Conservation Laws and Thermodynamics in Chemical Reaction Networks

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Many systems, including biological metabolism and prebiotic chemistry, can be modelled using the formalism of chemical reaction networks. An important quetion is, under what circumstances can such systems generate novelty and complexity? We show that when a very simple model of polymer chemistry is held away from thermodynamic equilibrium, autocatalytic cycles emerge, leading to exponential growth. This paves the way toward understanding how complex, self-producing phenomena could emerge in prebiotic chemistry in particular, and non-equilibrium systems in general.

1. Introduction

An important goal of complexity science is to understand how systems can generate novelty. That is, how is it possible for entirely new structures to form within a system, and in which kinds of system can such a process occur? This work represents a small step towards understanding such a question in the context of chemical reaction networks, but a general understanding of novelty generation would have applications in many fields, including artificial intelligence.

In chemistry, one way in which novelty can be generated is through the emergence of autocatalytic sets. That is, sets of chemical species that, collectively, catalyse one another's formation. Previous work on the emergence of autocatalysis has focused on quite complex systems. Most notably, the work of [Kauffman, 1986] and its successors focuses on collections of enzyme-like polymer molecules; while from a different direction, the work of [Fontana and Buss, 1994] looked for autocatalysis in chemistries where the molecules were represented as Lambda calculus expressions. [Ikegami and Hashimoto, 1995] looked for the emergence autocatalycity in networks of Turing machines and tapes under a noisy environment.

In this paper we show that when thermodynamic considerations are taken into account, autocatalytic cycles can emerge in much simpler systems. This suggests that the transition from chemistry to the first biological metabolism may have been easier than previously assumed, as well as providing evidence for the idea that thermodynamic considerations are important for self-organisation more generally.

2. The Model

We define a simple artificial chemistry, in which the set of species is written $A_1, A_2, \ldots A_n$, for some n. These are to be interpreted as polymers of different lengths, constructed from a single monomer type. All reactions must preserve the number of monomers. We therefore consider only reactions of the form $A_i + A_j \rightleftharpoons A_{i+j}$, where $i + j \leq n$. The double arrow indicates that the forward reaction $A_i + A_j \longrightarrow A_{i+j}$ and the reverse reaction both occur. This is required for consistency with thermodynamics.

Whether the net flow is in the forward or reverse direction depends upon the dynamics of the system.

We let every reaction occur at a net rate $R_{ij} = a_i a_j - k a_{i+j}$, where a_i is the molar concentration of species i, and k is the reverse reaction constant. (The forward rate has been set to 1 without loss of generality.) R_{ij} may be positive or negative, depending on the concentrations of the three reactants. The $a_i a_j$ term may be justified by noting that the ends of two polymer molecules must meet in order for them to undergo a ligation reaction, and assuming that the polymer tips behave like point particles in a well mixed system. (Such "mass action" assumptions are common in models of polymerisation kinetics.) The $-k a_{i+j}$ term simply means that, for every cleavage reaction, there is a constant probability per unit time that it will occur in a given molecule.

This leads to the following set of dynamical equations:

$$\dot{a}_i = \phi_i + \sum_{k=1}^{i-1} R_{k,i-k} - \sum_{j=1}^{i} R_{ij} \qquad (1)$$

where the R_{ij} are as defined above, and ϕ_i represents the flux of A_i in or our of the system, as explained below. The two summation terms arise from the fact that each species i is involved in reactions of the form $A_k + A_{i-k} \rightleftharpoons A_i$ as well as $A_j + A_i \rightleftharpoons A_{i+j}$.

2.0.1 Thermodynamic equilibrium properties

If we let the fluxes $\phi_i = 0$, the system will approach thermodynamic equilibrium. In such a state the reactions have the property of *detailed balance*, meaning that the forward and reverse rates are equal for every reaction. For a reaction $A_i + A_j \rightleftharpoons A_{i+j}$ this occurs when $a_i a_j = k a_{i+j}$. This can be related to thermodynamics by defining the chemical potential μ_i of species i to be $(i-1) \log k + \log a_i$ and noting that when the system is in thermodynamic equilibrium, $\mu_i + \mu_j = \mu_{i+j}$. Thermodynamic quantities such as Gibbs energy and entropy production may be calculated form this.

The equilibrium concentrations must satisfy $a_i = k e^{Ci}$, for some constant C, in order for detailed balance to hold. The value of C depends on the initial conditions.

In order to observe the operation of autocatalytic cycles, we must hold the system away from thermodynamic equilibrium. We do this by letting the fluxes ϕ_1 and ϕ_2 have
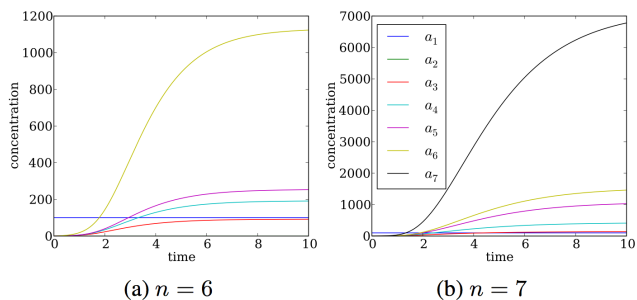
(a) $n = 6$ (b) $n = 7$

Figure 1: Time series of the concentrations in the model when $n = 6$ and $n = 7$. In both cases there is a period of exponential growth from $t = 0$ to about $t = 2.0$, indicating autocatalysis. This is followed by gradual saturation.
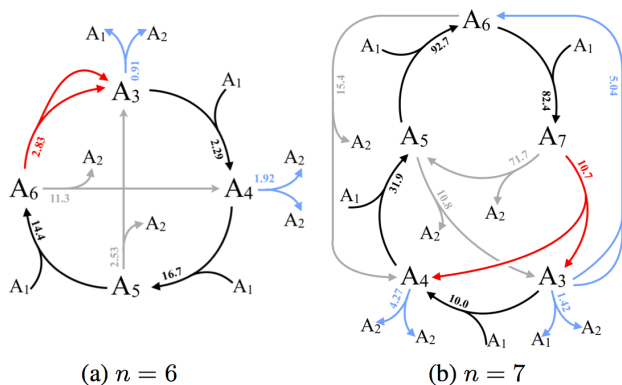

(a) $n = 6$ (b) $n = 7$

Figure 2: The reaction networks that form when $n = 6$ and $n = 7$. Propagating reactions are shown in black or grey, branching reactions in red, and terminating reactions in blue. Numbers represent the rate at which each reaction occurs once a steady state is reached, in multiples of 10^{-3} concentration units per time unit. Both networks contain several catalytic cycles, coupled to an autocatalytic cycle (highlighted in black). The reaction $A_6 \longrightarrow 2\,A_3$ is the key branching step when $n = 6$, but when $n = 7$ it runs in the opposite direction, becoming a depleting reaction instead.

nonzero values. In this paper we choose fluxes such that the concentrations a_0 and a_1 are held constant at 100 and 0.1 respectively. Conceptually, A_1 flows into the system, then undergoes a series of reactions until it is converted into A_2, at which point it is removed.

We use $k = 10$ in our simulations, and we initialise the system with concentrations $a_i = 10^{-i}$, so that every species is initially in equilibrium with A_2 but not with A_1, and most species initially have very low concentrations.

2.1 Results

Figure 1 shows the dynamics of the system when $n = 6$ and $n = 7$. In both cases there is a period of exponential growth followed by a period of saturation. Exponential growth is a key experimental sign of autocatalysis. (With $n \leq 5$ this effect does not occur.)

Figure 2 shows the reaction networks that arise once these

systems have reached a steady state. In both cases the mechanism behind the exponential growth is an autocatalytic cycle that produces two molecules of an intermediate for every molecule present initially; this exponential growth is countered by decay reactions once the concentrations become high. But the two systems use different autocatalytic cycles.

As n is increased further, more catalytic and autocatalytic cycles emerge. However, the steady-state concentrations increase rapidly as n is increased, leading to unrealistic results if we allow n to become large. This is related to the problem of side-reactions in prebiotic chemistry.

3. Discussion

Autocatalysis is important because it allows one set of species to "out-compete" others, ultimately providing the selectivity required for natural selection. The question of whether the origins of metabolism lie in an abiotically-generated autocatalytic cycle has been much discussed [Morowitz et al., 2000]. Our work suggests that such cycles may in fact occur easily in non-equilibrium systems. However, the problem of side-reactions remains. More generally, in more complex systems, autocatalysis can act as a mechanism for novelty generation. Our result suggests that this could occur more easily if reverse reactions, together with thermodynamic constraints are included in the model.

References

[Fontana and Buss, 1994] Fontana, W. and Buss, L. W. (1994). What would be conserved if "the tape were played twice"? *Proceedings of the National Academy of Sciences*, 91:757–761.

[Ikegami and Hashimoto, 1995] Ikegami, T. and Hashimoto, T. (1995). Active mutation in self-reproducing networks of machines and tapes. *Artificial Life*, 2(3):305–318.

[Kauffman, 1986] Kauffman, S. (1986). Autocatalytic sets of proteins. *Journal of Theoretical Biology*, 119:1–24.

[Morowitz et al., 2000] Morowitz, H., Kostelnik, J., Yang, J., and Cody, G. (2000). The origin of intermediary metabolism. *Proceedings of the National Academy of Sciences*, 97(14):7704–7708.