International Journal of Autonomous and Adaptive Communications Systems

ISSN online: 1754-8640 - ISSN print: 1754-8632
https://www.inderscience.com/ijaacs

A multi-level autopoietic system to develop an artificial embryogenesis process

Rima Hiouani, NourEddine Djedi, Sylvain Cussat-Blanc, Yves Duthen

DOI: 10.1504/IJAACS.2024.10047330

Article History:
Received: 20 August 2021
Accepted: 28 November 2021
Published online: 10 January 2024

A multi-level autopoietic system to develop an artificial embryogenesis process

Rima Hiouani* and NourEddine Djedi

LESIA Laboratory,
Biskra University,
BP 145 RP 07000, Biskra, Algeria
Email: rima.hiouani@gmail.com
Email: n.djedi@univ-biskra.dz
*Corresponding author

Sylvain Cussat-Blanc and Yves Duthen

University of Toulouse,
IRIT – CNRS UMR 5505, France
Email: sylvain.cussat-blanc@irit.fr
Email: yves.duthen@ut-capitole.fr

Abstract: This paper presents a new model for the self-creation of an artificial multicellular organism from one cell, which is inspired by 'The Autopoietic System Theory' at different levels. This theory has been proposed to define the universal self-organisation of living systems. We proposed MLAS, 'Multi-level Autopoietic System' to embody this autopoietic system. However, in contrast to the proposed system by Varela, we set it up according to various levels (organs autopoietic machine, tissues autopoietic machine, and cells autopoietic machine). Inside the level of the cell autopoietic machine, we proposed the second contribution in this paper, which is a Boolean artificial gene regulator network with an epigenetic part that leads the cells to create their history during evolution. Several interesting features have been observed in the developed organism through MLAS, as self-organisation and self-creation. Likewise, other processes that characterise the living system have appeared, such as evolution and diversity.

Keywords: autopoietic system; self-organisation; self-adaptation; artificial gene regulatory network; evolution; diversity.

Reference to this paper should be made as follows: Hiouani, R., Djedi, N., Cussat-Blanc, S. and Duthen, Y. (2024) 'A multi-level autopoietic system to develop an artificial embryogenesis process', *Int. J. Autonomous and Adaptive Communications Systems*, Vol. 17, No. 1, pp.39–67.

Biographical notes: Rima Hiouani received her Master degree in Image and Artificial Life from UMK University, Biskra, Algeria in 2013. She is currently a PhD candidate in Computer Science at the LESIA Laboratory at the same university. Her current research interests include self-organisation, intelligent system, bioinspired techniques and artificial life.

NourEddine Djedi is a Professor of Computer Science and conducts research in artificial life and natural phenomenon simulation team of the LESIA Laboratory at the University of Biskra. He received his PhD in Computer

Science in 1991 at the University Paul Sabatier (Toulouse), and worked successively in several fields such as image synthesis, bio-inspired techniques and artificial life.

Sylvain Cussat-Blanc is an Associate Professor of Computer Science, a senior member of VORTEX team in the Institute for Research in Computer Science of Toulouse (IRIT). He received his PhD from University of Toulouse in 2009; and he passed a post-doctoral in Brandeis University (USA) with the team of Jordn Pollack in 2012. His main research interests are artificial life, evolutionary computation, developmental model, gene regulatory networks. He has to his credit more than 100 publications in journals, books and conferences. He serves as an editorial member and a reviewer of several journals such *Artificial Life*, *ACM Transactions on Autonomous and Adaptive Systems*, *Genetic Programming and Evolvable Machines* and *IEEE Transactions on Neural Networks*.

Yves Duthen is a Professor of Computer Science and conducts research in artificial life and virtual reality team VORTEX of the Institute for Research in Computer Science of Toulouse (IRIT). He received his PhD in Computer Science in 1983 then HDR in 1993, he worked successively in several fields such image synthesis, parallel machines, behavioural simulation and artificial creatures.

This paper is a revised and expanded version of a paper entitled ‘A multi-level autopoietic system to develop an artificial organism’ presented at *14th European Conference on Artificial Life (ECAL 2017)*, Lyon, France, Volume: Late-Breaking Abstracts Booklet, September 2017.

1 Introduction

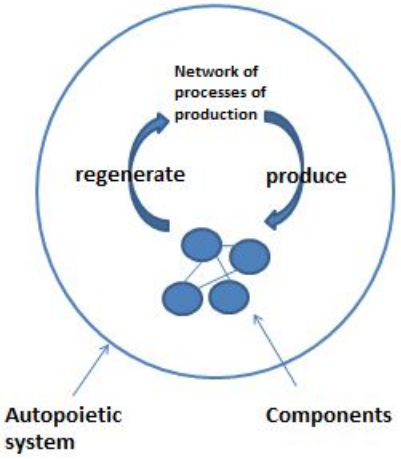
Maturana and Varela describe the autopoietic machine as an organisation of a living system which defines the universal self-organisation (Fuchs and Hofkirchner, 2009). In short, Maturana and Varela (1991) see that autopoiesis explain the autonomy of all living system, they believed that, although living systems are diverse, they still share a common organisation which we implicitly call ‘living’. They also claim that some biological processes such as reproduction and evolution are secondary to the establishment of this unitary organisation. Then they asked “what is the necessary and sufficient organisation for a given system to become a living unity?” they often argued that living organisation is characterised by specifying the network of interactions of components to form the living system as a whole ‘unity’. On this basis, they proposed the concept of ‘autopoiesis’ to define the system that produces itself, which means self-production or self-creation. They affirmed that the autopoietic mechanisms of self-production are crucial in understanding both the diversity and the uniqueness of the living system. And they give the following definition to this system, an autopoietic machine is

> “a machine organised (defined as a unity) as a network of processes of production (transformation and destruction) of components that produce the components which: (i) through their interactions and transformations continuously regenerate and realise the network of processes (relations) that produced them and (ii) constitute it (the machine) as a concrete unity in the space in which they (the components) exist by specifying the topological

> domain of its realisation as such a network." (Maturana et al., 1974), we have summed up this definition in Figure 1

Although the notion of autopoietic systems was first suggested in biology, it has since been applied to a variety of subjects, including sociology and the nature of creativity (Iba, 2010; Baraldi and Corsi, 2016; Bishop and Al-Rifaie, 2017; Meincke, 2019; Chettiparamb, 2020). Many artificial life researchers employ the autopoietic theory to try to comprehend and mimic the properties and capabilities of living systems. Varela clarifies the idea of autopoietic by using the substrate-catalyst-link (SCL) model to replicate an autopoietic cell that develops and maintains its membrane recurrently and dynamically (McMullin and Varela, 1997). Furthermore, the researchers extend the SCL model by integrating explicit membrane dynamics in Suzuki and Ikegami (2009), where they discovered that different membrane shapes cause distinct types of self-motility. Agmon et al. (2016) also present a spatial model of concentration dynamics. The configurations presented in this model demonstrate metabolism–boundary co-construction, precariousness, and self-repair. Other researchers show and explore the relationship between mechanisms of autopoiesis and behaviour in Computational Chemo-ethology (Egbert and Di Paolo, 2009). Beer makes an analysis of autopoiesis in game of life (GoL) and tries to utilise it as a simple universal model, in which we can explore in detail the various issues that arise when attempting to apply the definition of autopoiesis to a concrete system (Beer, 2015). Turney (2021) analyses autopoiesis and multicellularity in the Model-S, which is based on the evolution of seed patterns in Conway's Game of Life. They find that the fitness of evolved seed patterns in Model-S is correlated with the diversity and quantity of multicellular autopoietic structures.

Figure 1 The autopoietic machine (see online version for colours)



Authors in the field of morphogenetic engineering (ME) propose that the self-organisation system be elevated to a new level called 'programmable self-organisation,' or 'self-architecturing'. A concept that has yet to be fully explored, but which can be found in certain types of biological systems, such as embryogenesis and insect colonies, which have the ability to combine pure self-organisation and sophisticated architecture without the need for a great architect or ultimate plan. In embryogenesis the 'self-architecturing' is guided by the genetic and epigenetic information which is produced

throughout millions of years of evolution inside each cell (Doursat et al., 2012). Recreating such system and obtaining characteristics of the living system, as their autonomy, self-formation, and self-organisation capabilities to generate an automatic design of a complex system, as in the development of an entire artificial organism from one single cell, which exhibits the same 'strong' characteristics of the living system, recreating an artificial system has the capacity of biological system based on the definition of autopoietic theory, could help as to understand how this biological system began and how they evolved.

Many developmental models have been created to replicate the growth of virtual multicellular animals from a single cell, with varying degrees of biological realism. Morphogens play a crucial part in the developmental process in the environment. The morphogens are hand-coded in the environment in Chavoya and Duthen (2008), Cussat-Blanc et al. (2011), and in Chavoya and Duthen (2008), Cussat-Blanc et al. (2011). While cells in Joachimczak and Wróbel (2009), Knabe et al. (2008) and Pascalie et al. (2014) can distribute this information in the environment, they are the controllers of morphogen diffusion. The concentration of this chemical in the environment is represented by a gradient function in Disset et al. (2014), and the source of this diffusion is hand-coded. The development of these models (Chavoya and Duthen, 2008; Cussat-Blanc and al, 2011; Joachi unimczak and Wróbel, 2009; Knabe et al., 2008, p.9, Pascalie et al., 2014) is dependent on morphogens in the environment, where cells choose their actions based on this input morphogen, whether hand-coded, coded in the environment as a gradient, or controlled by other cells. In the other side, others research used a cell driver to guide the process of development (Fontana, 2010; Cussat-Blanc and Pollack, 2014). They have one type of cell guide the other cells and the process of the artificial embryogenesis. Despite the importance of the obtained results, they are still very far from biological realism.

The morphogenesis process, which permits live beings to fully develop from single cells, has proved particularly appealing for creating algorithms that control agent swarms, like in Barga et al. (2018). The morphogenesis process is also used in evolutionary robotics by Hockings et al (2020). The goal of these methods is to make it easier to create delicate and efficient robot mechanisms. Another researcher (Yu, 2020; Yang et al., 2017, 2020) was inspired by the traits and strategies of ant colonies to develop a cloud computing algorithm based on this biological autonomous system.

Though cells are the basic unity in these models (Chavoya and Duthen, 2008; Cussat-Blanc et al., 2011; Joachimczak and Wróbel, 2009; Knabe et al., 2008; Fontana, 2010; Cussat-Blanc and Pollack, 2014; Disset et al., 2014; Pascalie et al., 2014), all of them respond to the same stimulus in the same way. However, the biologists Bracken, Dietrich et al. (2006), confirm that even if cells have identical genomes, they can respond differently to the same stimulus because of their preprogrammed memory considered by 'The Polycomb group (PcG)'. Moreover, cells are considered as an autopoietic system, in which the external event (the outside of the cell) only triggers partial effects inside the system. The total and significant effect of the changes is defined by the internal dynamics of the system and not by the external (Maturana-Romesín and Mpodozis, 2000).

Authors of autopoietic theory attempt to provide a general definition of all living systems' self-organisation and autonomy; on the other hand, ME field attempts to replicate natural systems' self-organisation as artificial systems. In this study, we attempt

to design an artificial embryogenesis process using a simple system based on the technical details of Maturana and Varella's biological theory. Self-organisation and complex architecture are combined in this system. Scientists have only just begun the long task of simulating these intricate processes. Because it defines the organisation of the living system, we employ the theory of autopoietic machines to construct our system. This notion has also been used to explain biological evolution (Dekkers, 2017). Can we achieve evolution, variety, and reproduction as a second process of this machine, as Maturana suggests, in our quest to develop an artificial system capable of self-organisation and autonomy by using this theory?

We propose in this study two contributions, the first against the autopoietic system, we proposed a new kind of the autopoeitic system 'MLAS' pass from the cell autopoeitic system to an organism autopoeitic system, where the cells without an external controller develop an architectured organism. The second contribution is inside the cell, exactly in the Artificial GRN that controls the cell fate, where we proposed a new kind of GRN with epigenetic parts that lead the cell to be an autopoeitic system; the cells used by the researchers in ME is not an autopoeitic system.

We successfully applied the autopoietic theory at different levels in our MLAS system. MLAS has several levels of organisation: cell level, tissue level, and organ level, each individual at each level is an autopoietic machine in its process of production and regulation. Cells are controlled by an artificial GRN with an epigenetic part (the second contribution in this paper), this artificial GRN is self–regulated to create a pathway of actions and history inside the cells; the artificial GRN with an epigenetic part represents the network of creation of components in the autopoeitic cell.

The paper is organised as follows. Section 2 introduces the different levels in our system, Section 3 presents the parameters the system begin with, Sections 4 and 5 shows the different autopoietic individuals in each level and their identity, in Section 6, we present how MLAS create itself as a cyclic network of production in different levels, and how levels interact together, then in Section 7 we go deeper into the cell level, and we present here, the artificial GRN with an epigenetic part and its different layers of regulation inside the cell, while the next section presents the results, and the last section draws some conclusions and discusses a new viewpoint in the autopoietic system.

2 Multi-level organisation (the organisation and levels of MLAS)

Due to the complexity of embryogenesis, it would be difficult for a cell to devote the entire process to the creation of an organism. During embryogenesis, certain cells perform only one function: to build a specific tissue, rather than the entire creature. A multicellular organism's body structure has different levels of organisation, with cells considered the fundamental units of life (for example, tissues are groups of similar cells that work together to accomplish a specific task, and organs are made up of two or more tissues that are organised to carry out a specific function...). Therefore, we propose a hierarchical developmental model with three levels (Organ level, Tissue level, and Cell level) to create and regulate the different individuals (artificial organ, artificial tissue, and artificial cell) Figure 2.

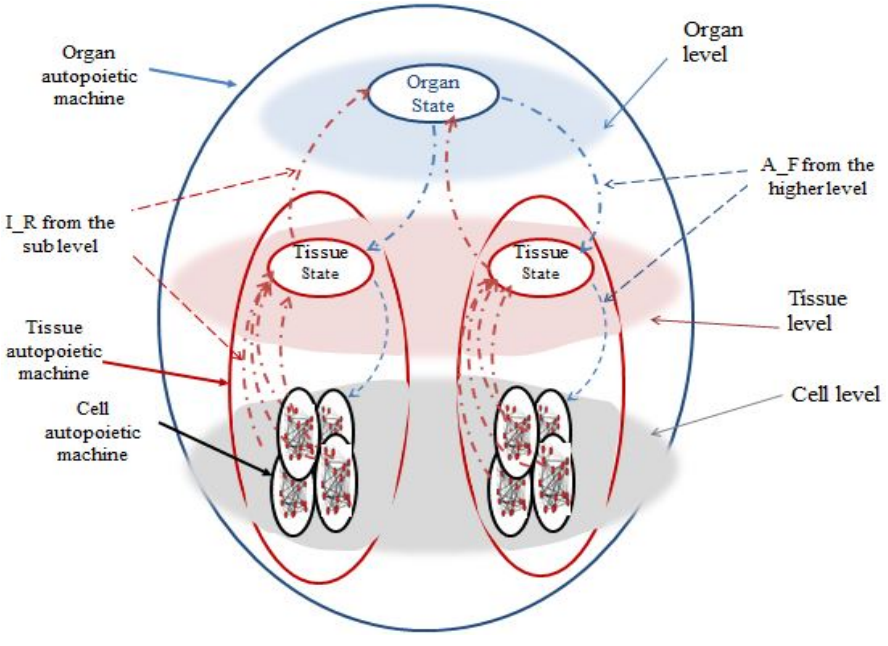
The concept of levels is a metaphor. They are a set of parameters that are calculated and regenerated by network components to produce the many autopoietic machines in the system; Figure 2 shows how they are organised:

1 the individual's state (Organ state, Tissue state, Cell state) represents the values that describe the individual's level of construction

2 individual report 'I_R'' floating value (between 0 and 1) is calculated and diffused by individuals of the sub levels

3 the Autopoietic Factor 'A F' is a floating value (between 0 and 1) that is derived from higher levels.

Figure 2 The cyclic network of creation of the different autopoietic system (cell, tissue, and organ) and the different interactions between them (see online version for colours)

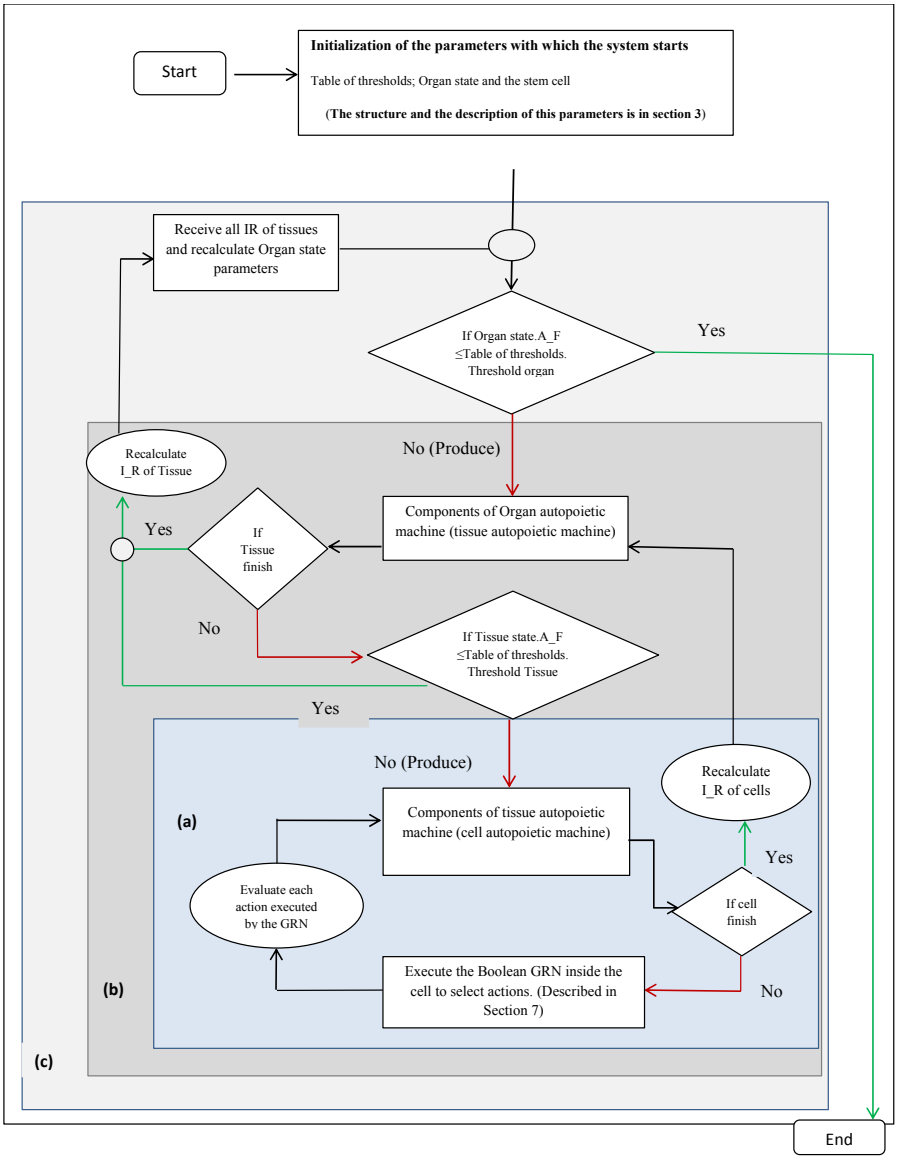


- Signals diffused by neighbours of the same level, it gives individuals information about their neighbours.

These parameters of the different levels regenerate the network of creation of individuals. More details about these parameters (structure...) are presented in the following sections.

In MLAS system we have nested autopoietic individuals and each one influence in the construction of the others, Figure 3 presents a flow chart that sketches the basic structure of MLAS.

Figure 3 This flowchart outlines the process for executing the algorithm of MLAS in the different individual levels: (a) cell autopoietic machine; (b) tissue autopoietic machine and (c) organ autopoietic machine. The initial parameters structure which the system begins with is described in Section 3; the calculation of the different parameters between levels is presented in Section 6; the Boolean GRN in cell section autopoietic machine is presented in Section 7 (see online version for colours)



3 The initial parameters of MLAS

The system's initial parameters are a table of thresholds, one stem cell, and the organ state.

Only with these three parameters, the system (MLAS) could create and regulate itself as an autopoietic system (self-creating and self-architecting without any external information), to develop an artificial embryogenesis process.

Table of thresholds: There is a required degree of construction for each individual in our process of self-creating individuals, which is represented in the table of thresholds (contain threshold of construction for each individual in each level) Figure 4(b), the value of the threshold for each individual is a float between 0 and 1. *Organ state*: Figure 4(a1). Structured as follow:

- State identifier (Org_Id) coded as an integer between 1 and P.
- Individual reports (I_Rorg) is coded as a float between 0 and 1, the value of this individual reports determine the success rate of the components that construct the organ. In the beginning, this I_Rorg is initialised by 0.
- Autopoietic factor (A_Forg) is coded as a float between 0 and 1, initialised by 1. A_Forg used to verify if the organ autopoietic machine should create new components or not.

These two concentrations ($I\_R_{org} = 0$ and $A\_F_{org} = 1$) demonstrate that the organ doesn't exist yet.

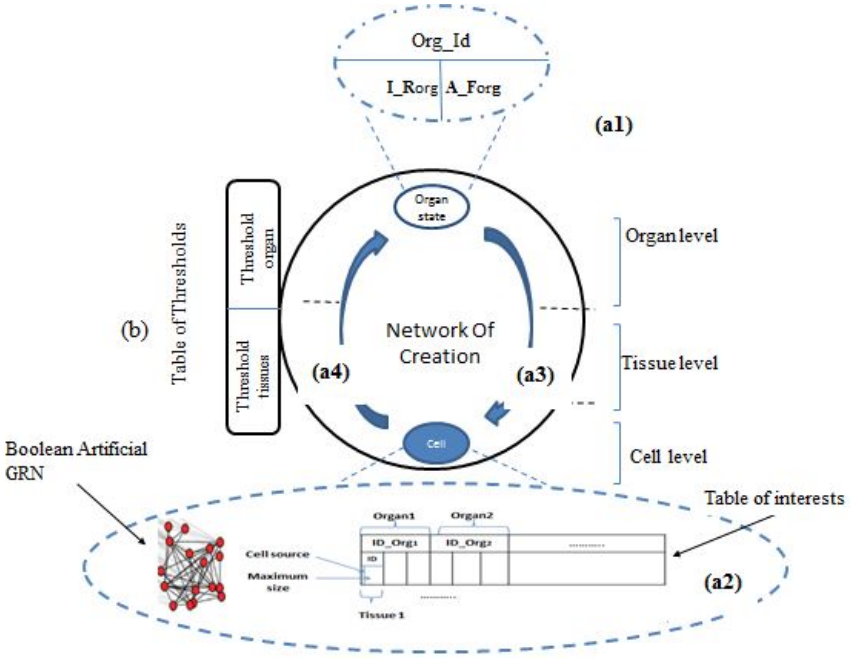
Stem cell: In addition to the table of thresholds and the organ state, one inactive stem cell is present in the system with irregular Boolean Artificial GRN and table of interest Figure 4(a2). This table represents all the possible global interests of the cell (global interests are described in Boolean Artificial GRN section). Many experiments suggest that the organ grows to reach its final predetermined mass and that it has intrinsic information about its final size (Conlon and Raff, 1999; Day and Lawrence, 2000; Klingenberg et al., 2002). In contrast, the techniques to set the limits of growth are not well characterised (Li et al., 2008).

Inside our cell, exactly in table of interests, we chose it to be the mechanism of setting the limits of growth for each tissue in our model of artificial embryogenesis. In each case of table of interests; we have Organ represented by its identifier organ 'ID_Org', which is coded as an integer between 1 and P, and a group of tissues that constructs this organ. Each tissue is represented by its:

- Identifier 'ID', represented as an integer between 1 and N.
- Cell source, the first cell begins the construction of this tissue.
- Maximum size represents the maximum length and width of the tissue, which is represented as an integer between 0 and m for the length, and 0 and n for the width. It is considered as the technique of setting the limit of growth for the tissue.

Since the organ is a group of tissues, the maximum size of its tissues set organ limits too. However, the final size of the organ and each tissue at the end of the development process depends on signals in the environment and the table of thresholds of the system.

Figure 4 The initialisation of MLAS in the different levels. (a1) the structure of organ state node; (a2) the boolean artificial GRN and the table of interests inside the stem cell; (a3) the first semi circle between organ state node and the stem cell; (a4) the second semi cercle between stem cell and organ state node and (b) the table of threashold that represent the requiered level of construction for each individual (see online version for colours)



4 The aim of MLAS and its different autopoietic individuals

To go from self-organisation to preprogrammed self-organisation system (self architecturing system), which is considered as a challenge in ME and artificial life, we propose (MLAS), a network with the aim of creating a system that has the capacity of self-creating and self-architecturing without external guide or planning, MLAS network adapts its different autopoietic individuals and components to develop the right architecture. On the other side, we want to see how this biological theory (autopoietic theory), which was proposed to define the organisation of the living system and its different characteristics, could influence the self-organisation systems in artificial life.

With the organ state and the stem cell, the MLAS network organises and creates itself to reach the required level of construction (table of thresholds) as an autopoietic machine inside an autopoietic machine at three levels.

This network of creation and regulation of individuals (MLAS) is created by the interaction between the different levels. Beginning from organ state node in the highest level to the stem cell network (Boolean Artificial GRN), the first semi-circle Figure 4(a3), and arrived at the first node (organ state) as a cyclic network Figure 4(a4). In each cycle of this network, different changes are produced (number of nodes, the organisation of individuals, and the state of the individual). Furthermore, new nodes

appear and new transformation between individuals is generated by the network to achieve the required degree of construction in the table of thresholds.

MLAS leads individuals to create themselves and combine between self-organisation and architecture. According to the different levels in the system, individuals are different from one level to another (Cell individuals, Tissue individuals, Organ individuals). At the first time, there is one individual inside the system (single stem cell) at the cell level. Cells are the basic unit of construction of all the other individuals. The tissue individual consists of several cells with similar structures and functions. An organ is made up of tissue groups which work together to accomplish the composition of a whole organ according to the required level of construction in table of thresholds.

Each individual in the system is an autopoietic machine in its process of creation and regulation. It creates and regulates itself as a closed organisation (without any information or guide from the exterior of the autopoietic machine) by a network of production of components, which produces the components of the individual. These components can interact together and regenerate the network of production, which leads again to create these components. This cyclic network of creation shows the capacity of the individual to organise and create itself without any external driving from the environment.

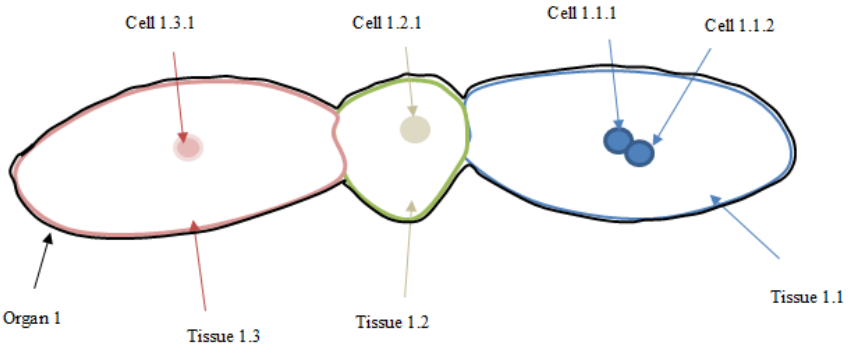
Due to the fact that autopoietic theory is interesting in biology 'in the natural system' and in other disciplines, the understanding of the biological system and recreate their capacity to generate systems has their capacity are the first aim in artificial life research. Thus, based on this theory, we propose a network of self-creating and organisation with hierarchical levels to develop a structured shape of organs without external or central control.

The first autopoietic machine, 'organ autopoietic machine' Figure 2, begins in the higher level of the system 'organ level' with the first node 'Organ state', and the components of this individual (tissues) are in the sub level. Highlighting that, these components (tissues) are another autopoietic machine with a network of production and components. Components in tissue autopoietic machine are cells, this last one 'cell' is also another autopoietic machine, the network of creation in cells is the Boolean Artificial GRN, and its components are the actions executed by this Boolean Artificial GRN, these actions regenerate and regulate the Boolean Artificial GRN, this means, the cell creates and regulates its pathway of actions and history.

5 Identity of individuals

Each Individual in the system has a vector of identity passing by the organ to the cell. Individuals (cell, tissue, organ) are represented by their states; Organ state, tissue state, and cell state, and their components, tissues, cells, and actions. Respectively, individuals' state contains the identity of the individual and its two reports (I_R, A_F). The aim of each individual is to maximise its I_R concentration. The length of the Identity depends to the level of the individual, which distinguishes its individual identity. In organ individual, the identity is represented by Organ ID= {Org_Id}, coded as an integer between 1 and P, for tissue individual is, Tissue ID= {Org_Id, T_Id}, 'T_Id' that is coded as integer between 1 and N, for the cell individual is, Cell ID= {Org_Id, Id_T, Id_C}, Id_C represents the cell number in the system coded as integer between 1 and k, Figure 5.

Figure 5 Different identities of individuals (see online version for colours)



This identity can distinguish also the function should accomplish by the individual. In cell individual, it consists of organ and tissue identifier that the cell works for. Example, the identifier of the $cell_x$ ID = {1, 3, 15}; the first number (1) represents the organ identity, the second (3) represents tissue identity, and the third (15) represents the cell. Therefore, this cell has to create tissue 3 of the organ 1. So, in table of interest of this cell will be activated in the region of the organ 1, and exactly in the tissue number 3 of this organ.

6 Cyclic network of creation (the execution of MLAS)

Multi-level autopoietic system (MLAS), is a dynamic cyclic network of creation, represented the autopoietic machine with its two sides, the nodes in this network represent the components, and the arcs between them represent the components interactions and transformations in three different levels. Components in the different levels (except cell components 'actions'), are others autopoietic machine, this makes the MLAS as a global cyclic network of creation of the global individual autopoietic machine (individual of the higher level), inside this global cyclic network, we find different sub cyclic networks of creation in different levels. That's mean cyclic network inside cyclic network of production Figure 2. In each cycle of these networks, new changes are produced, as the creation of a new node, arcs…

Initially, MLAS begins with a single node state 'Organ state' in the higher level, and one inactive stem cell 'one autopoietic machine' in the cell level. The aim of this cyclic network of creation (MLAS) is to create and regulate each autopoietic machine in the system to reach a degree of required construction for each individual. This is achieved by reaching a required level of construction for each individual node state (Organ state, Tissue state, and Cell state). This required level of construction is expressed in table of thresholds by a threshold of construction for each individual.

The organ is the first individual that begins to create itself by MLAS, the first node in this network of creation is 'Organ state', and the value of I_R_{org} and A_F_{org} in this node control the appearance of new nodes in the network, in each calculation of A_F_{org}, if the

value is superior to the threshold organ in table of thresholds, new node 'tissue state' is generated in the network (Figure 6).

$$A\_F_{org} > \text{Threshold organ} \rightarrow \text{New node of Tissue state} \quad (1)$$

This node 'Tissue state' creates the beginning of a new autopoietic machine in the sub level (tissue autopoietic machine). The network of creation of tissue begins by the 'Tissue state' node, in which its structure is different from 'Organ state' only in the state identifier. The 'Tissue state' has the identifier of the 'Organ state' and the identifier of tissue 'T_Id' that is coded as integer between 1 and N. The initialisation of the concentration of the two reports (I_R_{tissue}, A_F_{tissue}) in 'Tissue state' is similar to 'Organ state' ($I\_R_{tissue} = 0$ and $A\_F_{tissue} = 1$).

If A_Ftissue in 'tissue state' node is superior to the threshold tissue in table of thresholds, it will be received by inactive stem cell (cell which has no active region in its table of interest), and are responsible for the activation of a specific part in table of interest of the stem cell according to the identity of 'Tissue state'. When a specific part in this table of interest is active, the cell knows its global interest that it will work for in all its lifetime, as long as this part of table of interest is active (Figure 6(a)).

Also, A_Ftissue could be received by another tissue in the environment if there is no inactive stem cell (Figure 7). In this case, the tissue that receives it is random, then this tissue chooses from its components (cells) a random cell and signals it (UpS see section Boolean Artificial GRN).

Figure 6 The execution of the first semi-circle of MLAS, (a) a part of the table of interest is active 'coloured with different colour' (see online version for colours)

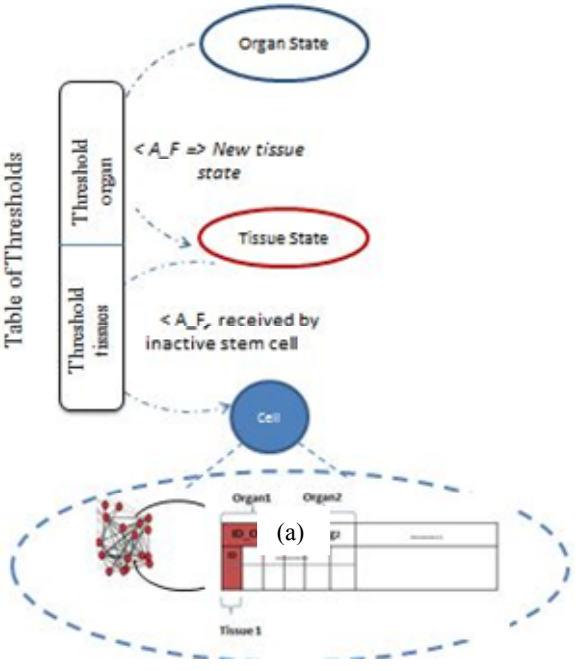
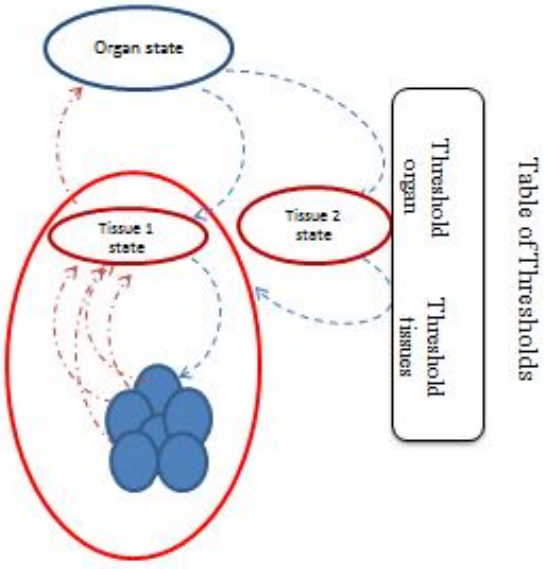


Figure 7 The second cycle of the production network of organ autopoietic system (see online version for colours)



When a specific part is active in table of interest of the cell, the third level of individual autopoietic machine will begin (cell autopoietic machine), the Boolean artificial GRN inside the cell interacts and chooses actions (is the final level of MLAS in the system, see Boolean Artificial GRN section). These actions create the pathway of the cell (suite of actions in time and space to reach the global interest of the cell), which regulates the Boolean artificial GRN. In each action chosen by the Boolean artificial GRN, the cell evaluates the action; this evaluation changes the memory system (part in the Boolean artificial GRN). When the cell finishes executing actions, it calculates its 'Individual Report (I_Rcell)'. The value of this I_Rcell expresses how the successfulness of the cell in the accomplishment of its global interest.

The evaluation of an action: Eva (Actioni [t]) is equal to 1, if it is 'good' action (influences positively in the global interest of the cell), else it is equal to 0 (see Boolean Artificial GRN exactly in TLOR section). The sum of Eva (Action) will be divided by the number of the actions executed by the cell 'N_A'. This report is between [0 and 1], in which the optimal result equal to one, when the individual executes only the 'good' actions. If 'N_A' is equal to 0, the I_Rcell will equal to one. This I_Rcell concentration was calculated by the equation (2):

$$\begin{cases} If\ N\_A > 0, \quad I\_R_{cell} = \sum_{i=1}^{N\_A} Eva(Action_i[t]) / N\_A\ , \\ If\ N\_A = 0, \quad I\_R_{cell} = 1 \end{cases} \tag{2}$$

In this time the second semi-circle will begin.

All the cells diffuse their I_Rcell. This I_Rcell is the input of the tissue state node, of the tissue the cell works for; when tissue state receives all the I_Rcell from its components (cells), it calculates its individual report by equation (3). I_Rn of the tissue

state is the total of all their components individual reports I_Ri (components here are cells), divided by the number of their component individuals 'Nind', if they are more than the minimal number. Else by the minimal number of individual 'Nb_min'.

$$I\_R_n = \sum_{i=1}^{N_{ind}} I\_R_i / ((N_{ind} + Nb\_\min) + || (N_{ind} - Nb\_\min) ||) / 2 \quad (3)$$

When all the cells diffused their I_Rcell to the tissue state node, we move from the cell individual to the tissue individual, this means, the group of cells that construct the same tissue will be one individual, that can interact with its neighbour and its higher level, this tissue has tissue state node and a group of similar cells Figure 7.

When tissue calculates its I_ Rtissue, it sends it to the organ level, in this step the tissue is considered as a component of the organ autopoietic machine. When the organ state receives the tissue report 'I_Rtissue', the first circle will finish in the system. Within this circle, the network created new nodes, arcs, and even changes the concentration in node state of individuals.

The organ state receives I_R from its components (tissues) and recalculates its I_R by (equation (3)). While it's A_F (which is the second report between the higher level and the sub-level) for all the different individuals (organ, tissue, cell) is calculated by the difference between the optimal value and its individual report (equation (4)):

$$A\_Fn = 1 - I\_Rn. \quad (4)$$

If the value of A_F is inferior to the threshold organ in table of thresholds, the individual has reached the required level of construction. Else, the second circle will begin by regenerating another node of tissue state. The same circle is repeated until the energy ends or the system reaches the required level of construction. In the case when the energy finished, the first stem cell in the environment takes all the experience of other cells and passes to the next generation (see Boolean Artificial GRN section).

7 Boolean artificial GRN with epigenetic part (MLAS in the cell level)

Most models of development are closely related to cell-based models of biological morphogenesis, starting from one single cell to a set of repeated functions (proliferation, differentiation, and apoptosis). Gene Regulatory Network (GRN) is the most important mechanism underlying this development, and many models are inspired by the GRN to simulate the growth of artificial embryogenesis.

During development, cells fate creates the growth of the multicellular organism. In which PcG proteins are the essential regulators of embryonic development and cell fate, by controlling their target gene, and they are considered as a part of an epigenetic blueprint for development and as a preprogrammed memory in the cell (Aloia et al., 2013; Bracken et al., 2006). The expression of the gene in cells depends on both, the morphogen and signals surrounding the cell and its created history during evolution (preprogrammed memory). Moreover, this cellular memory can be modified later in development (Maurange and Paro, 2002). The PcG proteins appear to form the molecular basis of cellular memory (Ringrose and Paro, 2004). They are also central players in various epigenetic phenomena (Bantignies and Cavalli, 2006), and later they are

considered as epigenetic gatekeepers of cellular memory processes (Schuettengruber and Giacomo, 2009).

Traditionally, Epigenetic have been studied in the domain of development. However, they can also play significant roles in evolution, when epigenetic changes are heritable (Mendizabal et al., 2014; Moore, 2015). Epigenetic inheritance adds another dimension to the modern picture of evolution. In Darwin's evolutionary theory the genome changes slowly through the process of random mutation and natural selection. In contrast, epigenetic change can happen in many individuals at once and pass this change to future generations (Youngson and Whitelaw, 2008). A key question is how this epigenetic change can be transmitted between generations? Some studies report the transgenerational epigenetic. That is the direct inheritance of epigenetic modification themselves transmitted from one generation to the other (Mendizabal et al., 2014; Youngson and Whitelaw, 2008; Daxinger and Whitelaw, 2012).

Inspired from the cell memory system, the role of PcG protein is controlling development, and they are a part of epigenetic blueprint in development, and the capacity of cells to make a change in their memory system during development. We propose a new kind of Boolean Artificial GRN with epigenetic part represented by cell memory system and Policy controller, which is the responsible for choosing cell actions since cells can add change in their memory system during development and make epigenetic change. To transmit this change between generations we relied on research that reports the direct inheritance of epigenetic that change themselves to the next generation 'transgenerational epigenetic'.

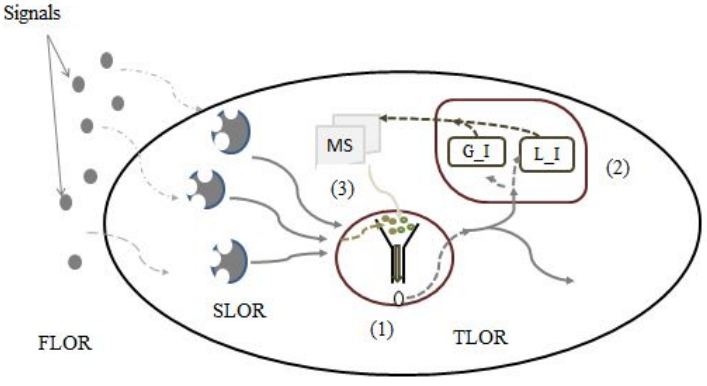
The use of this epigenetic part in our Boolean Artificial GRN should present some abilities. For example, even if we have the same genotype, we can get numerous phenotypes; in (Vogt et al., 2008) the results indicate that individual genotypes in biology can map different phenotype, despite being raised in the same environment. In our case, this is due cells could create different memory systems to solve the same problem, and its selection of actions which depends on the external signals and the internal history (memory system) of the cell.

To achieve an embryogenesis process, cells must know what they should execute as an action during the developmental processes. In our model, inside each cell, there is a Boolean Artificial GRN with epigenetic part. The main aim of this artificial GRN is to choose what the cell must execute in each step during the development process and to create its pathway of actions and history.

First Layer of Regulation (FLOR)

The first layer of regulation is outside the cell and represented by a group of different signals Figure 8 (FLOR). This last one has important roles in embryogenesis, but the development is more complex than guiding the process by the outside of the cell. Because of that, our developmental model uses the signals from the outside of the cell only as the first layer of regulation, where the change in the external of the cell could make a change in other layers of regulation inside the cell but not necessarily in cell fate (the cell's exterior only has partial influence on its fate).

Figure 8 The Boolean artificial GRN controlled cells, with its different layers of regulation; FLOR represented by a group of exterior signals, gives the cell information about its environment. SLOR is the second layer of regulation; contain a set of genes represents all the possible cell actions. TLOR represented by (1) (2) and (3), is the mechanism of choosing the action and evaluate it (see online version for colours)



Signals values in FLOR are Boolean. They give cell information about its neighbour, higher level, and its surrounded environment. Hence, they can be considered as the precondition of cell actions. Table 1 shows the different signals and their description and value.

Table 1 Different signals in FLOR and their value

	Signals of FLOR	
	Description	*Concentration*
S	Cell specialisation	=1, If cell not yet specialised (stem), =0, If cell are specialised.
N_T	The difference between cell and their neighbours in type	=1, if cell and its neighbour have the same type, =0, If not.
N_S	Signal diffused by neighbours 'one cell can receive more than one signal'	=1, if exist in the environment, =0, if not.
Up_S	Signal from the higher level (from tissue level)	=1, if exist in the environment, =0, if not.
N_F,	Neighbour position state	=1, if Neighbour position free, =0, if not.
E	Energy	=1, if Energy > 0, =0, if not.

These signals can activate more than one action at the same time in the second layer.

7.1 Second layer of regulation (SLOR)

The previous signals (First layer of regulation) regulate the second layer of regulation, inside the cell, where a set of genes represents all the possible actions (division, differentiation, dedifferentiation, apoptosis, and attack). It is the link between the external and the epigenetic part of the cell Figure 8 (SLOR). Its objective is to ensure that all external signals for each action are present in the environment during each step.

To activate one or more of these genes we need different types of proteins. 'Complex Protein' is composed of several signals from the outside. For that, each gene needs a fixed number of signals from the first layer that we denoted Nb. Table 2 shows the different gene actions and their needed signals. In Apoptosis, cell needs Ns signals from its four neighbours. To calculate the status (active or inactive) for each gene in this layer we use the following equation:

$$Gene[t]_{actioni} = \sum_{j=1}^{Nb} FLOR[t]_{ij} \,/\, Nb \tag{5}$$

If all the necessary signals for the Genei (FLOR proteins) are present, the gene is active.

The output of the Second layer is an activation or inhabitation protein, and these outputs will be used as inputs of the 'Policy controller'.

7.2 Third layer of regulation (TLOR)

This layer has as an input all the active actions from the SLOR. TLOR contains the epigenetic blueprint for the development process which is represented by a programmed memory in the cell Figure 8 (TLOR). This was created and programmed during evolution, and the cells (cells with the same type) evolved their memory system to reach together their global interest (active part in table of interest of the cell). Cells use this layer as an attempt to choose the appropriate action between all the active actions during each step of development. It executes a loop of three principal parts (Evaluation module, Memory System and Policy protein).

Table 2 Different actions of the cell and their needed signals

	FLOR						
Gene actions	*S*	*NT*	*Ns*	*Ups*	*Nf*	*E*	*Nb*
Differentiation	×					×	2
Division					×	×	2
Apoptosis			×			×	5
Dedifferentiation				×		×	2
Attack		×				×	2

Evaluation module: Figure 8 (SLOR (2)) with two evaluation functions:

Local interest: is integrated into individual behaviour, since its appearance in the environment, it never changes in all its lifetime. It is considered as the survival and reproduction instinct for each cell as follows:

Stay alive: Individual Cells, their first local interest is to stay alive as much as they can.

Divide: The second local interest for the individual cells is to reproduce a copy of itself.

Apoptosis is the action that does not support the local interest of the cell, by contrast, the rest of actions (except division) have a neutral influence.

Global interest when a specific parts of the table of interest of the cell are active, the global interest is specified for the cell. It represents a specific tissue, and the cell will work during its lifetime to participate in the construction of this tissue.

The global interest will stay the same for the cell during all its lifetime as long as the cell ID does not change. Actions that support global interest can differ from a cell to another even if they have the same global interest, either the action adds to the construction of the right tissues or not. The division will support the global interest only if the daughter cell is within the specific tissue boundary. By contrast, apoptosis beyond the specific tissue boundaries supports the global interest of the cell even if it does not support the local interest, the same thing if the cell changes its type (differentiation or dedifferentiation actions), If the cell type is the same as the tissue, this will support the global interest, otherwise, it will not, and signalisation action will be represented as neutral.

Choosing the action by Policy controller (The third part of this layer) was evaluated by these two functions, and a note was given. Neutral actions were noted by '0' in the two interest functions (global and local). By contrast, actions that support 'local interest' are noted by '+1', else '–1', and in 'global interest' actions evaluation should be more influenced in the system. Actions that support this interest are noted by '+2', else '–2'. The final report is the sum of the previous two reports. If its value is more than or equal to zero, then it will be considered as a good action. If not it is a bad action.

This can be summarised in "I, individual, work for my personal benefit, local interest, as long as it does not adversely affect the global interest". The final report of evaluation (action with its note) is stocked in the second part of the layer 'memory system'.

The memory system: (Figure 8 (SLOR (3), Figure 9)

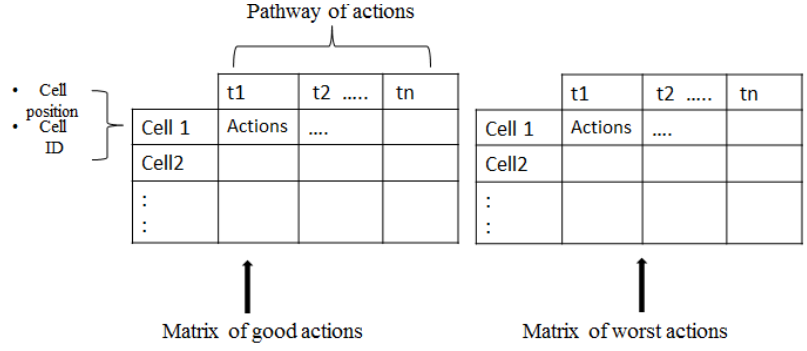
Memory system 'MS' in cells is represented by two matrices. The first is 'good actions' and the second is 'bad actions'. MS contains cells and their pathway of actions (pathway of good in the first matrix and bad in the second), in which cells are represented by their position and ID of the cell. The pathway is a suite of actions in each step of the cell's life. For each step in this pathway; we could find more than one action. These two matrices are considered as the memory system in cells. When cell appear in the system, it chooses the closest 'cell's pathway' to it in the memory system (same position and same global interest) if it exists.

Cells used memory system in two ways. The first way, Policy controller uses it to choose between actions. Likewise, Policy controller uses the experiences of the cell from previous generations that exist in the memory system. In the other way, cells update these memory systems by adding their own experiment at the end of the process, knowing that in the first generation the memory system is empty. From one generation to another, the evaluation module created cell history 'memory system'. Ultimately, one cell passes to the next generation after taking a direct inheritance of all the change that happened to the memory system through cell's 'transgenerational epigenetic'.

Policy controller: Figure 8 (SLOR (1))

Policy controller is the mediator between the epigenetic and the genetic parts in the cell. In the first hand, it is the gatekeeper of cell memory, by taking into consideration the history of the cell when choosing the action. On the second hand, it receives all the active genes of actions (from SLOR) which can be implemented by the cell, actions have all the necessary signals from the outside, Policy controller combining between the history of the cell (MS) and the signals that exist in the environment, which expressed by the SLOR layer. To select the right action in each step of development, Policy protein uses a strategy to choose between the possible actions from (SLOR).

Figure 9 The memory system inside the cell



In the first time policy controller looks to the memory system. If it was empty (no history for the cell), policy controller chooses between actions from SLOR randomly. If not, it uses a filter step, computes the intersection between possible actions from SLOR and the actions in the best action matrix, if there are actions from the result of this intersection, Policy controller chooses between the actions of the intersection depending on its note (the preferred choice is the action that has the higher note), if there is more than one action that has the same note, Policy controller chooses between them randomly. Furthermore, If there are no actions after this intersection, Policy controller uses another filter but with the matrix of worst action. Here it can choose randomly between actions that do not belong to the intersection.

The action that Policy controller chooses will enter in the Evaluation Module.

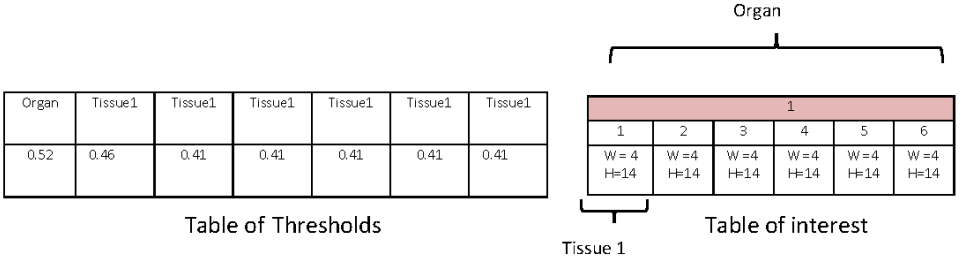
8 Results

Different shapes of organs have been developed using the MLAS in different environment condition. Our MLAS has successfully created different individuals as an autopoietic machine, and proves the capacity of these machines in self-regulation, self-creating, and self-organisation. Each individual creates and regulates its components through its network of components of production as a closed organisation.

In all the different experiments, we begin the simulation with the same stem cell in the environment. This stem cell has an empty memory system, irregular Boolean artificial GRN, and the same parameters in table of interest. Figure 10(b) presents the number of

tissues and the predetermined size of each one, while energy in all the next experiments equal to 500.

Figure 10 In the left side: (a) the initialisation of thresholds for each tissue and organ. In the right side and (b) the initialisation of the table of interest inside the cell, 'W' represents the width and 'H' represents the height for each tissue (see online version for colours)



8.1 Self-regulation, self-creating and self-organisation

In addition to the first stem cell, we have a table of thresholds defines the required level of construction (Figure 10(a)). The first stem cell evolves and regulates itself with other cells that appear in the system, to reach the required level of construction. We run the system 60 times with the same initial parameters (table of interest and table of thresholds). In each run, the system creates and regulates itself in different ways to reach the required level of construction. Figure 11 shows one of the created morphologies by the system to reach its table of thresholds. The left side shows the final morphology that is developed by the system in the different generations of the evolution. The development of these morphologies begins with one cell. On the right side, the diagram presents the execution of actions in the Boolean Artificial GRN level. In each time step of the development process, the number of cells that execute actions in a random way (cells do not know what they should execute as actions to develop the required tissue) is represented by 'tissue random', and the number of cells that know what they should execute depending on their memory system (cell history) is represented by 'tissue regulated'. In the first generation, all cells in the system randomly chosen actions, and there are no regulated actions; this goes back to the empty memory system inside cells. Actions that choose randomly were not necessarily bad actions. They could be either bad or good actions, this will be decided in the evaluation module of the Boolean Artificial GRN. On the other hand, the system develops just one tissue, this due to the unlimited division. In which cells in this stage do not know when they should stop division. Generation after generation cells acquire experience and create its history (memory system), which this helps the Boolean Artificial GRN to choose the right actions in the right time and space. This means creating the components (actions) of the autopoietic machine (cells). This self-regulation of the Boolean Artificial GRN inside each cell leads the cells to develop and create the required level of construction of the specific tissue (the tissue they work for construct it). In other words, cells (components of tissue autopoietic machine) lead the tissues to create themselves as we can see in the different generations, the global autopoietic machine (organ autopoietic machine) creates news components (tissues) during evolution, and this last one (tissues autopoietic machine) regulates and creates its components (cells autopoietic machine), the organ autopoietic machine

finishes its self-creating when it reaches the required level of construction that is defined in table of thresholds.

The developed morphologies of each tissue are not the same; even we have the same specific size inside the table of interest of the cell, the required level of construction (table of thresholds) play the essential role with the table of interest of the cell to create the final morphology.

As generations go by, the cell actions grow more and more organised (Figure 11); they create their pathway of actions (memory system). In the last generation, we have four tissues all of them are regulated their cell actions to create the tissue with its required level of construction, tissue5 is not regulated yet in generation 37, but the evolution is stopped, because the organ autopoietic machine reaches its required level. Thus this autopoietic machine (organ), with its current tissues developed, creates the required organ (It does not have to regulate or add other tissues).

Figure 11 The right side, shows diffrent generations of the development of the organ to reach the table of thresholds. In left side, presents the diagram of cell actions that are executed in the boolean artificial GRN level in each time step of the development process (the attached file 'PPT.Video' show the development in each generation) (see online version for colours)

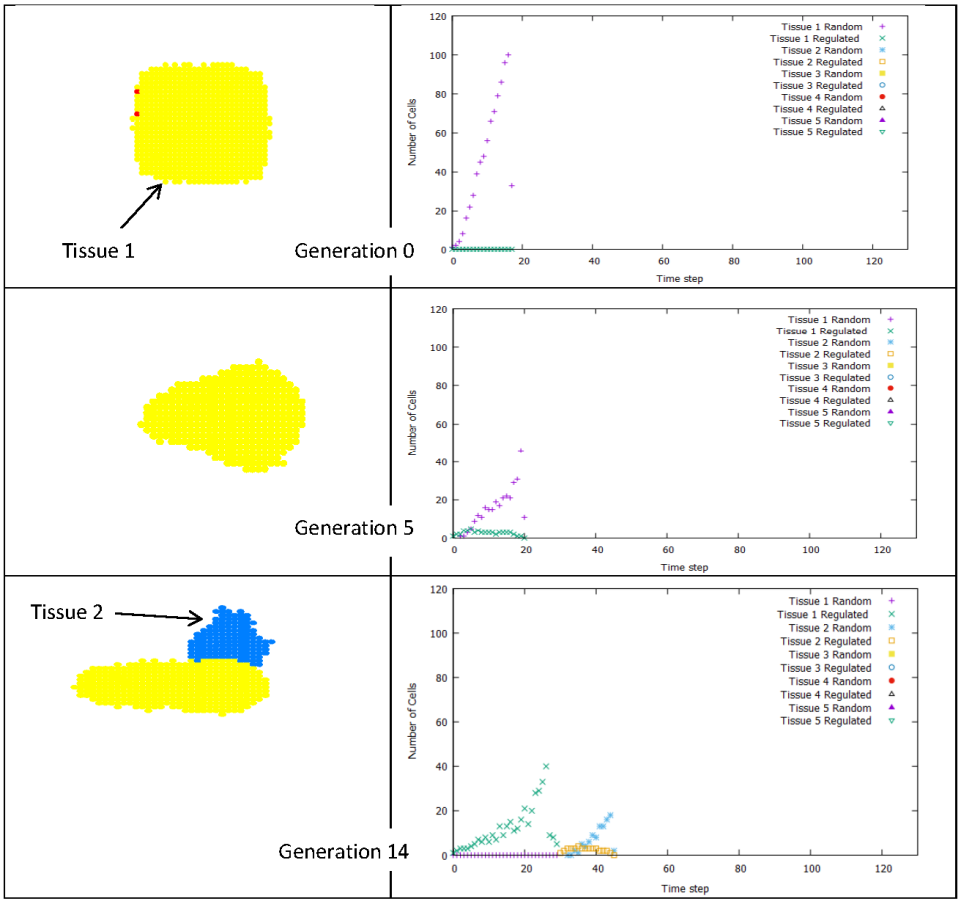
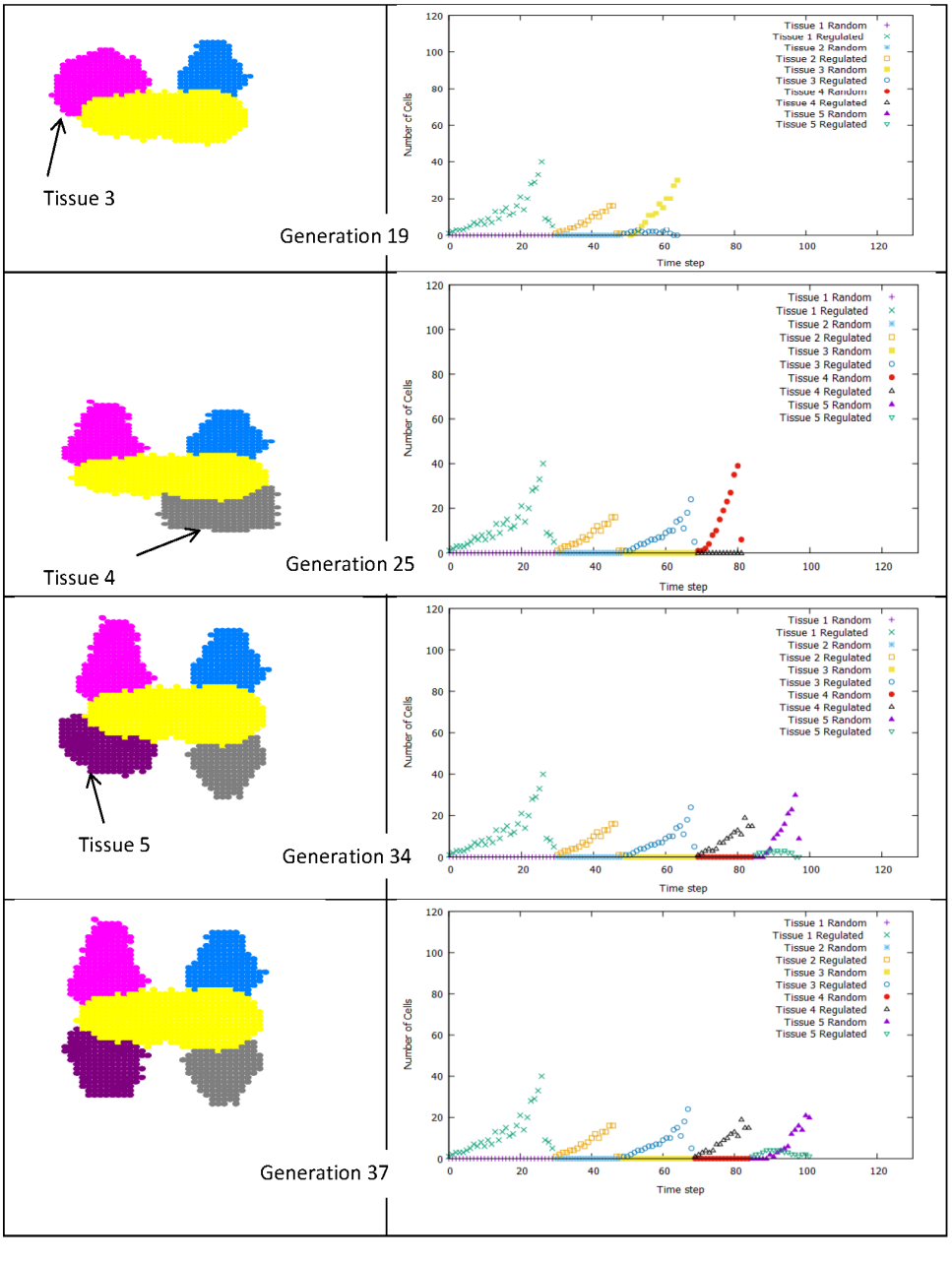


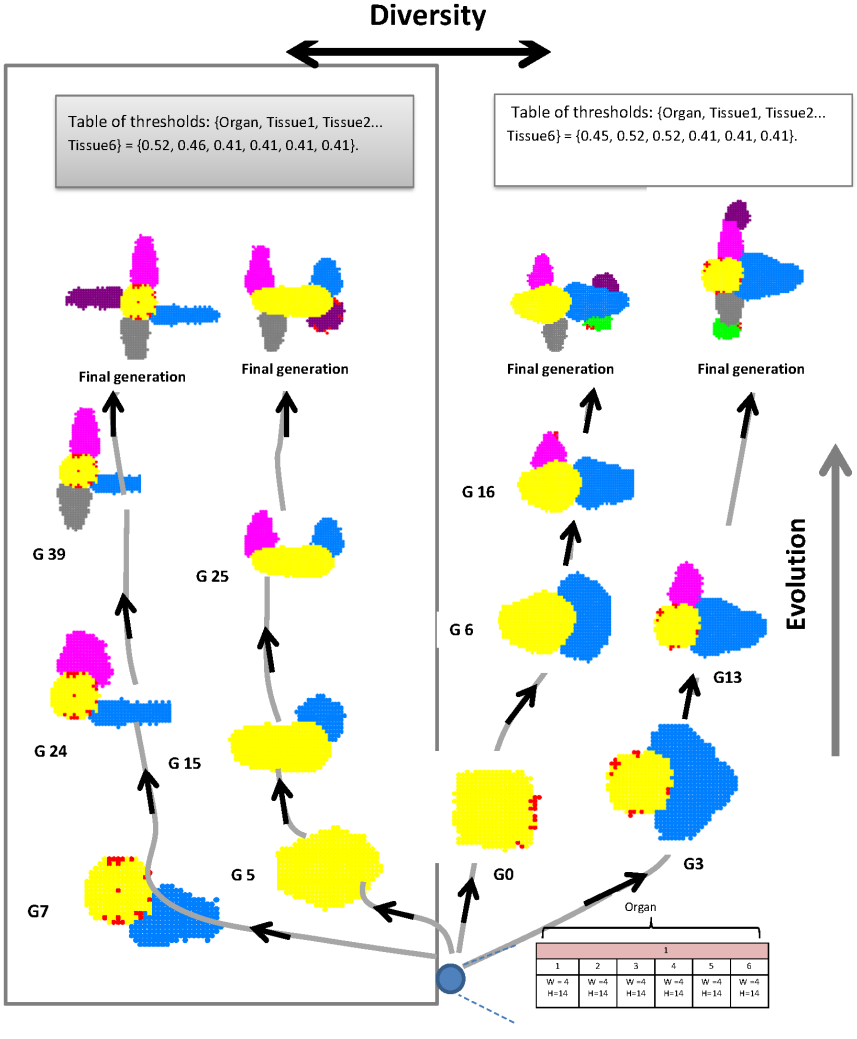
Figure 11 The right side, shows diffrent generations of the development of the organ to reach the table of thresholds. In left side, presents the diagram of cell actions that are executed in the boolean artificial GRN level in each time step of the development process (the attached file 'PPT.Video' show the development in each generation) (see online version for colours) (continued)



8.2 Evolution and diversity as a second process of the autopoietic machine

After we saw how our MLAS could create and regulate itself as a closed organisation in the precedent section. We present here different experiments with different table of thresholds, but with the same stem cell (same number and size of tissues) Figure 12. For the same experiment we lance the system 60 times, we present two experiments each one with different table of thresholds with different required level of construction of individuals (organ and its tissues). In each experiment, we choose some of the organs that are evolved and developed by our MLAS to reach the required level of construction. We notice here that the system in all the 60 runs reaches the objective, with organs converged and diverged in shapes and some of them show symmetric.

Figure 12 Differents evo-devo creatures in different environment conditions, begin with the same cell. Each generation (G = generation) represent the development of the multicellular organ that begin with one single cell. From a generation to another we have an evolution in the morphology of the multicelluar organ (see online version for colours)



The evolution in organ shape is the result of the experience gained by cells from one generation to another. In the early stages of evolution, the system develops less number of tissues for each organ with different shapes and size, but in the advanced stages of evolution, some tissues minimise their size, and other new tissues appear (new changes in the components of organ autopoietic machine) to reach the organisation of the system. The evolution finishes when the system creates and regulates all its components to reach the table of thresholds, otherwise the system passes to the next generation and makes the change in the level of its components (adds new components, changes their regulation or their size).

In the second hand, the two experiments show diversity in the solutions of the generated system (Figure 12), which is caused because the regulation of the Boolean artificial GRN inside each cell, exactly in the memory system. Each cell creates its own different pathway of actions (history of the cell) depending on the random selection of actions by the Policy controller and the evaluation module. Moreover each cell fixes its memory system when they achieve the required level of construction of its autopoietic machine (tissue), or the required level of construction of the whole system (organ). The different regulations of the memory system for each cell, which is the different regulation and creation of cell components (actions), lead to creating diversity in the morphologies of organs.

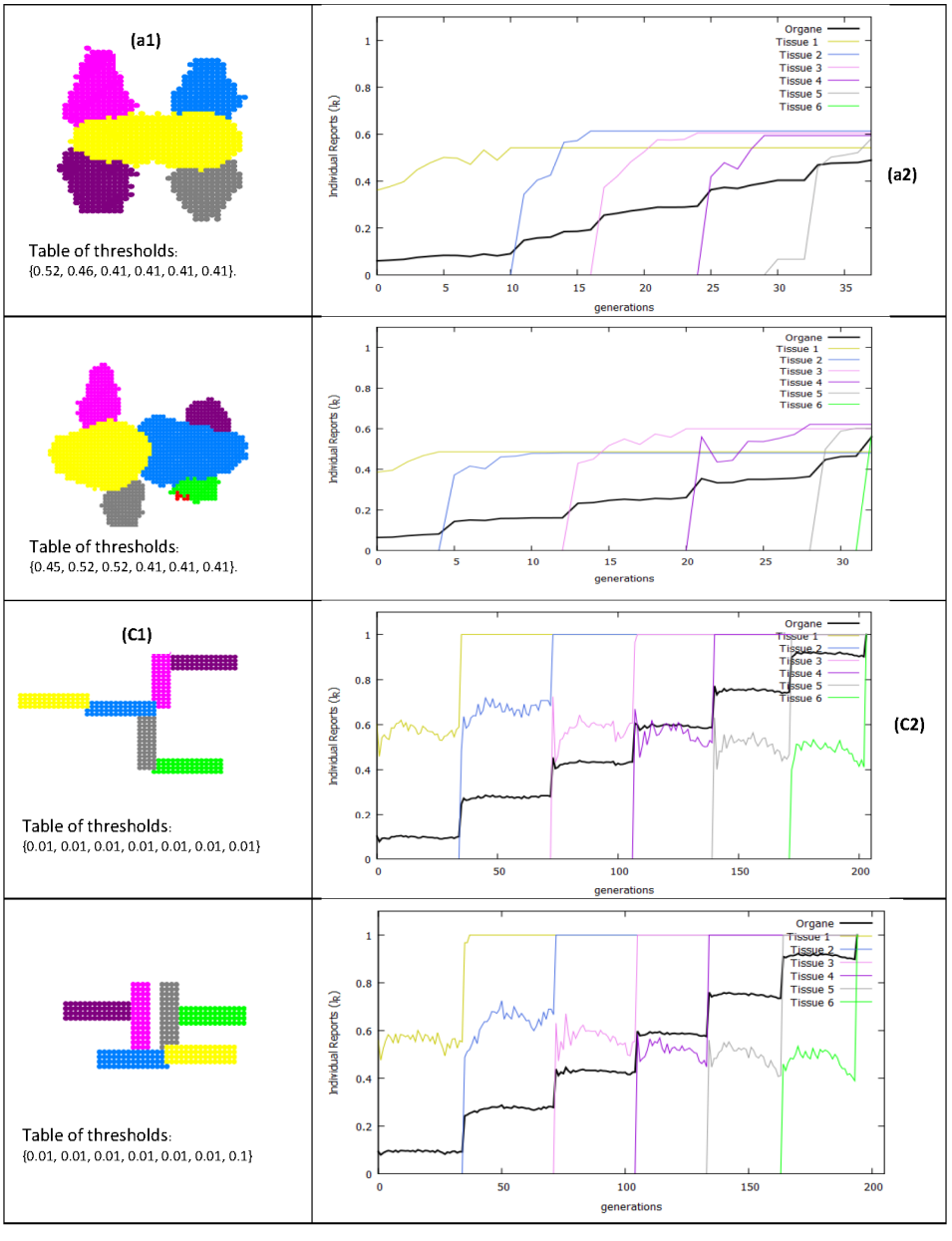
Figure 13, in the left side shows different creatures developed to reach different table of thresholds (the parameters of the first stem cell is the same in all the experiments). While in the right side the diagram shows I_R concentrations for each creature respectively. In each diagram we found the individuals reports (I_R) of the organ and their tissues, and how each individual evolves its reports to reach the required level of construction.

In each generation, individuals (cells, tissues, organs) at the end of their development process calculate and diffuse their own Individual Report (I_R) in the environment, which gives the status of success of each individual at each generation. For each individual, when the I_R reaches its required level of construction, this means the individual completes successfully its development and its process of regulation is finished.

In the next generations, the new experiences gained by cells make an evolution in the concentration of the constructed individuals (organ or tissue). I_R of tissues in some iteration appears as if it does not evolve. Figure 13(c2), in iteration between 0 and 34, the concentration of I_R protein of the first tissue is fluctuating, and the concentration does not evolve significantly. In iteration 35, the concentration is much improved, and it reached the threshold of the required level. This is due to the fact that before iteration 34 cells learned and gained experience, however, some other cells remain wrong. But we notice here, that if organ individual reaches its required level of construction, we can see some tissue does not yet reach their threshold of construction or they did not appear at all in the environment, this is due to the fact that when the autopoietic machine reaches its requested level of construction, it stops the regeneration of its network of components, which is obvious in tissue 5 (Figure 13(a2)) where the tissue does not reach its threshold of required level. Adding to that in the table of interest inside the cells, the number of tissue is 6, in Figure 13(a1), while the system develops just 5 tissues, this is enough to reach the table of thresholds. But when we minimise the threshold of the required level, the system creates more tissues (Figure 13(c1)) in this execution (Figure13(c1)) we minimise the threshold to approaching 0, all the tissues appeared and the size of each

tissue was very close to what was defined exactly in table of interest of the cell. Therefore, the final morphology of organ autopoietic machine depends on table of thresholds and table of interest of the cell where the size of tissue is defined. However the system takes more time to reach the required organ when the thresholds in table of thresholds close to 0.

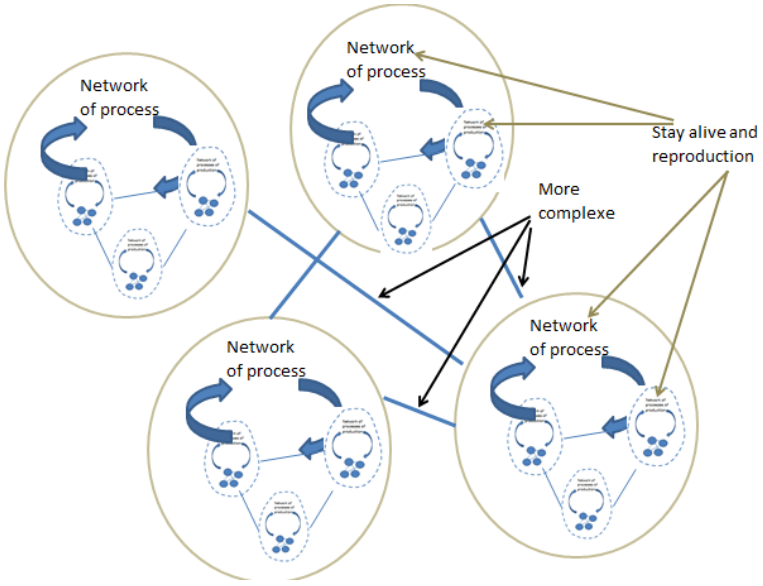
Figure 13 In the left side, different organs developed by MLAS with different table of thresholds, and in the right side, the evolution the individual reports(I_R) for each organ and tissue in the environment (see online version for colours)



9 Discussion and future work

In this work, we try to use artificial life (AL) to implement a biological theory that defines the organisation and the autonomy of living organisms, as an automatic system, maybe could it give as a better understanding of the theory of life. This field of research (self-organisation, self-creating, and autonomy) still one of the most important areas in AL, the study and the implementation of this theory in AL will develop systems has some living systems capabilities. The results generated by our MLAS show the capacity of autopoietic system in self-organisation and the self-creating of each artificial organism developed and all their components (autopoietic machine in all the different level of the system), this organisation of our artificial organisms leaves our artificial organs creating themselves by a closed organisation, which gives rise to an emerging or global coherence of the system without the need of a central controller. We notice too, that the MLAS could generate more than one solution, and this is one of the properties of living organisms, this property is the basis of diversity in life, which is an important point to understand the origin of life besides the evolution, that was appeared as a second process by MLAS, this unexpected result appeared in this kind of system based on autopoietic theory confirms the suggestion of Maturana and Varella about the appearance of all the other biological processes. This then will be a secondary result of the theory that defines the organisation of living system 'autopoietic system'.

Figure 14 Different autopoietic machines at higher levels (see online version for colours)



The results obtained by this MLAS and the different interesting capacities shown by the system as (self-creating, self-organisation, evolution and diversity), even with simple objective, in our case, to develop a required level of construction of individuals defined in table of thresholds, encourage us to think about the capacity of this systems based on this theory in more higher levels with complex objectives, Figure 14 presents different autopoietic systems in higher levels (eco-system or organisms) that contain components.

These components also are other autopoietic systems and so on... Thus, the objective we propose in the future is to 'stay alive'. Because all-natural systems create and organise themselves and find strategies (work together or against themselves) to stay alive, they share the same principal objective in their lives.

If the system organises itself to reach this objective 'stay alive', with higher levels, the components of this autopoietic machine will create new relations and transformations between them to lead this autopoietic machine to stay alive. Thence we wonder if we could see reproduction as a second process of this machine as Maturana suggest, and if the Darwin evolution theory will be a result of this machine that is created just by the interactions and transformations between individuals (components). Do we live inside an autopoietic system, and are we an autopoietic system from some level. And moreover, does the origin of life begin with these machines (chemistry level)! Obviously, it is not an easy task to answer these questions. But if we study this kind of systems in AL deeply and provide results that support what we have in the biological level, this can bring us closer to answer some of these hard questions.

References

Agmon, E., Gates, A.J., Churavy, V. and Beer, R.D. (2016) 'Exploring the space of viable configurations in a model of metabolism–boundary co-construction', *Artificial Life*, Vol. 22, No. 2, pp.153–171.

Aloia, L., Di Stefano, B. and Di Croce, L. (2013) 'Polycomb complexes in stem cells and embryonic development', *Development*, Vol. 140, No. 12, pp.2525–2534.

Bantignies, F. and Cavalli, G. (2006) 'Cellular memory and dynamic regulation of polycomb group proteins', *Current Opinion in Cell Biology*, Vol. 18, No. 3, pp.275–283.

Baraldi, C. and Corsi, G. (2016) *Niklas Luhmann: Education as a Social System*, Springer, Cham.

Beer, R.D. (2015) 'Characterizing autopoiesis in the game of life', *Artificial Life*, Vol. 21, No. 1, pp.1–19.

Bishop, J.M. and Al-Rifaie, M.M. (2017) 'Autopoiesis creativity and dance', *Connection Science*, Vol. 29, No. 1, pp.21–35.

Bracken, A.P., Dietrich, N., Pasini, D., Hansen, K.H. and Helin, K. (2006) 'Genome-wide mapping of polycomb target genes unravels their roles in cell fate transitions', *Genes and Development*, Vol. 20, No. 9, pp.1123–1136.

Braga, A.L., Goldschmidt, R.R. and Rosa, P.F.F. (2018) 'Morphogenesis-based multidimensional shape formation of swarms', *2018 IEEE Congress on Evolutionary Computation* (*CEC*), IEEE, July, Rio de Janeiro, pp.1–8.

Chavoya, A. and Duthen, Y. (2008) 'A cell pattern iteration model based on an extended artificial regulatory network', *Biosystems*, Vol. 94, Nos. 1–2, pp.95–101.

Chettiparamb, A. (2020) 'Autopoietic interaction systems: micro-dynamics of participation and its limits', *International Planning Studies*, Vol. 25, No. 4, pp.427–440.

Conlon, I. and Raff, M. (1999) *Size Control in Animals Cell*, Vol. 96, pp.235–244.

Cussat-Blanc, S. and Pollack, J. (2014) 'Cracking the egg: virtual embryogenesis of real robots', *Artificial Life*, Vol. 20, No. 3, pp.361–383.

Cussat-Blanc, S., Bredeche, N., Luga, H., Duthen, Y. and Schoenauer, M. (2011) 'Artificial gene regulatory networks and spatial computation: a case study', *Proceedings of the European Conference on Artificial Life (ECAL□11)*, MIT Press, Cambridge, MA.

Daxinger, L. and Whitelaw, E. (2012) 'Understanding transgenerational epigenetic inheritance via the gametes in mammals', *Nat. Rev. Genet.*, Vol. 13, pp.153–162.

Day, S.J.L. and P.A. (2000) 'Measuring dimensions: the regulation of size and shape', *Development*, Vol. 127, pp.2977–2987.

Dekkers, R. (2017) 'Autopoietic systems', *Applied Systems Theory*, Springer, Cham, pp.193–210.

Disset, J., Cussat-Blanc, S. and Duthen, Y. (2014) 'Self-organization of symbiotic multicellular structures', *Fourteenth International Conference on the Synthesis and Simulation of Living Systems-ALIFE. 2014*, New York, p.541.

Doursat, R., Sayama, H. and Michel, O (Eds.) (2012) *Morphogenetic Engineering: Toward Programmable Complex Systems*, Springer, New York.

Egbert, M.D. and Di Paolo, E. (2009) 'Integrating autopoiesis and behavior: an exploration in computational chemo-ethology', *Adaptive Behavior*, Vol. 17, No. 5, pp.387–401.

Fontana, A. (2010) 'Devo co-evolution of shape and metabolism for an artificial organ', *The Conference Artificial Life XII*, MIT Press, Boston, pp.16–23.

Fuchs, C. and Hofkirchner, W. (2009) 'Autopoiesis and critical social systems theory', Bingley, U.K Emerald Bovenkant formulier, pp.111–129.

Hiouani, R., Cussat-Blanc, S., Djedi, N. and Duthen, Y. (2017) 'An autopoietic machine to achieve pure self-organization', *Morphogenetic Engineering Workshop', at the European Conference on Artificial Life* (*ECAL*), September, pp.14–15.

Hiouani, R., Ouannes, N., Djedi, N., Duthen, Y. and Cussat-Blanc, S. (2016) 'Intelligent cell using on-line GRN policy enzyme', *Morphogenetic Engineering Workshop' (MEW 2016), at 15th International Conference on the Synthesis and Simulation of Living Systems-ALIFE*, July, Cancun, pp.12–13.

Hockings, N. and Howard, D. (2020) 'New biological morphogenetic methods for evolutionary design of robot bodies', *Frontiers in Bioengineering and Biotechnology*, Vol. 8, p.621.

Iba, T. (2010) 'An autopoietic systems theory for creativity', *Procedia-Social and Behavioral Sciences*, Vol. 2, No. 4, pp.6610–6625.

Joachimczak, M. and Wróbel, B. (2009) 'Evolution of the morphology and patterning of artificial embryos: scaling the tricolour problem to the third dimension', *10th European Conference on Artificial Life*, Springer Verlag.

Klingenberg, C.P. (2002) 'Morphometrics and the role of the phenotype in studies of the evolution of developmental mechanisms', *Gene*, Vol. 287, No. 1, pp.3–10.

Knabe, J., Schilstra, M. and Nehaniv, C. (2008) 'Evolution and morphogenesis of differentiated multicellular organisms: autonomously generated diffusion gradients for positional information', *Artificial Life, XI*, pp.321–328.

Li, Y., *et al.* (2008) 'Control of final seed and organ size by the DA1 gene family in arabidopsis thaliana', *Genes and Development*, Vol. 22, No. 10, pp.1331–1336.

Maturana, H.R. and Varela, F.J. (1991) *Autopoiesis and Cognition: The Realization of the Living* (*Vol. 42*), Springer Science and Business Media.

Maturana, H.R., Varela, F.J. and Uribe, R. (1974) 'Autopoiesis: The organization of living systems, its characterization and a model', *BioSystems*, Vol. 5, pp.187–196.

Maturana-Romesín, H. and Mpodozis, J. (2000) 'The origin of species by means of natural drift', *Revista Chilena De Historia Natural*, Vol. 73, No. 2, pp.261–310.

Maurange, C. and Paro, R. (2002) 'A cellular memory module conveys epigenetic inheritance of hedgehog expression during drosophila wing imaginal disc development', *Genes and Development*, Vol. 16, No. 20, pp.2672–2683.

McMullin, B. and Varela, F.R. (1997) 'Rediscovering computational autopoieses', in Husband, P. and Harvey, I. (Eds.): *Proceedings of the 4th European Conference on Artificial Life*, MIT Press, Cambridge, MA, pp.38–47.

Meincke, A.S. (2019) 'Autopoiesis, biological autonomy and the process view of life', *European Journal for Philosophy of Science*, Vol. 9, No. 1, pp.1–16.

Mendizabal, I., Keller, T.E., Zeng, J. and Yi, S.V. (2014) 'Epigenetics and evolution', *Integrative and Comparative Biology*, Vol. 54, No. 1, pp.31–42.

Moore, D.S. (2015) *The Developing Genome: An Introduction to Behavioral Epigenetics*, 1st ed., Oxford University Press, ISBN 978-0199922345.

Pascalie, J., Doursat, R., Potier, M., Spicher, A., Kowaliw, T., Giavitto, J.L. and Michel, O. (2014) 'Soft to wet: morphogenetic engineering in synthetic biology', *Workshop', Exploiting Synergies Between Biology and Artificial Life Technologies*' (*EVOBLISS 2014*), *at 14th International Conference on the Simulation and Synthesis of Living Systems* (*Alife 14*), July.

Ringrose, L. and Paro, R. (2004) 'Epigenetic regulation of cellular memory by the polycomb and trithorax group proteins', *Annu. Rev. Genet.*, Vol. 38, pp.413–443.

Schuettengruber, B. and Giacomo, C. (2009) 'Recruitment of polycomb group complexes and their role in the dynamic regulation of cell fate choice', *Development*, Vol. 136, No. 21, pp.3531–3542.

Suzuki, K. and Ikegami, T. (2009) 'Shapes and self-movement in protocell systems', *Artificial Life*, Vol. 15, No. 1, pp.59–70.

Turney, P.D. (2021) 'Evolution of autopoiesis and multicellularity in the game of life', *Artificial Life*, pp.1–18.

Vogt, G., Martin, H., Markus, T., Gerald, V.B., Oliver, J. and Schmitz, C.S. (2008) 'Production of different phenotypes from the same genotype in the same environment by developmental variation', *Journal of Experimental Biology*, Vol. 211, No. 4, pp.510–523.

Yang, Y., Liu, X., Deng, R.H. and Yingjiu, L. (2020) 'Lightweight sharable and traceable secure mobile health system', *IEEE Transactions on Dependable and Secure Computing*, Vol. 17, No. 1, pp.78–91.

Yang, Y., Zheng, X., Liu, X., Shangping, Z. and Chang, V. (2017) 'Cross-domain dynamic anonymous authenticated group key management with symptom-matching for e-health social system', *Future Generation Computer Systems*, Vol. 84, pp.160–176.

Youngson, N.A. and Whitelaw, E. (2008) 'Transgenerational epigenetic effects', *Annual Reviews in Genomics and Human Genetics*, Vol. 9, pp.233–57.

Yu, J. (2020) 'Research on cloud computing user privacy protection based on dynamic adaptive ant colony algorithm', *International Journal of Autonomous and Adaptive Communications Systems*, Vol. 13, No. 2, pp.178–194.