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Competitive Exclusion of Disjoint Hypercycles

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Dedicated to Prof. Dr. Peter Schuster
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A conjecture of Eigen and Schuster (1979) concerning the competitive exclusion of disjoint hypercycles is finally proved.

A *hypercycle,* as introduced by Eigen and Schuster [1], is a system of n self-replicating macromolecules, coupled together by a closed loop of catalytic reactions, such that each species catalyses the self-reproduction of the next one. Such hypercycles have been postulated as missing links in the prebiotic evolution from simple self-replicating elements with enzyme-free copying mechanism to the early forms of RNA.

One open problem concerns an exclusion principle for competing, disjoint hypercycles, conjectured in [1]. This principle plays a crucial role in explaining the uniqueness of the genetic code within the hypercycle theory, see [4]. It will be proved in the present paper.

The mathematical model behind this are differential equations of the form

$$\dot{x}_i = x_i(k_i x_{\pi(i)} - \overline{F}), \quad i = 1, \dots, n, \quad \overline{F} = \sum_{i=1}^{n} k_i x_i x_{\pi(i)} . \tag{1}$$

Here x_i denotes the concentration of the ith species, $k_i > 0$ are rate constants, π is a permutation of $\{1, \dots, n\}$. The flux term $\overline{F}$ ensures that the total number of elements remains constant and (1) defines a flow on the simplex $S_n = \{x \in \mathbf{R}^n : x_i \geq 0 \text{ and } \sum_{i=1}^{n} x_i = 1\}$.

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If π is a cyclic permutation, such as $\pi(i) = i - 1$ (modulo n), then (1) is called the *hypercycle equation*. If the permutation π consists of m cycles then (1) describes the competition of m disjoint hypercycles.

In the first case ($m = 1$) the dynamics of (1) is now rather well understood. It has been shown already in [1] that the unique interior equilibrium E of (1) is globally asymptotically stable if $n \leq 4$. Since the eigenvalues at E are essentially the nth roots of unity (except 1), E is unstable for $n \geq 5$. Still, as shown in [4] and [3, ch. 13.3]), the hypercycle is *permanent*: There is a $\delta > 0$ such that for all initial values $x(0) \in \operatorname{int} S_n$, $\liminf_{t\to\infty} x_i(t) \geq \delta > 0$. Moreover, as conjectured in [1] and shown in [2], there exists an asymptotically stable periodic orbit for $n \geq 5$, and every orbit of (1) in $\operatorname{int} S_n$ converges either to E or to a periodic orbit.

In the second, general case ($m > 1$) the following has been conjectured [1, p. 54ff]: *For almost all initial conditions* $x(0) \in S_n$, (1) *leads to the establishment of a unique hypercycle, the other* $m - 1$ *going to extinction.* This conjecture has been shown in [4] and [3, ch. 13.4] if each of the cycles of π has at most 3 resp. 4 members. The purpose of this note is to prove this conjecture in general.

More generally we consider equations of the form

$$\dot{x}_i = x_i(F_i(x) - \overline{F}), \quad i = 1, \dots, n, \quad \overline{F} = \sum_{i=1}^{n} x_i F_i(x). \tag{2}$$

We assume that there is a partition into m disjoint subcommunities, $\{1, \dots, n\} = \bigcup_{\alpha=1}^{m} C_\alpha$, that do not interfer directly with each other (only indirectly through the flux term $\overline{F}$).

(A1) $\frac{\partial F_i}{\partial x_j} = 0$ if i and j belong to different subcommunities.

Further assumptions on (2) are:

(A2) The functions $F_i : \mathbf{R}^n_+ \to \mathbf{R}$ are homogeneous of degree $q > 0$: $F_i(sx) = s^q F_i(x)$.

(A3) At least one subcommunity is 'productive': $\exists \alpha : \sum_{i\in C_\alpha} F_i(x) > 0$ for all $x \in S_n$ with $\sum_{i\in C_\alpha} x_i > 0$.

These assumptions are obviously satisfied for the hypercyclic interaction term $F_i(x) = k_i x_{\pi(i)}$ of (1). We can now state the exclusion principle.

Theorem. *Under the above assumptions* (A1), (A2) *and* (A3), *for almost all initial conditions* $x(0) \in S_n$, *there is an* α *(that depends on* $x(0)$*) such that* $x_i(t) \to 0$ *for all* $i \notin C_\alpha$ *and hence* $\sum_{i\in C_\alpha} x_i(t) \to 1$ *as* $t \to \infty$.

The *proof* is divided into four steps.

1) Let us consider a modified differential equation on the nonnegative orthant $\mathbf{R}^n_+$,

$$\dot{y}_i = y_i(F_i(y) - 1)\,, \quad i = 1, \dots, n\,. \tag{3}$$

In view of (A1) this system on $\mathbf{R}^n_+$ obviously decouples into m independent subsystems of the form

$$\dot{y}_i = y_i(F_i(y) - 1), \quad i \in C_\alpha \tag{3_α}$$

for $\alpha = 1, \dots, m$. The systems (2) and (3) are essentially dynamically equivalent: Consider a solution $y(t) \neq 0$ of (3), and define $z(t) = Q\,(y(t))$, where $Q : \mathbf{R}^n_+ \setminus \{O\} \to S_n$, $Q(y) = y / \sum_{i=1}^n y_i$ is the radial projection onto the simplex S_n. It is easy to check, that

$$\dot{z}_i = z_i\left(F_i(y) - \sum_{j=1}^n z_j F_j(y)\right) = z_i\left(F_i(z) - \sum_{j=1}^n z_j F_j(z)\right) \cdot \left(\sum_{j=1}^n y_j(t)\right)^q, \tag{4}$$

using the homogeneity assumption (A2). Systems (2) and (4) differ only by a positive factor and generate the same orbits. More precisely, $z(t)$ traces out a portion of the orbit of (2) through $x(0) = z(0) \in S_n$. One should be aware that while solutions of (2) are defined for all t due to the compactness of S_n, solutions of (3) will not be in general. If $\sum_{j=1}^n y_j(t) \to \infty$ in finite time, as $t \uparrow \tau$ then $z(t)$ traces out the positive orbit of $x(0) = z(0)$ already in finite time. On the other hand, if $\sum_{j=1}^n y_j(t) \to 0$ as $t \to \infty$ then $z(t)$ will trace out only a finite portion and come to a stop at a certain point $x(\tau)$ on the orbit of (2) through $x(0) = z(0)$. Hence we cannot recover the full positive orbit of (2) from a solution $y(t)$ converging to 0.

2) The origin O is asymptotically stable for (3), or each subsystem (3_α), as seen by linearization, and hence its basin of attraction $B_\alpha(O)$ is open. Hence, for each subcommunity C_α there is a function $s_\alpha : \mathbf{R}^n_+ \to \mathbf{R}_+ \cup \{\infty\}$, such that for $y \in \mathbf{R}^n_+$ we have: if $0 \le s < s_\alpha(y)$ then $sy \in B_\alpha(O)$ and if $s = s_\alpha(y) < \infty$ then sy lies on the boundary $\operatorname{bd} B_\alpha(O) = M_\alpha$ of the basin. $s_\alpha(y)$ depends only on the components y_i with $i \in C_\alpha$ and it is homogeneous of degree -1, *i.e.*, $s_\alpha(qy) = q^{-1}s_\alpha(y)$. Since the basin $B_\alpha(O)$ is open, s_α is lower–semicontinuous. Solutions $y(t)$ in the invariant manifold M_α exist for all time $t \ge 0$ (being limits of solutions in $B_\alpha(O)$) and satisfy $\sum_{i \in C_\alpha} y_i(t) \ge c > 0$ for some $c > 0$, for all t.

3) For those α that correspond to a productive subcommunity C_α according to (A3), $s_\alpha(y)$ is finite for all positive $y \in \operatorname{int} \mathbf{R}^n_+$. This can be seen as follows. For $P(y) = \prod_{i \in C_\alpha} y_i$ one has $\dot{P}/P = \sum_{i \in C_\alpha}(F_i(y) - 1)$. Using (A3), (A2), and compactness of the simplex we find a constant $c > 0$ such that $\sum_{i \in C_\alpha} F_i(y) \ge c(\sum_{i \in C_\alpha} y_i)^q$. This implies that the sets $\{y : P(y) \ge p_1\}$ are forward invariant for large p_1 and in these sets P goes to infinity (in finite time)

along solutions. Since every positive ray from the origin hits this region, $B_\alpha(O)$ is bounded along every positive ray and $s_\alpha(y) < \infty$ for each $y \in \operatorname{int} \mathbf{R}^n_+$. (For boundary rays this need not be true, as the example of the hypercycle shows.) With other words, the boundary manifold $M_\alpha = \operatorname{bd} B_\alpha(O)$ is hit by each positive ray from the origin (in exactly one point).

4) Let now

$$s(y) = \min_{1 \le \alpha \le m} s_\alpha(y) < \infty \,. \tag{5}$$

Consider an initial point $x \in \operatorname{int} S_n$. Then $y := s(x)x$ is the 'first' point where the ray from the origin through x hits one of the manifolds M_α. For almost all $x \in S_n$ there is a unique α such that $s(x) = s_\alpha(x)$ while for all $\beta \neq \alpha$ we have $s(x) < s_\beta(x)$. (Homogeneity of the functions s_α implies that for each pair $\alpha \neq \beta$, the set $\{x : s_\alpha(x) = s_\beta(x)\}$ has Lebesgue measure zero.) Then $y_i(t) \to 0$ for $i \in C_\beta$ $(\beta \neq \alpha)$, as $t \to \infty$, but $\sum_{i \in C_\alpha} y_i(t) \ge c > 0$ for all $t \ge 0$. Consider again the projection $z(t) = Q(y(t))$. Then $z_i(t) \to 0$ in (4), and hence $x_i(t) \to 0$ in (2), as $t \to \infty$ for $i \in C_\beta$, $\beta \neq \alpha$, and only members of the α-subcommunity can survive. □

Remarks. 1. Whenever the functions s_α are continuous (like for the competition of hypercycles (1), see Remark 3 below) the sets $\{x : s_\alpha(x) \neq s_\beta(x)\}$ are open and dense for each pair $\alpha \neq \beta$. Then the exclusion principle holds also for generic initial conditions, i.e., in the topological category.

If the minimum in (5) is attained for several α, that means several manifolds M_α are hit at the same value s, two or more subcommunities can simultaneously survive. This occurs only within codimension 1, namely on the projection under Q of the intersection of two manifolds M_α. Survival of all m subcommunities is possible only if $s_1(y) = \cdots = s_m(y)$, which happens only on an $(n-m)$-dimensional manifold of initial conditions in S_n.

2. The result obviously extends to equations of the form

$$\dot{x}_i = G_i(x) - x_i\overline{G}(x)\,, \quad i = 1, \ldots, n, \quad \overline{G}(x) = \sum_{j=1}^n G_j(x)\,,$$

which do not leave the boundary of S_n invariant but define semiflows on S_n instead. (A1) and (A2) have to be modified in an obvious way.

3. The 'productivity' assumption (A3) which is used in step 3 of the proof could be replaced by other conditions satisfied by (1) such as monotonicity $\frac{\partial F_i}{\partial x_j} \ge 0$ for $i \neq j$ together with the existence of an interior fixed point for (3_α), see the proof of Lemma 1.3 in [2]. In this case, the functions s_α and the manifolds M_α are at least Lipschitz continuous.

4. It is not clear, how important the homogeneity assumption (A2) is. Certainly the present proof makes essential use of it. For a similar exclusion result

without (A2) consider systems of the form

$$\dot{x}_i = x_i(f_i(x_i) - \overline{f}), \quad i = 1, \dots, n, \quad \overline{f} = \sum_{j=1}^{n} x_j f_j(x_j), \tag{6}$$

(case $n = m$) where f_i are strictly monotonically increasing functions of x_i. Such systems (6) have a Ljapunov function $V(x) = \sum F_i(x_i)$ where F_i is an antiderivative of f_i, *i.e.*, $F_i'(x_i) = f_i(x_i)$, see [3, Ex. 24.3.2]. Since f_i is increasing, V is strictly convex, and has maxima only at the corners of the simplex. Hence for most initial conditions, only one species will survive.

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