramid. The other faces of π are dealt with similarly.

Letting P_1 vary from e_1 to C and repeating the construction, one obtains a nested family of pyramids having the line l as their intersection. Thus all orbits converge towards l, i.e., (3.3) is valid.

3.c. *Competition of Short Hypercycles*

Consider now a system consisting of N 2-hypercycles and M 3-hypercycles. We may describe this by an equation of the type (3.1), namely

$$
\begin{aligned}
\dot{x}_1^{(i)} &= x_1^{(i)}(k_1^{(i)} x_2^{(i)} - \Phi) \\
\dot{x}_2^{(i)} &= x_2^{(i)}(k_2^{(i)} x_1^{(i)} - \Phi)
\end{aligned}
\right\} \quad \text{for} \quad i = 1,\dots, N;
$$

$$(3.4)$$

$$
\begin{aligned}
\dot{x}_1^{(i)} &= x_1^{(i)}(k_1^{(i)} x_3^{(i)} - \Phi) \\
\dot{x}_2^{(i)} &= x_2^{(i)}(k_2^{(i)} x_1^{(i)} - \Phi) \\
\dot{x}_3^{(i)} &= x_3^{(i)}(k_3^{(i)} x_2^{(i)} - \Phi)
\end{aligned}
\right\} \quad \text{for} \quad i = N+1,\dots, N+M,
$$

on the simplex S_{2N+3M}. By (3.a) and (3.b) all orbits in int S_{2N+3M} converge to the invariant subset S^* defined by the relations

$$k_1^{(i)} x_2^{(i)} = k_2^{(i)} x_1^{(i)} \qquad i = 1,\ldots, N$$

$$k_1^{(i)} x_3^{(i)} = k_2^{(i)} x_1^{(i)} = k_3^{(i)} x_2^{(i)} \qquad i = N-1,\ldots, N+M.,$$

which is an $(N-M)$-simplex. As coordinates on S^*, we use y_i ($i = 1,\ldots, N+M$), where

$$y_i = x_i^{(i)} q_i^{-1}$$

with

$$q_i = \frac{k_1^{(i)} k_2^{(i)}}{k_1^{(i)} + k_2^{(i)}} \qquad \text{for} \quad i = 1,\ldots, N$$

and

$$q_i = \frac{k_1^{(i)} k_3^{(i)}}{k_1^{(i)} k_3^{(i)} + k_2^{(i)} k_1^{(i)} + k_3^{(i)} k_2^{(i)}} \qquad \text{for} \quad i = N+1,\ldots, N+M.$$

Note that on S^*, $y_i \geqslant 0$ and $\sum_{i=1}^{N+M} y_i = 1$. The relation $y_i = 1$ means that there exists just the ith hypercycle, in internal equilibrium. The restriction of (3.4) to the invariant subsimplex S^* becomes

$$\dot{y}_i = y_i(q_i y_i - \Phi)$$

$$(3.5)$$

$$\text{with} \quad i = 1,\ldots, N+M \qquad \text{and} \qquad \Phi = \sum_{i=1}^{N+M} q_i y_i^2.$$

(3.5) is particularly easy to analyse, since the quotients (y_i/y_j) grow or decay according to whether they are larger or smaller than (q_i/q_j). It follows that the attractors are the vertices and their basins of attraction the [...] $y_i \in S_{N+M}$ with $y_i > 0$ and $y_i > y_j$ for all $j \neq i$. This implies that the only ω-limits of orbits of (3.4) in int S_{2N+3M} are the ω-limits in S^*, and that the only attractors whose basins are of positive measure are the vertices of S^*. Thus for almost all initial conditions, only one hypercycle survives and reaches internal equilibrium.

We do not know how to prove a corresponding exclusion principle for the competition of longer hypercycles, nor how to describe their attractors.

Finally, let us note that for the competition of two 2-hypercycles (i.e. (3.4) with $N = 2$, $M = 0$) one obtains by a simple computation that

$$\frac{k_2^{(1)} x_1^{(1)} - k_1^{(1)} x_2^{(1)}}{k_2^{(2)} x_1^{(2)} - k_1^{(2)} x_2^{(2)}} = \text{const.}$$

This shows that the plane through the line joining the two attractors $A_1(k_2^{(1)} x_1^{(1)} = k_1^{(1)} x_2^{(1)}, x_1^{(2)} = x_2^{(2)} = 0)$ and $A_2(x_1^{(1)} = x_2^{(1)} = 0, k_2^{(2)} x_1^{(2)} = k_1^{(2)} x_2^{(2)})$ are invariant.

It means that the internal equilibration of the two hypercycles occurs in a well-balanced way. It would be interesting to know whether a corresponding fact holds for longer hypercycles.

4. DISCUSSION: THE FORMATION AND SELECTION OF HYPERCYCLES

Any attempt to explain the evolution of the genetic code has to deal with a kind of "existence and uniqueness" problem:

(A) it has to show how such an extremely improbable machinery could emerge;

(B) it must account for the very strange fact that there is only one such code for the multitude of living cells on earth. The biochemical theory of hypercycles as developed in [2] is a step towards the solution of this double task. We want to show here how the simple mathematical model (1.1) reflects this.

Problem (A) relates to the notion of self-reproductive automata. As v. Neumann showed in [4], the "complexity" of such an automaton has to be above a certain threshold. This level can be estimated in the biochemical context: as shown in [1] and [2] it exceeds the capacity of the primitive biopolymers likely to be found in the "primordial soup," so that they have to cooperate in order to fulfill their task. The hypercycle is a biochemical device allowing macromolecular information carriers of comparatively low grade to pool their information. The theorem in Section 2 means that this form of cooperation is stable in the sense that small perturbations cannot "kill off" members of the hypercycle.

The proof in Section 2 proceeds in a way which sheds some light on a possible course of hypercycle formation. We have to assume that the species are formed by mutations, i.e. by random fluctuations introducing from time to time small positive concentrations x_i. We start with a system which is not yet complete, i.e. where $x_j = 0$ for some j's. By Lemma 1, the $\mathbf{x}(t)$ approaches the fixed point set and asymptotically seems to be inert. All but the concentrations of the "end species" (where $x_i > 0$ but $x_{i+1} = 0$) are extremely small. Consider some mutation which introduces one of the previously non existing species without yet completing the hypercycle: the system still remains on the boundary and after some (possibly drastic) changes in concentration approaches again some seemingly inert state. But when finally the system is completed by a mutation creating the last missing member, the state $\mathbf{x}(t)$ enters int S_n and the long term behaviour changes its character. The attractor now lies in the interior of the concentration simplex and apart from the low dimensional cases no longer consists of fixed points. From a seemingly dead quasi-equilibrium emerges a pulsating form of dynamical cooperation.

Problem (B) has to do with the competition of hypercycles. While we cannot prove an exclusion principle in full generality, we may account for the "once for ever" decisions if we make the natural assumption that fluctuations leading to efficient mutations are very small and do not occur frequently.

Thus consider the competition of the hypercycles H_l ($1 \leqslant l \leqslant N$) without common species. With $x_1^{(l)},\dots,x_{n_1}^{(l)} \geqslant 0$ as the concentrations of the species of H_l, the system is described by

$$\dot{x}_i^{(l)} = x_i^{(l)}(x_i^{(l)} x_j^{(l)} - \Phi) \tag{4.1}$$

where $j = i - 1 + n_l \delta_{1n_l}$; $i = 1,\dots,N$; $k_i^{(l)} > 0$;

$$\sum_{l=1}^{N}\sum_{i=1}^{n_l} x_i^{(l)} = 1 \quad \text{and} \quad \Phi = \sum_{l=1}^{N}\sum_{i=1}^{n_1} k_i^{(l)} x_i^{(l)} x_j^{(l)}.$$

Note first that Lemma 1 remains valid, so that if H_l is incomplete, all concentrations except those of the end-species converge to 0. As long as no hypercycle is completed, the system is asymptotically inert.

Suppose now that a mutation completes the first hypercycle, H_1 say. Let G be the subset of the concentration simplex where $x_i^{(1)} > 0$ for $i = 1,\dots,n_1$ and

$$k_{i'}^{(l)} x_{j'}^{(l)} < k_i^{(1)} x_j^{(1)} \tag{4.2}$$

for $l = 2,\dots,N$; $1 \leqslant i \leqslant n_1$; $1 \leqslant i' \leqslant n_l$; $j = i - 1 + n_1 \delta_{i1}$ and $j' = i - 1 - n_l \delta_{1n_l}$. G is an open neighborhood of the attractors of the "pure" hypercycle H_1 (the set where $x_i^{(l)} > 0$ iff $l = 1$). Since in G one has

$$\left(\frac{x_{i'}^{(l)}}{x_i^{(1)}}\right)^{\cdot} = k_{i'}^{(l)} x_{i'}^{(l)} \left(\frac{x_{j'}^{(l)}}{x_{i'}^{(l)}} - \frac{k_i^{(1)}}{x_i^{(1)}}\right) < 0,$$

the set G is forward invariant, the $x_{i'}^{(l)}$ vanish and all orbits converge to the attractors of H_1.

Let E denote the invariant subset of the concentration simplex where $x_i^{(1)} > 0$ for $1 \leqslant i \leqslant n_1$ and all other concentrations except those of one or several end-species $x_i^{(l)}$ are 0. Since $x_j^{(l)} = 0$ and $\Phi > 0$, $x_i^{(l)}$ is decreasing and $\sum_{i=1}^{n_1} x_i^{(1)}$ remains bounded away from 0. A minor modification shows that the theorem in Section 2 is still valid for the $x_i^{(1)}$ and thus that Φ remains bounded away from 0. Hence $x_i^{(l)}$ converges to 0, i.e. all orbits from E enter G. The same holds for all orbits starting from some suitable open neighborhood V of E in the concentration simplex.

If the time interval which precedes the mutation completing H_1 is large enough, the concentrations of those species which are not end-species have become so small that the fluctuation sends the system into some state in V. Hence the system will converge to some attractor of the pure hypercycle H_1.

If the time interval up to the next fluctuation is sufficiently large, the state will not leave G under such a small perturbation and hence will still converge to an attractor of H_1. This is valid even if further hypercycles H_l are completed: the concentrations of all their species will vanish. This does not mean, of course, that evolution ends with the first hypercycle. But it shows that the only possible concurrents of H_1 are those hypercycles having some species i in common with H_1. Such a hypercycle H will supersede H_1 iff i is a better catalysator for its H-successor than for its H_1-successor. (Indeed, $k_{i-1}^{(1)} < k_{i+1}$ implies $(x_{i+1}^{(1)}/x_{i+1}) \rightarrow 0$ etc.). Hence mutations introducing new species may yield "improved" hypercycles and extinguish their ancestors.

The inheritance of members of the previous hypercycle is a mathematical paraphrase of the "once for ever" decisions in the formation of the cellular mechanism, where we have "linear descendency" of prebiotic organisms instead of the familiar, many-branched "descendency tree" of Darwinian evolution. This fact is amply validated biochemically by the universality of the genetic code, the uniqueness of chiralities etc.

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