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Abstract

The Graded Autocatalysis Replication Domain (GARD) model described here depicts an early primordial scenario, prior to the emergence of biopolymers, such as RNA or proteins. The model describes, with the help of statistical chemistry computer simulations, a collection of organic molecular species capable of rudimentary selection and evolution. The GARD model provides a rigorous kinetic analysis of simple sets of chemicals that manifest mutual catalysis. It is shown that catalytic closure can sustain self replication up to a critical dilution rate, related to the extent of mutual catalysis. The capacity for self replication in a mutually catalytic set is shown to be a graded property, quantitated by a critical parameter $\lambda_{ci}$. GARD could be a simple model for a primordial scenario, in which replication and catalysis are performed by the same set of molecules.

GARDobes are proposed to be entities that embody a GARD system, endowed with a non-DNA "compositional genome", and are presumed to have replicated slowly and imperfectly through mutually catalytic networks. Therefore, they are not bound by the standard cellular size constraints: GARDobes may be as small as a few nanometers, with 20-50 nanometers being rather large and elaborate. Active GARDobes, if ever found on earth or on other planets, would be distinguished by a highly biased organic chemistry, i.e. having only a small subset of the possible molecules of any given class. Their fossils might still bear the hallmarks of such a bias, with narrow spectra of molecules such as Polycyclic Aromatic Hydrocarbons or even with enantiomeric excesses.

Keywords: Self replication, mutual catalysis, autocatalysis, chemical kinetics, computer modelling, numerical analysis, chemical selection, compositional genome, minimal life.
**Introduction**

Primordial evolution requires self replication of chemical species. Autocatalysis and template-mediated replication of individual molecules have been pursued as the basis for such a process (Eigen, 1971; Swetina and Schuster, 1982; Küppers, 1983; Lifson, 1987; Orgel, 1992; Li and Nicolaou, 1994; Siever and Von Kiedrowski, 1994). In parallel, it has been suggested (Dyson, 1985; Farmer, Kauffman et al., 1986; Kauffman, 1993; Stadler, Fontana et al., 1993; Fontana and Buss, 1994) that sets of biopolymers with mutual catalysis may undergo replication (due to "catalytic closure", (Farmer, Kauffman et al., 1986; Kauffman, 1993)), even if none of the individual components is autocatalytic. The latter scenario has been proposed to represent a primitive self-propagating metabolism without a genome (Wächtershäuser, 1990; Kauffman, 1993). We describe here a kinetic model which strongly supports the feasibility of self replication in mutually catalytic sets, and provides a quantitative measure of self replication of species in such sets. The results address a potential scenario for rudimentary replication behavior in a primordial, very heterogeneous mixture of organic molecules (Miller, 1953), members of which may be expected to display weak and non-specific catalysis. Such scenario could predate a much later stage, at which self-replication began to be performed by more complex information-carrying or catalytic biopolymers (Eigen, 1971; Orgel, 1992).

Recently, we introduced the GARD model (Segré et al., 1996, Segré et al., 1998, Segré and Lancet 1999), as a novel approach that combines rigorous chemical kinetics with realistic assumptions on molecular processes that could occur prebiotically. This model is described below and its implications to bioastronomy are discussed.

**Results and Discussion**

A simplified representation of a catalytic set (cf. (Kauffman, 1993)) is shown in Figure 1. In this model (cf. (Lancet, Kedem et al., 1994)), N chemical species (A<sub>i</sub>) are generated from a high energy precursor A<sub>0</sub> supplied from outside the system ("food set", (Kauffman, 1993)). This generation takes place in a set of reversible unimolecular reactions with rate constants k<sub>i</sub>, k<sub>−i</sub>. The specific model considered here is useful for analyzing the most fundamental features of mutual catalysis and catalytic closure. More elaborate embodiments, with two or more food set species and a comprehensive reaction topology (Farmer, Kauffman et al., 1986; Kauffman, 1993; Stadler, Fontana et al., 1993; Fontana and Buss, 1994), may be similarly analysed, but with considerable augmentation of mathematical complexity.

In previous analyses (Farmer, Kauffman et al., 1986; Kauffman, 1993), each species A<sub>i</sub> (symbolizing any organic compound, conceivably including amino acids, nucleotides and their oligomers) was deemed as a potential catalyst for one or more of the system's chemical reactions. The present model considers such a generalization, in which each of the species A<sub>i</sub> could potentially catalyze more than one of the reactions. In the most general case, mutual catalysis is defined by an NxN matrix β,
whose element \( \beta_{ij} \) is the catalytic enhancement factor by the substance \( A_j \) of the rate of the reaction \( A_0 \leftrightarrow A_i \) (\( i=j \) signifies autocatalysis).

The time dependent concentration of the species \( A_i \) obeys the differential equation:

\[
\frac{dA_i}{dt} = k_i A_0 - k_{-i} A_i + \sum_{j=1}^{N} k_j \beta_{ij} A_0 A_j - \sum_{j=1}^{N} k_{-j} \beta_{ji} A_i A_j \quad (i=1, \ldots, N)
\]

The first two terms in Eq. 1 represent the uncatalyzed (spontaneous) formation and decomposition of \( A_i \), that are expected to be very slow. The last two terms represent the mutually catalyzed forward and backward reactions. In reality, most \( \beta_{ij} \) may be equal to zero (no catalysis), and the occasional non-zero elements in the \( \beta \) matrix may be rather small, as expected for random interactions between organic molecules (Bar-Nun, Kochavi et al., 1994; Kirby, 1994).

In the present analysis we wish to stress the differential effect of mutual catalysis, rather than that of pure thermodynamics or basal kinetics, as the basis for time-dependent differences in the \( A_i \) concentrations. We therefore impose that the species \( A_i \) are equally favorable thermodynamically (\( K_i = k_i / k_{-i} \) equal for all \( i \)). We further assume for simplicity that all \( A_i \) have also identical basal kinetic constants (\( k_i, k_{-i} \) are equal for all \( i \)). The only difference among \( A_i \) is thus in their respective \( \beta_{ji} \). Obviously, other sets of parameters in which such equalities are not obeyed may be analysed as well.

A central question to be addressed in this paper is what are the kinetic properties of a set of chemicals which may allow it to undergo self-replication. For this, we consider an enclosed sub-system (e.g. a vesicle) containing the \( A_i \) components (Figure 1), whose wall is impermeable to all the \( A_i \) species, except \( A_0 \). \( A_0 \) is kept constant within the system through fast equilibration with a large external pool, as appropriate for a "food set" substance. Self replication may then be defined as a process that, through mutual catalysis, provides for making additional copies of all molecular species \( A_i \) from the precursor \( A_0 \). We name such a system GARD: Graded Autocatalysis Replication Domain (see Figure 1). Consider a process in which the volume available for the GARD's components increases 2 fold, but all concentrations \( A_i \) are preserved by further synthesis, i.e. the GARD's composition remains unchanged. The copy number of each of the \( A_i \) molecules will thus increase by a factor of 2, and if a GARD split into two separate volumes, a simple replication process may be thought to have occurred. As shown below, this may happen under steady state conditions, far from equilibrium, whereby a conjectural composition preserved by mutual catalysis is being propagated. Thus, it is suggested that self replication in a set of interconvertible chemicals, such as represented in a GARD, is equivalent to the homeostatic preservation of the steady state attained under conditions of persistent dilution. This is analogous to previous definitions of replicative steady states (Eigen, 1971) except that here the individual components are not assumed to be self replicating information carriers, and information is manifested in
the composition of the set as a whole (Segré and Lancet, 1999).

If the available volume in a GARD increases exponentially, as would be the case for vesicles that expand and undergo splitting (Rashevsky, 1960; Bachmann, Luisi et al., 1992; Luisi, Walde et al., 1994), i.e. $V(t) = V(0) \cdot \exp(\lambda t)$, then equation 1 becomes (see appendix A):

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

The balance between the reactions and the dilution expressed in equation (2) is rather general, and may also refer to other mechanisms, such as desorption in a set of surface-adsorbed chemicals. Eq. 2 predicts a steady state, which depends on the balance between the decline of all $A_i$ due to expansion-related dilution, and the (potentially catalyzed) generation of each $A_i$.

Figure 2A shows a numerical solution of Eq. 1 (or of Eq. 2 with $\lambda=0$) for a system with $N=20$, an arbitrary selection of the elements of the matrix $\beta_{ij}$, and the initial condition $A_i = 0$ for all $i>0$. This shows the time-dependent concentration changes for each of the chemical species $A_i$ as the reaction progresses from an initial state of pure $A_0$ to an equilibrium with all $A_i$ present at equal concentrations. It may be seen that the $A_i$ species form at different rates, which reflect the degree of catalysis exerted upon them by all $A_j$ species. The kinetic behavior of $A_i$ species that are subjected to mutual catalysis is similar to that of a single autocatalyst (bold broken line). This is an explicit kinetic demonstration that mutual catalysis can give rise to a dynamics similar to that observed in autocatalysis (see also Figure 3B, legend). However, it should be emphasized that the effect of catalysis under the conditions examined here is a faster convergence to the same equilibrium attained in absence of catalysis.

Next we consider what happens upon expansion, i.e when $\lambda \neq 0$. Figure 2B shows a numerical solution of Eq. 2 with $\lambda=10^{-7} \text{Sec}^{-1}$ and with all $A_i$ species initially at their (equal) equilibrium concentrations. After a transient change, each of the $A_i$ species attains a unique steady state concentration, the size of which depends on the degree of mutual catalysis exerted upon it. These results indicate that, under conditions of persistent dilution, catalysis may change the steady state concentration of thermodynamically identical species. In other words, dilution leads to a unique steady state composition, which is very different from equilibrium, at which all $A_i$ are equal.

The introduction of $\lambda$ as an externally imposed expansion rate parameter allows one to quantify the self-replication capacity of each chemical species within the GARD.

If $\lambda$ is increased continuously, each of the $A_i$ species will show a different behavior, which again depends on the extent of mutual catalysis exerted upon it (Figure 3A). It
is possible to define $\lambda_{ci}$ as the critical value of $\lambda$ at which the steady state concentration for a given $A_i$ drops to $1/e$ of its value at $\lambda=0$ (no dilution) (Figure 3A). It may be seen that at arbitrarily chosen $\lambda=\lambda^*$ (Figure 3A), the $A_i$ species for which $\lambda_{ci}>>\lambda^*$ become dominant, while other $A_i$ species decline appreciably. Such dominance is attained solely because of a kinetic advantage, since all $A_i$ species are chosen as equally favorable thermodynamically.

The dependence of the steady state concentrations on the strength of mutual catalysis $\beta^*$ shows a sigmoidal behavior (Figure 3B). This indicates that for a given expansion rate $\lambda$ there is a critical range of $\beta^*$ values in which catalysis is very effective in leading to catalytic closure. At lower $\beta^*$ values, even though every one of the component is catalyzed, they will not be able to cope with expansion. In other words, catalytic closure is a necessary but not a sufficient condition for self replication. On the other hand, above a certain $\beta^*$ value, a more efficient catalysis does not contribute to better replication capacity.

In order to demonstrate some additional properties of the GARD model, we analyzed a few specific cases of GARDs with $N=20$, in which the elements of the $\beta$ matrix may only assume two values: zero or $\beta^*\neq 0$. Thus, we consider a matrix with $\Omega$ non-zero elements and $N^2-\Omega$ elements that are equal to zero. This is in accordance with previous analyses of mutually catalytic sets, in which catalysis was considered as an all or nothing phenomenon (Kauffman, 1993). A detailed analysis of the case in which $\beta_{ij}$ is sampled out of a graded distribution (Lancet, Sadovsky et al., 1993) is discussed elsewhere (Lancet, Kedem et al., 1994), (Pilpel et al in preparation).

Figure 4A shows a simple case, in which all $\beta_{ij}=0$ except $\beta_{55}=\beta^*=1000$ M$^{-1}$ ($\Omega=1$). This amounts to a set in which one and only one of the components is autocatalytic, and the rest are uncatalyzed. In this case, the behavior of the autocatalyst ($A_5$) is described by the solid line of Figure 5, while all the others obey the broken line in this figure. The value of $\lambda_{ci}$ in the case where $A_i$ is an autocatalyst is given by Eq.3 (see appendix B).

$$\lambda_{ci} = k_{i-1}(e^{-1}) + \beta^*k_iA_0(1-1/e).$$

If $\beta_{6,18}=\beta_{18,6}=\beta^*$ and all other $\beta_{ij}=0$ (dual catalysis, Figure 4C), then these two mutually catalytic components are found to obey the solid line of Figure 5 and Eq.3, i.e. behave in a way identical to that of a single autocatalyst.

It should be noted that even for the case in which all $\beta_{ij}=0$, i.e. where no mutual catalysis takes place (Figure 4B), $\lambda_{ci}$ has a non-vanishing value $\lambda_{ci} = k_{i-1}(e^{-1})$. This is an indication that there is a rudimentary capacity for the GARD components to make additional copies of themselves due to the basal reaction kinetics. However, without mutual catalysis this effect amounts to trivial relaxation to equilibrium of all the GARD components.
Figure 4G shows the case of $\Omega=20$, with the constraint that each $A_i$ species is catalyzed exactly once, thus forming a GARD in which the entire set of species fulfills the condition of catalytic closure (Kauffman, 1993). In this case, all the $A_i$ show a behavior identical to that of an autocatalyst or a dual catalyst (Figure 5, solid line). In Figure 4E, seven of the species form a catalytic cycle while 13 others remain uncatalyzed. In this case, again those species that take part in mutual catalysis are found to behave according to the solid line of Figure 5, typical of autocatalysis, dual catalysis and the fully connected cycle, while the other components follow the broken line. The expanding GARD is seen in this case to propagate a unique composition ($A_4$, $A_6$, $A_{10}$, $A_{13}$, $A_{15}$, $A_{18}$, and $A_{20}$), although none of these components is autocatalytic or dually catalytic. In contrast, all the other 13 species are quickly diluted to a relatively low steady state concentration.

An important aspect of the model is depicted in Figure 4I. This model allows each $A_i$ to be catalyzed by more than one $A_j$, i.e. a gradation of mutual catalysis may take place. Here, we consider the case of $\Omega=60$, keeping $\Omega \beta$ the same as in the case of Figure 4G (taking $\beta^*=33.3$). In addition, we impose here an equal number of catalytic events (three) that each species is subjected to. The results of the calculations show again the same dependence on $\lambda$ (solid line in Figure 5). This demonstrates that synergy of multiple weak rate enhancements for each species $A_i$ by several other $A_j$'s yields an identical self-replication behavior. Showing a kinetic equivalence between a simple cycle and a more dense network of weaker catalytic values is important, since weak catalysis may be more probable among primordial chemicals with poorly evolved recognition capacity and low specificity.

An essential feature of the case of Figure 4I is that eliminating one non-zero value of the $\beta$ matrix (as in Figure 4J) has a relatively small effect on $\lambda_{ci}$ of even the slowest component (Figure 6D). In contrast, when a similar deletion is performed in the cases of dual catalysis (Figure 4C), a partial cycle (Figure 4E), or a complete cycle (Figure 4G), yielding respectively figures 4D, 4F and 4H, a more complex behavior, depicted in the respective figures 6A,B,C is obtained. Here, the slowest component behaves according to the broken line of Figure 5, and other $A_i$ species show a variety of behaviors. Such sensitivity to the elimination of one catalytic event will have a strong deleterious effect on the potential replication capacity of the entire set, in analogy to the case of a deleted hypercycle (Eigen, 1971).

Concluding remarks and implications to bioastronomy

We describe a Graded Autocatalysis Replication Domain (GARD) model for mutual catalysis in a set of simple reversible reactions, that occur within an enclosed volume. The model is based on previously developed concepts of mutually catalytic sets and catalytic closure. It is applicable to a scenario in which a heterogeneous mixture of organic molecules has already formed from simple precursor(s), while complex information carriers or biocatalysts are not yet present. A vital point of the model, similar to previous descriptions for mutual catalysis, is its portraying a system in which the catalysts and the catalyzed entities belong to the same set of molecules.
The GARD model further allows a rigorous kinetic analysis of the behavior of the mutually catalytic components, providing a quantitative assessment of their self replication capacity as a unified set. We demonstrate that components of mutually a catalytic set, none of which is necessarily autocatalytic, might resemble in their collective behavior the kinetics of a single autocatalyst. The GARD model provides a natural and simple quantitative definition of self replication capacity of members of catalytic sets. This is based on a graded measure ($\lambda_{ci}$) of the ability of the set's components to maintain their concentrations under dilution. A GARD with multiple catalysis events for each chemicals is shown to be endowed with a remarkable capacity to withstand mutation-like changes, in which one or a few catalytic events are deleted. Heterogeneous GARDs, in which a subset of the components shows efficient mutual catalysis, while other components show weaker interaction, may constitute a simple system for chemical selection and evolution. The analysis of such phenomena is currently in progress, using a more elaborate version of the GARD model, involving continuous distribution of catalytic potencies.

The GARD model has broad implications to bioastronomy. An entity based on the GARD model, with a rudimentary capacity to replicate, undergo mutation-like changes and simple evolution, may be much smaller and simpler than the any known free-living organism. The GARD concept allows bioastronomers to free themselves of the bias of the assumption that extraterrestrial life should resemble terrestrial living cells, with DNA, RNA and proteins. The concept of the Compositional Genome (Segre and Lancet 1999) allows for information content and transmission without a DNA-based genome, as well as a translationa dn transcription machinery. Therefore it provide much different estimates on the minimal size of a primordial or extraterrestrial eraly organisms. A "GARDobe" may be a few nanometers in diameters and still constitute a bona-fide early life form.

Furthermore - a GARDobe may be much more stable to environmental hazards - high temperature and pressure, as well as extremely dry conditions. This would greatly augment the window of time and conditions for the origin of life. An additional constraint to be relaxed is that of the specific chemistry to be expected. No more looking for amino acids (let alone those 20 found in our own life), no more looking for the specific nucleotides. Rather, it is possible that life would begin with any arbitrary organic chemistry that would fulfill the broad requirements of the GARD formalism. Yet, an interesring prediction of the GARD model is that wherever life began, a restricted collection of organic chemicals wil be found.This is because the GARD scenario begins with "Random Chemistry" but continues with narrowing the chemical spectrum of low molecular weight monomers, prior to the appearance of higher polymeric forms (Segre and Lancet 1999). Thus, the GARD model provides a set of novel guidelines to a "galactic traveller" in search of life's first rudiments on earth and in the universe.
Appendices

Appendix A
In an expanding vesicle of volume $V(t)$, the time dependent concentration of the GARD components relates both to the kinetics of the chemical conversions $A_0 \leftrightarrow A_i$ (basal and catalyzed), and to the rate of expansion. For derivation of Eq.2 from Eq.1 we shall account for the change in concentration due to expansion. Since expansion does not involve a change in the amount of material $Q$, we can say that $Q= A_i \cdot V$ is a constant in time and hence (denoting with "prime" the time derivative):

$$Q = A_i \cdot V$$

Therefore

$$A_i' = - \frac{V'}{V} \cdot A_i$$

If we assume $V(t)=A_0 \cdot \exp(\lambda \cdot t)$, then

$$V' = \lambda \cdot A_0 \cdot \exp(\lambda \cdot t)$$

and

$$\lambda = \frac{V'}{V}$$

thus $A_i' = -\lambda \cdot A_i$ is the contribution of the expansion to the derivative of the concentration added in Eq.2.

Appendix B
In order to derive an expression for $\lambda_{c1}$ in the case of $N=1$ we impose in Eq.2 the condition:

$$A_1 \text{ (steady state)} = (1/e)A_1 \text{ (equilibrium)} = (1/e)(A_0 k_1 / k_{-1}).$$

We obtain therefore:

$$0 = k_1 A_0 - k_{-1} (A_0 k_1 / k_{-1})/e + k_1 A_0 \beta (A_0 k_1 / k_{-1})/e - k_{-1} \beta [(A_0 k_1 / k_{-1})/e]^2 - \lambda (A_0 k_1 / k_{-1})/e$$

which solved for $\lambda = \lambda_{c1}$ gives Eq. 3.

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References

Legends

Fig. 1
A schematic depiction the GARD model. The term GARD (Graded Autocatalysis Replication Domain) denotes a collection of N types of organic molecules, that are chemically interconvertible through common precursor(s), and are contained in a spatial domain with a defined volume. GARD is governed by graded mutual catalysis and its kinetic properties resemble those of a replicating molecular autocatalyst (see text).

A GARD vesicle contains the components $A_0$, $A_1$, $A_2$, ..., $A_N$. Solid thin lines represent the reversible chemical conversions $A_0 \leftrightarrow A_i$ with the respective kinetic constants $k_i$, $k_i^{-1}$ shown on the chemical reaction arrows. The catalysis arrows connecting $A_j$ with the reaction $A_0 \leftrightarrow A_i$, represent the catalytic effect of $A_j$ on the formation and degradation of $A_i$ with a rate enhancement factor $\beta_{ij}$. The $A_0$ transport arrows represent the inward and outward free passive diffusion of the "food set" material $A_0$ which is buffered across the vesicular wall. The vesicle expansion arrows indicate the volume increment $\Delta V(t)$ in the time interval $\Delta t$.

Subsequent figures show the results of numerical solutions of Eqs. 1, 2 for this reaction mechanism.

Fig. 2
The kinetic behavior of GARD components. All the results shown here and in the next figure were obtained using the GRIND software (De Boer, 1983) on a Silicon Graphics Indy 2 computer. In a large number of numerical experiments only solutions of Eqs. 1,2 that lead to a single steady state with all $A_i>0$ were obtained, in accordance with previous analyses (Stadler, Fontana et al., 1993; Schlosser and Feinberg, 1994). The parameter values used throughout this work are:

$\lambda_1=1\times 10^{-5}$ sec$^{-1}$, $\lambda_1^{-1}=1\times 10^{-8}$ sec$^{-1}$, $A_0=1\times 10^{-4}$M.

A. The time dependent concentrations of the components of a GARD system with $N=20$, computed by numerical solution of Eq. 1 (or Eq. 2 with $\lambda=0$, i.e. no expansion). The initial concentration of all $A_i$ (for $i>0$) is equal to zero. In the case shown, the elements of the $\beta$ matrix are chosen arbitrarily in the range of 0-1000 M$^{-1}$, so that different species $A_i$ differ with respect to the number and magnitude of the of catalytic effects they are subjected to. Consequently, each $A_i$ has a different time course, but they all reach the same plateau, corresponding to chemical equilibrium, as determined by their equal thermodynamic constants $K_i$.

B. A similar analysis of Eq. 2, with a non-zero expansion rate of $\lambda=10^{-7}$ sec$^{-1}$ and with the initial concentration of all $A_i = 0.1$ M (for $i>0$) (equal to the equilibrium concentrations attained in Figure 2A). All other parameters are as in Figure 2A. Each $A_i$ reaches a different steady state plateau, depending on the degree of mutual catalysis.
Fig. 3
A. The dependence of the steady state concentrations of the chemical species A on the expansion parameter $\lambda$, derived by computations as in Figure 2B for many $\lambda$ values. The $\lambda_{ci}$ values for a given $A_i$ is that $\lambda$ at which the $A_i$'s steady state concentration declines to $1/e$ of its initial equilibrium value. $\lambda^*$ is an arbitrary intermediate value of $\lambda$ (see figure 3B and text).

B. The dependence of steady state concentrations on the degree of mutual catalysis. This curve is computed for the case of a single autocatalyst (GARD with $N=1$), with increasing $\beta_{11}$. The same curve is obtained in the case of a GARD with $N=20$, having a cycle of mutual catalysis (Figure 4E) with equal catalytic enhancement factors $\beta^*$. This $\beta^*$ dependence is computed at a specific expansion value $\lambda=\lambda^*=10^{-7}$ sec$^{-1}$ (see Figure 3A). The steady state concentration for the $A_{11}$ autocatalyst (or for any of the $A_i$ in the case of cycle) is computed for increasing $\beta^*$ values using Eq. 2.

Fig. 4
A depiction of 10 different cases of a GARD with $N=20$, the behavior of which is shown in Figures 5 and 6. All the $\beta$ matrices are "binary", having either $\beta_{ij}=0$ or $\beta_{ij}=1000M^{-1}$ (except cases I, J). Every occurrence of a $\beta_{ij} \neq 0$ is represented by a directed arrow leading from species $A_j$ to species $A_i$. The specific cases are:
A. A single species autocatalysis (the only non-zero element is $\beta_{5,5}$).
B. No catalysis (all $\beta_{ij}=0$).
C. Mutual catalysis between $A_6$ and $A_{18}$ (All $\beta_{ij}=0$ except $\beta_{6,18}=\beta_{18,6}=\beta^*$)
D. Unidirectional mutual catalysis (same as C with $\beta_{6,18}=0$).
E. Mutual catalysis sub-cycle involving 7 species out of the total 20 ($A_4$, $A_6$, $A_{10}$, $A_{13}$, $A_{15}$, $A_{18}$, and $A_{20}$). Since each of these 7 species is catalyzed once, they constitute a catalytically closed subset of the original GARD.
F. Same as E, with one catalysis step missing ($\beta_{4,20}=0$).
G. A cyclic network of catalysis, where $\beta_{2,1}=\beta_{3,2}=\beta_{4,3}=\ldots=\beta_{20,19}=\beta_{1,20}=\beta^*$.
H. The same cycle as in D, "broken" at one position ($\beta_{2,1}=0$).
I. A dense network of catalysis, where each species is catalyzed by three other species with $\beta^*=1000/3$.
J. The same network as in F, lacking of one catalytic connection ($\beta_{2,1}=0$).

Fig. 5
Plots of the $\lambda$-dependence of the steady state concentrations of the chemical species $A_i$ for the specific cases in Figure 4 A, B, C, E, G, I. The solid line represents the behavior of all the species $A_i$ for which catalytic closure obtains: Figure 4A ($A_5$), Figure 4C ($A_3$ and $A_9$), Figure 4E ($A_4$, $A_6$, $A_{10}$, $A_{13}$, $A_{15}$, $A_{18}$, and $A_{20}$), Figure 4G (all $A_i$), Figure 4I (all $A_i$). The broken line refers to all other (uncatalyzed) $A_i$ species in cases A, B, C, E, G, I.
Fig. 6
A similar analysis as in Figure 5 applied to Figures 4D, F, H, J.
In all the case shown here A, B, C, D which refers to Figures 4D, 4F, 4H, and 4J respectively, the solid lines refers to the species that are subjected to various degrees
Steady state concentration (M)

Fig. 3A

\[ \lambda (\text{sec}^{-1}) \]

\[ \text{Steady state concentration (M)} \]
Fig. 3B

Steady state concentration (M)

$\beta^* (M^{-1})$

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Fig. 5

Steady state concentration (M) vs. \( \lambda (\text{sec}^{-1}) \)

- Solid line represents the steady state concentration.
- Dashed line indicates another concentration profile.

Log-log scale for both axes.
Fig. 6