



The information capacity of hypercycles

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ABSTRACT

Hypercycles are information integration systems which are thought to overcome the information crisis of prebiotic evolution by ensuring the coexistence of several short templates. For imperfect template replication, we derive a simple expression for the maximum number of distinct templates n_m that can coexist in a hypercycle and show that it is a decreasing function of the length L of the templates. In the case of high replication accuracy we find that the product $n_m L$ tends to a constant value, limiting thus the information content of the hypercycle. Template coexistence is achieved either as a stationary equilibrium (stable fixed point) or a stable periodic orbit in which the total concentration of functional templates is nonzero. For the hypercycle system studied here we find numerical evidence that the existence of an unstable fixed point is a necessary condition for the presence of periodic orbits.

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1. Introduction

Most of the modern theoretical work on prebiotic evolution was prompted by the seminal paper of Eigen (1971) which explored the fate of a population of competing macromolecules in an environment with limited resources. The main conclusion of Eigen's work is that the length of a replicating polymer (i.e., a RNA-like template) is limited by the replication accuracy per nucleotide, and so primordial replicators would have to replicate with implausible high accuracy in order to reach the length of today's RNA viruses (about 10^3 – 10^4 nucleotides). This finding, together with the observation that distinct templates cannot coexist in the competition-only scenario (Swetina and Schuster, 1982), come to be known as the information crisis of prebiotic evolution.

In fact, this information crisis would be resolved by the coexistence of several distinct, short templates, i.e., by the splitting of the information in short modules, similarly to the division of the genome in chromosomes found in many present-day organisms. In this case, the total information content of the template pool is the product of the number of different templates and the maximum information coded per template (roughly the template length L), provided the template types have the same concentration. But template coexistence can be achieved only if some sort of cooperation between templates is imposed *a priori* to the molecular population. To this end Eigen and Schuster (1979) proposed a cyclic reaction scheme, termed hypercycle, in which

each replicator would aid in the replication of the next one, in a regulatory cycle closing on itself. An alternative proposal confines the templates in packages or prebiotic vesicles which are deemed viable provided it encloses a number n of distinct functional templates (Niesert et al., 1981; Szathmáry and Demeter, 1987; Zintzaras et al., 2002; Fontanari et al., 2006).

Perhaps because hypercycles and vesicle models are more difficult to analyze than the naked-gene (quasispecies) scenario, the all-important question of whether these information integration systems exhibit a similar phenomenon as the error threshold of the quasispecies model was put off. Only recently a re-examination of a prototypical package model—the model of Niesert et al. (1981)—revealed that package models in general suffer from the same malady as the quasispecies model: in the case of imperfect replication an increase in the number n of distinct templates confined in the vesicle must be followed by a decrease of their lengths, otherwise the package becomes unviable. As a result, the product nL (i.e., the total information content of the package) tends to a constant value that depends essentially on the spontaneous mutation rate per nucleotide (Silvestre and Fontanari, 2007, 2008). Our aim in this contribution is to investigate whether a similar restriction to the total amount of information in the pool of templates holds for hypercycle systems as well.

The dynamics of hypercycle systems in the presence of a variety of mutant types was extensively investigated by Stadler and Schuster (1992) and Happel and Stadler (1998). We refer the reader to Bresch et al. (1980), Szathmáry and Demeter (1987) and Sardanyés and Solé (2007) for an emphasis on the destabilizing effects of mutant parasites and to Boerlijst and Hogeweg (1991) and Cronhjort and Blomberg (1994) for an analysis of the

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robustness conferred by spatial organization against those mutants. However, the formulation of Campos et al. (2000) in which the mutants form an error tail class seems more appropriate to study the error threshold phenomenon and so our analysis will build heavily on that paper.

The sole motivation of this contribution is to show that the condition for the viability of the hypercycle derived in Campos et al. (2000) is in fact valid for all n and not only for the regime where fixed points are stable, i.e., for $n \leq 4$. This is so because we found numerically that a necessary condition for the presence of stable periodic orbits is the existence of an unstable fixed point. For the purpose of completeness, in the following section we describe the model and re-derive the main results regarding the existence of fixed point (and hence of stable periodic solutions) for the hypercycle system.

2. Model

The hypercycle system we consider here is composed of n 'functional' elements I_1, \dots, I_n and its error tail I_e . The templates are capable of self-replication with productivity values A_i ($i = 1, \dots, n$) and A_e . As usual, we introduce the kinetic constants K_i that measure the strength of the influence of template I_{i-1} on the growth promotion of template I_i . The key ingredient in the modeling is that in both processes of growth of template I_i the probability of success is given by the parameter $Q \in [0, 1]$, so that an erroneous copy, which will then belong to the error tail, is produced with probability $1 - Q$. Back-mutations from the error class to the functional class, as well as mutations between elements of the functional class, are neglected. This formulation is equivalent to considering polynucleotides of length $L \rightarrow \infty$ whose mutation probability per nucleotide u goes to 0 such that the replication accuracy per genome is finite, i.e., $\exp(-Lu) \rightarrow Q$.

The concentrations x_i ($i = 1, \dots, n$) of the hypercycle functional elements and the concentration x_e of the error tail evolve in time according to the kinetic equations (Campos et al., 2000)

$$\dot{x}_i = x_i(A_i Q + K_i x_{i-1} Q - \Phi), \quad i = 1, \dots, n \quad (1)$$

and

$$\dot{x}_e = x_e(A_e - \Phi) + (1 - Q) \sum_{i=1}^n x_i(A_i + K_i x_{i-1}), \quad (2)$$

where $x_0 \equiv x_n$ and

$$\Phi = \sum_{i=1}^n x_i(A_i + K_i x_{i-1}) + x_e A_e \quad (3)$$

is a dilution flux that keeps the total concentration constant, i.e., $\sum_{i=1}^n \dot{x}_i + \dot{x}_e = 0$. As usual, the dot denotes a time derivative. Henceforth we will assume that

$$\sum_{i=1}^n x_i + x_e = 1. \quad (4)$$

In accord with the usual assumption of package models that functional templates and parasites are selectively neutral (Niesert et al., 1981; Silvestre and Fontanari, 2008) we set $A_i = A_e = a$, and $K_i = K > 0$ for $i = 1, \dots, n$, resulting in the so-called symmetric hypercycle. Hence by measuring the self-replication productivity a and the time t in units of K we can set $K = 1$ without loss of generality.

3. Analysis of the steady state

Here we focus only on the fixed-point solutions $x_i > 0$ for $i = 1, \dots, n$. In this case, the condition $\dot{x}_2 = 0$ yields $\Phi = Q(a + x_1)$

which, inserted in the equations $\dot{x}_3 = \dots = \dot{x}_n = \dot{x}_1 = 0$, yields $x_1 = x_2 = \dots = x_n$. Using these results in Eq. (3) we find that x_1 is given by the roots of the quadratic equation

$$n x_1^2 - Q x_1 + a(1 - Q) = 0, \quad (5)$$

which has two real positive roots provided the condition

$$Q^2 - 4na(1 - Q) \geq 0 \quad (6)$$

is satisfied.

The analysis of the roots of Eq. (5) and the numerical evaluation of the Jacobian eigenvalues indicate that the smaller root is always unstable, whereas the larger root is (locally) stable for $n \leq 4$. In addition, the disordered fixed point $x_i = 0, \forall i$ and $x_e = 1$ is always stable (Campos et al., 2000).

It is well known that for $n > 4$ the steady state of the hypercycle is characterized by stable periodic solutions (Eigen and Schuster, 1979; Hofbauer and Sigmund, 1988; Hofbauer et al., 1991) where the concentrations x_i vary wildly reaching values dangerously close to zero, which would certainly doom a finite-population system (Nuño and Tarazona, 1994). Nevertheless, here we take an optimistic stance and assume that the hypercycle is an acceptable information integrator even in the regime where it exhibits periodic solutions: the n templates do coexist in this regime after all, albeit with (very) distinct concentrations. The issue is then to determine the region in the space of the parameters Q and a where the steady-state solution is such that $\sum_{i=1}^n x_n = 1 - x_e$ is nonzero.

The search for steady-state solutions with nonvanishing concentration of functional templates can be carried out straightforwardly through the numerical integration of the differential equations (1)–(2). The procedure is illustrated in Fig. 1 for $n = 12$: for a fixed value of a we decrease Q until we reach a threshold value below which the only steady-state solution is $x_e = 1$.

Remarkably, through this numerical analysis we find that the region of viability of the hypercycle (i.e., the region in the space (Q, a) characterized by a nonzero concentration of functional templates, regardless of whether the stable solution is a fixed point or a periodic orbit, as shown in Fig. 2 for $n = 5$) is determined by the condition of existence of real fixed points, Eq. (6). We are not aware of a mathematical proof for this result. For $n = 2$, index theory can be used to show that inside the region enclosed by a periodic orbit there must exist at least one fixed

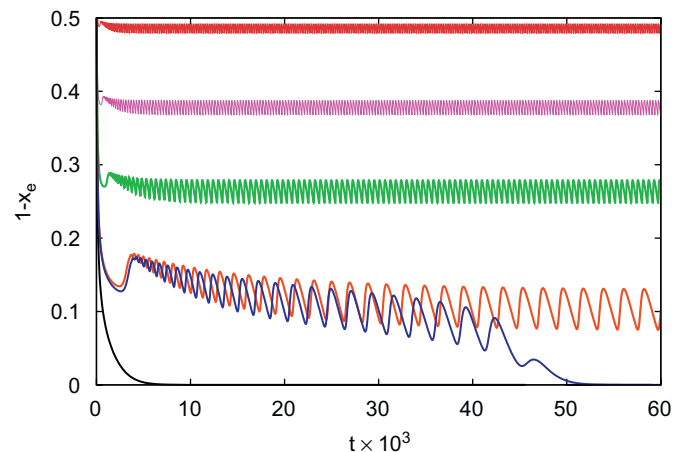


Fig. 1. Time evolution of the total concentration of functional templates for $n = 12$, $a = 0.001$ and (top to bottom) $Q = 0.5, 0.4, 0.3, 0.2, 0.19639, 0.1$. The periodic solutions disappear at $Q \approx 0.19639$, the value at which the condition (6) for the existence of a nontrivial equilibrium is violated. We have no proof for this remarkable coincidence. For lower values of replication accuracy the dynamics converges to the trivial fixed point $x_e = 1$, which is always stable.

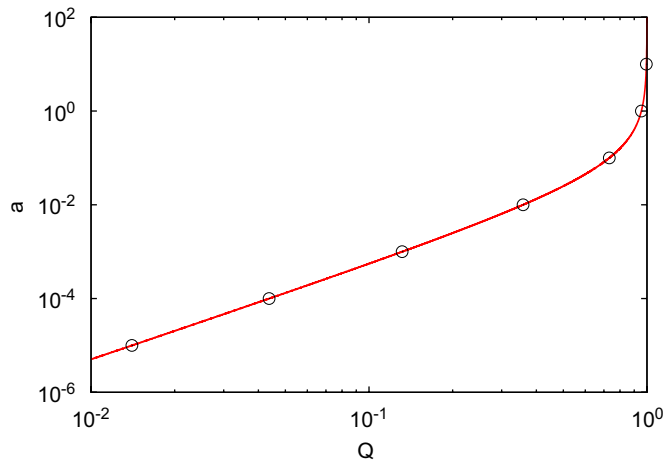


Fig. 2. Bifurcation diagram in the space (Q, a) for $n = 5$. Periodic stable solutions exist only in the region above the curve, where inequality (6) is satisfied. The symbols \circ are the results obtained using the numerical procedure illustrated in Fig. 1.

point so that the absence of fixed points precludes the existence of periodic orbits (Guckenheimer and Holmes, 1983, p. 51). It seems, however, that this result cannot be extended to $n > 2$. The theorem proved by Hofbauer et al. (1991) is not helpful either: it asserts that for a hypercycle system with no error tail (i.e., $Q = 1$) if the (unique) fixed point becomes unstable then there is a stable periodic orbit, whereas our conjecture is that if there is a stable periodic orbit then there must be at least one unstable fixed point.

In summary, we find that the hypercycle system is viable provided the number of functional templates n satisfies the condition $n \leq n_m$ where

$$n_m = \frac{Q^2}{4a(1-Q)}. \quad (7)$$

Since n_m is a monotonously increasing function of $Q \in [0, 1]$ and Q , in turn, is a monotonously decreasing function of L (recall that $Q = \exp(-uL)$) we find that n_m decreases with increasing L . Hence, all other things being equal if the number of functional templates n is increased then their lengths L must decrease accordingly so as to guarantee that $n \leq n_m$ is fulfilled. This remark shows that an information preservation principle similar to that derived for package models holds for the hypercycle as well, which suggests a reconsideration of the whole approach based on the coexistence of distinct templates to address the information crisis of prebiotic evolution.

4. Conclusion

In our analysis we have opted for the choice of parameters that most favored the stability of the hypercycle. For instance, introduction of other interactions such as the catalytic promotion of the growth of the templates in the error tail by functional templates—an assumption implicit in the package models—can only reduce the value of n_m . (We have verified that the catalytic coupling between functional templates and the error tail does not produce any qualitatively new result.) Similarly, the parameter setting that corresponds to the elementary hypercycle in which $A_i = 0, \forall i$ but $A_e = 1$ results also in a reduction of n_m . Asymmetric hypercycles in which the templates have distinct productivities A_i

leads to internal competition and again to the decrease of n_m (Campos et al., 2000). Hence Eq. (7) must be seen as an upper bound to the maximum number of functional templates in the hypercycle.

The effect that a change δL causes on n_m is given by

$$\frac{\delta n_m}{n_m} = -u \left(2 + \frac{Q}{1-Q} \right) \delta L. \quad (8)$$

In the case the functional templates have a high replication accuracy (i.e., $1 - Q \approx uL \approx 0$) we find that the product $n_m L$ tends to a constant value, similarly to the findings for the package models (Silvestre and Fontanari, 2007, 2008).

We stress that Eq. (7) is worthful because its validity is not restricted to the regime where the nontrivial fixed point is stable: it holds also in the regime where the only stable solutions are periodic orbits. We provide only numerical evidence to support this remarkable finding which is based on the conjecture that the existence of an unstable fixed point is a necessary condition for the presence of stable periodic orbits in the system of ordinary differential equations (1)–(2). It would be very interesting to find a proof for this conjecture.

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