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## Minimal model of a cell connecting amoebic motion and adaptive transport networks

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#### ABSTRACT

A cell is a minimal self-sustaining system that can move and compute. Previous work has shown that a unicellular slime mold, Physarum, can be utilized as a biological computer based on cytoplasmic flow encapsulated by a membrane. Although the interplay between the modification of the boundary of a cell and the cytoplasmic flow surrounded by the boundary plays a key role in Physarum computing, no model of a cell has been developed to describe this interplay. Here we propose a toy model of a cell that shows amoebic motion and can solve a maze, Steiner minimum tree problem and a spanning tree problem. Only by assuming that cytoplasm is hardened after passing external matter (or softened part) through a cell, the shape of the cell and the cytoplasmic flow can be changed. Without cytoplasm hardening, a cell is easily destroyed. This suggests that cytoplasmic hardening and/or sol–gel transformation caused by external perturbation can keep a cell in a critical state leading to a wide variety of shapes and motion.

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#### 1. Introduction

A new paradigm of computing which utilizes biological or natural intelligence has been advocated ([Paun et al., 1998;](#page--1-0) [Adamatzky, 2007a](#page--1-0); [Paun, 2002](#page--1-0); [Agladeze et al., 1997](#page--1-0)). It has been shown that a unicellular system, Physarum, can solve a maze ([Nakagaki et al., 2000;](#page--1-0) [Nakagaki, 2001\)](#page--1-0), compute a logical operation [\(Tsuda et al., 2004, 2006](#page--1-0)), and solve a spanning tree problem [\(Adamatzky, 2007a\)](#page--1-0) by means of an adaptive network. Physarum's intelligence is described as the ability to remove redundant paths from all possible paths [\(Tero et al., 2007\)](#page--1-0). Since a cell has not only intelligence but the ability of self-movement, amoebic motion has been studied in terms of the physicochemical interaction of actin fibers [\(Bottino et al., 2002;](#page--1-0) [Karakozova et al., 2006](#page--1-0)) and dynamic boundary [\(Varela, 1979;](#page--1-0) [McMullin and Varela, 1997](#page--1-0); [Zeleny, 1979](#page--1-0); [Suzuki and Ikegami,](#page--1-0) [2007\)](#page--1-0). However, no proposal has been made to connect amoebic motion with network formation. The relationship between them plays an essential role in computing, since computing redundant paths, for example, is carried on by the cytoplasmic flow encapsulated in a membrane([Adamatzky, 2007b](#page--1-0)) thus producing amoebic motion. The mechanism of amoebic motion is implemented by cytoplasmic flow accompanying cytoskeleton trans-

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port, and the effective cytoplasmic flow is guided by the assembly of fibers [\(Verkhovsky et al., 1999;](#page--1-0) [Pollard and Borisy, 2003\)](#page--1-0). Many cell movements appear to be driven by polymerization of the cytoskeleton, such as actin filaments, and that cell movement is dependent on the distribution of the cytoskeleton, and motion reorganizes the distribution. Although network formation of Physarum can be driven by the same mechanism, most researchers do not pay attention to the mechanisms with respect to Physarum's intelligence.

The interplay between microscopic and macroscopic mechanisms is a very fundamental issue in biological processes. For example, if a biochemical reaction is expressed by ordinary differential equations (ODE), the degree of freedom is invariant, where the variable implies the concentration of biochemical substrate, i.e.,  $10^{23}$  order molecules. Even if the concentration of substrate is decreased, it is neither zero nor lost in the macroscopic ODE perspective. Recently, some attempts have been made using a multi-set to express reactions based on a small number of molecules [\(Dittrich and Fenizio, 2007](#page--1-0)) in order to reveal the loss of the substrate. It is likely that the interplay between the microscopic and macroscopic viewpoints essentially contributes to the real biochemical reaction. The interplay between local cytoplasmic flow and global change of the pattern of unicellular motion is a typical example of such interplay. Both optimization based on global estimation and amoebic motion based on local cytoplasmic flow can be obtained from the interplay.





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A cell is also regarded as a minimal life form which makes its own boundary from membrane components, in the context of the origin of life [\(Ganti, 2003;](#page--1-0) [Szostak et al., 2001](#page--1-0); [Luisi, 2006\)](#page--1-0). Models for a proto-cell based on cellular automata [\(McMullin and](#page--1-0) [Varela, 1997](#page--1-0); [Suzuki and Ikegami, 2007](#page--1-0)) and their chemical implementations [\(Bachman et al., 1992;](#page--1-0) [Zepik et al., 2001\)](#page--1-0) have been proposed. In these, researchers focus on the self-sustainability of a cell that is implemented by the stable bonding of the membrane components. Due to the stable bondage, the shape of model cells is maintained not far from being oval, and never forms a network like Physarum. The question arises whether selfsustainability of a cell can allow a variety of cell shape from an amoeba to a network form.

Here we show that our cell model, CELL, moving like an amoeba can form an adaptive network to solve a maze, Steiner minimum tree problem and a spanning tree problem. By giving up the usual strong bonding of membrane components and introducing the rapid flexibility of cytoplasm, CELL produces a fragile but dynamic motion. Cytoplasmic flow is modeled by the sol–gel transformation. A CELL continually takes in external matter (i.e., sudden softening), which leads to shape modification and a selfsustaining structure. Softened part is transported with fibers that can be deposited somewhere in a CELL. It is assumed that soon after transportation the cytoplasm hardens and loses the ability to flow and this creates an adaptive network from a sponge-like structure. Through the transport of external matter, the computing system interacts with its own boundary. When this transportation is combined with the rapid flexibility of the cytoplasm, the interplay between the computing system and its boundary is enhanced in a way which robustly sustains the system.

#### 2. Definition of model

Although our cell model, CELL, is very simple, it is consistent with many properties of real cells. CELL is based on the following assumptions: (i) a cell is a mass of cytoplasm surrounded by a membrane, (ii) the membrane is the marginal part of a cell where the cytoskeleton is concentrated and hardened, (iii) once a cytoskeleton assembly is de-polymerized and part of the membrane is softened, the cytoplasm distributed in other areas in the cell rushed for the softened part. This leads to shape modification and cell locomotion, and (iv) cytoplasmic flow is accompanied by transportation of the cytoskeleton, and is guided by the distribution of cytoskeleton assemblies.

The model CELL has two phases: a development phase and a foraging phase. In the development phase, an aggregation of cell components is derived from an initial seed. This makes CELL satisfy the property (i) and (ii) mentioned above. CELL in the foraging phase corresponds to the vegetative state of Physarum and/or an amoeba. Given a planar lattice, each site has state of 0, 1,  $..., m$  (final state, natural number) or  $-1$  and a neighborhood (north, south, east and west). The state transition rule is shown in Fig. 1A, and the neighbors of each site are shown in Fig. 1B. Given a seed with state 1, neighbors of a seed that are state 0 become state 2, and the state 1 seed also becomes state 2. This leads to a diamond-shaped aggregation consisting of sites in state 2. Eventually, we obtain a diamond-shaped aggregation consisting of sites in state m. Since site in state m whose neighbors are all in state  $m$  becomes a site in state  $-1$ , we obtain an aggregation of sites in state  $-1$  surrounded by sites in state  $m$  (Fig. 1C). The size of a CELL is given as  $m^2+(m-1)^2$ . This aggregation is the initial configuration of a CELL. After the development phase, a cell always consists only of states the boundary,  $m$  and the inside,  $-1$ . Thus, we hereafter label the state of the boundary by 2 and the state of the inside by 1. In most simulations we set  $m = 8$ .



Fig. 1. (A) The transition of rule of state, where state is given by an integer. An arrow with a label represents the transition of state with a particular condition represented by the label. The symbol  $N_{MAX}$  means the greatest state of neighbors,  $N_{MIN}$  means the least state of neighbors. Thus  $N_{MIN} = m$  means that all neighbors are in state m. (B) The neighbors of shaded site. (C) Time development from a single seed with state 1. We set  $m = 8$  in simulating studies and the size of neighborhood is given as 4.

A CELL is described as an aggregation of lattice sites in a particular state: the inside (state 1) is surrounded by a boundary (state 2) in a lattice space consisting of the outside (state 0) (property (i)). It is assumed that the boundary state corresponds to an assembly of cytoskeleton fibers (property (ii)). After a development phase, a CELL "eats 0", and this gives rise to both migration and modification of the CELL. Eating 0 or invasion of the outside into a CELL corresponds to the process of softening a particular part of the membrane (property (iii)). Cytoplasmic flow toward the softened area is implemented by the transportation of the ''eaten 0'', which we call a bubble. During this transportation, the bubble is accompanied by cytoskeleton (i.e., state 2), which leads to a re-organization of the distribution of the cytoskeleton (property (iv)). The algorithm of ''eating 0'' is the following:

- (1) Choose one site with state 2, and call the site the stimulus point.
- (2) Randomly choose one of the stimulus point's neighbors in state 0. Replace the state of the stimulus point with the state of the chosen neighbor, and vice versa. Thus 0 invades the CELL, and that 0 is called a bubble.
- (3) State 1 is replaced by 2. Thus all sites of the CELL are now in state 2. Set the number of moves to 0.
- (4) Mark the site at which a bubble is present.
- (5) Decide whether s sites of the bubble's neighbors are in state 0 or not. If yes, go to (8), otherwise go to (6). In the simulations we set  $s = 3$ .
- (6) Decide whether the number of moves exceeds the threshold  $n$ or not. If yes, go to (8), otherwise go to (7).
- (7) Randomly choose one of the bubble's non-marked neighbors, which is in state 2. Replace the state of the bubble with the state of chosen neighbor, and vice versa. It means the transportation of the bubble. If there is no bubble's nonmarked neighbor, the bubble does not move. Add 1 to the number of moves, whether the bubble moves or not. Go to (4).
- (8) Re-organize the boundary and the inside, and i.e., if a site with state 2 is surrounded only by neighbors with state 2, its state is changed to 1. Return to (1).

Our model CELL consists of four parameters: size of the CELL (i.e., the number of CELL components,  $N = m^2 + (m-1)^2$ ), moving

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