Asymmetrical division in protocells

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Abstract

The sustained growth of a population of protocells which undergo symmetrical division (where each individual splits into two equal daughter protocells) requires synchronization between the two processes of (i) duplication of the genetic material and (ii) fission of the lipid container. It has however been observed that one often encounters uneven division, where daughters of different sizes may be generated. Here we analyze the case of asymmetrical division, where each protocell has exactly two daughters of different sizes. In this case no true synchronization is possible, and we introduce the notion of homogeneous growth which guarantees that sustained population growth is possible. We consider different abstract models of protocells growth and reproduction and we show by simulation that homogeneous growth is encountered, both in Surface Reaction Models, where the replicators are located in the membrane, and in Internal Reaction Models where they are found in the internal water phase, under a broad set of different kinetic equations. We argue that, when there are different kinds of replicators, it is legitimate to identify the "chemical signature" of the protocell with the set of the ratios between the quantities of these replicators at fission time: it is shown that, in the case of linear kinetic equations, the ratios and therefore the chemical identity are conserved through generations.

Introduction

Cell fission is usually preceded by duplication of its genetic material, to assure that every daughter cell gets a full copy. While present-day cells host sophisticated control mechanisms which assure that fission does not start before DNA duplication has occurred [1], it is highly unlikely that such control mechanisms were in place in the early days of primordial protocells.

It is fair to say that, while several interesting intermediate results have been obtained [2-4], full-fledged protocells, able to continuously generate several successive generations, have not yet been achieved. Given the time and cost of actual wet experiments, mathematical and computational models are extremely important to indicate directions of research and to test the suitability of the different proposals. These models are also important since they allow one to experiment freely with different parameter values, which can be difficult to achieve, and to observe the values of all the variables, including those which are difficult to measure in a laboratory experiment.

Lipid vesicles are interesting supramolecular structures, which are spontaneously formed under a broad set of conditions, in aqueous solutions of amphiphiles [5-8] and which resemble cells in that their aqueous interior is surrounded by an approximately spherical membrane, which is composed by a lipid bilayer. If further lipids are supplied, the size of vesicles can grow and, under some experimental conditions, their splitting has been observed [2,9-11]. The resemblance of this process to cell fission is probably the main reason why vesicles have been proposed as the starting point of most hypothesized protocell architectures. In this work we indeed consider broad classes of mathematical and computational models of protocells, all based upon lipid vesicles which will be assumed to spontaneously undergo fission when they reach a certain size. Moreover, it will be assumed that each protocell hosts some chemicals ("replicators") which are able to collectively self-replicate, and that some of these replicators also increase the rate of growth of the vesicle lipid membrane (e.g. by catalyzing the synthesis of its amphiphiles). For simplicity, we consider a single type of lipid in aqueous environments, so the replicators determine the cell properties. In particular, it will be assumed that the set of ratios of the quantities of replicators at splitting time defines the "identity" of the protocell.

For symmetry reasons, one can hypothesize that the sizes of the two daughter protocells are identical. In this case, the two different processes that take place in these vesicles, i.e. (i) cell reproduction by fission and (ii) duplication of the genetic material, should take place at the same rate in order to allow sustained growth of the protocell populations [12-14].

Asymmetrical division

However, different phenomena have also been observed in real vesicles, which may sometimes give rise to offsprings of largely different sizes [15]. In this paper we will consider the case where a protocell splits in two daughters of different sizes, using both models Surface Reaction Models (SRMs), where the replicators are found in the lipid membrane, and Internal Reaction Models (IRMs), where they inhabit the internal aqueous phase. These models are quite abstract (for example, replicators are defined by their kinetic equations, without any explicit reference to their chemical identity) so they can represent several different more specific models.

When the offsprings are born different, the issue can no longer be that of synchronization since, in general, they will reach the critical size for division at different times. Sustainable growth through generations will take place if the daughters are similar to how their parents were, when they were born. We will refer to this situation as homogeneous growth: synchronization implies homogeneous growth, but homogeneous growth can be achieved even without strict synchronization of the two processes. In order to claim that a generation is similar to the previous one, it may be requested that, at splitting time, the chemical compositions of the cells be the same. Since we assume that there is a single type of lipids, and that the size of splitting is the same, the chemical composition of a cell is determined by the total quantities of different replicators, or rather by their ratios. We therefore observe homogeneous growth if the ratios of the quantities of different types of replicators are the same in different generations, when they divide.

The model equations during the continuous growth phase are the following. At time t, let C denote the quantity of lipid in a protocell, and let $\boldsymbol{X}$ denote the quantities of the q types of replicators $X_1 \ldots Xq$; then the kinetic equations during continuous growth are:

$$\begin{cases} \dot{C} = f(C, \vec{X}) \\ \dot{\vec{X}} = g(C, \vec{X}) \end{cases}$$

For simplicity, in the following the function $f(C,\boldsymbol{X})$ will be considered linear in $\boldsymbol{X}$. When the critical quantity of lipids θ is reached, the cell splits in two parts, which contain $\omega\theta$ and $(1-\omega\theta)$ lipids (ω being the lipid fraction inherited from one of the two daughter protocells). In the case of the IRM models, depending upon the details of the division process, there may (or may not) be loss of internal material: however, assuming that fission is a fast process, this does not significantly influence the dynamics of the system, as confirmed by the simulations performed in both modalities.

Results

Simulations have been performed allowing growth for a long time, keeping the overall population size limited so to simulate finiteness of resources. In order to achieve such limitation, the asynchronous update procedure is such that, if at time T a cell reaches its critical size, its two daughters are generated and added to the current population; the mother cell disappears and, in order to keep the total population size fixed, another randomly chosen protocell is removed. The main results, widely discussed in ref [16] are the following.

In the case of SRMs, homogeneous growth is observed under a number of different kinds of linear and nonlinear kinetic equations in $g(C,\boldsymbol{X})$. It is not found in the case of quadratic or higher order kinetics, but this seems to be cured in a slightly more complicated model which explicitly takes into account the finite diffusion rate of replicator precursors across the membrane. The final population is composed by two types of protocells, i.e. those which were born small and those which were born large. Even in the case of noise, so that ω is not the same for every division but is randomly chosen within a given range, the overall behavior is remarkably similar to the case with fixed ω.

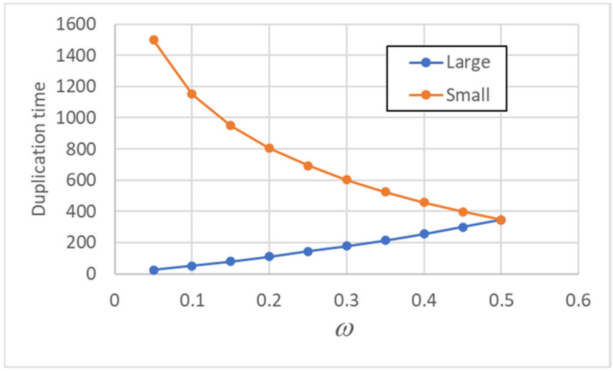

Fig.1 SRM model: duplication times of a stable protocell population as asymmetry varies. Values on the X axis show the fraction of lipids inherited from the smaller protocell, whereas the duplication times of the "born small" and "born large" protocells are shown on the y axis.

In the case of IRMs there are still two types of individuals, i.e. those which were born small and those which were born large. The different embedding of membrane lipids (inserted in a two-dimensional structure) and replicators (contained in a three-dimensional space) leads the system to present relatively narrow distributions, rather than deltas as in the case of SRM models. The distributions reflect the different proportions in the population of small-born and large-born protocells, while the average values present the properties presented here below.

It is highly remarkable that, if the dependence of the function $g(C,\boldsymbol{X})$ upon the various X_q is linear, then the ratios of the various X_q/X_m at division time become constant through generations. So the chemical identity of the protocells is conserved. It should also be observed that, if one follows the two daughters of a single protocell until they reach their own division times (which can be largely different, depending upon the degree of asymmetry w), one observes that the overall quantity of their replicators is twice as much as that of the mother protocell, as it is necessary to assure homogeneous growth.

Some suggestions for further work include the study of a larger set of kinetic equations, a thorough analysis of asymmetrical division in the case of finite diffusion rates of precursors across the membrane, and the possible effects of age-dependent removal of existing protocells.

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