

# Simulation of a large network of autocatalytic reactions within a vesicle

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## Abstract

A chemical reaction is called autocatalytic if one of the reaction products is itself a catalyst for the chemical reaction [1]. Part of the reason for the interest in these types of reactions stems from the fact that even if only a small amount of the catalyst is present, the reaction may start off slowly, but will quickly speed up once more catalyst is produced. If the reactant is not replaced, the process will again slow down producing the typical sigmoid shape for the concentration of the product. All this is for a single chemical reaction, but of greater interest is the case of many chemical reactions, where one or more reactions produce a catalyst for some of the other reactions. Then the whole collection of constituents is called an autocatalytic set [2].

Autocatalytic reactions have been invoked in the context of studies on the origin of life as a possible solution of the famous Eigen's paradox. This is a puzzling logic concept which limits the size of self replicating molecules to perhaps a few hundred digits. At odd with this conclusion, almost all life on Earth requires much longer molecules to encode their genetic information. This problem is handled in living cells by the presence of enzymes which repair mutations, allowing the encoding molecules to reach sizes on the order of millions of base pairs. In primordial organisms, autocatalytic cycles might have provided the needed degree of microscopic cooperation to prevent the Eigen's evolutionary derive to self- destruction to occur.

With reference to this latter application, the reactions might have occurred within vesicles, small cell-like structures in which the outer membrane takes the form of a lipid bilayer. Vesicles represent a sort of minimal living cells and despite the dramatic reduction in complexity they still display many fascinating properties, as revealed in laboratory experiment. They grow due to inclusion of lipid constituents, progressively adjust they shape and eventually divide to produce daughter vesicles. Moreover, vesicles are semi-permeable and allow for different chemical entities to enter the enclosed volume hence sustaining the reactions cycles.

The study of the dynamical evolution of interacting species of homologous quantities defines the field of population dynamics, which finds particularly important applications within the realm of life science. Population is indeed a technical term which is referred to various, completely distinct fields of applications ranging, from e.g. the level of expression of a protein in a cell, to the number of animals in a finite ecosystem.

The classical approach to population dynamics relies on characterizing quantitatively the densities of species through a system of ordinary differential equations which incorporate the specific interactions being at play. In other words, the analytical expression for the fields includes pure competition, predator-prey interactions, or even cooperative effects. Moreover, a specific delay might be required to account for the processing time which is needed for a system under scrutiny to react to an external stimulus or signal. This is a paradigmatic problem of many biological pathways. More than one independent variable is often to be assumed, which in turn implies dealing with the partial differential equation for an exhaustive modelization effort. However, and despite the degree of coarse-graining intrinsic to the model, all these are phenomena can be tackled via the population viewpoint, namely focusing on the evolution of homogeneous family of constituents as whole, and solely allowing for effective (global) interactions between microscopic elements. It is customary to refer to this level of description as to the deterministic theory. Noise and other disturbances can be eventually hypothesized to alter the ideal deterministic, hence reproducible, dynamics

but always act as a macroscopic bias.

As opposed to this formulation, a different level of modeling can be invoked which instead focuses on the individual-based description. This amounts to characterizing the microscopic dynamics via explicit rules governing the interactions among individuals and with the surrounding environment. This former approach has been recently adopted in various contexts such as predator-prey interactions, metabolic reactions, and epidemic models [3?, 4]. These models are usually implemented numerically through algorithms which use random numbers, and for these reason we refer to these models with the term stochastic. The stochasticity is now intrinsic to the systems and stems from the microscopic finiteness of the investigated medium.

Those alternative, conceptual strategies translate into different tools for characterizing a given phenomenon under inspection, and it is therefore of interest to highlight similarities, and/or discrepancies, in the associated predictions. A viable method that enables us to bridge the gap between the two levels of description is the so-called van Kampen's system size expansion [5]. Starting from the stochastic scenario and performing a perturbative development with respect to a small parameter which encodes the amplitude of finite size fluctuations, one recovers, at the leading order, the mean-field equations. These latter govern the coupled evolution of the average population amount, as in the spirit of the deterministic representation. Including the next-to-leading order corrections, one obtains a description of the fluctuations, as a set of linear stochastic differential equations. Such system can be hence analyzed exactly, so allowing us to quantify the differences between the stochastic formulation and its deterministic analogue.

Again, let us emphasize that fluctuations do not arise from an external noise. Despite the evidence that it is always present in actual population dynamics and that it is an essential ingredient of life processes, noise is often omitted. When instead considered, it is frequently assumed to act as a source of disorder and it is included in the dynamics as an external element. At variance, the individual-level approach allows us to investigate the unavoidable intrinsic noise, which originates from the discreteness of the system and that has to be considered in any sensible model of natural phenomena.

Building on this knowledge, we aim at resolving the interplay between the microscopic dynamics of the chemical constituents and the macroscopic evolution of the vesicle container: spontaneously emerging spatio-temporal oscillations of the chemical quantities might seed instabilities which could drive changes in the vesicle shape, eventually yielding to the dynamical splitting.

Inspired to this rationale, we recently set down analyzing the model proposed by Togashi and Kaneko [6, 7], where  $k$  species are made to interact according to an auto-catalytic scheme inside a closed volume. The volume of the container enters the model as an external parameter and can be in principle adjusted as sought. In a recent paper [8], we revised the aforementioned model and focused via combined numerical and analytical approaches on the emergence of large temporal oscillations in the concentration amount, which develop as a resonant effect induced by the discreteness of the simulated medium. Macroscopic ordered patterns hence arise from the disordered sea of microscopic constituents, an interesting self-organization ability which we believe might have important consequences in the expression of key biological functions. When low concentration develop, fluctuations do matter and the effects of the intrinsic discreteness need to be properly accounted for. In other words, continuous kinetic equations prove inadequate, finite size corrections becoming significant.

Starting from this background, we are now proposing to take one crucial loop forward by incorporating the notion of space, as an additional explicit ingredient to the model. So far, in fact, following the original prescriptions of Kaneko and collaborator, the diffusion was regarded as a purely effective mechanism resulting in a net mass exchange between the inside and the outside. At variance, we here suggest to take a more realistic viewpoint by solely allowing for the migration between spatially close regions. This requirement will eventually enable us to monitor the emergence of organized spatio-temporal structures and to identify the portion of the admissible parameters' space yielding to such collective behaviours.

To this end, we have already elaborated a spatial version of the autocatalytic model discussed in [8]. The idea is to introduce a spatial coarse graining at the level of small micro-cells which are supposed to uniformly cover the volume occupied by the vesicle. In each microscopic cell autocatalytic reactions as specified in [8] do occur. Migration between neighbours cells is allowed. As a simplifying ansatz, we first imagine a periodic geometry and focus on a chain of microscopic cells situated at the frontier with the external membrane. This hypothesis is put forward so to restore the translational invariance, so allowing for a straightforward perturbative treatment of governing master equation which serves as solid backup for our planned, extensive numerical investigations.

To perform realistic simulations of a large network of auto-catalytic reactions we have represented the vesicle as a bounded domain in two dimensions which we assume partitioned in a large ensemble of small patches. Diffusion (migration) of species between adjacent patches are allowed. The system is made to evolve according to the Gillespie algorithm, a dedicated Montecarlo scheme which allows to respect the intrinsic stochastic nature of the simulated process [9]. Numerical runs performed through powerful computing facilities, and assisted by a dedicated analytical

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