Journal of Theoretical Biology 254 (2008) 741–751

Contents lists available at ScienceDirect

Journal of Theoretical Biology

journal homepage: www.elsevier.com/locate/yjtbi

Sufficient conditions for emergent synchronization in protocell models

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ARTICLE INFO

Article history:
Received 22 January 2008
Received in revised form
8 July 2008
Accepted 8 July 2008
Available online 16 July 2008

Keywords:
Protocell
Self-replication
Dynamical model
Synchronization

ABSTRACT

In this paper, we study general protocell models aiming to understand the synchronization phenomenon of genetic material and container productions, a necessary condition to ensure sustainable growth in protocells and eventually leading to Darwinian evolution when applied to a population of protocells.

Synchronization has been proved to be an emergent property in many relevant protocell models in the class of the so-called surface reaction models, assuming both linear- and non-linear dynamics for the involved chemical reactions. We here extend this analysis by introducing and studying a new class of models where the relevant chemical reactions are assumed to occur inside the protocell, in contrast with the former model where the reaction site was the external surface.

While in our previous studies, the replicators were assumed to compete for resources, without any direct interaction among them, we here improve both models by allowing linear interaction between replicators: catalysis and/or inhibition. Extending some techniques previously introduced, we are able to give a quite general analytical answer about the synchronization phenomenon in this more general context. We also report on results of numerical simulations to support the theory, where applicable, and allow the investigation of cases which are not amenable to analytical calculations.

1. Introduction

Several attempts are currently under way to obtain protocells capable of growth and duplication, endowed with some limited form of genetics (Oberholzer et al., 1995; Rasmussen et al., 2004; Szostak et al., 2001; Mansy et al., 2008). The interest for these systems is motivated either by the quest to understand which are the minimal requirements for a life form to exist and evolve, or by the search for indications about the way in which primitive life might have emerged on Earth.

In order to study how protocells can develop, given that they do not yet exist, it is necessary to consider "simplified models able to capture universal behaviors, without carefully adding complicating details" (Kaneko, 2006). A protocell should comprise at least one kind of "container" molecule (typically a lipid or amphiphile) and one kind of replicator molecule—loosely speaking "genetic material", hereafter called, genetic memory molecule, GMM for short. This is typically a linear polymer which can be copied or a system of two or more kinds of replicators which catalyze each other's synthesis—e.g., proteins and nucleic acids. There are therefore two kinds of reactions which are crucial for the working of the protocell, which in this paper will be called "key" reactions: those which synthesize the container molecules and those which synthesize the GMM replicators.

The two key reactions may take place at different rates. However, to achieve sustained protocell growth and avoid death by dilution, it is necessary that the two proceed at equal rates, i.e., that the genetic material has doubled when the protocell splits into two—a condition referred to as *synchronization*, to ensure that each offspring will contain the same amount of genetic material as the mother. Indeed, if replication were slower than duplication, the concentration of genetic material would eventually vanish (we refer to the splitting of a protocell as duplication, and to the doubling of genetic polymers as replication). In the opposite case, its concentration would grow unbounded. Of course, the requirement of doubling of the genetic material at duplication time refers to the average behavior, while each single event is affected by noise and random fluctuations.

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doi:10.1016/j.jtbi.2008.07.008

Note that synchronization has a further important property, namely that, even in the case where the kinetic equations for the GMMs have sub-linear growth terms (Rasmussen et al., 2003; Munteanu et al., 2006), it leads to exponential growth of the population of protocells (a straightforward consequence of constant doubling time)[1] and therefore to strictly Darwinian selection among protocells.

Most of the different protocell architectures which have been proposed can be divided in two main families, according to the region of cell space where these key reactions occur. Some proposals, which have been called *surface reaction models* (Serra et al., 2007a)—SRM for short, assume that the key reactions take place on the surface of the cell membrane, as hypothesized for the Los Alamos bug (Rasmussen et al., 2003, 2004). Other architectures exist, for instance the RNA-cell (Oberholzer et al., 1995; Szostak et al., 2001), where the key reactions develop in the interior of the vesicle. For this reason we call our model, whose inspiration has been drawn from this latter case, *internal reaction model*—IRM for short.

In this paper, we address the synchronization question for both proposed architectures, exhibiting a unified analysis; in fact we are able to prove that working with quantities (of chemicals) instead of concentrations allows us to map one model on the other and thus to provide a unified view.

In the case of SRM, we are also able to consider cases (see Section 3.4) where the "genetic molecules" are actually the same lipids that compose the "container", allowing us to consider models close to the GARD—model (Segré et al., 1998) or to the one proposed by Kaneko and Yomo (2002), although in this paper we limit ourselves to considering only linear interactions. In these models the (compositional) information is carried by the diversity of lipids in the vesicle or micelle, thus the synchronization problem here can be restated in terms of the reproduction of the whole set of molecules before division occurs, so as to guarantee the maintenance of information content.

The problem of synchronization has already been studied in previous works by means of a class of abstract surface reaction models of protocells (Serra et al., 2007a, b) and it has been shown that in several cases synchronization is an emergent property, in the sense that, through successive generations of protocells, the doubling times of both container and replicators, tend asymptotically to the same value even if at the beginning they were different. This was contrasted to earlier models, like the well–known Chemoton (Carletti and Fanelli, 2007; Gánti, 1997; Munteanu and Solé, 2006), where synchronization was achieved by *ad hoc* hypotheses concerning the form of the kinetic equations.

In models involving a single GMM, synchronization is always achieved once the growth of the lipid container is linear with respect to the quantity of the replicator (Serra et al., 2007a). This result has been generalized to models where the replicator equation is non-linear or when the growth of the container is given by a non-linear function of the amount of genetic materia (Serra et al., 2007b).

In models where more than one GMM coexist in the same protocell, but limiting the treatment to the case where there is no direct interaction among them, synchronization was achieved: if the replicator kinetics is linear, only the fastest replicator asymptotically survives, while if it is parabolic there is coexistence of different replicators in the long time limit (Serra et al., 2007a).

[1] Here we ignore further terms which might limit the growth of the whole population of protocells, e.g., competition for limited resources or growth in a limited volume.

The fact that several different hypotheses lead asymptotically to synchronization raises the question whether this is a general property of the SRM or even of a larger class also including the IRM. In the present paper we therefore explore this wider class of models taking into account direct interaction, positive and negative, among the replicators. We consider the case of linear replication kinetics, finding sufficient conditions to guarantee synchronization: note however that, since protocell division is taken into account, the overall model is non-linear, so its analysis is far from being trivial. We are aware that such assumptions limit the application of our method to a limited class of models, and that relaxing them we cannot obtain such analytical results, nevertheless we support our choice with the following two reasons. First, we have proved (Serra et al., 2007b) that synchronization arises under general assumptions of non-linear coupling between container growth and GMMs or non-linear kinetics for GMMs replication; second, we stress once again that we are looking for simplified models able to capture universal features, neglecting specific, model-dependent details, hence the linear assumptions are a reasonable starting point. For this same reason we here neglect higher order phenomena like diffusion and permeation processes, whose influence can be important but whose analyses go beyond the scope of the present work.

The treatment of the subject is mostly analytical; we nevertheless present some numerical simulations both to support our results and to explore cases where the rigorous analysis cannot be performed.

The paper is organized as follows. In Section 2 we will briefly introduce the two protocell architectures that somehow inspired our models: the Los Alamos bug and the RNA–cell. Then we will introduce our models: the surface reaction model and the internal reaction model; and finally we will discuss the relevant equations describing their dynamics. Section 3 will contain a full analysis of the dynamics of these models and the proof that synchronization can be achieved, provided some conditions on the involved coefficients are satisfied. Finally in Section 4 an in-depth discussion of these conditions and of their physical meaning will be provided together with some comments on possible further directions of research.

2. Two protocells models

The aim of this section is to introduce our models describing two possible architectures for living protocells, inspired by some current bio-chemical researches. First, for the sake of completeness we will briefly introduce the models and then our approach will follow.

2.1. Two possible artificial minimal cells

According to Rasmussen et al. (2004), the Los Alamos Bug is a synthetic organism that integrates three functionalities: a lipid container, a photo-metabolic system and a hydrophobically anchored templating polymer that influences metabolic kinetics.

The role of the proto-container is to hold together the other two key aggregates. Moreover, authors assumed that the interior lipid phase as well as the water/lipid interface possess very different physico-chemical properties with respect to bulk water, in such a way that the high concentrations determined by the spatial proximity of anchored molecules will enhance the chemical reactions: i.e., both the lipid phase and the lipid/water interface act as catalysts.

The assumed GMMs are lipophilic PNA or PNA-like nucleic acids; this choice has been motivated by the stronger interactions with the lipid phase of such molecules, thanks to their