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Mutual catalysis in sets of prebiotic organic molecules: Evolution through computer simulated chemical kinetics

D. Segré, Y. Pilpel, D. Lancet *

Department of Membrane Research and Biophysics, Weizmann Institute of Science, Rehovot 76100, Israel

Abstract

A thorough outlook on the origin of life needs to delineate a chemically rigorous, self-consistent path from highly heterogeneous, random ensembles of relatively simple organic molecules, to an entity that has rudimentary life-like characteristics. Such entity should be endowed with a capacity to express variation, undergo mutation-like changes and manifest a simple evolutionary process. For simulating such system we developed the Graded Autocatalysis Replication Domain (GARD) model for explicit kinetic analysis of mutual catalysis in sets of random oligomers derived from energized precursor monomers. The kinetic properties of the GARD model are based on vesicle enclosure and expansion. With the additional assumption of spontaneous vesicle splitting, a GARD evolution scenario is envisaged as a consequence of pure chemical kinetics. Here we show how the GARD model can serve as a platform for investigating the dynamics of self-organization mechanisms in molecular evolutionary processes. © 1998 Elsevier Science B.V. All rights reserved.

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1. Introduction

It is of no surprise to anybody that a large variety of physical phenomena can be explained by means of few general laws with the help of mathematical formalisms. In contrast, for biological phenomena, the existence of underlying fundamental laws is less easily demonstrated. It has been proposed [1] that for a specific topic of biological

* Corresponding author. E-mail: bmlancet@weizmann.weizmann.ac.il.

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research, namely the origins of life, progress could be made through a search for such general laws. We rationalize this statement as follows:

(1) The origin of life is a historical event, so far away in time that we cannot hope to trace back the path of early prebiotic evolution. It is highly unlikely that any specific scenario purporting to explain how exactly life started will be proven right by experimental evidence. Still, a deeper understanding of the emergence of life may come from a general model. Such a model should assume some non-biological initial conditions, and explain through physical and chemical laws how entities with characteristics of living organisms could gradually arise [2,3]. The emphasis here is on the path from the non-living to the living, rather than on the the exact specification of the initial conditions.

(2) The origin of life has many similarities to the study of complex phenomena in physics. The emergence of life cannot be inferred easily by examining molecular shapes or binding energies. Likewise, the details of a pattern cannot be easily derived from the elementary laws that govern a complex dynamic system. The problem of the origins of life begins with a set of molecules [4], governed by physical and chemical laws. Concepts such as self-replication, information carriers or metabolism are allowed only as emergent properties. Insights on self-organization of complex systems could have important consequences in the study of the origins of life [9].

The model that we have proposed for approaching the problem of the origin of life (Graded Autocatalysis Replication Domain, GARD), utilizes chemical kinetics to simulate the behavior of mutually catalytic sets [5–8]. In the present work we wish to show how the GARD model can shed light to the temporal behavior and the dynamics of a molecular evolutionary process. We will also discuss some limitations of the present model, and describe some features of novel, more powerful extensions.

2. Results

It has been suggested that mutual catalysis in sets of simple organic molecules could lead to a process akin to self-reproduction [9,10]. The GARD model extends this concept, and provides a quantitative analysis of mutual catalysis among members of a set of random molecules derived from energized precursor. The simplest embodiment of GARD consists of a set of N types of molecules (A_i) generated from a common precursor (A_0) by a set of reversible reactions, with forward and backward rates k_i and k_{-i}, respectively. A network of mutual catalysis events among GARD members can sustain self-replication of the entire ensemble. The components of GARD may be any organic molecules, endowed with sufficient complexity to allow for structural diversity and a measure of mutual complementarity. The mutual catalytic rate enhancement exerted on the species A_i by the species A_j is denoted by a matrix element β_{ij}. For GARD simulations we use a formalism that allows one to assign likelihood values for any degree of catalysis between two randomly chosen species A_i and A_j. This is

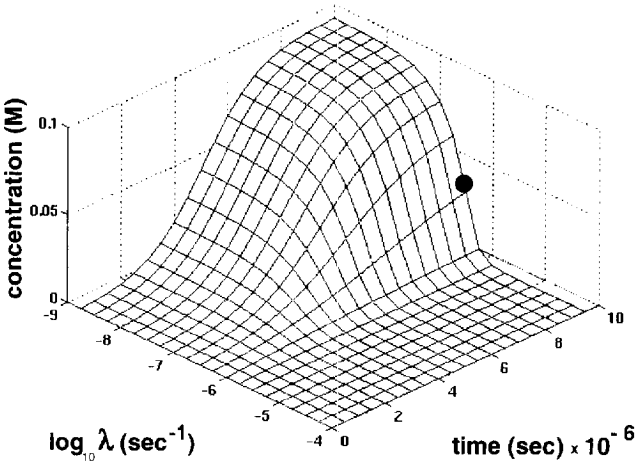

Fig. 1. The dependence of the concentration of a GARD species on time and expansion rate λ. For any given value of λ, the concentration reaches a steady state with a sigmoidal time course typical of autocatalysis. As the expansion rate λ increases, the steady-state concentration diminishes. This decline is steepest around a critical λ value (λ_c, large dot).

described in the form of a probability distribution

$$\Phi(\beta_{ij}) = \mathrm{Binom}[n, p, c_1 \log_{10}(\beta_{ij}) + c_2], \tag{1}$$

analogous to our previously developed Receptor Affinity Distribution (RAD) model [5,11]. It is further assumed that GARD components are spatially enclosed, e.g. in a lipid-like vesicle [12], whose potential expansion with time exerts a selective force on the members of the mutually catalytic set. A law of the kind $\exp(\lambda t)$ for this expansion [13] leads to the following GARD differential equations:

$$\frac{dA_i}{dt} = (k_i A_0 - k_{-i} A_i)\left(1 + \sum_{j=1}^{N} \beta_{ij} A_j\right) - \lambda A_i, \quad i = 1, \ldots, N. \tag{2}$$

We demonstrated that the quantifiable self-reproduction capacity of this entire molecular ensemble is formally related to the degree of mutual catalysis among its members. In the GARD formulation, vesicle expansion is assumed, and a graded metric of self-reproduction (λ_c) is computed based on how well the internal composition is preserved in face of the expansion-related dilution flux (Fig. 1) [8].

A finite value of the parameter λ_c may be ascribed to any collection of molecules, with any amount of mutual catalysis. It applies equally to very simple entities, such as single autocatalysts, and to evolved proto-organisms. This allows one to trace with continuity a process of prebiotic evolution from sets with feeble self-replication capacity up to more elaborate and fast self-replicating entities. A useful aspect of λ_c is demonstrated in a simple evolutionary process in which a simulated chemical set is allowed to undergo minute compositional changes, and λ_c is used as a fitness parameter for a "selective" process. We consider a large population of small GARD vesicles,

each with N molecule types, randomly sampled out of a global number $N_G \gg N$ of chemically allowed species, all interconverting with A_0. A certain range of λ_c values might be attainable in a random mixture of organic molecules of the kinds suggested to have occurred on the surface of primordial earth. In such spontaneously formed GARD vesicles, further discrete changes in chemical composition could ensue, akin to mutations among replicating information carriers [14,15]. These could result in a gradual evolution-like change, leading to increasingly higher λ_c values with progressively lower probability [8]. We simulate such a process by numerically solving Eq. (2), and calculating iteratively the value of λ_c for the current GARD vesicle. Changes in the β matrix are induced by replacing one of the species by another, randomly chosen molecule. This amounts to changing one row and one column in the β matrix. Such changes are accepted only if they give rise to a vesicle with higher self-replication capacity [8]. While at the initial steps in this simulated process few instances of strong mutual catalysis are present, the later stages result in the formation of a chemical network that is well-connected in terms of mutual catalysis. In Fig. 2a, λ_c is plotted against time for such a simulated evolutionary process. The evolution curve manifests punctuated equilibrium behavior [16], with periods of inactivity, alternated with burst of improvement, independently of the observed time scale.

This result has been obtained for a GARD with $N = 20$, and with parameters for the probability distribution $\Phi(\beta_{ij})$ (Eq. (1)) as in Fig. 2. The same kind of behavior has been observed in simulations with different values of N, and different parameters for the catalytic potencies distribution. Some insight about the dynamics of the system can be obtained by examining the network formed by arrows corresponding to catalytic enhancement higher than a threshold (Fig. 2). The network of Fig. 2c corresponds to a long plateau, indicating a condition of high stability, potentially a local λ_c minimum in the landscape of possible vesicle compositions. In network of Fig. 2c it is possible to note the presence of a number of species catalyzing each other in a cyclic fashion (bold arrows). Cycles of any size constitute powerful catalytic domains capable of catalyzing a number of other species in branched stems. In the simulated evolutionary process, the first step that destabilizes the system (leading to network given in Fig. 2d), breaks the large cycle that was present in network of Fig. 2c, because of a mutation that has occurred in position 6. A whole class of new configurations becomes suddenly available to the system. After a few rearrangements (the more significant being the mutation at position 10), a new stable situation is reached, correspondent to network of Fig. 2e. The presence of this kind of dynamics has been already noticed in other simulated evolutionary processes, and the possibility that Self-Organized Criticality [17] plays a fundamental role in the evolution of living organisms has been suggested [18]. Indeed, the distribution of the length of the plateaus (L) (Fig. 2b) seems to obey a power law L^{α} with $\alpha = -1.07 \pm 0.03$ suggesting, perhaps, that molecular evolution could show hallmarks of a self-organized critical phenomenon as well [9].

The GARD model affords the possibility of relating the connectivity of a catalytic network composed of an arbitrary set of molecules to the time behavior of its potential evolution. This can be a powerful tool for translating the GARD model assumptions

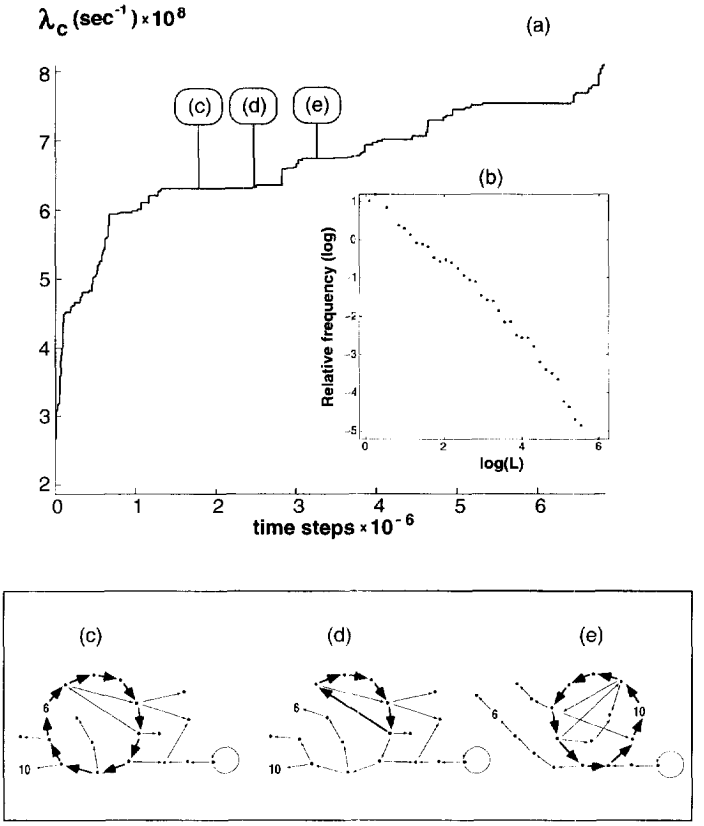

Fig. 2. (a) A curve of the evolutionary process simulated for a GARD system. The parameters for the $\Phi(\beta_{ij})$ distribution are $n = 15$, $p = 1/8$, $c_1 = 2$, $c_2 = 4$. The points labeled (c)–(e) correspond to the catalytic networks drawn below. (b) Distribution of plateau lengths L relative to the curve in (a). The number of analyzed plateaus is 380. A fit to a power law L^{α} gives $\alpha = -1.07 \pm 0.03$ (for the linear fit in a log–log scale, the correlation coefficient is -0.99). (c)–(e) Networks of catalysis: only the values above a threshold of 30 are indicated. Bold arrows evidence the largest cycles present at the different stages.

into predictions about real molecular evolution properties. The challenge of making such predictions calls though for an improvement towards a more realistic model. A first aspect that we see as a limiting factor for such development is the assumption of externally imposed expansion for the GARD vesicle. For this reason, we are now developing a variant model which includes vesicle-forming amphiphils among the molecular species of the GARD (the Amphiphil-GARD) [20]. Vesicle expansion becomes in this way a direct consequence of the catalyzed reactions, and a deeper interpretation of the GARD vesicle as an explicit computer model for a "minimum protocell" [19] might begin to emerge. In addition, we are moving in the direction of modeling chemical reactions through stochastic simulations. This approach is different from that described above, which utilizes differential equations to simulate chemical kinetics. The novel approach, that we name Single Molecule Algorithms for Complex Chemistry (SMACC),

considers random encounters of molecules as potential reaction events [5]. Among the advantages of SMACC, we wish to mention the possibility of dealing with a large and variable number of possible molecular species – important for simulating prebiotic scenarios. Moreover, the compositional mutations previously performed artificially on the GARD vesicles become now a natural consequence of random fluctuations of the composition of ensembles permanently exchanging material with the surrounding environment. Preliminary results from such an extended version of the GARD model, show an evolutionary process that bears some resemblance to that shown in Fig. 2. This is now achieved without assuming an imposed expansion, and the simulation manifests spontaneous compositional mutations. Further analysis will allow us to provide a more accurate description of the kinetic and thermodynamic behavior of mutually catalytic sets in a primordial setting.

3. Conclusions

We have shown how the GARD model, a tool for explicit kinetic analysis of mutually catalytic sets under prebiotic conditions, can serve as a platform for simulated experiments of molecular evolution. The dynamics of the system could allow one to extract general patterns of behavior in the evolution of mutually catalytic sets. Such patterns could be related to fundamental stages of the origins of life.

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