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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.

1. Introduction

A new paradigm of computing which utilizes biological or natural intelligence has been advocated (Paun et al., 1998; Adamatzky, 2007a; Paun, 2002; Agladeze et al., 1997). It has been shown that a unicellular system, *Physarum*, can solve a maze (Nakagaki et al., 2000; Nakagaki, 2001), compute a logical operation (Tsuda et al., 2004, 2006), and solve a spanning tree problem (Adamatzky, 2007a) 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). Since a cell has not only intelligence but the ability of self-movement, amoebic motion has been studied in terms of the physico-chemical interaction of actin fibers (Bottino et al., 2002; Karakozova et al., 2006) and dynamic boundary (Varela, 1979; McMullin and Varela, 1997; Zeleny, 1979; Suzuki and Ikegami, 2007). 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) thus producing amoebic motion. The mechanism of amoebic motion is implemented by cytoplasmic flow accompanying cytoskeleton transport, and the effective cytoplasmic flow is guided by the assembly of fibers (Verkhovsky et al., 1999; Pollard and Borisy, 2003). 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) 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; Szostak et al., 2001; Luisi, 2006). Models for a proto-cell based on cellular automata (McMullin and Varela, 1997; Suzuki and Ikegami, 2007) and their chemical implementations (Bachman et al., 1992; Zepik et al., 2001) 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 self-sustainability 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 self-sustaining 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 $m = 8$.

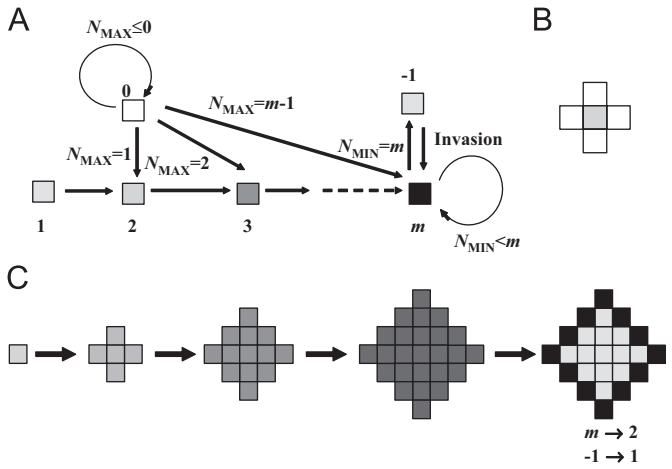

Fig. 1. (A) The transition of rule of state, where state is given by an integer. An arrow with a label represents the transition of state with a particular condition represented by the label. The symbol N_{MAX} means the greatest state of neighbors, N_{MIN} means the least state of neighbors. Thus $N_{MIN} = m$ 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 non-marked 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

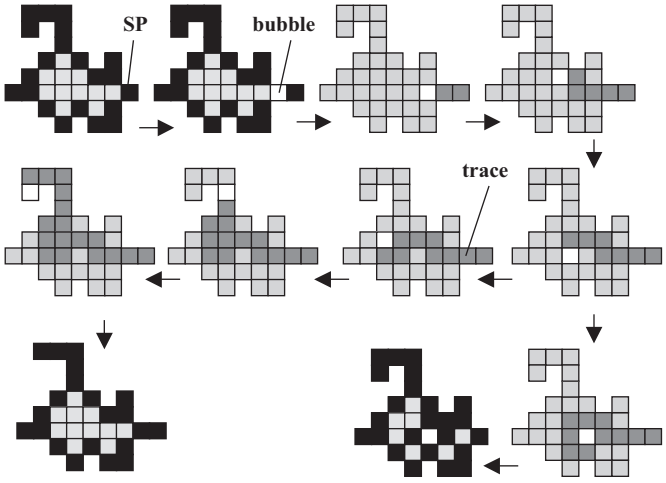

Fig. 2. The transport of a bubble in a CELL. A CELL consists of the boundary (state 2, black) and the inside (state 1, pale gray) components. A boundary site is randomly chosen (indicated by SP for "stimulus point"), and the external state (state 0, white), called a bubble, invades the CELL by swapping sites. After invasion, the inside and boundary are identified with state 2 (pale gray). The bubble diffuses in a CELL and never crosses the path of its own diffusion (shaded area). This makes the bubble move toward a new area. If the bubble is transported along an open-end branch (tentacle), the bubble moves toward the open end and is excluded. After excretion of a bubble, the boundary and interior components are re-organized and the tentacle has been shrunk (left bottom). If the bubble is not excluded and is deposited in the CELL, it is surrounded by cytoskeleton (state 2) (right bottom).

time limitation of a bubble (n), the criterion for the bubble explosion (s), and the probability of heterogeneity of stimulation. In the simulation, m, n and s are fixed. In the simulation of an amoeboid cell, except for that of *Physarum*, $m = 8$, $n = 1000$, $s = 3$. In the case of simulation that mimics *Physarum*, we first set the aggregation of the CELL components that are the boundary states. By applying procedure (8) to the aggregation, the CELL is divided into the boundary and the inside state. In this case we prepare the size of the cell as N independent of $m^2+(m-1)^2$.

Fig. 2 shows how a CELL is modified by applying the algorithm. We call the transportation of a bubble without crossing its own trace "memorized flow". The memorized flow is implemented by procedures (4) and (7). Invasion of a bubble, that is, "softening of the cytoplasm" (Postma et al., 2004), into a part of the CELL that is very thin and tiny will result in the part broken by the invasion flowing to the tentacle. If, however, the bubble invades a large area of the CELL, the part broken will flow toward the outside. In the former case, a thin tube is cut and shrunk, and in the latter case, cytoplasm flows toward the active zones. Both cases arise from the same mechanism of softening of the cytoplasm.

3. Basic behavior of CELL

The algorithms (1)–(8) is common for all simulation studies described here. If the choice of a stimulus point is made randomly, a CELL moves like an amoeba. If a stimulus point is chosen from several active zones, a CELL forms an adaptive network. If there are several active zones, the forces moving a CELL oppose each other and a CELL forming an adaptive network stays in one place. Whether a CELL shows amoebic behavior or forms an adaptive network depends only on the way of choosing a stimulus point. A CELL allows a bubble to occur inside it. Due to the transition rule, the bubble is surrounded by the boundary component of sites in state 2. Thus we can choose a stimulus point inside the CELL such as the boundary of a bubble. If we do so, the existing bubble is moved and can be excluded from a CELL. If the position at which a bubble is present is not checked (step 4 is omitted), then there is no memorized flow. Without step 4 a CELL is easily destroyed.

Step 5 gives the condition for whether a bubble is excluded or not. In our simulations, s is set 3 or 4. This means that if at least three neighbors of a bubble have state 0, then the bubble is considered to be excluded from a CELL, the movement of the bubble is stopped and a new stimulus point is chosen. Step 6 limits the number of moves a bubble can make. In our simulations, $n = 1000$. Due to step 8, an aggregation of state 2 sites is changed to an aggregation of state 1 sites surrounded by state 2 sites. That is, the boundary and the interior are re-organized. Steps 3 and 8 mean that the boundary of an aggregation is always maintained at the outer edge of a CELL, and that external matter (bubble) is always combined with fibers (boundary component) when being transported. Due to step 7, a bubble avoids its own path, and that produces a memorized flow for the bubble. Memorized flow is why a bubble can easily explore new areas in a CELL such as narrow areas called tentacles (Fig. 2). On the other hand, memorized flow can easily lead to a bubble being deposited in a CELL if the bubble proceeds in a spiral way to reach a dead end (Fig. 2).

Here we particularly focus on how self-sustainability of the CELL is influenced by the moving time limitation of a bubble (n). The moving time limitation of a bubble is set as the time required for the bubble to explore all sites in the CELL in all simulations, that is, the number of components of a CELL$<n$. Thus, we set $n = 1000$ for the simulation with $m = 8$. The shorter n is, the more bubbles are deposited in the CELL, which can break its unity. Fig. 3 shows the probability of CELL sustainability against the moving time limitation of a bubble, where $m = 8$ and the size of the CELL is 113. It is clear that there is a phase transition near the value of $n = 30$–80. The CELL is considered destroyed if the number of CELL components that are in contact with each other is reduced, where it is defined that CELL component A is in contact with the other component B if B is a neighbor of A. Thus, if some components are temporarily located outside of the neighboring sites of any components, it is determined that the CELL is destroyed. For this reason the probability of sustainability is saturated under 100%, thus never meaning that the CELL is destroyed in the case of $n = 90$–100.

3.1. Amoebic motion

Eaten 0 passes through the CELL giving rise to the modification of the CELL shape. It reveals an amoebic motion. One site of the

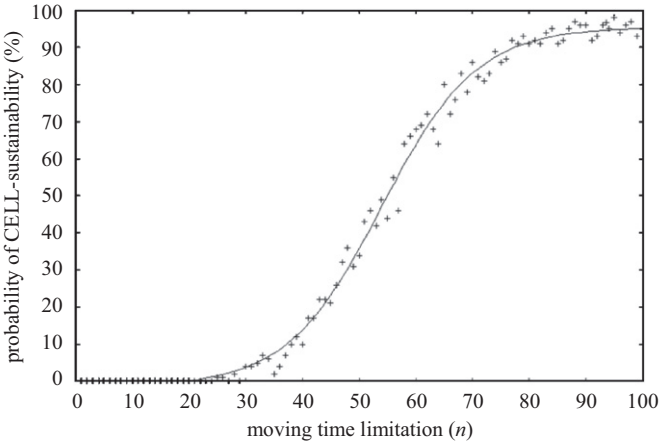

Fig. 3. The probability of CELL-sustainability plotted against the moving time limitation of a bubble (n). The eating 0 process is applied to CELL ($m = 8$) and is iterated. A CELL is defined to be destroyed if the number of CELL-components bonded with each other is reduced. The probability of CELL sustainability is the number of CELL-destruction per 1000 experiments. A solid line represents a fitting curve by a tanh function.

boundary (state 2) is randomly chosen, and its neighboring state 0 site swaps state with the chosen boundary site. This results in the invasion of a site of state 0 into the CELL, which we call a bubble. Once a bubble invades a CELL, it diffuses in the CELL till the bubble is excluded or the step-wise motion of the bubble is terminated. It is assumed that a bubble never crosses its own path (Fig. 2). By this "memorized flow" we refer to effective cytoplasmic flow toward the front of motion, guided by the assembly of fibers (Verkhovsky et al., 1999; Pollard and Borisy, 2003), because the cytoplasmic flow is implemented by reverse 0-flow. This "eating 0" is iterated, and that makes a CELL move or causes it to be modified.

A bubble sometimes remains and grows in a CELL (Fig. 4A). Fig. 4A shows how the memorized flow contributes to the complex amoebic motion, where $m = 8$, $s = 3$, and $n = 1000$. A bubble grows bigger and makes a large chamber of sites in state 0 in the CELL. Due to the transition rule, the bubble is surrounded by boundary material (also see Fig. 2). When a bubble stops moving in the boundary, the chamber is broken and that makes a tentacle. Once a bubble is transmitted along the tentacle, it is immediately expelled via the open end because the memorized flow prohibits reverse flow or bubble's wandering along the tentacle. Thus a tentacle is shrunk by one bubble length. Even when a part of the CELL exhibits amoebic behavior and the rest of it is left as a long tentacle, the tentacle is shrunk and the oval shape of the CELL is recovered (Fig. 4A). If a bubble flows without regard to its previous path, it is more difficult to exclude a bubble, and more bubbles remain in the CELL. This destroys the CELL itself (Fig. 4B). It shows that memorized flow keep CELL in critical state. The memorized flow sometimes drives a bubble into dead end in CELL (Fig. 2 right bottom), and that makes a big 0-chanmer and many branches in CELL. It is close to destruction of CELL. However, also due to the memorized flow, any tentacles are shrunk and CELL cannot be broken (Fig. 2, left bottom).

3.2. Adaptive network

The formation of adaptive networks by *Physarum* can also be explained only by "eating 0" process or by the mechanism of tentacle formation in a CELL (Fig. 5). The simulation is conducted where $N = 1600$, $s = 3$, and $n = 2000$. The similar results are obtained where $N = 400$, $s = 3$, and $n = 1000$. The body of *Physarum* consists of tubular actin–myosin fibers and cytoplasm. If fibers are distributed heterogeneously, the body becomes a sponge. If fibers are transported by cytoplasmic flow in a preferred orientation, a tube is made up of fibers (Naib-Majani et al., 1982; Stockem and Brix, 1994). Since the transport of a bubble entails the deposition of the boundary material (state 2 sites) in the CELL, the boundary material can be interpreted as fibers. The binding of state 2 sites leads to a tubular structure in the CELL. When given active sites made by food in a triangular layout *Physarum* forms an adaptive network connecting the three sites with an approximation to the minimal path (Nakagaki et al., 2004). Given an expanded CELL, we let bubbles invade the CELL from the boundary within three active zones (Fig. 5 top left). Iterated invasion grows the parts of the CELL in the active zones, and many bubbles are left in the CELL. Coalescence of bubbles leads to the formation of a large chamber of state 0 sites (Fig. 5 top center and top right). The boundary is destroyed and tentacles are formed. An open ended tube always shrinks like a tentacle (Fig. 5 bottom). This can lead to the removal of redundant paths, where the paths are continually generated and destroyed through the transport of fibers. The CELL approximates the minimal path connecting the three active zones like *Physarum* does. Once a loop structure is removed, a network is maintained by a CELL. Fig. 6 shows the formation of adaptive network under the four active zones. As well as three active zones, the CELL approximates the skeleton connecting active zones. Figs. 5 and 6 show that a CELL can solve Steiner minimum tree problem.

3.3. Maze-solving

While it is known that *Physarum* solves a maze (Nakagaki et al., 2000; Nakagaki, 2001), it is easy to see that CELL has the ability of solving a maze. After generating a CELL along a maze, we set two active zones representing the start and the goal of a maze (Fig. 7A left). Because of the transport of a bubble invading a CELL mainly (probability of 0.7) from the active zones, cell components with state 1 (the inside) are transported from the maze area to the active zones (Fig. 7A center). Finally the minimal path connecting the start and the goal is left, and most of the CELL is at the active zones (Fig. 7A right). CELL mimics *Physarum*'s maze solving by cytoplasmic flow from the maze area to the active zones. The simulating result is obtained where N is about 3600 that corresponds to the amount of CELL-components filling the maze, $s = 3$, and $n = 4000$. The heterogeneity of the stimulating points contributes to the choice of minimal path. This effect is discussed in the Section 4.

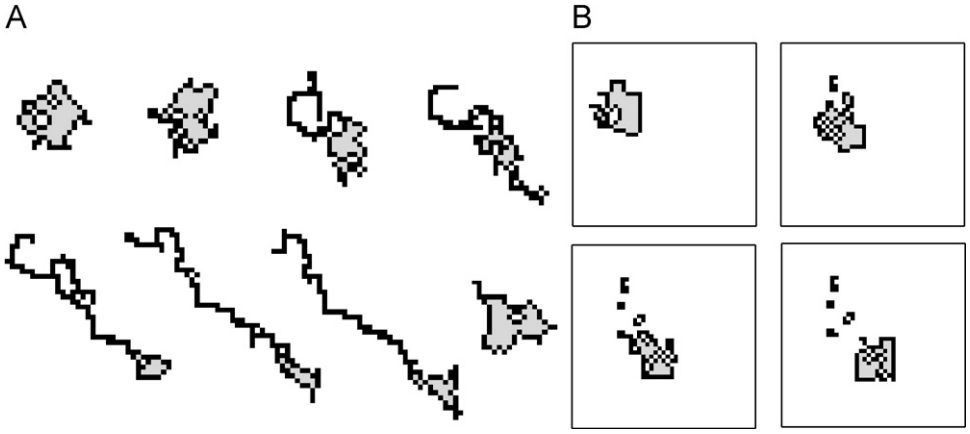

Fig. 4. (A) Amoebic behavior of a CELL with memorized flow. Since the diffusion of a bubble avoids its own path, long tentacles cannot be cut and that gives rise to complex amoebic behavior. Time proceeds from left to right and from top to bottom. (B) CELL moves rightward and downward without memorized flow. Because of deposited bubble excess CELL is destroyed. Time proceeds from left to right and from top to bottom.

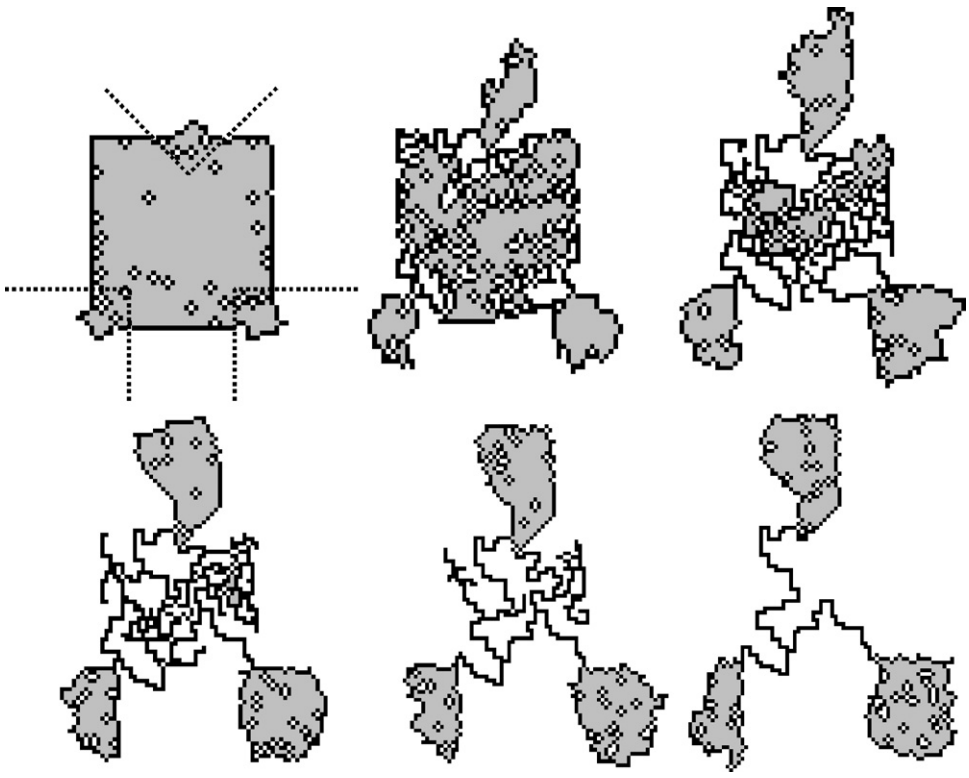

Fig. 5. Development of an adaptive network in a CELL, where black, gray and white dots represent sites with state 2, 1 and 0, respectively. Time proceeds from left to right and from top to bottom. First a CELL is generated as a square, and it is assumed that a bubble invades from the boundary within the active zones surrounded by broken lines. For a while many bubbles surrounded by boundary components are deposited in CELL, and bubble chambers grow. This results in network formation. Finally the CELL reveals an acyclic graph representing rough approximation of shortest paths connecting the three active zones.

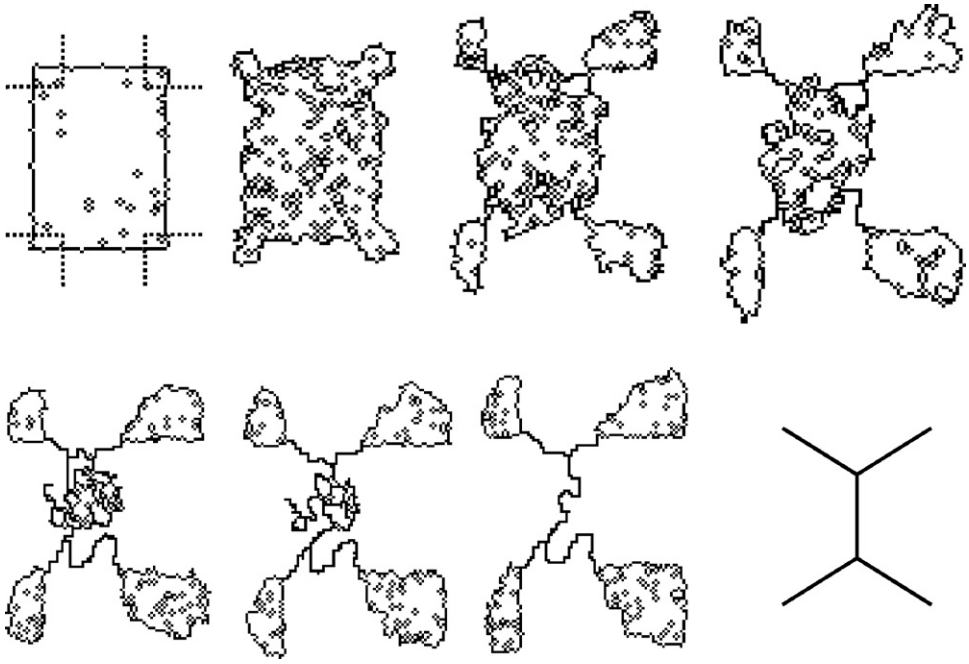

Fig. 6. Development of an adaptive network in a CELL, given four active zones. First a CELL is generated as a square, and it is assumed that a bubble invades from the boundary within the active zones surrounded by broken lines. Finally the CELL approximates the "skeleton" connecting the four active zones (right bottom).

3.4. Spanning tree problem

It is also known that *Physarum* can solve a spanning tree problem. Given points of planar set, if all points are connected with minimal edges and without loops, the graph is called a spanning tree. If points are set as active zones made of food, *Physarum* approximates the spanning tree. In Fig. 7B, a CELL eats 0 from any boundary, then it moves like an amoeba. When the CELL

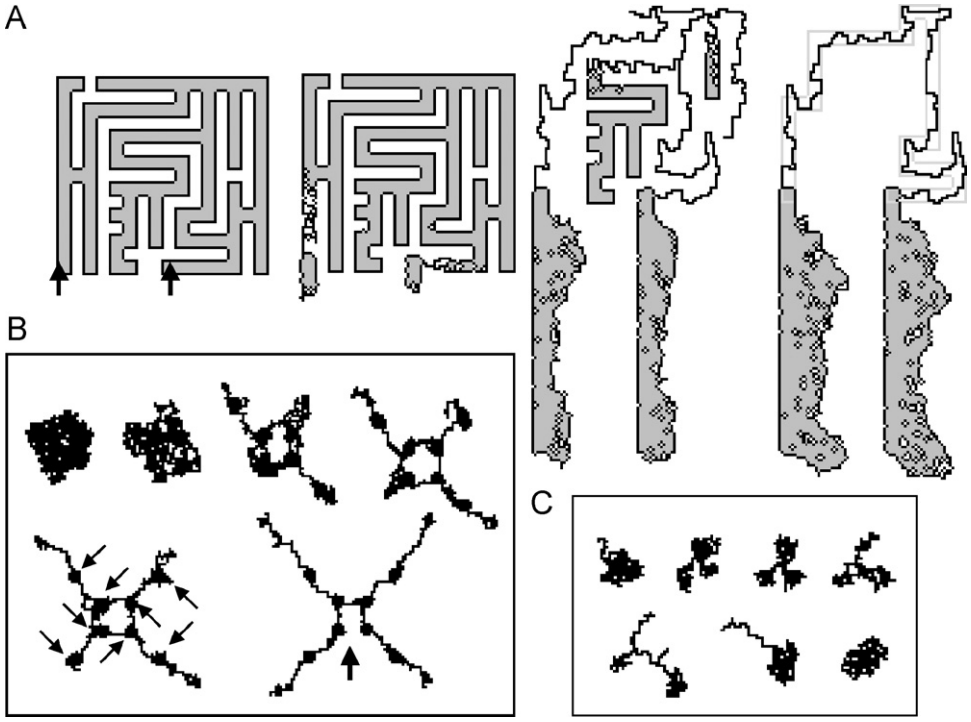

Fig. 7. (A) The process of maze solving by a CELL. Given a CELL in the shape of the maze, it is assumed that a bubble invades CELL mainly from two active zones indicated by thick arrows (left). When a bubble invades a maze, the inside component of the CELL is transported toward the active zones. This results in the shrinking of the CELL in the maze area and in a thin network of state 2 sites including loops (center left). Eventually loops are cut and redundant paths are removed (center right). Finally the CELL approximates the solution of the maze. The gray corridor represents the minimal path. (B) The process of spanning tree solution by a CELL, where both states 1 and 2 are represented by black dots (from left to right and from top to bottom). First the CELL behaves like an amoeba, and finds eight active zones indicated by black thin arrows. Finally a loop is removed as indicated by the thick arrow, and the CELL approximates the spanning tree. (C) The transition between amoebic behavior and transport network of a CELL. Both states 1 and 2 are represented by black dots. A foraging CELL finds three active sites, then forms an adaptive transport network. After that the CELL returns to being an amoeba again.

encounters active zones, bubbles invade the CELL mainly from the active zones. Then the state 1 sites of the CELL are concentrated in active zones and other regions are shrunk. Although loops are kept for a while, they are finally removed and a spanning tree is obtained.

3.5. *Amoeba encountering food*

Fig. 7C shows that a CELL moving like an amoeba forms an adaptive network and then moves again. In this simulation three active zones are fixed in a plane, where "food" is assumed to be limited (i.e., the number of bubble-invasion is limited). Stimulus points of CELL are chosen randomly before CELL's encountering active zones. Thus, CELL first moves like an amoeba to search for food (Fig. 7C top left). Once a CELL encounters active zones, cytoplasm of CELL (state 1) flows toward active zones and then CELL shows a pattern connecting three active zones like reverse V-shaped pattern. After that CELL approximates the minimal path connecting three active zones, in showing reverse Y-shaped pattern. In this simulation, mass of cytoplasm of CELL is so small that cytoplasm concentrated at active zones is unstable and is perpetually moved. However, CELL concentrated at three active zones are dynamically changed, the minimal path can be kept till the food is consumed (Fig. 7C top). The CELL breaks up the adaptive network after finishing eating, and the three regions are unified again (Fig. 7C bottom).

4. Discussion

We explain how the memorized flow of a bubble plays a part in making and withdrawing a tentacle and solving a maze. Fig. 8A shows how a loop is cut and tentacles are withdrawn. The left-hand diagram shows a CELL with a loop and a tentacle. If many bubbles are connected in a CELL, a big chamber consisting of state 0 appears. That leads to a loop in this CELL. Assume that a stimulus point is chosen randomly. The candidates are all black sites of the left-hand diagram of Fig. 8A. If a point on the loop is chosen (indicated by thick arrow), it is transported either downward or upward. Assume downward. The bubble is transported to the chamber consisting of state 1 (gray), and it may enter the loop again. Assume that it enters the loop again. Since a bubble cannot cross its own path, it stops at the very position where a bubble invaded. As the number of moves is finite (step 6 in the algorithm), the stopped bubble cuts the loop at this position where the bubble invaded. Once a loop is cut, it produces tentacles, and we obtain the right-hand diagram in Fig. 8A. It is easy to see that any tentacle is withdrawn into a CELL. If a bubble invades from the boundary of a chamber consisting of state 1 and enters a tentacle, it eventually reaches the end of the tentacle since the threshold number of moves is large enough for it to reach that point (see step 6). If a bubble invades a CELL on a tentacle, it is transported either toward a chamber or the end of a tentacle. If it goes to the chamber, the tentacle is not changed. If it goes to the end of the tentacle, the tentacle is shrunk by one bubble length. That is why, eventually, any tentacle is withdrawn.

Fig. 8B shows how the shorter path is chosen to connect two chambers. Given the left-hand diagram of Fig. 8B, assume that a stimulus point is chosen randomly. If it is chosen from the boundary of two chambers, the bubble can be excluded through the boundaries of chambers and, with respect to the two paths, nothing happens. If a stimulus point is chosen from points on the long path, it is possible that a bubble is transported from the point

indicated by thick arrow, to the one of chambers, to the short path, to the other chamber, and to the long path again. Note that the diagram contains a loop. As mentioned above in the tentacle discussion, the bubble stops at the position indicated by the thick arrow, and the long path is cut. In general, it is the longer path, which is cut because the probability of choosing a stimulus point is dependent on the length of paths. Therefore, longer paths are invaded by a bubble more frequently. Since cut paths are withdrawn, we obtain the right-hand diagram of Fig. 8B. Now there is no loop in this diagram. Therefore, even if a bubble invades from a path, it is transported into either of two chambers, and never enters a path again due to the "memorized flow" (i.e., step 7). Thus the remaining path is robustly kept.

The properties of a CELL mentioned above: (i) loop cutting, (ii) tentacle withdrawal, and (iii) choice of shorter paths—yield a mechanism for solving a maze or a spanning tree problem. In previous models for explaining the adaptive network of *Physarum*, the essential mechanism of solving a maze is Kirchhoff's law (the sum of flows on a node is 0) and removal of redundant paths. Although this mechanism looks consistent with the real *Physarum*, we focus on the mechanism of the interplay between the local constrained cytoplasmic flow and the global shape of *Physarum* cell. Whether a path is longer or shorter, thinner or thicker is dependent on the shape of the boundary that is caused by the cytoplasmic flow. In reality, the deletion of a path occurs by the decomposition of tubes into free actin–myosin fibers. This means that any tubular path is continually exposed to decomposition, and redundant longer paths have high probability of being decomposed. The CELL implements this tendency as a longer path has higher probability of being invaded, and that leads to the three properties (i), (ii) and (iii) mentioned above. In a CELL, memorized flow (i.e., sol–gel transformation) contributes to the formation of the boundary shape. Thus, a CELL's ability to solve a maze is based on a realistic mechanism. The model CELL has an important additional property: (iv) fibers are created from the sponge structure. A CELL contains the process for making the distribution of fibers and paths.

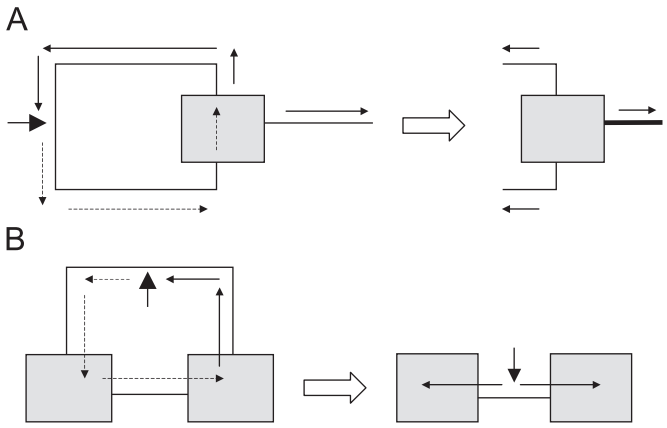

Fig. 8. (A) Schematic diagram showing how a loop is cut and an open end branch is shrunk. (B) Schematic diagram showing how a shorter path remains when two chambers are connected by two paths.

We here show the detailed process of solving a maze by CELL (Fig. 9). The CELL follows the procedure given in steps 1–8, where the stimulus points are chosen specially for a given maze. The bubble invades from two active zones with probability of 0.7, and otherwise it invades from the maze area. Given a CELL distributed along a maze, it is assumed that a bubble invades the CELL mainly (probability of 0.7) from two active zones indicated by arrows in Fig. 9. Actually there are two rectangular areas located below the points represented by arrows. A position with the boundary state (state 2, indicated by black dot) in these rectangular areas is chosen randomly, and a bubble invades the CELL at that position. Since a bubble is replaced with the inside state (state 1, indicated by a gray dot), the inside cell-components are transported to two rectangular areas as shown in Fig. 7A. In Fig. 9, the two rectangular zones in which gray components are deposited are omitted. Although a corridor is filled with a CELL at first, cell components are removed. This makes a thin, wandering network.

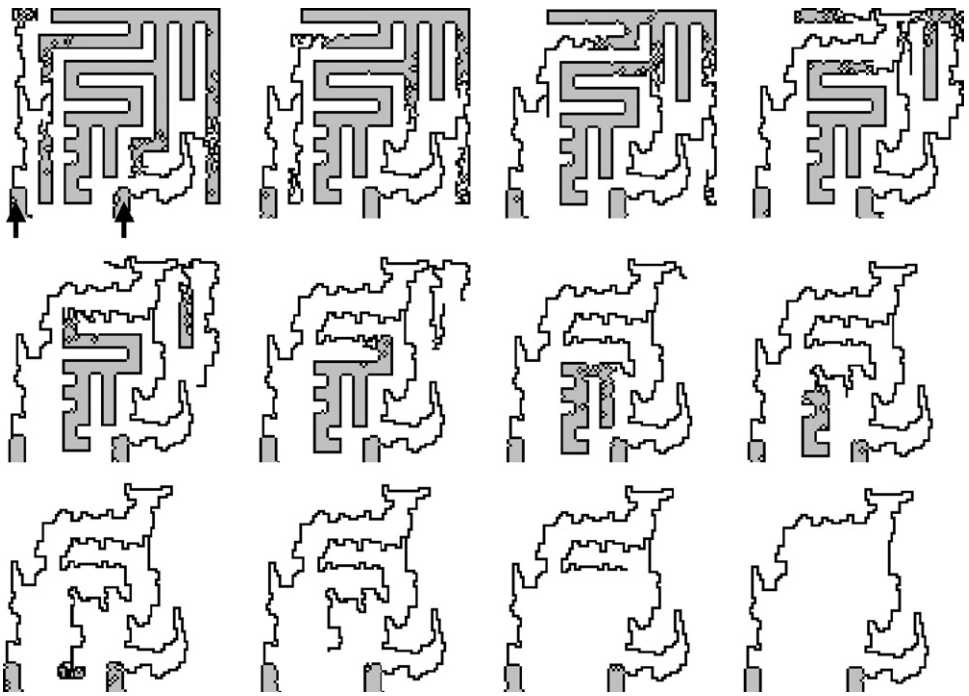

Fig. 9. The process of solving a maze, from left to right and from top to bottom. Black and gray dots represent boundary state 2 and inside state 1, respectively. As bubbles invade a CELL from active zones, cell components with the inside state are transported to the active zones.

Due to the properties (i)–(iv), loops are cut and open ended branches are withdrawn, until a short path remains. As a result, the CELL approximates the minimal path connecting the start and the goal. That is, it solves the maze.

The heterogeneity of stimulating points can be introduced to achieve more efficient computation of the minimal path. In the previous condition, we set the heterogeneity of stimulating points through division into the active zone with probability p and other areas with $1-p$. Now we divide the stimulating points into the active zones and thin structure of the boundary state, where the thin structure is defined as a horizontal or vertical triplet array of the boundary state. Fig. 10 shows how the heterogeneity of stimulating points in terms of thin structures contributes highly efficient finding of the minimal path. In this simulation the bubble invades from two active zones with the probability of 0.7, and from the thin structures with the probability of 0.3. As a result, the CELL can find the shorter path with a probability of 0.78. If the bubble invades from thin structures more frequently (i.e. higher ratio of heterogeneity) in an oval CELL, the marginal area of the CELL has much more branching structures. As a result the CELL shows not a massive but a dendritic pattern.

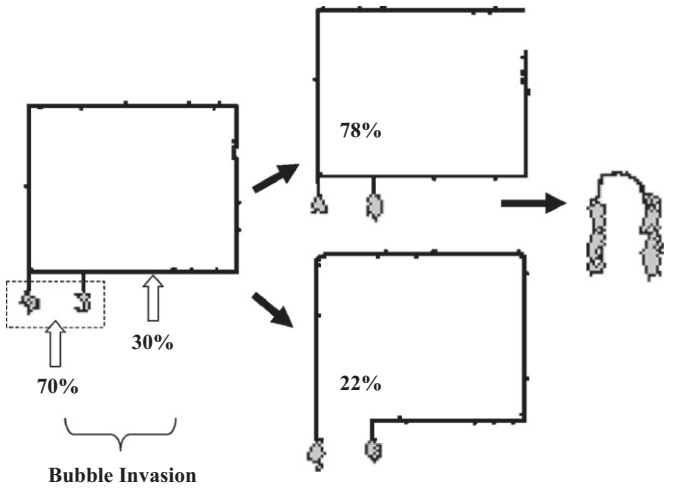

Fig. 10. Heterogeneity of stimulating points can contribute highly efficient finding of the minimal path. A bubble invades a CELL from two active zones (surrounded by broken lines) with the probability of 0.7 and from thin structures with the probability of 0.3. As a result, we obtain the shorter path with the probability of 0.78.

We introduce the heterogeneity of stimulating points in term of thin structures in maze simulation (Fig. 11). The parameter settings and two active zones shown in Fig. 11 are the same as those in Fig. 9, where the bubble invades from two active zones with the probability of 0.7 and from thin structures (not from whole maze area) with the probability of 0.3. It is clear that the CELL solves a maze and we obtain the minimal path. While the solution is indicated by a thick corridor, the CELL finds the minimal path in this corridor. When the marginal area of the CELL is fluffy or has many thin structures, the pattern is actively re-organized and re-distributed as shown in Fig. 11 (middle). Compared with the pattern in Fig. 9, it is complex and distributed over a large area. These patterns can contribute to finding other active zones or food. Thus we can say that the preferred invasion of a bubble (biologically this refers to a softening of the fine structures) into thin structures can play a role not only in finding the minimal path efficiently but also in exploring for other food sources. It can weaken the trade-off between optimization and exploration.

5. Conclusion

Physarum computing can contribute to graph theoretical computations. It is experimentally demonstrated in Adamatzky (2007b) that Physarum can implement Kolmogorov–Uspensky machine (Kolmogorov and Uspensky, 1963), is a type of storage modification machine based on a graph with bounded in- and out-degrees. While *Physarum* can be regarded as a living undirected tree, the mystery remains as to the relationship between path generation and information flow in the body. The key is the transport of fibers within a robust body surrounded by tube materials. We found that memorized flow produces both robust transport and dynamic graph modification. If some fibers are left and deposited in the path of the transportation, it can inhibit cytoplasmic flow in such an area and it plays as an obstacle. If many bubbles aggregate to form a large vacant chamber, the boundary of the chamber becomes a path for the cytoplasmic flow and the wall of the chamber is eventually

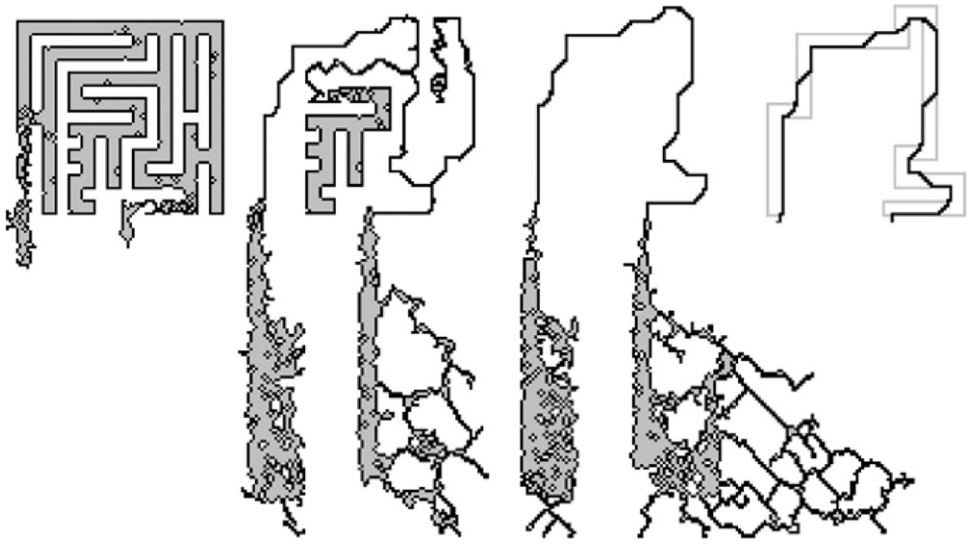

Fig. 11. The process of maze solving by a CELL under the condition of preferred stimulating. In the simulation, the area of a maze and two active zones are the same as those in Fig. 9. Other parameter setting of n and s is also the same as that in Fig. 9. A bubble invades from the active zones with the probability 0.7, and from thin structures with the probability of 0.3. If the marginal pattern of CELL is fluffy or featured by thin structures, marginal areas are actively re-distributed and reveal a complex network pattern.

broken. The continual repetition of this process creates tubular networks from a sponge-like structure.

Memorized flow yields a huge diversity of CELL shapes. Memorized flow can make a bubble stay in a dead end surrounded by its own trajectory, which causes the outer boundary to be broken. This leads to complex outer shapes with many tentacles—a situation which is close to autonomous destruction. However, also due to the memorized flow, any open ended branch will be shrunk. It is clear to see that memorized flow leads to amoebic motion driven by the continuous alternation of cytoplasmic hardening and softening. Since cytoplasmic hardening and softening is realized by the polymerization and de-polymerization of cytoskeleton filaments, the time scale of the hardening–softening switch is different from that of cytoplasmic flow. This difference of time scales inhibits free cytoplasmic flow, leads to the stagnation of the softened or hardened cytoplasm, and produces the heterogeneous distribution of cytoplasm in a cell. The alternation of hardening and softening plays a key part in both amoebic motion and intelligent computing.

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