Toward a Computational Model of Actin Filament Networks

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Abstract: Actin is one of the most important proteins responsible for a reaction of cells to external stimuli (stresses). There are monomeric actin or G-actin and polimeric actin or F-actin. Monomers of G-actin are connected into double helical filaments of F-actin by the processes of nucleation, polymerization, and depolymerization. Filaments are of 7-8 nm in diameter. They are of several microns in length. Furthermore, filaments can be organized as complex networks of different forms: unstable bunches (parallel unbranched filaments), trees (branched filaments), stable bunches (cross-linked filaments). Actin filament networks can be considered a natural computational model of cells to perform different responses to different external stimuli. So, in this model we have inputs as different stresses and outputs as formations and destructions of filaments, on the one hand, and as assemblies and disassemblies of actin filament networks, on the other hand. Hence, under different external conditions we observe dynamic changes in the length of actin filaments and in the outlook of filament networks. As we see, the main difference of actin filament networks from others including neural networks is that the topology of actin filament networks changes in responses to dynamics of external stimuli. For instance, a neural network is a sorted triple (N,V,w), where N is the set of neurons/processors, V is a set of connections among neurons/processors, and w is a weight for each connection. In the case of actin filament networks we deal with a variability of filaments/processors. Some new filaments/processors can appear in one conditions and they can disappear in other conditions. The same situation when the computational substratum changes during the time of computations is faced in the so-called swarm computing, e.g. in slime mould computing. In this paper we propose a swarm computing on the medium of actin filament networks.

1 INTRODUCTION

In machine learning there have been used some biologically inspired networks such as *artificial neural networks*, where we have a fixed number of processors involved into computations. However, elementary computational units understood as processors in real biological networks are never fixed. They are being built and rebuilt permanently in responses to different stresses as external conditions. One of the best examples of these units in biological networks is presented by *actin filaments*. Their networks are most important in remodelling cell configurations and in the cell motility. The point is that actin filament networks are engaged in changing the cell shape, for example in the division of one cell into two daughter cells and in the protrusion of parts of the cells, e.g. in the cell deformation by means of growing pseudopodia during phagocytosis. Meanwhile, the actin filaments are being assembled and disassembled during the time. As a consequence, we face a permanent assembly and disassembly of actin filament networks. These changes in networking are cell responses to different stimuli. For instance, actin filament networks by the own reconstruction can transmit internal stresses and govern the spatial organization of the cytoskeleton. So, these networks can provide signal transduction pathways and make a mechanical equilibrium of the cell and its environment.

The actin filament networks react to external stresses. These stresses are inputs for the networks. There are three main types of the actin filament networks: *unstable bunches* (parallel unbranched filaments), *trees* (branched filaments), *stable bunches* (cross-linked filaments), see: (Furukawa et al., 1993; Steinmetz et al., 1997). Outputs are different for different network types. For unstable bunches and trees, the outputs are represented by chemotaxis, cell spreading, nerve growth-cone movement, etc. For stable bunches, the outputs have the form of mechanic stress transduction such as (i) a tensional stress in the distortion to the network; (ii) a curvature stress in the deformation of the network; (iii) an orientational stress in the deformation of the network.

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Due to actin filaments, the amoeboid cell motility is possible. In robototechnics, one species of the Mycetozoan group of the Amoebozoa, which is characterized by this kind of motility, is best studied. It is *Physarum polycephalum*. In the project *Physarum Chip Project: Growing Computers From Slime Mould* (Adamatzky et al., 2012) supported by FP7 we have designed an unconventional computer on plasmodia of *Physarum polycephalum*. Each *plasmodium* has both an external stationary ectoplasm and an internal liquid endoplasm that moves to pseudopodia. The amoeboid motility is classified by the following three stages: (i) the stage of growing pseudopodia; (ii) the stage of attaching the pseudopodium to a substrate; (iii) the stage of dragging up the rest of the cell (Fackler and Grosse, 2008; Pollard and Borisy, 2003). Such a movement requires an oscillatory mode of contractility system where an actin filament network is being assembled and disassembled for an equilibrium between ectoplasm and endoplasm (Furuhashi et al., 1998). Hence, the *Physarum polycephalum* plasmodium motility that is so intelligent and can be programmed by using chemotaxis so that we can design computers on their media is based on some actin filament network properties.

Actin filament networks are a universal mechanism in the reception and further transmission of external stimuli/stresses in any biological organism. By chemicals it is possible to govern an actin polymerisation and depolymerisation, i.e. the filament assembly and disassembly. For instance, on the one hand, cytochalasin B, the cell-permeable mycotoxin, strongly inhibits the formation of actin filament networks. On the other hand, the mycotoxin of *Amanita phalloides* strongly activates the aggregation of all cell G-actin into filaments which become Ph-actin and cannot be depolymerised and thus this taxin avoids any dynamics of cytoskeleton.

Hence, theoretically we can assume that it is possible to synthesize and then govern/program an *artificial actin filament network*. This network is fundamental in any cell reaction to stimuli. As a result, this artificial network could be considered a biological computer/chip as such. Its computational processes would be primary for organic intelligence in principle. Some computational features of actin filament network are as follows:

- We deal with a system (N', V', w'), where (i) N' is a non-well-founded set of processors called "filaments"; this set is non-well-founded, because it is impossible to divide N' into atoms or even just into excluded subsets n_j which form a partition of $N' = \bigsqcup_j n_j$; in other words, processors are being redesigned permanently and they can appear and disappear and ever change own features; (ii) V' is a set of tuples $\{(i_t, j_t) \colon i_t, j_t \in N'\}$ whose elements are connections between filament i_t and filament j_t at time step t; hence, the set V' is non-well-founded, too, as its cardinality can change during the time t; (iii) w' is a function from V' to ${}^*\mathbf{R}$, where ${}^*\mathbf{R}$ is a set of hyperreal numbers such that $w'(({}^*i, {}^*j))$, where ${}^*i = i_0 i_1 i_2 i_3, \ldots$ and ${}^*j = j_0 j_1 j_2 j_3 \ldots$, for short $w_{{}^*i,{}^*j}$, is called the weight of the connection between filament ${}^*i$ and filament ${}^*j$ at each time step $t = 0, 1, 2, 3, \ldots$; notice that a filament ${}^*i$ can be hidden (not present) at actual time.

- Each filament behaves as an *artificial organism* (e.g. as an artificial cell): (i) it can grow up; (ii) its behaviour can be attracted/directed by chemotaxis. In cells there are ever filaments, some of them 'die' and some others 'born'.

- Each unstable actin filament network behaves as an *artificial swarm*: (i) it can grow up; (ii) its behaviour can be attracted/directed by chemotaxis (Van Haastert and Devreotes, 2004); (iii) there can be a fusion of two swarms (two actin filament networks) into one swarm (one network); (iv) there can be a splitting of one swarm (one network) into two swarms (two networks). In cells there are ever some actin filament networks.

- Each cross-linked actin filament network behaves as a *metaswarm*: it reacts to mechanical external stimuli and it can be partly reorganized.

Thus, in constructing the actin filament network (N', V', w') we have the following three levels of computations: (i) an artificial organism (filament); (ii) an artificial swarm (unstable bunch or tree); (iii) a metaswarm (stable bunch). On all three levels we face an instability of computation substratum. So, we assume that an *actin filament chip* changes its configurations during the computation processes. In designing this chip we can appeal to swarm computing, e.g. to slime mould computing. In the same measure as the neural networks, the actin filament networks can be used in pattern recognitions. So, due to the actin filament networks any slime mould can recognize its dynamic environment and occupy the pieces of food/attractants.

In this paper we consider some basic features of artificial actin filament networks. In Section 2 we concentrate on computational properties of unstable actin filament networks. In Section 3 on properties of stable actin filament networks. All constructions of this paper are pioneering.

2 ACTIN FILAMENTS AS SWARMS

In any cell there is a huge number of actin monomers or globular actin (the so-called G-actin) denoted by A_i. Monomers are involved into computations only within actin filaments, minimally consisting of three actin monomers. G-actin A_i can assemble into double helical filaments of 7-8 nm in diameter and of several microns in length.

Filaments are (re)designed by the processes of nucleation, polymerization, and depolymerization:

- *Nucleation*. For nucleation that allows monomers to be assembled into filaments it is enough to bound three G-actin monomers at first. Then for enlargement an actin filament must be polarised with a barbed end that is plus at which monomer addition is faster than at the pointed end that is minus. So, actin filaments are morphologically asymmetric with different kinetic characteristics at two ends, and this fact helps to polymerize filamentous actin (the so-called F-actin) from the head (plus end) to the tail (minus end), see please (Holmes et al., 1990; J. Hu et al., 2007).
- *Polymerization*. It is an association of new filaments mediated by actin cross-linking proteins: α-actinin, fascin, fimbrin, and filamin. This assembly is carried out on the basis of adding new monomers at the barbed end. Meanwhile, at the steady state, when a filament finishes to grow, the net rate of disassembly matches the rate of assembly at the plus end (Goldmann et al., 1998).
- *Depolymerization*. It is a dissociation of filaments which takes place when the critical concentration for actin polymerization is less than the dissociation constants at the two filament ends (Coluccio and Tilney, 1983).

Thus, an actin filament consists of two filament strands in the helical form. For each actin monomer A_i in both strands there are three possible states: *bound on the left*, lA_i; *bound on the right*, rA_i; and *bound on both sides*, bA_i. Out of any filament, the monomer A_i is considered *free*, fA_i, or turned off. Monomers in the first strand are distinguished by $sA_i^\bullet$, where $s \in \{l,r,b\}$. Monomers in the second strand are distinguished by sA_j°, where $s \in \{l,r,b\}$.

Definitions 1. *Polymerization is a process calculus defined as follows:*

$$names \ ::= \ fA_i\,|, lA_i^\bullet\,|\,rA_i^\bullet\,|\,bA_i^\bullet\,|\,lA_j^\circ\,|\,rA_j^\circ\,|\,bA_j^\circ;$$

$$\&, bounding \ ::= \textbf{ if } fA_j^\star \& rA_i^\star, \textbf{ then}$$
$$fA_j^\star \hookrightarrow_\& rA_{i+1}^\star \textbf{ and } rA_i^\star \hookrightarrow_\& bA_i^\star \ |$$
$$\textbf{if } fA_j^\star \& lA_i^\star, \textbf{ then}$$
$$fA_j^\star \hookrightarrow_\& lA_{i-1}^\star \textbf{ and } lA_i^\star \hookrightarrow_\& bA_i^\star \ |$$
$$\textbf{if } lA_j^\star \& rA_i^\star, \textbf{ then}$$
$$lA_j^\star \hookrightarrow_\& bA_{i+1}^\star \textbf{ and } rA_i^\star \hookrightarrow_\& bA_i^\star \ |$$
$$\textbf{if } bA_{i+i}^\star \& lA_i^\star, \textbf{ then}$$
$$\textbf{if } lA_i^\star \hookrightarrow_\& bA_{j+1}^\star, \textbf{ then } bA_{i+1}^\star \hookrightarrow_\& bA_{j+2}^\star \ |$$
$$\textbf{if } rA_{i+i}^\star \& lA_i^\star, \textbf{ then}$$
$$\textbf{if } lA_i^\star \hookrightarrow_\& bA_{j+1}^\star, \textbf{ then } rA_{i+1}^\star \hookrightarrow_\& rA_{j+2}^\star \ |$$
$$\textbf{if } rA_{i+i}^\star \& bA_i^\star, \textbf{ then}$$
$$\textbf{if } bA_i^\star \hookrightarrow_\& bA_{j+1}^\star, \textbf{ then } rA_{i+1}^\star \hookrightarrow_\& rA_{j+2}^\star \ |$$
$$\textbf{if } fA_i^\star \& fA_j^\star, \textbf{ then}$$
$$fA_i^\star \hookrightarrow_\& rA_{j+1}^\star \textbf{ and } fA_j^\star \hookrightarrow_\& lA_j^\star \textbf{ or}$$
$$fA_i^\star \hookrightarrow_\& lA_i^\star \textbf{ and } fA_j^\star \hookrightarrow_\& rA_{i+1}^\star,$$

where $\star \in \{\circ,\bullet\}$ *and* A $\hookrightarrow_\&$ B *is a renaming of monomer* A *by a new name* B *after the bounding;*

$$P, processes \ ::= \ \& \ | \ P_1 | P_2.$$

In this definition we have defined filaments as growing from the right side. So, a free monomer $fA_i^\star$ can interact with another free monomer $fA_j^\star$ and, as a result, we can have a strand $rA_{j+1}^\star lA_j^\star$ or a strand $rA_{i+1}^\star lA_i^\star$. A free monomer $fA_i^\star$ can also interact with a monomer $lA_j^\star$, and, as a result, we obtain a strand $\ldots bA_j^\star lA_{j-1}^\star$. A free monomer $fA_i^\star$ can also interact with a monomer $rA_j^\star$, and, as a result, we obtain a strand $rA_{j+1}^\star bA_j^\star \ldots$. A monomer $rA_i^\star$ can associate with a monomer $lA_j^\star$ to give a strand $\ldots bA_{i+1}^\star bA_i^\star \ldots$

Definitions 2. *Depolymerization is a process calculus defined as follows:*

$$names \ ::= \ fA_i\,|, lA_i^\bullet\,|\,rA_i^\bullet\,|\,bA_i^\bullet\,|\,lA_j^\circ\,|\,rA_j^\circ\,|\,bA_j^\circ;$$

$$\overline{\&}, unbounding \ ::= \textbf{ if } bA_{i+1}^\star \overline{\&} bA_i^\star, \textbf{ then}$$
$$bA_{i+1}^\star \hookrightarrow_{\overline{\&}} lA_j^\star \textbf{ and } bA_i^\star \hookrightarrow_{\overline{\&}} rA_i^\star \ |$$
$$\textbf{if } bA_{i+1}^\star \overline{\&} lA_i^\star, \textbf{ then}$$
$$bA_{i+1}^\star \hookrightarrow_{\overline{\&}} lA_{i+1}^\star \textbf{ and } lA_i^\star \hookrightarrow_{\overline{\&}} fA_i^\star \ |$$
$$\textbf{if } bA_j^\star \overline{\&} rA_{j+1}^\star, \textbf{ then}$$
$$bA_j^\star \hookrightarrow_{\overline{\&}} rA_j^\star \textbf{ and } rA_{j+1}^\star \hookrightarrow_{\overline{\&}} fA_{j+1}^\star \ |$$
$$\textbf{if } rA_{i+i}^\star \overline{\&} lA_i^\star, \textbf{ then}$$
$$rA_{i+1}^\star \hookrightarrow_{\overline{\&}} fA_{i+1}^\star \textbf{ and } lA_i^\star \hookrightarrow_{\overline{\&}} fA_i^\star,$$

where $\star \in \{\circ,\bullet\}$ *and* A $\hookrightarrow_{\overline{\&}}$ B *is a renaming of monomer* A *by a new name* B *after the unbounding;*

$$P, processes \ ::= \overline{\&} \ | \ P_1 | P_2.$$

Hence, a monomer $lA_i^\star$ can dissociate from a strand $\ldots bA_{i+1}^\star lA_i^\star$ or a strand $rA_{i+1}^\star lA_i^\star$ and to become a free monomer $fA_i^\star$. A monomer $rA_{i+1}^\star$ can dissociate from a strand $rA_{i+1}^\star lA_i^\star$ or a strand $rA_{i+1}^\star bA_i^\star \ldots$ and to become a free monomer $fA_{i+1}^\star$. A strand $\ldots bA_{i+1}^\star bA_i^\star \ldots$ can be divided into two strands $\ldots lA_{i+1}^\star$ and $rA_i^\star \ldots$.

Let $[sA_i^\star]$, where $s \in \{l, r, b\}$, mean a value of $sA_i^\star$: (i) $[sA_i^\star] = 1$ iff $sA_i^\star$ is excited; and (ii) $[sA_i^\star] = 0$ iff $sA_i^\star$ is not excited. A signal is transmitted in filaments $\ldots bA_{i+1}^\star lA_i^\star$ form the left to the right hand and the signal transmission defined as follows:

$$[bA_i^\circ] = \begin{cases} 1, & \text{if either } [bA_{i+1}^\circ] \wedge [bA_{i+1}^\bullet] = 1 \text{ or} \\ & [bA_i^\circ] \wedge [bA_i^\bullet] = 1; \\ 0, & \text{otherwise.} \end{cases}$$

$$[bA_i^\bullet] = \begin{cases} 1, & \text{if either } [bA_{i+1}^\bullet] \wedge [bA_{i+1}^\circ] = 1 \text{ or} \\ & [bA_i^\bullet] \wedge [bA_i^\circ] = 1; \\ 0, & \text{otherwise.} \end{cases}$$

$$[lA_i^\circ] = \begin{cases} 1, & \text{if } [bA_{i+1}^\circ] \wedge [bA_{i+1}^\bullet] = 1; \\ 0, & \text{otherwise.} \end{cases}$$

$$[lA_i^\bullet] = \begin{cases} 1, & \text{if } [bA_{i+1}^\bullet] \wedge [bA_{i+1}^\circ] = 1; \\ 0, & \text{otherwise.} \end{cases}$$

Each filament is instable because of the faster net loss of G-actin at the pointed end than at the barbed end and the faster net addition at the barbed end than at the pointed end. If there is an equilibrium of two rates of association and dissociation, it gives rise to a *treadmilling* when there is a net flow of actin subunits through the filament (Svitkina and Borisy, 1999). The rate of treadmilling may be altered by the inhibition of disassembly at the pointed end, e.g., by mM phosphate (Coluccio and Tilney, 1983). Increasing the rate of monomer dissociation at the pointed end, e.g., by cofilin can accelerate treadmilling, also. Proteins that control treadmilling of actin filaments and their adhesions are classified as follows:

$$C, control \ ::= \ \text{SeqP} \mid \text{CrossP} \mid \text{SevP} \mid \text{NucP},$$

where

- SeqP are *sequestering proteins*: (i) β-thymosins which sequester G-actin to prevent spontaneous nucleation; (ii) profilin which interacts with actin monomers to enhance nucleotide exchange (Carlier et al., 1994);
- CrossP are *cross-linking proteins*: (i) α-actinin which cross-links the actin filaments; (ii) vinculin, talin, and zyxin which link the cortex to the plasma membrane (Chhabra and Higgs, 2007; Choi et al., 2008);
- SevP are *severing proteins*: (i) cofilin (actin depolymerization factor) which sever F-actin to generate more filament ends for assembly or disassembly and enhances subunit dissociation; (ii) gelsolin and the Arp2/3 complex (containing the actin-related proteins, Arp2 and Arp3) which cap filament ends to regulate addition or loss of actin subunits, see: (Iwasa and Mullins, 2007);
- NucP are *nucleating proteins*: (i) formin, the Arp2/3 complex which nucleate filament growth; (ii) integrins which nucleate the formation of assemblies of structural and signaling proteins for filament adhesions (Balaban et al., 2001).

Actin filaments can be organized as bunches in response to the activation of signalling pathways by external stimuli. The basic processes in filament bunching are as follows:

- *Anchoring*. As response to external stimuli the actin filaments anchor to membranes. Meanwhile, filaments are attached at their plus ends so that the filament elongation occurs at anchored ends which can cause a membrane deformation in the form of growing pseudopodia.
- *Parallel orientation*. Usually, actin filaments are short, randomly oriented, and not bundled. External stimuli organize actin filaments in linear patterns with orientation of filament heads towards stimuli.
- *Branching*. The Arp2/3 complex anchors the pointed end of the future daughter filament to the existing mother filament. Then the daughter filament grows up at its barbed end. As a result, a branch appears. Continuing in the same way, a tree is assembled. More often the Arp2/3 complex nucleates the tree assembly close to the cell membrane at the point of external stimulus.
- *Cross-linking*. The actin filaments are cross-linked and bound to the cytoskeleton due to the actin-bounding proteins: profilin, the Arp2/3 complex, filamin, spectrin, and α-actinin. These proteins transform unbundled actin filaments with small adhesions into the bundled actin filaments with larger adhesions. Notice that the actin cytoskeleton built up by cross-linkers is used then for mechanotransduction and signal transmission.
- *Adhesion*. Integrins and myosin II are mainly responsible for adhesion and actin organization as bunches. For adhesion stability talin activates integrins and links them to actin. Adhesions disassemble at the back edge of the lamellipodium, which is a region of active actin depolymerization.

Each actin filament is attracted by a stimulus so that the filament grows up towards this stimulus. In case we have many actin filaments in one bunch, they behave as a swarm in front of stimuli attracting each individual of that bunch. This grouping behaviour can be represented as the following process calculus:

Definitions 3. *Let $P_{bunch} = \{n_1, n_2, \ldots, n_k\}$ be initial states of transitions for k filament bunches, $A_{bunch} = \{a_1, a_2, \ldots, a_j\}$ be a set of external stimuli (stresses) localized at different places, $V_{bunch} = \{r_1, r_2, \ldots, r_i\}$ be a set of filament trees. Then the bunch transition system, $TS_{bunch} = (S_{bunch}, E_{bunch}, T_{bunch}, I_{bunch})$, is defined in the following manner:*

- $\sigma : P_{bunch} \cup A_{bunch} \to S_{bunch}$ *assigning a state to each original point of bunches as well as to each external stimulus;*
- $\tau : V_{bunch} \to T_{bunch}$ *assigning a transition to each filament tree attracted by one stimulus;*
- $\iota : P_{bunch} \to I_{bunch}$ *assigning an initial state to each bunch localization.*

Each event of the set of events E_{bunch} is assigned to bunch transitions in accordance with the following process types:

- direction *(the filament tree grows from one state / localization / initial point to another state / stimulus),*
- fusion *(the filament tree grows from different states / localizations to the same one state / stimulus),*
- splitting *(the filament tree grows from one state / localization / initial point to different states / stimuli),*
- repelling *(the filament tree can dissociate).*

The system TS_{bunch} just defined behaves like the slime mould computer (Adamatzky et al., 2012) and it can solve the same tasks: transporting net optimization, pattern recognition, etc. Hence, in TS_{bunch} we can design reversible logic gates (Schumann, 2015). Let us remember that in these gates the number of inputs and outputs is the same. Let us show how we can implement the CNOT gate (the 2-bit controlled-NOT gate) into filament trees. In the CNOT gate, the four possible input bit strings are 00, 01, 10, 11 and these are mapped into 00, 01, 11, and 10 respectively (see Table 1).

Table 1: The CNOT gate in the matrix form.

	00	**01**	**10**	**11**
00	1	0	0	0
01	0	1	0	0
10	0	0	0	1
11	0	0	1	0

In the unexcited state filaments are chaotically oriented. Let us consider an artificial plane cell with the four zones on the cell surface: *a*, *b*, *c*, *d*, see Figure 1. Assume that two external stimuli are transmitted from both fronts: *ab* and *cd*. At the same time, suppose that the protein pool of the cell activates the polymerization and branching of filaments only in the four possible ways pictured in Figures 1, 2, 3, 4. Then the cell can be regarded as the *CNOT gate*. In this gate, mechanical stimuli generate a filament tree building in accordance with proteins which control treadmilling of actin filaments and their adhesions.

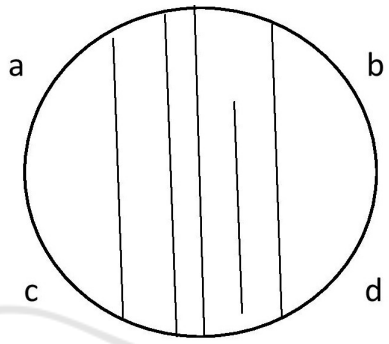

Figure 1: The first possible state of reacting to two stimuli (one from *ab* and one from *cd*): mapping 00 into 00, i.e. the string [*ab*] is mapped into the string [*cd*].

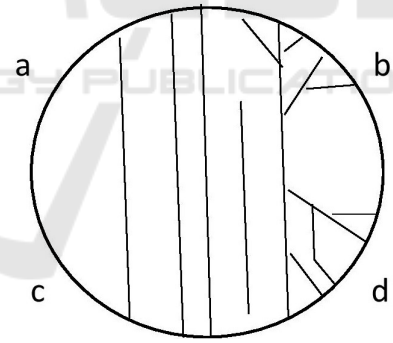

Figure 2: The second possible state of reacting to two stimuli: mapping 01 into 01.

In Figure 1, there are no mechanical stimuli and, as a consequence, there is no transmission of signal from *ab* to *cd* or from *cd* to *ab*, i.e. there are no filament trees and, therefore, we have a transmission from 00 to 00. In Figure 2, we have one mechanical stimulus at the zone *b* (or at the zone *d*) that implies a tree building at the whole right side of the cell and we have a transmission of signal from 01 to 01. In Figure 3, we have two mechanical stimuli at the zones *a* and *b* (or one mechanical stimulus at the zone *c*) that result a tree building at the zones *a*, *b*, and *c* and from that we have a transmission of signal from 11 to 10 (or from 10 to 11). In Figure 3, we deal with

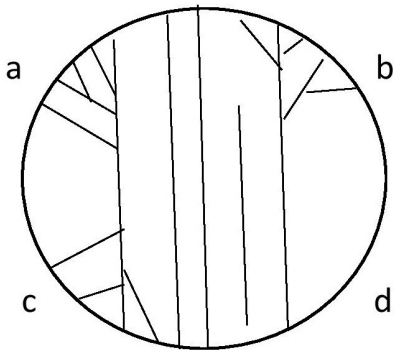

Figure 3: The third possible state of reacting to two stimuli: mapping 11 into 10.

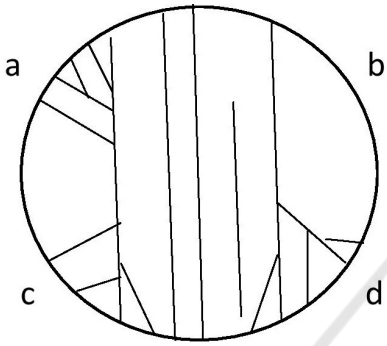

Figure 4: The fourth possible state of reacting to two stimuli: mapping 10 into 11.

one mechanical stimulus at the zone a (or with two mechanical stimuli at the zones c and d) that causes a tree building at the zones a, c, and d and we observe a transmission of signal from 10 to 11 (or from 11 to 10).

3 ACTIN FILAMENTS AS METASWARM

Highly cross-linked filaments are used in cells for transferring the mechanical stimulus resulted by mechanical forces applied to cell surfaces. These forces generate elastic stress waves which rapidly propagate through actin stress fibers. Such external mechanical stresses can imply a diffusion of actin filament networks if filaments were uncross-linked semidilute (Kas et al., 1995). So, the rotation around their axis cause colliding with other filaments for uncross-linked filament networks, but in the case of cytoskeleton the mechanical stimulus is being transmitted by filament strands. As a consequence, in response to the physical force the stress fiber displacement is activated in the cytoskeleton (Hotulainen and Lappalainen, 2006; K. Hu, 2007; Ridley et al., 2003). Some forms of that displacement which transmit the external stress: fiber inertia, fiber viscoelasticity, and cytosolic damping. Hence, if highly cross-linked actin filament networks are organized in parallel arrays of filaments, they become stress fibers with the following kinds of deformation which strongly influence on transmitting signals (ben Avraham and Tirion, 1995; Guo and Wang, 2007; Higuchi et al., 1995; Xu et al., 1998):

- *Shear deformation*. In a highly cross-linked actin filament network both sides do not change their lengths under shear, but the diagonals are stretched and compressed respectively. This stretch or compression causes a large tensional stress in the actin filament network.
- *Bending deformation*. It is a curvature stress that is a result of force that is generated by the local extension of the material on the convex side and compression of the material on the concave side of the bend.
- *Orientation deformation*. It is a mechanical stress, when the orientation changes.

Thus, we can consider all the possible states in the cell deformation as a form of signal transmission by filaments. Each deformation state is caused by an appropriate mechanical force. In turn, the mechanical signal generated by the force is transmitted in different ways according to a kind of the cell deformation. So, the cell can be regarded as a reversible logic gate which has the same number of inputs (mechanical stresses) and outputs (stress transmissions by deformation). The form of the cell deformation is a form of signal transmission. Let us examine an artificial plane cell pictured in Figure 5. Then let us concentrate on the four zones on the cell surface: a, b, c, d. Each letter runs over the two values: 1 or 0. It has the value 1 if a mechanical stress goes through an appropriate zone. Notice that the stress transmission depends on the cytoskeleton structure and there may be zones, where the mechanical stress cannot go through at all. Let us suppose that the cell pictured in Figure 5 can have only four kinds of deformation in transmitting mechanical signals: from Figure 6 to Figure 9. Then this cell can be regarded as the CNOT gate.

In this gate we assume that a compression of zone x means the value $[x] = 1$ and a stretching of zone x means the value $[x] = 0$. Hence, in Figure 6, we deal with the cell deformation where all four zones a, b, c, d are stretched and, as a result, we have a transmission from 00 to 00. In Figure 7, zones a and c are stretched and zones b and d are compressed and, therefore, we have a transmission from 01 to 01. It is a bending in the right side of the cell from b to d and vice versa. In

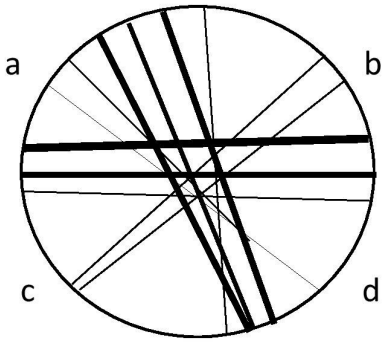

Figure 5: The artificial cell considered the CNOT gate. Its cytoskeleton is at the normal stage without external stresses. We assume that after stresses the string $[ab]$ is transformed into the string $[cd]$ and vice versa.

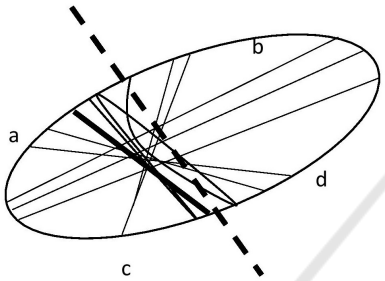

Figure 6: The first possible state of the cell after one mechanical stress: mapping 00 into 00.

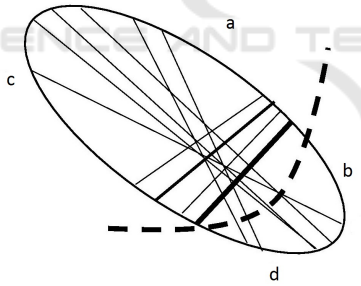

Figure 7: The second possible state of the cell after one mechanical stress: mapping 01 into 01.

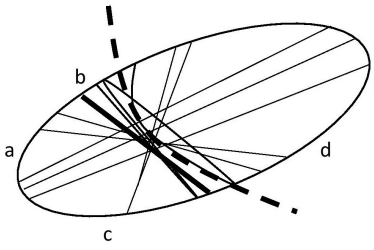

Figure 8: The third possible state of the cell after one mechanical stress: mapping 11 into 10.

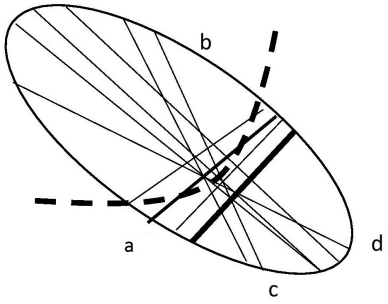

Figure 9: The fourth possible state of the cell after one mechanical stress: mapping 10 into 11.

Figure 8, zones a, b, and c are compressed and zone d is stretched and we have a transmission from 11 to 10 (or from 10 to 11). It is a bending from a, b, c to d and vice versa. In Figure 9, zones a, c, and d are compressed and zone b is stretched and, hence, we have a transmission from 10 to 11 (or from 11 to 10). It is a bending from a, c, d to b and vice versa.

Any deformation of cells is a transduction of mechanical stress to their neighboring cells. This allows us to construct artificial networks uniting thousands cells with a fixed number of neighbors for each cell. Let us suppose that for each cell with n inputs and k outputs we have just $n+k$ neighbor in our actin filament network. For instance, in the CNOT gate we deal with 2 inputs and 2 outputs, thus, we have 4 neighbors: for each zone from a to d pictured in Figure 5 we have just one neighbor. So, the cell deformation of Figure 6 implies no mechanical stress transduction for the four neighbors of the cell. The cell deformation of Figure 7 is a mechanical stress transduction for the two neighbors of the cell at zones b and d. The cell deformation of Figure 8 is a mechanical stress transduction for the three neighbors of the cell at zones a, b, and c. And, finally, the cell deformation of Figure 9 is a mechanical stress transduction for the three neighbors of the cell at zones a, c, and d.

4 CONCLUSIONS

We have considered two types of actin filament networks as a computational substratum: branched filaments (Section 2) and cross-linked filaments (Section 3). In both cases we can design reversible logic gates. In the second case we can design actin filament networks with thousands cells which by their deformations transmit mechanical stresses to their neighbors.

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REFERENCES

Adamatzky, A., Erokhin, V., Grube, M., Schubert, Th., Schumann, A. 2012. Physarum Chip Project: Growing Computers From Slime Mould. *International Journal of Unconventional Computing*. 8(4):319-323.

Balaban, N. Q., Schwarz, U. S., Riveline, D., Goichberg, P., Tzur, G., Sabanay, I., Mahalu, D., Safran, S., Bershadsky, A., Addadi, L. et al. 2001. Force and focal adhesion assembly: a close relationship studied using elastic micropatterned substrates. *Nat. Cell Biol.* 3:466-472.

ben Avraham, D., Tirion, M. M. 1995. Dynamic and elastic properties of F-actin: a normalmodes analysis. *Biophys. J.* 68:1231-45.

Carlier, M. F., Valentin, R. C., Combeau, C., Fievez, S., Pantoloni, D. 1994. Actin polymerization: regulation by divalent metal ion and nucleotide binding, ATP hydrolysis and binding of myosin. *Adv. Exp. Med. Biol.* 358:71-81.

Chhabra, E. S., Higgs, H. N. 2007. The many faces of actin: matching assembly factors with cellular structures. *Nature Cell Biology* 9:11101121.

Choi, C. K., Vicente-Manzanares, M., Zareno, J., Whitmore, L. A., Mogilner, A. and Horwitz, A. R. 2008. Actin and alpha-actinin orchestrate the assembly and maturation of nascent adhesions in a myosin II motor-independent manner. *Nat. Cell Biol.* 10:1039-1050.

Coluccio, L. M., Tilney, L. G. 1983. Under physiological conditions actin disassembles slowly from the nonpreferred end of an actin filament. *J. Cell. Biol.* 97:1629-1634.

Fackler, O. T., Grosse, R. 2008. Cell motility through plasma membrane blebbing. *J. Cell Biol.* 181:879-884.

Furuhashi, K., Ishigami, M., Suzuki, M., Titani, K. 1998. Dry stress-induced phosphorylation of physarum actin. *Biochem. Biophys. Res. Commun*. 242:653-658.

Furukawa, R., Kundra, R., Fechheimer, M. 1993. Formation of liquid crystals from actin filaments. *Biochem.* 32:12346-52.

Gimona, M., Mital, R. 1998. The single CH domain of calponin is neither sufficient nor necessary for F-actin binding. *J. Cell. Sci.*

Goldmann, W. H., Guttenberg, Z., Tang, J. X., Kroy, K., Isenberg, G., Ezzell, R. M. 1998. Analysis of the F-actin binding fragments of vinculin using stopped-flow and dynamic lightscattering measurements. *Eur. J. Biochem.* 254:413-419.

Guo, W. H., Wang, Y. L. 2007. Retrograde fluxes of focal adhesion proteins in response to cell migration and mechanical signals. *Mol. Biol. Cell.* 18:4519-4527.

Higuchi, H., Yanagida, T., Goldman, Y. E. 1995. Compliance of thin filaments in skinned fibers of rabbit skeletal muscle. *Biophys. J.* 69:1000-1010.

Holmes, K., Popp, D., Gebhard, W., Kabsch, W. 1990. Atomic model of the actin filament. *Nature*. 347:44-49.

Hotulainen, P., Lappalainen, P. 2006. Stress fibers are generated by two distinct actin assembly mechanisms in motile cells. *J. Cell. Biol.* 173:383-394.

Hu, J., Matzavinos, A., Othmer, H. G. 2007. A theoretical approach to actin lament dynamics. *Journal of Statistical Physics*. 128(1/2):111138.

Hu, K., Ji, L., Applegate, K. T., Danuser, G., Waterman-Storer, C. M. 2007. Differential transmission of actin motion within focal adhesions. *Science*. 315:111-115.

Iwasa, J.H., and R. D. Mullins. 2007. Spatial and temporal relationships between actin-lament nucleation, capping, and disassembly. *Current Biology*. 17:395406.

Kas, J., H. Strey, J. X. Tang, D. Finger, R. Ezzell, E. Sackmann, and P. A. Janmey. 1995. F-actin, a model polymer for semiflexible chains in dilute, semidilute and liquid crystalline solutions. *Biophys. J.* 70:609-625.

Pollard, T. D. and Borisy, G. G. 2003. Cellular motility driven by assembly and disassembly of actin filaments. *Cell* 112:453-465.

Ridley, A. J., Schwartz, M. A., Burridge, K., Firtel, R. A., Ginsberg, M. H., Borisy, G., Parsons, J. T. and Horwitz, A. R. 2003. Cell migration: integrating signals from front to back. *Science*. 302, 1704-1709.

Schumann, A. 2015. Conventional and unconventional reversible logic gates on Physarum polycephalum. *International Journal of Parallel, Emergent and Distributed Systems*. DOI: 10.1080/17445760.2015.1068775 .

Steinmetz, M., K. Goldie, and U. Aebi. 1997. A correlative analysis of actin filament assembly, structure, and dynamics. *J. Cell Biol.* 138:559-574.

Svitkina, T. M. and Borisy, G. G. 1999. Arp2/3 complex and actin depolymerizing factor/cofilin in dendritic organization and treadmilling of actin filament array in lamellipodia. *J. Cell Biol.* 145:1009-1026.

Van Haastert, P. J. and Devreotes, P. N. 2004. Chemotaxis: signalling the way forward. *Nat. Rev. Mol. Cell Biol.* 5:626-634.

Xu, J. Y., Schwarz, W. H., Kas, J. A., Stossel, T. P., Janmey, P. A., Pollard, T. D. 1998. Mechanical properties of actin filament networks depend on preparation, polymerization conditions, and storage of actin monomers. *Biophys. J.* 74:2731-2740.