The influence of different kinetic rates on the dynamics of a simple model of catalytic reaction network

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Abstract. An ODE-based model of a simple catalytic reaction network is discussed, with particular attention to the influence of the kinetic rates of the various reactions on the overall dynamical behavior.
Several distinct scenarios are described and analyzed, highlighting the importance of the fine tuning of the kinetic parameters in regard to the competition for survival of different dynamical structures, i.e. autocatalytic cycles, on the one hand, and linear reaction chains, on the other, which access the same limited resources.
Finally, the importance of a possible compartmentalization of this dynamical system within protocell-like structures is discussed, with explicit regard to the competitive advantage that is supposed to characterize the dynamics of autocatalyitic cycles.

1 Introduction

The emergence of *autocatalytic set of molecules* in a prebiotic environment is considered to be an important step toward the emergence of life [4,5,20,18,2,16]. Several distinct models (e.g. [5,20,2,17,29,9]) have been developed in the last decades to address the questions on how complexity initially emerged from the interaction of basic entities and on how billions of years of evolution gradually molded the life as we know it today.
To this end, a relatively recent discipline named complex systems biology [19] aims at joining the concepts and methods provided by the science of complex systems with the network-based approach typical of systems biology [21,22,1], with the explicit goal of investigating the generic dynamical properties of biological systems of particular interest.
Within this methodological framework, our objective is to decipher and characterize the robustness of autocatalytic cycles, by analyzing a deterministic ODE-based model of a catalytic reaction network. In particular, the attention is focused on the analysis of the influence of the kinetic rates of the different reactions of the system on the overall dynamical behavior.

In section 2 a description of the model is provided, while section 3 is devoted to the results of the numerical simulation. In section 4 the results are commented and finally section 5 is dedicated to some conclusions and further evolutions of the research.

2 Description of the model

Conversely to our recent works [11,13,9,12,10,7], we adopt here a deterministic description of a simple catalytic reaction network by means of a system of ODEs[4].
In general, the model describes the dynamics of a simple network of catalytic reactions that involves species that can be substrates, products or catalysts according to the different reactions in which they participate. The reactions are simple conversions of a species (i.e. substrate) into another one (i.e. product), which occur by means of the catalytic activity of another species (i.e. catalyst). We suppose that the system evolves in a well stirred chemostat with an incoming flux of nutrients, i.e. the substrates, and an outgoing flux affecting all the molecules present in the reactor.

The system is composed of two simple reaction pathways only, the former forming an autocatalytic cycle (i.e. a closed reaction chain in which one of the products of a specific reaction is also a catalyst of one of the other ones) and the latter forming a linear reaction chain. Both pathways compete for the same limited substrates and, therefore, the overall speed of each pathway is fundamental in order to dominate within a competitive scenario (represented in fig. 1). We decided to choose this particular model because it represents one of the simplest yet not trivial possible systems, which can actually shows complex dynamical behaviors, despite the relatively limited parameters and variables space. The final goal is to disentangle and characterize the specific effect of a variation in some key parameters on the overall dynamics, mostly considered that this would be a way tougher task as the number of parameters and variables of the model increases.

The overall reaction scheme is described in the following:

1. $A + S_1 \xrightarrow{k_1} B + A$

[4] The software used to simulate is *Dizzy* [28] available at http://magnet.systemsbiology.net/software/Dizzy/. Although *Dizzy* is actually developed to perform stochastic simulations, it provides also a useful tool for the simulation of deterministic systems. Once that the reactions scheme has been created, the user has the possibility to choose which kind of simulation performs. With regard to these analysis we adopted a finite difference method ODE solver, specifically the 5th-order Runge-Kutta algorithm with an adaptive stepsize controller.

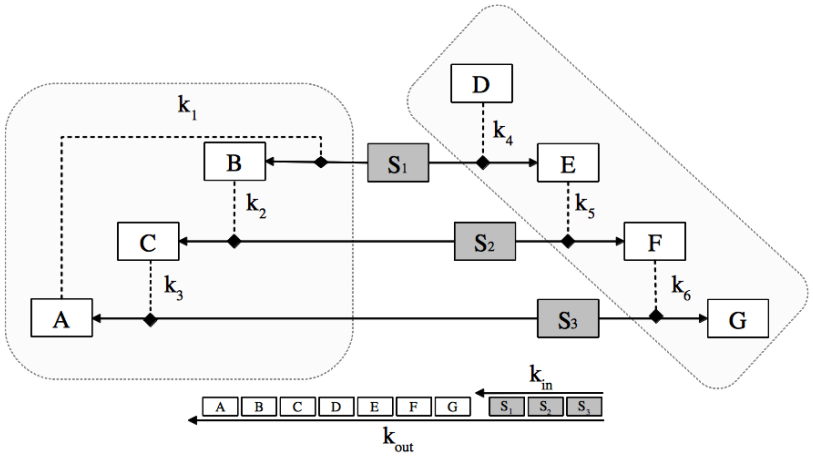

Fig. 1. The scheme of a simple catalytic reaction network composed of two different reaction pathways is represented. The species are represented by capital letters, arrows represent reactions and dot lines are catalyses. On the left side the autocatalytic cycle composed of the species A, B and C is shown. On the right side the reaction channel composed of the species D, E, F and G is shown. S_1, S_2 and S_3 are the substrates involved in both the reaction pathways. The kinetic rates are indicated by k_n with $n = 1, ..., 6$, k_{in} stands for the incoming flux rate of the substrates (moles per sec. in a unitary volume) and k_{out} stands for the outgoing flux rate of all the species (and proportional to their concentrations).

2. $B + S_2 \xrightarrow{k_2} C + B$
3. $C + S_3 \xrightarrow{k_3} A + C$
4. $D + S_1 \xrightarrow{k_4} D + E$
5. $E + S_2 \xrightarrow{k_5} E + F$
6. $F + S_3 \xrightarrow{k_6} F + G$
7. $\xrightarrow{k_{in}} S_1, S_2, S_3$
8. $A, B, C, D, E, F, G, S_1, S_2, S_3 \xrightarrow{k_{out}}$

In this work different competitive scenarios have been considered, varying the nature of the reactions composing the linear reaction chain only and letting those involved in the autocatalytic cycle unchanged. For each different setting the modification of the scheme is described in the specific section.

3 Results

3.1 Competition between an autocatalytic cycle and a reaction chain

The reactions scheme of the first scenario is that represented in fig. 1 in which an autocatalytic cycle and a reaction chain compete for the same limited resources. Figure 2a shows the behavior of a system in which all the reactions occur with identical kinetic rates.
Once that species D (which is neither produced by the dynamics nor fed in from the influx) is completely diluted by the outgoing flux, the conversion of the substrates in the species present in the reaction chain (right side of the scheme) is no longer viable, the choice of kinetic rates being not influential. As a consequence, the autocatalytic cycle is the only dynamical structure that can survive, at least under certain conditions.
It is important, in fact, to remark that the sustainability of the autocatalytic cycle depends on the velocity of the outgoing flux as well. If the overall rate of the dilution is faster than the rate of the formation of the species belonging to the autocatalytic set, it would be diluted as well.
Figure 2b shows the behavior of the species when the kinetic rates regarding the reactions not belonging to the ACS are ten times faster. According with what we said above, after a first transient in which the species belonging to the chain seem to overbear, the dilution of the first specie of the chain stops the chain production and, eventually, the ACS dominates the system's dynamics.

3.2 Introduction of an autocatalytic loop in the first step of the reaction chain

With the addition of an autocatalytic loop at the beginning of the reaction chain[5] the reaction 1 of the scheme is modified as $D + S_1 \xrightarrow{k_4} 2D + E$ and this dramatically affects the dynamics.
In the specific case in which all the reactions are characterized by the same kinetic rates the system allows the coexistence of all the species. In particular,

[5] For the sake of clarity it is important to notice that, with the insertion of a loop, the reactions pathway is no longer a simple reaction chain. Nevertheless, we keep the same denomination in order to distinguish from the autocatalytic cycle represented in the left side of the reactions scheme shown in fig. 1.

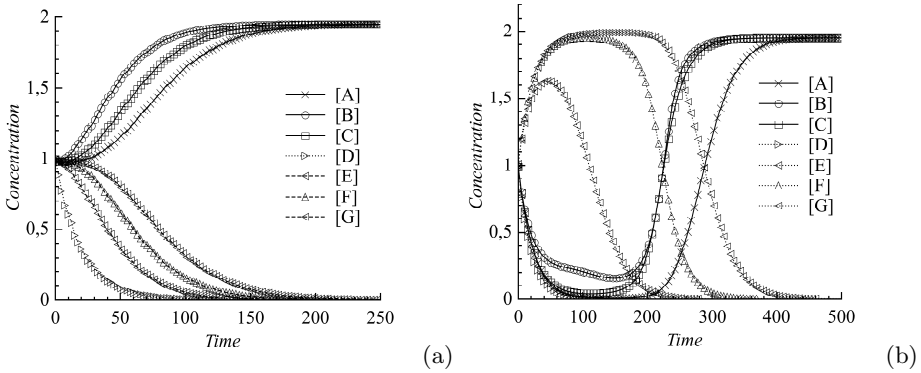

Fig. 2. The graphs show the concentrations of the species in function of time. On the left panel (a) the behavior of a system characterized by $k_1 = k_2 = k_3 = k_4 = k_5 = k_6 = 1$ is shown while on the right panel (b) the kinetic rates of the reactions belonging to the reaction chain are ten times greater than the kinetic rates belonging to the autocatalytic set, $k_1 = k_2 = k_3 = 1$ and $k_4 = k_5 = k_6 = 10$. In both panels $A_{(0)} = B_{(0)} = C_{(0)} = D_{(0)} = E_{(0)} = F_{(0)} = G_{(0)} = 1$, $k_{in} = 0.1$, $k_{out} = 0.05$.

all the species reach the same fixed point, i.e. the same concentration (fig. 3a)[6]. On the other hand, a little increment in the kinetic rates of the reactions of the chain is sufficient to disrupt the equilibrium and influence the relative possibility of survival (fig. 3b).

This outcome hints at another interesting issue, that is the importance of the linear chains that originate from the ACSs, i.e. the *branches* of the reaction graph. One finer analysis may take also this more complex structures into account, but this would go further than the objective of the current work. The interest reader is referred to Filisetti et al.[10,9] for a review on the structural properties of complex catalytic reaction networks.

3.3 Introduction of an autocatalytic loop in the last reaction of the reaction chain

A different behavior is observed when the autocatalytic loop is added to the final step of the reaction chain. Accordingly, the reaction 6 of the scheme is modified as:

$$F + S_3 \xrightarrow{k_6} 2F + G.$$

If all the reaction rates are identical (fig. 4a) even though the species involved

[6] Notice that a (possibly analytical) stability analysis concerning this and other specific results could be important and highly effective in a exhaustive description of these phenomena. Nevertheless, because of the lack of time it was not possible to perform this kind of analysis in course of this work, while it will be inserted in our future (and more extended) article on this model.

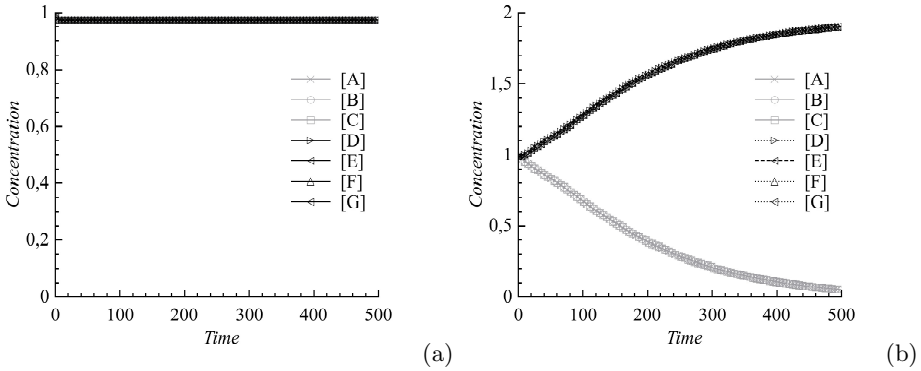

Fig. 3. The graphs show the concentrations of the species in function of time after the modification of the first reaction of the right side of the scheme represented in fig. 1. On the left panel (a) the behavior of a system characterized by $k_1 = k_2 = k_3 = k_4 = k_5 = k_6 = 1$ is shown; it is possible to observe a perfect overlap of the concentrations of the different species. On the right panel (b) the kinetic rates of the reactions belonging to the reaction chain are 1.1 times greater than the kinetic rates belonging to the autocatalytic set, $k_1 = k_2 = k_3 = 1$, $k_4 = k_5 = k_6 = 1.1$. In both panels $A_{(0)} = B_{(0)} = C_{(0)} = D_{(0)} = E_{(0)} = F_{(0)} = G_{(0)} = 1$, $k_{in} = 0.1$, $k_{out} = 0.05$.

in the loop[7] survive with very low concentrations, the autocatalytic set eventually dominates. Nonetheless, is possible to observe that, since the substrate S_3 is shared between reaction 3 (belonging to the ACS) and reaction 6 (the autocatalytic loop), the concentration of the species A, that is the product of the reaction 3, is lower than those of the species B and C.
Moreover, the autocatalytic nature of F allows it to survive with no regard to the eventual dilution of D.
Increasing the kinetic rates of the reactions depicted in the right side of the scheme in fig. 1 the dynamical equilibrium of the system changes according to the variation of the kinetics (fig. 4b). Species D and E are always diluted by the outgoing flux and the concentrations of the species D and F increase to the detriment of A.

3.4 Introduction of an inorganic catalyst in the reaction chain

The last setting that we decided to investigate concerns the introduction of an *inorganic catalyst* (*I.C.*), an hypothesis taken into account in different scenarios concerning the origin of life [15,24,14,6].
Let us assume that the species D is an inorganic catalyst, e.g. a clay catalyst, hence it is not affected by the outgoing flux and its concentration (or quantity) remains constant in time. Assuming for simplicity all the kinetic rates equal to one, figures 5a, 5b and 5c show that the overall behavior of the system is ruled by the total amount of the *I.C.*.

[7] F is the autocatalytic species, while G is the product of the autocatalytic loop.

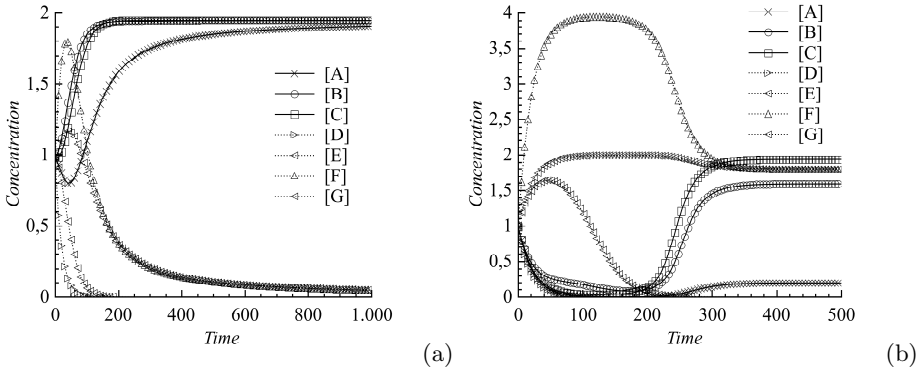

Fig. 4. The graphs show the concentrations of the species in function of time after the modification of the last reaction of the right side of the scheme represented in fig. 1. On the left panel (a) the behavior of a system characterized by $k_1 = k_2 = k_3 = k_4 = k_5 = k_6 = 1$ is shown. On the right panel (b) the kinetic rates of the reactions belonging to the reaction chain are 10 times greater than the kinetic rates belonging to the autocatalytic set, $k_1 = k_2 = k_3 = 1$, $k_4 = k_5 = k_6 = 10$. In both panels $A_{(0)} = B_{(0)} = C_{(0)} = D_{(0)} = E_{(0)} = F_{(0)} = G_{(0)} = 1$, $k_{in} = 0.1$, $k_{out} = 0.05$.

4 Discussion

The analysis of the distinct scenarios presented above clearly highlights the importance of the reaction kinetics, even in a simple system composed of two reaction pathways only, i.e. an autocatalytic set of molecules and a linear reaction chain.

One first important conclusion is that the presence of an autocatalytic set is not in itself sufficient in order to achieve a self-sustainable structure able to evolve and proliferate.

The simplest case presented in section 3.1 shows, instead, the unsustainable nature of a reaction chain in which the reactants are not introduced from the external environment within the chemostat. This outcome is clearly expected, considered that the presence of an outgoing flux compels the species which are not supplied into the feed to be produced by the reactions network and, otherwise, they are diluted by the flux.

However, it is interesting to observe that if one increases the kinetic rates of the reactions belonging to the reaction chain, i.e. increasing the uptake of the substrates by means of the species of the chain, the production of the species of the chain is greater than the production of the species of the ACS, at least up to the complete dilution of D. At that time ACSs can gain the control of the system by virtue of their higher robustness.

In the other analyzed cases we have shown that it is sufficient to slightly modify the nature of the reactions composing the reaction chain in order to dramatically influence the dynamical evolution of the system. Especially in the last scenario, section 3.4, with the presence of an inorganic catalyst, we demonstrated that its

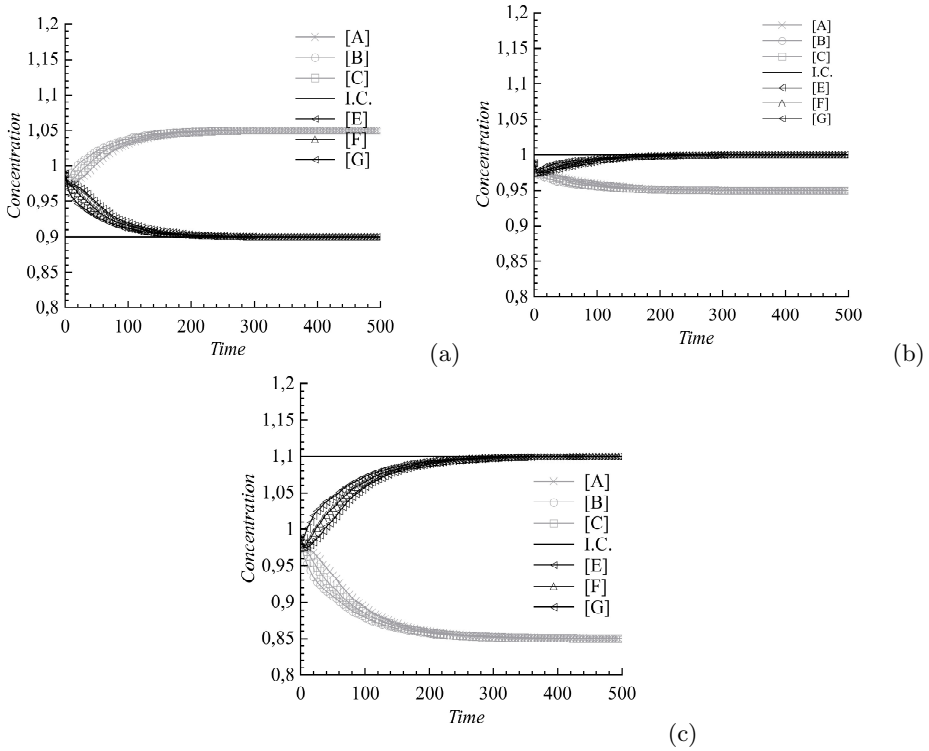

Fig. 5. The graphs show the concentrations of the species in function of time substituting the species D with an inorganic catalyst "$I.C.$". To better detect the contribution of the quantity of $I.C.$ present in the system all the kinetic rates are fixed to 1, hence $k_1 = k_2 = k_3 = k_4 = k_5 = k_6 = 1$. Panel (a) $\rightarrow D = 0.9$, panel (b) $\rightarrow D = 1$ and panel (c) $\rightarrow D = 1.1$. In all panels $A_{(0)} = B_{(0)} = C_{(0)} = E_{(0)} = F_{(0)} = G_{(0)} = 1$, $k_{in} = 0.1$, $k_{out} = 0.05$.

abundance is sufficient to modify the concentrations of either the ACS or the reaction chain.

We remark that one could perform analyses on the equilibrium states of systems such this, but in this case we preferred to focus our attention on the noteworthy (and sometimes counterintuitive) dynamics that emerge during the transients, which could actually lead to important bifurcations in the dynamical trajectory of the system.

Some further considerations. It is reasonable to hypothesize that in a prebiotic environment only a few molecular species were involved in the formation of autocatalytic structures and that, conversely, the number of directed reaction channels full of different reaction pathways uptaking most of the (limited) resources might be sensibly higher. Therefore, in this context the chances for autocatalytic structures to self-maintain and to be evolutionally favored would be much lower, given the large predominance of linear reaction pathways in the

overall dynamics.
Nevertheless, a different situation may be encountered introducing *surfactants* able to self-assembly and capture the available molecular species present in the bulk [25,24]. In this case the chance to observe the formation of an autocatalytic sets within a vesicle, instead, would depend on the probability that all the elements of the ACS are entrapped in the vesicle after its closure. In Stano et al. [31] it has been shown that once that some of the molecules begin to remain entrapped, the probability that also the other molecules are captured is significantly higher than the one expected from statistical mechanics calculations [27]. The encapsulation, in fact, would allow the new species to increase their concentrations without being diluted by the flux and, moreover, the presence of a semi-permeable membrane would protect them from possible "killer" species present in the bulk.
Assuming that only the short species, i.e. the substrates, can cross the semi-permeable membrane, the material contained in the vesicles characterized by only reaction chains will be totally diluted through successive divisions.
On the other hand, a competition for the limited resources will start among the vesicles containing all the necessary species forming an ACS.
Finally, if the vesicle containing the fastest ACS is also able to growth and duplicate synchronizing the processes of membrane growth and replication of the species [30,3,8], the higher rate of duplication and the consequent exponential growth of the number of vesicles would lead to a proliferation, and eventually to the extinction of the other vesicles, according to the Darwinian evolution triggered by the exponential nature of the population growth [23,26].

5 Conclusions

The very simple model proposed in this work helped us to investigate the importance of the dynamics in the theoretical studies concerning catalytic reaction networks of molecules, with specific regard to reaction kinetics. Although in our previous works we have already shown how the emergence of autocatalytic cycles in stochastic models of catalytic reaction networks is an indeed unlikely event despite the theoretical formulations, in this paper we concentrated our attention on a simple ODE-based deterministic system, composed of two reaction pathways only, focusing on the impact of a variation of the kinetic rates and of the structures of the reactions on the overall behavior.
One first conclusion is that the autocatalytic closure implicates a remarkable competitive advantage, mostly in regard to the higher robustness of cycles with regard to different kinds of perturbations. Nevertheless, this positive feedback is triggered only under certain conditions and, in this specific case, when the kinetic parameters are opportunely tuned. Moreover, also in the case of favorable conditions, if a single or a few ACSs emerge within a scenario characterized by the presence of a large majority of reaction chains, they would reasonably be dominated in the competition for the same limited resources.
Especially in this regard, another major issue faced in the final part of the work

concerns the importance of the encapsulation of the autocatalytic set within proto-cellular structures as vesicles. To this end, we are setting up several simulations aimed at deciphering the role of compartmentalization in the evolution of such structures, with particular regard to the concept of protocell.

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