Cellular Evolution in a 3D Lattice Artificial Chemistry

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Abstract. We introduce a three-dimensional model of the formation of proto-cell structures. Our model is based on an artificial chemistry extended from an earlier two-dimensional realization by Ono and Ikegami. This model describes the chemical reactions of a primitive metabolic system and the spatial interactions of simple amphiphilic molecules which organize into membrane-like structures. The results demonstrate the emergence of dynamic three-dimensional cellular structures from a "primordial soup", and a variety of self-maintaining structures may be observed, depending on initial conditions.

1 Introduction

Theoretical studies of reaction-diffusion systems in non-equilibrium environments [1, 2] have shown that self-organizing and self-reproducing chemical patterns can be demonstrated in quite simple chemical systems without relying on complex molecular devices. However, the dynamics of these patterns are such that it is impossible for different regions of a particular pattern to have any significant degree of individuality. To distinguish living organisms from mere dissipation structures, a new phenomenology of biological systems seems required.

Maturana and Varela [3] focussed on an essential feature of living organisms - "autopoiesis", their ability to produce and maintain their own boundaries. While they only considered a two-dimensional case, they stated that a three-dimensional extension to their model would be a simple one not involving any conceptual obstacles. While we indeed found this to be the case, in three dimensions there is a much greater diversity of structures to be found. Luisi[4] and others showed that some vesicles of amphiphilic lipids had a catalytic activity enabling them to assimilate resources so that they could reproduce themselves automatically.

Molecular simulations of the self-assembly of amphiphilic lipids have been studied thoroughly. However, because realistic simulation of lipid molecules is

a computationally difficult task, various models based on simpler discrete dynamics have been proposed [5–7]. Another issue is the metabolism of membrane molecules. Though there are various attempts to simulate realistic chemical pathways in the cell [8] we instead focus on abstract models of artificial chemistry [9] since our purpose is to understand primitive, minimal forms of life. In the spirit of Zeleny's and Varela's work, there have been studies of the organization and maintenance of proto-cell structures in computational models [10, 11]. Along this line, Ono and Ikegami presented a model called "Lattice Artificial Chemistry" (LAC) [12, 13] which simulates both spatial interactions and chemical reactions of abstract molecules within a simple consistent framework using a lattice method [14]. In the 2D version of the model, evolution of cellular structures from a random soup, maintenance and self-reproduction of cell structures, and evolution of catalysts through cellular selection were observed. In the present 3D case however, a vastly greater number of possible cellular morphologies is expected. Therefore, we expect the transition from 2D to 3D to produce qualitatively different behaviour.

One issue we wish to emphasize is that cell membranes are not merely vehicles which contain rich chemical networks. We argue that it may be the other way around: perhaps it is the membrane structures themselves that determine what kind of chemical reactions may occur within them. For example, we wonder if chemical reactions may proceed differently when constrained to occur in quasi-1D structures such as tube-like membranes. Such questions are themselves of interest, besides the problem of the origin of cells. In the next section, we first explain some details of our model. Essentially, we perform a natural extension of the chemical potential between hydrophilic and hydrophobic particles from 2D to 3D.

2 The Model: A 3D Lattice Artificial Chemistry

Here we extend Lattice Artificial Chemistry ([12, 13]) to three-dimensional space.

Chemicals are represented by abstract particles which move on a cubic lattice. Note that any nonnegative integer number of particles are allowed to coexist on each lattice site. In the simulations reported in this paper the lattice size is 64^3 (with periodic boundaries) and there are 300 particles per site, on average. We consider here only the simplest autocatalytic chemical reactions which can produce membrane formation, and chemicals which can diffuse spatially.

i) Chemical reactions occur probabilistically according to the chemical potentials associated with them, though reactions on any particular site may be promoted by catalytic particles on that site. We use a system composed of two metabolic cycles of autocatalysts and membranes. An autocatalyst **A** catalyzes the reproduction of another such **A** and the production of membrane particles **M**. Resource particles are supplied from an external source at a constant rate, which is the energy supply driving the system. Further details of the model appear in [12, 13].

ii) Diffusion of chemicals is biased according to the spatial gradient of the potential of particles in the local cubic neighbourhood (of size 27), which is computed by calculating the repulsive potential of all particles in the neighbourhood.

iii) In order to simulate the organization of membrane-like structures, we consider hydrophobic interactions. Specifically, we model the repulsion between two primary classes of particles, hydrophobic and hydrophilic, as being stronger than the repulsion between other particles. We also introduce neutral particles which are not strongly repelled by hydrophobic particles, so that they can diffuse through membranes.

Membrane molecules are represented as hydrophobic particles which have an anisotropic potential field. Figure 1) illustrates an example of the repulsion around a membrane particle. When phase separation occurs due the repulsion

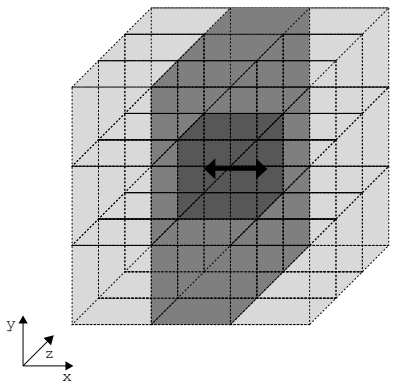

Fig. 1. The anisotropic repulsion field around an membrane particle. Deeper gray indicates stronger repulsion

between hydrophilic and hydrophobic particles, thin, membrane-like structures form as a result of this anisotropy. We assume that autocatalysts and resources are hydrophilic and neutral, respectively.

Below, we explain the details of the repulsive potential as this is a key part of the present model.

We model hydrophobic interaction using the following simple functions. First, the repulsion between hydrophilic and neutral particles depends only on the distance between the two particles

$$\phi_T(\mathbf{dr}) = R_T 2^{-dr^2} (T \in \{WW, WN, NN\}) \tag{1}$$

where R_T is the corresponding given constant of the repulsion coefficient for hydrophilic-hydrophilic, hydrophilic-neutral, and neutral-neutral interactions, and dr denotes the Manhattan distance between the particles in lattice units (i.e. $dr = 0, 1, 2$ or 3).

Second, elements of membranes (small clusters of membrane molecules) are represented by oriented particles as shown in Fig.2. Taking the symmetry of cubic lattice into account, we consider thirteen unique orientations. Thus, at each lattice site there are thirteen seperate populations of membrane particles, one for each orientation. In addition to diffusion, the rotation of membrane particles (i.e. the migration of membrane particles from one of the thirteen populations to another) is also biased according to the local potential field.

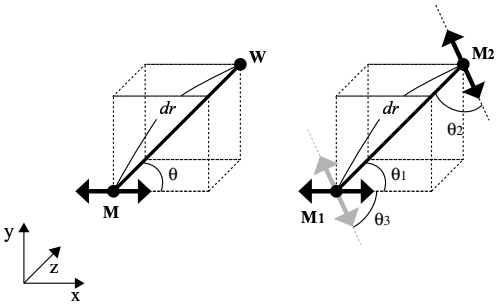

Fig. 2. The configuration of two particles.

The repulsive potential between hydrophobic and hydrophilic particles is calculated as follows:

$$\phi_T(\mathbf{dr}) = (R_{T_0} + R_{T_1} \sin^8(\theta)) 2^{-dr^2} (T \in \{WM, NM\}) \tag{2}$$

where R_{T_0} and R_{T_1} are given constant coefficients and θ denotes the angle between the orientation of the membrane particle and the position vector $\mathbf{dr}$ (see Fig2a).

Due to the second term, hydrophilic and neutral particles tends to avoid the "side" of membrane particles. The repulsion between membrane particles and hydrophilic particles is so strong that it causes phase separation between them. On the other hand, we assume that the repulsion to neutral particles is much weaker.

Finally, the repulsion between two membrane particles depends on both their orientations and their configuration. We calculate the repulsion between two membrane particles as follows:

$$\begin{aligned} \phi_T(\mathbf{dr}) = (R_{T_0} + R_{T_1}/2(\cos^4(\theta_1) + \cos^4(\theta_2)) \\ + R_{T_2} \sin^8(\theta_3)) * (2^{-|dr|^2})(T \in \{MM\}) \end{aligned} \tag{3}$$

where R_{T_0}, R_{T_1} and R_{T_2} are given constants, θ_1, θ_2, are the angles between their orientations and the position vector, and θ_3 is the difference of their orientations. Due to the second term, membrane particles tend to avoid having their "heads" near each other and the third term makes them tend to align in the same direction.

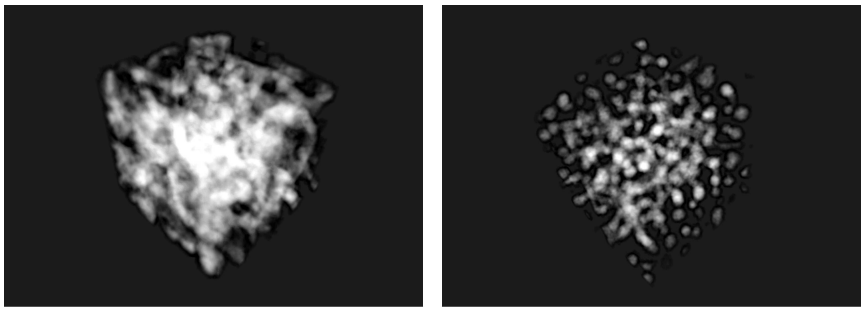

Fig. 3. Clouds of membrane particles (left) slowly relax into a low-energy configuration

3 Results

As will be demonstrated in this section, this system exhibits a variety of qualitatively different behaviours. However, these may be classified into four categories, which arise from different levels of physical and chemical evolution:

	weak diffusion	strong diffusion
weak reaction	relaxation	simplification
strong reaction	cellular formation	cellular evolution

3.1 Relaxation

In this region, neither the chemical composition nor the physical structure of the system changes significantly over time. While random initial conditions demonstrate a slow phase separation-like behaviour between hydrophobic and hydrophilic particles, any features present in the initial conditions are preserved for long periods of time. Figure 3) shows the formation of dense "membrane clouds" - diffusive forces are weak enough that clusters of membrane particles are not encouraged to form a hollow core, and chemical reactions occur at a low, steady rate such that the clusters do not grow or decay. Over sufficiently long time scales, the system will relax into a low energy configuration such as the hexagonal packing of circles in 2D, or the face-centered cubic packing of spheres in 3D.

3.2 Simplification

In this region, while the populations of the different particle types remain steady, any membrane structures exhibit a strong tendency to degenerate or "simplify" into structures of lower genus or dimension. Stable structures such as a hollow sphere or flat sheet of membrane particles can survive for long periods of time, but introducing even minor defects into them leads to their rapid decay under

the strong diffusive forces. For example, a punctured sphere flattens out into a sheet (see Figure 4), while two punctures in a flat sheet quickly coalesce into a single, larger defect.

3.3 Cellular Formation

When there are sufficient resource and catalytic particles available to allow the formation of membrane particles, a number of different cellular structures may be formed. We say that a cell has formed whenever a region of space is completely enclosed by a non-zero number of membrane particles. From random initial conditions, the evolution typically consists of the spontaneous formation of thin filaments of membrane particles, which begin to grow in diameter. Once they grow sufficiently, thin membrane surfaces may begin to form between nearby and similarly-aligned filaments (Figure 5). Since the diffusion term is proportional to the angle between membrane particles, any sharp corners in surfaces that are formed are smoothed out and the original thin filaments either become more rounded, or disappear. Figure 6) is an example of tube formation given specific initial conditions. While initial structure is often preserved, a variety of new structures also form. Instead of spherical cell structures, tubes grow to connect two parallel membranes. However, outside the regime of cellular evolution, the structures that are formed change slowly over time, and do not exhibit cell division.

3.4 Cellular Evolution

As soon as a number of filaments successfully transform into cells, these cells may begin to grow, compete for resources, and divide. A cell grows by absorbing resource particles from its neighborhood, which may or may not include other cells. As a cell grows, it is possible that it produces more membrane particles than it needs to maintain its structure. If this occurs, these excess particles can gather to seed the growth of a new membrane near the center of the cell. Eventually, this new membrane may grow to span the original cell completely, dividing it into two or more new, smaller cells. It is important for cells to maintain their structural integrity - if there is a defect in the membrane, catalysts may leave the cell by diffusing through the defect. If too many catalysts escape, those that

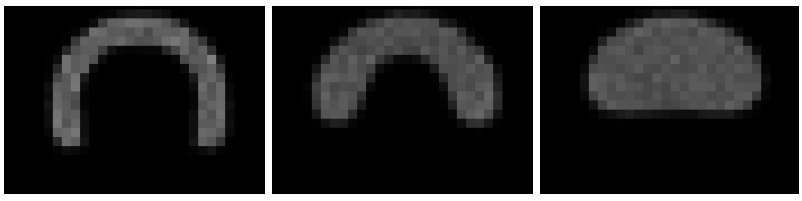

Fig. 4. Cross section: a punctured sphere rapidly loses its structure (800 timesteps)

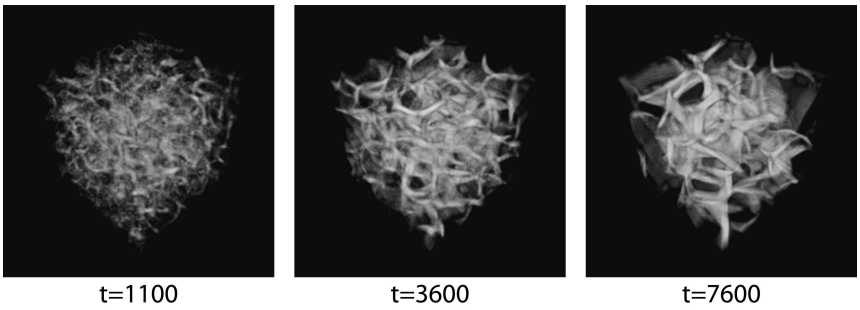

Fig. 5. From a random homogeneous initial configuration, filaments form and begin to organize

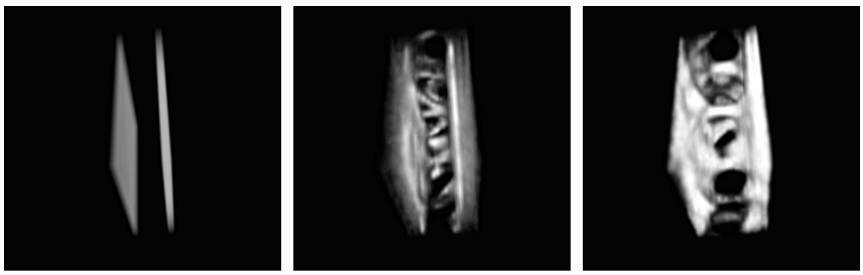

Fig. 6. From an initial configuration of two parallel membranes, tubular structures form to connect them

remain will be insufficient to maintain the cell membrane, and eventually the cell will decay completely. Thus, in this region there is a crucial interaction between diffusion and reaction: the two can interact only as long as cellular structures exist. Figure 7) is an example of this behaviour. Figure 8) shows that while for a given set of model parameters the emergence of cells is robust, the detailed dynamics of cellular evolution may vary considerably. We hypothesize that this is due to our model having a sensitive dependence on initial conditions. While the initial state for every run in Figure 8) was uniformly random, in the cases where the standard deviation of catalytic densities was particularly low, this may have prevented the early formation of membranes in specific areas, which might otherwise have been able to grow by simply aggregating other membrane particles produced nearby. This would lead to a higher cell population of smaller, shorter-lived cells. Had the initial random distribution contained any significant deviations, these deviations would have seeded the early growth of a few membranes which could then grow to dominate the volume, as in Figure 5). One interesting aspect of cell division in our model is that cells do not have any mechanism with which to select an internal axis of division. Therefore, cell division does not resemble mitosis: when cells divide, they do not displace each

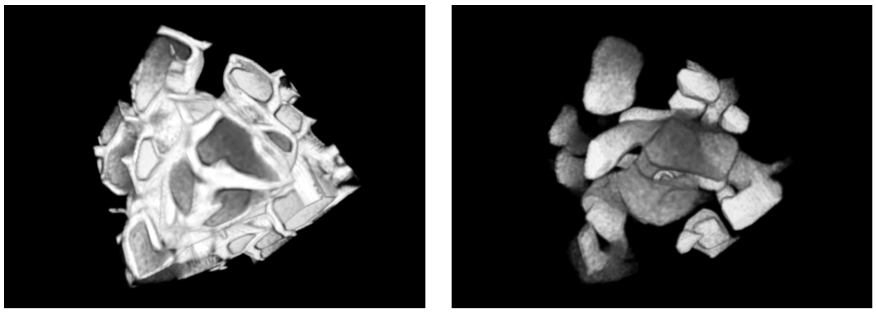

Fig. 7. Fully formed cellular structures (left) and the distribution of catalytic particles in the same structure (right). The effect of competition for resources is evident: A previously homogeneous distribution of resources has given way to cellular 'hoarding'.

other, but instead share a newly formed membrane surface. Furthermore, unlike real cell division, in our model there can often be a high degree of asymmetry between the "child" cells that are created. This leads to rapid disintegration of the smaller child cells, and the resources they would otherwise have consumed become available for another child cell to grow to closely resemble its parent. This phenomenon leads to the cyclic fluctuations in cell populations that can be observed in Figure 8).

4 Discussion

We have presented a three-dimensional model for the evolution of cellular structures. From random initial configurations, we have observed the emergence of proto-cells. These cells exhibit a significant degree of homeostasis in addition to the ability to spontaneously divide into smaller cells. The mechanism for this evolution consists of three stages: (1) local metabolism which produces membrane particles, (2) the formation of proto-cell structures, i.e. cellular structures which maintain their own membranes, in spite of external physical and chemical influences, including competition for resource particles from neighbouring cells, and (3) the division of those proto-cells successful enough to have an excess supply of membrane particles.

This behaviour is generally insensitive to the changing of model parameters, so long as the changes are not so severe as to completely prohibit the formation of membrane particles or to disallow the diffusion of other particles through membranes. In the present model, changing parameters may lead to different cell sizes, shapes and division rates, but the qualitative behaviour remains the same.

We note that while our model is at best an extremely primitive one, we feel that it is a promising approach to modelling proto-cells - that is, structures capable of self-maintenance and self-reproduction - within a physicochemical

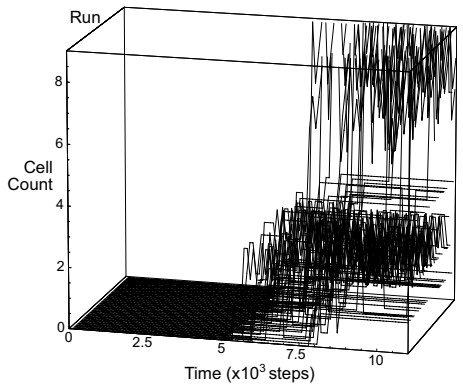

Fig. 8. The population dynamics of several runs from random initial conditions. For a significant length of time, the volume is devoid of cells. Eventually, cells may form, though only certain populations remain successful.

framework. In particular, we believe that it is the combination of membrane dynamics (driven by Gibbs energy) and physicochemical dynamics (supported by autocatalytic particles) which is key to any life-like behaviour observed.

In the simulations presented here, the supply of resource particles was homogeneous. If instead one enforces an inhomogeneous distribution of resources, one may observe cellular formation only in the region where there are sufficient resources. However, once cells are formed, they are able to migrate to and survive in regions of lower resource density.

Only the simplest reaction pathways exist in the present model. Moreover, cells are not generally formed in isolation, but adjacent to each other. This may limit the emergence of higher-order phenomena (such as cell differentiation and nontrivial interactions between groups of cells). Removing these limitations is one area of current work.

Lastly, the variety of types of membrane formation evident in the present 3D simulations tells us that possible proto-life forms may be radically different from the living structures we see today. In the 2D case, cellular reproduction of hexagonal shapes and some connected compartments is observed. In the 3D case, we observe stranger topologies. Taking Figure 6) as an example, two membrane sheets which are initially separate and parallel, if separated by an appropriate distance, will generate pipes between them. Catalytic particles can be transfered from one side to the other through these pipes, which reminds us of slime molds. With such connected membrane boundaries, preconceptions of self-reproduction become irrelevant. Instead of taking the concept of self-reproduction as primary, we should determine the necessary dynamics and environment that favour self-reproduction rather than connected units. Our message is that "vehicle takeover", not just the genetic takeover proposed by Cairns-Smith [15], deserves further investigation.

5 Acknowledgments

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