# Impact of Fixed Boundary Conditions on the Basins of Attraction in the Flower's Morphogenesis of *Arabidopsis Thaliana*

Jacques Demongeot[1], Michel Morvan[2,3], and Sylvain Sené[1,3]

[1] UJF-Grenoble, TIMC-IMAG, Faculté de Médecine, 38706 La Tronche cedex, France
[2] Université de Lyon, LIP, 46, allée d'Italie, 69364 Lyon cedex 07, France
[3] IXXI, Rhône-Alpes Complex Systems Institute, 5 rue du Vercors, 69007 Lyon, France

**Abstract.** Variations of fixed boundary conditions have been proven to have a significant influence in dynamical biological systems following a Hop-field-like rule such as genetic regulatory and neural networks. Classically, theoretical studies focusing on biological systems are based on toric networks, which does not seem to be coherent with the biological reality. We think that the dynamics of biological networks is also regulated by fixed boundaries, illustrated for instance by external magnetic fields, chemical potentials or environmental constraints. The aim of this paper is to go further in the study of the impact of fixed boundary conditions by showing that they significantly affect the relative size of certain basins of attraction. We argue that this is a critical point in real biological networks by giving an example of boundary influence in the genetic regulatory network of the flower's morphogenesis of the plant *Arabidopsis thaliana*.

*Keywords:* Complex systems, biological networks, boundary conditions, basins of attraction.

## 1 Introduction

The robustness of complex systems tends to become a central question in many disciplines to achieve a good understanding of some phenomena happening in complex systems such as their ability to adapt to natural constraints. Besides, the literature on this subject is numerous and presents a lot of relevant studies (see [1,2] for studies in the context of theoretical biology). In a context at the frontier between theoretical computer science and biology, the purpose of this paper is to present a study about the influence of boundary conditions in a specific network in order to give indications about what more generally can happen in the underlying dynamical system.

More precisely, this paper gives indications about what happens in finite threshold Boolean networks when they are not only regulated by the actions of nodes able to change their state but also by the actions of fixed boundaries which correspond to nodes whose state is fixed by their environment during all

time steps of the evolution of the system. The interest of this approach is that such networks are closer to the reality of biological systems than infinite toric networks. For instance, an eukaryotic cell is separated from its neighbours by the cytoplasmic membrane. This membrane, composed by two layers of lipids, plays the role of a boundary. However, that does not mean that interactions between cells do not exist. Indeed, if we consider the case of a plant, it has been shown that flows of hormones, such as auxin, propagate from cell to cell by going through the cellular membrane in order to accelerate the cell proliferation and improve the metabolic pathways transforming the nutrients necessary for the plant to develop. Consequently, studying the impact of stable boundaries in biological systems such as Hopfield-like networks seems to be relevant to understand what happens in real systems.

In previous papers [3,4], we focused on the influence of fixed boundary conditions in neural networks defined on lattices on $\mathbb{Z}^d$ following a stochastic transition rule, where $d$ corresponds to the dimension of the lattices. In such a theoretical framework, we have shown that the impact of different fixed boundary conditions could not be made explicit in one dimension whereas it was the case in two dimensions. Indeed, we have emphasised that the influence of boundary conditions in square grids on $\mathbb{Z}^2$ was characterised by phase transitions for specific values of parameters.

The purpose of this paper is to realise a step in the direction of biologists by proposing an exhaustive study of the impact of a specific fixed boundary in a real biological network whose evolution follows a deterministic transition rule. This network models the flower's development of a highly studied plant: *Arabidopsis thaliana*. The results obtained in this case show that boundary conditions have a significant influence as well as on the relative sizes of the basins of attraction of this discrete dynamical system as on the relative distances between them.

In this paper, Section 2 gives the main preliminary definitions that are used in this work. It specifically focuses on two notions: the attractors and the attraction basins of discrete dynamical systems, and also the centre and the boundary of networks. Then, it details the properties of the model on which this study is based on. Section 3 presents the network of our study and exposes the measures which seemed to be relevant in order to point out the links existing between the boundary conditions and the basins of attraction. Section 4 gives the results emphasising that fixed boundary conditions can significantly affect the relative sizes of the attraction basins of the dynamical system describing the developmental process of the *Arabidopsis thaliana*'s flower. This paper will be finally concluded by a discussion about the main perspectives of this work.

## 2 Definitions

The objective of this section is to give some basic definitions from the dynamical systems and graphs theories before detailing the model of networks on which we decided to base our study.

### 2.1 Discrete dynamical system, attractor and basin of attraction

A *discrete dynamical system* is a system composed by elements that interact with each others over time. More formally, a discrete dynamical system is defined by a triple $(X, T, f)$, where:

- $X$ is a finite set, called the space of configurations.
- $T$ equals $\mathbb{Z}$ and is called the time space.
- $f$ is the flow generated by a map $F : X \times T \mapsto X$ and satisfies $f(x, 0) = x$ and $f(f(x, t_1), t_2) = f(x, t_1 + t_2)$.

Let us consider a subset $A$ of $X$ and denote by $B(A)$ the *basin of attraction* of $A$. $B(A)$ is the subset of $X$ such as all its elements have their limit set of $f(x, T)$ in $A$, this limit set being the subset of $X$ whose elements evolve towards a configuration of $A$ after a succession of applications of the flow $f$.

Furthermore, let us consider a configuration $x$ of $X$ and apply successively to it a flow $f$. Since the space of configurations is a finite set, whatever the flow $f$ is, it is trivial that $x$ evolves in a finite time towards either a configuration which cannot evolve anymore, *i.e.* a *fixed point*, or a sequence of configurations which repeat themselves indefinitely, *i.e.*, a *limit cycle* (in the Poincaré's definition, a limit cycle has a non empty basin of attraction but, here, we do not impose this restriction [5,6]). These configurations, resulting from successive applications of the flow $f$ on a discrete dynamical system are called the *attractors* of the system (see Figure 1).

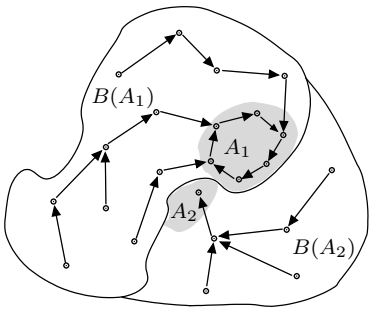


**Fig. 1.** Representation of the transitions in the space of configurations of a discrete dynamical system admitting two different attractors $A_1$ and $A_2$, respectively a limit cycle and fixed point. The black dots represent the different configurations belonging to the space of configurations and the arrows illustrate the transitions between the configurations resulting from the applications of $f$.

### 2.2 Oriented graph, centre and boundary

Biological *regulatory networks* are particular cases of discrete dynamical systems that have been developed to model interactions dynamics occurring between genes, proteins or cells. One denotes by $N$ a regulatory network made of $n$ nodes. Such a network can be represented by an oriented graph $G = (V, E)$, where $V$ is the set of vertices (nodes) and $E$ is the set of edges (interactions). Let us recall the useful definitions of the graph theory in our context [7].

Let $v_i$ and $v_j$ be two distinct nodes of $N$ and $P$ be a subset of $E$ defined by $P = \{e_1, e_2, \ldots, e_l\}$. $P$ is a *path* from $v_i$ to $v_j$ if the beginning of the edge $e_1$ is the vertex $v_i$, the end of the edge $e_l$ is the vertex $v_j$ and the final vertex of each edge of $P$ is the beginning vertex of the next edge of $P$. The *length* of a path equals the number of edges that compose it. The $L1$-*distance* between two vertices $v_i$ and $v_j$ is the length of the shortest path from $v_i$ to $v_j$.

The *eccentricity* of a vertex $v_i$ is the maximum $L1$-distance between $v_i$ and any other vertex of the graph $G$. The minimum and not null eccentricity of the graph is called the graph *radius* and the maximum eccentricity of $G$ is called the *diameter* of the graph.

The *centre* of a graph $G$ is the set of vertices whose eccentricity equals the graph radius. We will say that such vertices are *central*. In the same way, the *boundary* of a graph $G$ is the set of vertices whose eccentricity equals the graph diameter. We will say that such vertices are *peripheral* (see Figure 2).

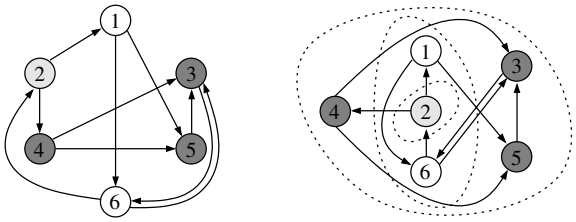


**Fig. 2.** Two representations of the same oriented graph $G = (V, E)$ where $|V| = 6$ and $|E| = 9$. Its diameter equals 4, its radius is 2. The centre (in light grey) of $G$ is $\{2\}$ and its boundary (in dark grey) is $\{3, 4, 5\}$. Let us remark that the first representation is arbitrary whereas the second is created by placing successively the vertices by increasing order of eccentricity.

Let us add that the computation of the centre (and consequently of the boundary) of an arbitrary graph corresponds to the computation of all the shortest paths for all the couples of vertices. So, in the general case, it needs a time complexity of $O(|V|^3)$ by using the algorithm of Dijkstra [8] for each vertex. However, in the case of sparse graphs, *i.e.*, where $|E|$ is significantly less than

$|V|^2$, the algorithm of Johnson [9] is more appropriate thanks to its complexity in $O(|V|^2 \cdot log|V| + |V| \cdot |E|)$.

### 2.3 The model of regulatory networks

In [10], Hopfield proposed a deterministic model with collective computational abilities which seemed to show a good correspondence with real neural networks. Lots of researches have then been deployed on Boolean networks following the Hopfield law in different fields of Science, from theoretical mathematical studies (*e.g.*, about the computational power of artificial neural networks in [11]) to applications in biology (see [12]). This section aims at presenting the definitions of a model of genetic regulation based on the Hopfield approach.

We have decided to focus on threshold Boolean networks following the Hopfield law, *i.e.*, on networks whose evolution is governed by a deterministic updating rule.

More precisely, the studied network $N$ is a set of $n$ nodes. Each node has two possible states named activity states. If we call $\sigma(t) = (\sigma_i(t))_{i \in N} \in \Omega = \{0,1\}^n$ the current configuration of the network $N$ at time $t$, the states of the nodes of this configuration are defined by :

$$\forall i \in N,\ \sigma_i(t) = \begin{cases} 0 & \text{if } i \text{ is inactive} \\ 1 & \text{else} \end{cases}$$

We define $W_{n \times n}$ as the interaction matrix (also called the synaptic weights matrix in the context of neural networks) giving the interaction structure between the nodes of $N$ in which the coefficient $w_{ij} \in \mathbb{R}$ gives the interaction weight that the node $j$ has on the node $i$. When this coefficient is negative (resp. positive), the node $j$ is called an inhibitor (resp. activator) of the node $i$ and when it is null, the node $j$ does not act on the node $i$. Let us also note that $\mathcal{N}_i$ represents the neighbourhood of the node $i$ in which the interaction weight that the node $j$ has on the node $i$ does not vanish. More formally, we have for given $i \in N,\ j \in N$: $j \in \mathcal{N}_i \Leftrightarrow w_{ij} \neq 0$.

We can now define the temporal evolution of such a network. The deterministic version of the Hopfield law is defined by:

$$\sigma_i(t+1) = H(\mathcal{H}_i(\sigma(t)) - \theta_i)$$

where $H$ is the Heaviside step function ($H(x) = 1$ if $x > 0$ and $H(x) = 0$ if $x \leq 0$), $\mathcal{H}_i(\sigma(t)) = \sum_{j \in \mathcal{N}_i} w_{ij} \cdot \sigma_j(t)$ is the activation potential of the node $i$ such that $i \in N$ and $\theta_i \in \mathbb{R}$ is the activation threshold of the node $i$.

Finally, let us note that there exist three different kinds of nodes updating over time:

– The nodes of a network can be updated simultaneously at each step of time. We then speak about the *parallel* updating iteration mode.
– An arbitrary sequence of nodes is fixed in advance. At each time step, depending on the chosen sequence, the state of only one node is updated. This updating iteration mode is called *sequential*.
– The nodes are grouped in blocks. The inter-block updating is sequential and the intra-block updating is parallel. This corresponds to the *block-sequential* case.

Let be $U_n$ the number of updating iteration modes for a network composed of $n$ nodes. In [13], $U_n$ is defined by:

$$U_n = \sum_{i=0}^{n-1} \binom{n}{i} \cdot U_i \text{ where } U_0 = 1$$

## 3 The network and the study protocol

The purpose of this section is to present the network of the flower's morphogenesis of the plant *Arabidopsis thaliana* on which we focus and to present the method that we used and the parameter that we decided to study in order to emphasise the impact of boundary conditions on the basins of attraction.

### 3.1 Variations around the "Mendoza network"

In 1998, Mendoza and Alvarez-Buylla isolated eleven genes of the plant *Arabidopsis thaliana* involved in its flower's morphogenesis: EMBRYONIC FLOWER 1 (EMF1), TERMINAL FLOWER 1 (TFL1), LEAFY (LFY), APETALATA 1 (AP1), CAULIFLOWER 1 (CAL), LEUNIG (LUG), UNUSUAL FLORAL ORGANS (UFO), AGAMOUS (AG), APETALATA 3 (AP3), PISTILLATA (PI), SUPERMAN (SUP). By using a genetic algorithm in order to obtain the interactions between these genes with their potential, they proposed a genetic regulatory network whose the mathematical study of the dynamics presents a strong closeness with the reality of its flower's morphogenesis.

Indeed, by considering that this network follows the deterministic version of the Hopfield law defined in Section 2 with a specific updating iteration mode, the authors show the existence of only six basins of attraction, all leading to fixed points. One of the most interesting points in this study is that among these six fixed points, four exactly correspond to the four specific tissues of the flower of this plant (sepals, petals, carpels and stamens), one corresponds to inflorescence meristematic cells and the last one corresponds to cells that have not already been seen in the nature but that are said to be experimentally induced (see [14] for more details). Let us note that, in the following tables and figures, we will speak about these six types of cells by abbreviating sepals by *Sep*, petals by *Pet*, carpels by *Car*, stamen by *Sta*, inflorescence by *Inf* and the not already seen in

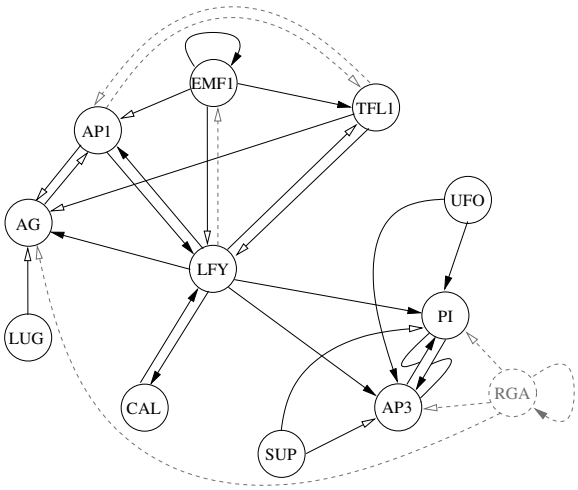


**Fig. 3.** A new genetic regulatory network representing the flower's morphogenesis of the plant *Arabidopsis thaliana* exhibiting the repressing power of RGA on floral genes. The repressions (resp. activations) are represented by empty arrows (resp. full arrows) and all the nodes and interactions added to the Mendoza network are indicated in dashed grey.

nature "cell" by *New*. The index 1 (resp. 2) will be associated to the not fixed (resp. fixed) boundary case.

The network on which this study is based corresponds to the one described in [14] in which we added all the non hypothetical interactions presented in [15] without adding any vertex. Thus, we have added the three following inhibitions by assuming that their potential is minimal: LFY $\xrightarrow{-1}$ EMF1, AP1 $\xrightarrow{-1}$ TFL1 and TFL1 $\xrightarrow{-1}$ AP1.

Furthermore, in [16], the authors emphasise that the genes AG, AP3 and PI are the targets of an inhibition by a gene called RECOMBINATION ACTIVATING GENE (RGA). Hence, we add one node representing RGA whose activation threshold equals 0. By assuming that RGA self-activates, we add also four interactions: RGA $\xrightarrow{-1}$ AG, RGA $\xrightarrow{-1}$ AP3, RGA $\xrightarrow{-1}$ PI and RGA $\xrightarrow{+1}$ RGA. An illustration of this new network is given in Figure 3.

Let us note that the values given to the interaction potentials are minimal (*i.e.*, their absolute value are equal to 1) because of our wish to focus more on the structure of the network than on the specific values that have few chances to be realistic whatever they are.

The diameter (resp. the radius) of this network is 4 (resp. 1) (cf. [13]). Its boundary (resp. centre) is {LUG, RGA} (resp. {LFY}). Let us remark that the

particular nature of the interactions between AP3 and PI prevents their consideration as central genes of the network. Since the two interactions between them are both dependent on their states of these two genes, we decided to consider that their eccentricity is not equal to 1 but to $1+\varepsilon$, where $0<\varepsilon<1$ represents the expression of the dual dependence of these two genes.

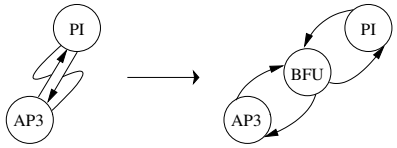


**Fig. 4.** Interpretation of the interactions between AP3 and PI for the model.

On this point, like in [14], in order to fix the impossibility for this kind of interaction to be directly captured by the model proposed in Section 2, we implement a "virtual" heterodimer gene named BURST FORMING UNIT (BFU) composed by the two genes AP3 and PI, that plays the role of an activating transcription factor for them (see Figure 4).

Let us now give the threshold vector $\theta$ and the interaction matrix $W$ where the columns are ordered with the following sequence: RGA, EMF1, TFL1, LFY, AP1, CAL, LUG, UFO, BFU, AG, AP3, PI, SUP.

$$W = \begin{pmatrix}
1 & 0 & 0 & 0 & 0 & 0 & 0 & 0\,0 & 0 & 0\,0 & 0\\
0 & 1 & 0 & -1 & 0 & 0 & 0 & 0\,0 & 0 & 0\,0 & 0\\
0 & 1 & 0 & -2 & -1 & 0 & 0 & 0\,0 & 0 & 0\,0 & 0\\
0 & -2 & -1 & 0 & 2 & 1 & 0 & 0\,0 & 0 & 0\,0 & 0\\
0 & -1 & -1 & 5 & 0 & 0 & 0 & 0\,0 & -1 & 0\,0 & 0\\
0 & 0 & 0 & 2 & 0 & 0 & 0 & 0\,0 & 0 & 0\,0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\,0 & 0 & 0\,0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\,0 & 0 & 0\,0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\,0 & 0 & 1\,1 & 0\\
-1 & 0 & -2 & 1 & -2 & 0 & -1 & 0\,0 & 0 & 0\,0 & 0\\
-1 & 0 & 0 & 3 & 0 & 0 & 0 & 2\,1 & 0 & 0\,0 & -2\\
-1 & 0 & 0 & 4 & 0 & 0 & 0 & 1\,1 & 0 & 0\,0 & -1\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\,0 & 0 & 0\,0 & 0
\end{pmatrix} \quad \theta = \begin{pmatrix}
0\\0\\0\\3\\-1\\1\\0\\0\\1\\-1\\0\\0\\0
\end{pmatrix}$$

### 3.2 Protocol of study

As we mentioned in the introduction of the paper, we wish to show the influence of fixed boundary conditions in the network defined in the previous paragraph. In this study, we essentially focus on the impact of one of the two boundary genes, namely RGA.

RGA is a good candidate to be studied as a boundary of the network because it is not only mathematically defined as a peripheral node but is also shown to be highly regulated by a hormone named GA (for Gibberellin). So, if we consider an arbitrary cell from which such an interaction network is isolated, the graph distance between RGA and the cell membrane from whichcomes GA is taken equal to 1. Indeed, the distance between RGA and the flow of GA is 1 and the flow go through the cellular membrane.

To show the influence of boundary conditions in such a network, we decided to emphasise the links existing between its boundary and its basins of attraction. To do that, we have chosen to show the differences between results obtained when the boundary RGA can change its state and when it is fixed to 0 on two kinds of measures. The first measure that seemed to be of interest is the relative size of each basin of attraction which, for a given basin, correspond to the probability to choose uniformly an initial configuration in this basin. The second measure corresponds to the relative distance between the basins of attraction. The relevance of this measure comes from the fact that it gives indications about the probabilities for an initial configuration belonging to a basin $B(i)$ to fall over in a basin $B(j)$ after perturbations. Let us consider three basins of attraction $B(i)$, $B(j)$ and $B(k)$. If the distance between $B(i)$ and $B(j)$ is smaller than the distance between $B(i)$ and $B(k)$, small perturbations on a configuration belonging to $B(i)$ have indeed more chances to send it into the basin $B(j)$ than to the basin $B(k)$.

Consequently, the protocol of our study is composed by three steps for the two different exposed cases:

- the study of the dynamics of the network for all the $2^{13}$ (resp. $2^{12}$) possible initial configurations when the boundary can evolve (resp. is fixed to 0), *i.e*, the computation of the attractors and the extraction of their basins of attraction;
- the computation of the relative sizes of these basins of attraction in terms of number of elements and proportion;
- the computation of the distribution of the minimal Hamming distances between the basins of attraction, for all couples of attraction basins $(B_1, B_2)$ and all couples of configurations $(c_1, c_2)$ respectively belonging to $B_1$ and $B_2$.

Finally, as it is said in Section 2, the dynamics of a network can be studied by using different updating iteration modes. Depending on the updating iteration mode chosen to let evolve the network of Section 3, we know that we can obtain different attractors. Indeed, by using the parallel iteration mode, the set of attractors contains limit cycles, which is not the case by choosing sequential iteration mode that results in the obtention of fixed points only. Let us note that these fixed points exactly correspond to those pointed out in [14] by using a block-sequential updating iteration mode. Consequently, as we want here to conserve only the fixed points and since we have no experimental data about the hierarchical place of RGA in the block-sequential updating iteration mode given

in [14], we choose a simple sequential iteration mode defined by the following ordered partition of the set of genes:
(RGA)(EMF1)(TFL1)(LFY)(AP1)(CAL)(LUG)(UFO)(BFU)(AG)(AP3)(PI)(SUP)

## 4 Results on the basins of attraction

This section aims at detailing the three steps of our study presented in the previous section. So, we give the dynamics of the network such that is has been updated and we expose the significant results obtained about the relative sizesof its basins of attraction and their relative distances when the network is subjected to a specific boundary condition or not.

### 4.1 Dynamics of the network and relative sizes

With the chosen sequential updating iteration mode, in the case where RGA can change its state, the network can evolve towards the eight following distinct fixed points whose correspondance with the cell lineages of *Arabidopsis thaliana* is indicated:

$$\begin{aligned}
(0000100000000) &\longleftrightarrow \text{Sep}\\
(0000100010110) &\longleftrightarrow \text{Pet}\\
(0000000001000) &\longleftrightarrow \text{Car}\\
(0000000011110) &\longleftrightarrow \text{Sta}\\
(0110000000000) &\longleftrightarrow \text{Inf}\\
(0110000010110) &\longleftrightarrow \text{New}\\
(1000100000000) &\longleftrightarrow \text{Sep}\\
(1110000000000) &\longleftrightarrow \text{Inf}
\end{aligned}$$

Of course, as in the work of Mendoza and Alvarez-Buylla, when we fix the boundary RGA to 0, we obtain the six first attractors above. Since only the notion of cell lineage is relevant from the biological point of view, we choose to merge the basins of attraction corresponding to identical lineages. So, in the sequel, in the case of not fixed boundary, we will assume that the basin of attraction of the sepals is the union of the basins of attraction of the fixed points (0000100000000) and (1000100000000) and that the one of the inflorescence cells is the union of the basins of attraction of the fixed points (0110000000000) and (1110000000000). Thus, we exactly retrieve the number of six attraction basins in the two cases, which allows us to realise comparisons between the results obtained in these different cases.

Figure 5 (left) illustrates with an histogram the relative sizes in number of configurations of the six different basins of attraction. It shows that, in the case of the boundary fixed to 0 compared to the one of not fixed boundary, all the $2^{12}$ removed configurations are parts of the two basins corresponding to the sepal cells and the inflorescence cells. So, only the sizes of the sepal and inflorescence basins are affected. Let us also remark that three quarters (resp. one quarter) of

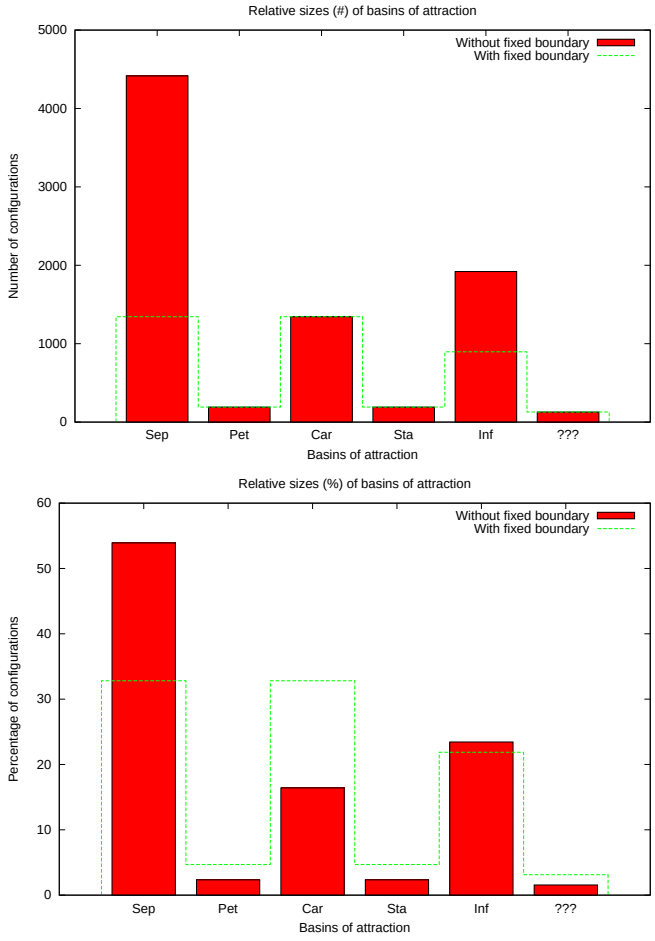


**Fig. 5.** Relative sizes of the six basins of attraction in (left) number of configurations and in (right) proportion. For the case of not fixed boundary, the results are presented with red boxes. For the other case, the results are presented with green steps.

the $2^{12}$ supplementary configurations in the case of not fixed boundary are parts of sepal (resp. inflorescence) basin.

Another representation of these relative sizes gives us more information. This representation is given in Figure 5 (right) and presents the probabilities for any basin to choose uniformly a configuration into it. When the boundary can change its state, we can remark a significant disequilibrium between the relative sizes of basins of attraction. 54.91 (resp. 23.44) percent of the initial configurations leads to sepal (resp. inflorescence) cells whereas only almost 21.09 percent of them

leads to petal, carpel and stamen cells. The forced inhibition of the boundary highly reduces this disequilibrium since the probability for an initial configuration to belong to one of the three latter cell types is multiplied by 2. Biologically, that means that the forced inhibition of RGA thanks to the repressive flow of Gibberellin (GA) significantly improves the chances that the plant has to develop normally, which was experimentally proven in [16].

Consequently, these first results confirm that the dynamics of the flower's morphogenesis of the plant *Arabidopsis thaliana* is highly dependent on the state of the boundary played in this case by RGA. Now let us go further in the study of the impact of the boundary on the basins of attraction by focusing on the distances separating them.

### 4.2 Relative distances

| | $Sep_1$ | $Sep_2$ | $Pet_1$ | $Pet_2$ | $Car_1$ | $Car_2$ | $Sta_1$ | $Sta_2$ | $Inf_1$ | $Inf_2$ | $New_1$ | $New_2$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $Sep_{1/2}$ | 0.00 | 0.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.23 | 1.50 | 2.00 | 2.50 |
| $Pet_{1/2}$ | 2.61 | 1.71 | 0.00 | 0.00 | 2.71 | 2.71 | 1.00 | 1.00 | 3.63 | 3.21 | 1.50 | 1.50 |
| $Car_{1/2}$ | 1.44 | 1.00 | 2.00 | 2.00 | 0.00 | 0.00 | 1.00 | 1.00 | 2.10 | 1.50 | 2.50 | 2.50 |
| $Sta_{1/2}$ | 2.91 | 2.71 | 1.00 | 1.00 | 1.71 | 1.71 | 0.00 | 0.00 | 3.63 | 3.21 | 1.50 | 1.50 |
| $Inf_{1/2}$ | 1.33 | 1.33 | 2.33 | 2.33 | 1.33 | 1.33 | 2.33 | 2.33 | 0.00 | 0.00 | 1.00 | 1.00 |
| $New_{1/2}$ | 3.59 | 3.05 | 1.33 | 1.33 | 3.05 | 3.05 | 1.33 | 1.33 | 2.13 | 1.71 | 0.00 | 0.00 |

**Table 1.** Average distances between attraction basins for not fixed (resp. fixed) boundary condition, given at the intersection of columns and rows which represent respectively the initial and the final basin. For example, the average distance from sepal to petal basins is 2.61 (resp. 1.71).

First of all, let us give the formal definition of *distance* used in this paper. We define the distance from a set $S_1$ to another set $S_2$ by $d(S_1, S_2) = \mathrm{Min}_{i \in S_1, j \in S_2}(d_H(i, j))$ where $d_H(i, j)$ is the Hamming distance between the elements $i$ and $j$.

In this subsection, we are going to analyse the relative distances between basins of attraction, by comparing the results obtained on the not fixed boundary case and on the fixed boundary case.

Let us focus on the average distances between basins (cf. Table 1). We remark that we have no difference on the not fixed boundary case (case 1) and on the fixed boundary case (case 2) for small size basins (petal, carpel, stamen and new). Moreover, a coarse to fine study of these basins has confirmed the absence of difference between these two cases. That is why we restreint in the sequel our study to large size basins (sepal and inflorescence). Indeed, these two basins

show significant differences. In the case 1, the arithmetic average of the computed distances, when the initial basin is the sepal (resp. inflorescence) one and the final is any of the others, is equal to 2.38 (resp. 2.54) whereas, in the case 2, this arithmetic average equals 1.96 (resp. 2.26). So, for these two basins, finer studies on the distances are relevant.

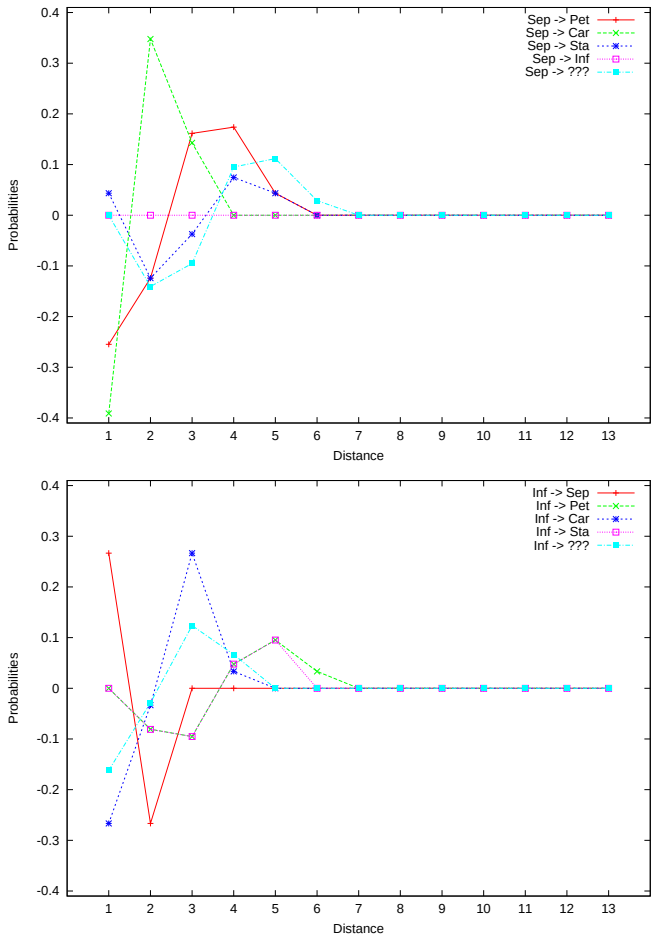


**Fig. 6.** Differences of probabilities of having a given distance (from 0 to 13) for not fixed minus fixed boundary condition. On the left (resp. right), the initial basin corresponds to the sepal (resp. inflorescence) cells. On the two graphics, when, for instance, the green curve disappears, it is confounded with the violet curve

To go further, we have focused on the differences between the probabilities distributions of the distances. As well as for the sepal basin as for the inflorescence basin, the two graphics given in Figure 6 illustrate the fact that the fixed boundary allows to highly reduce the probability to choose an initial configuration far from the other basins. Let us note that, for the two large size basins and for almost all the small distances, the differences between the probabilities distributions in the case 1 minus the ones of the case 2 are negative. A first conclusion on this point is that the fixed boundary decreases the distances between these two attraction basins and the others and, more, increases thus the probability for an arbitrary configuration of one of these two basins to be sensible to small perturbations changing so its attractor.

Let us now give more details about the probabilities distributions of distances for these two basins (see Tables 2 and 3). These tables give precise indications about the impact of the fixed boundary condition on the dynamics of the network. To illustrate this high influence, let one consider for the sepal basin the distances separating it from the petal ($i$) and the carpel ($ii$) ones. For the inflorescence basin, let we focus on the distance between it and the carpel one ($iii$):
($i$) the forced inhibition of the boundary brings to a two units reduction of the maximum of computed distances. In this case, 85.71 percent of the sepal configurations are at distance 1 and 2 to the petal basin whereas this measure represents only 47.83 percent of the configurations in the other case;
($ii$) there too, the fixed boundary brings to a two units reduction of the maximum of computed distances. Furthermore, in this case, all the sepal configurations are at distance 1 to the carpel basin. In the other case, this proportion equals 60.87 percent;
($iii$) the forced inhibition of the boundary gene allows a reduction of two units of the distance. The proportion of inflorescence configurations at distance 1 to the carpel basin is 23.33 percent in the case 1 and 50.00 percent in case 2.

Hence, globally, the fixed boundary significantly reduces some distances between the basins of attraction. The relations between basins concerned by this general statement are: sepal towards petal, sepal towards carpel and inflorescence towards carpel. As we could expect, the significant changes occurring on the distributions of distances between basins take place on basins whose relative size in number of configurations significantly changes too. Consequently, we can expect from this study that boundary conditions may have an impact in an arbitrary network, not only on the relative sizes of their basins of attraction but also on the distances between them.

## 5 Conclusion and perspectives

After having studied the influence of boundary conditions on stochastic neural networks in previous papers, we have presented here some results about the important impact that these conditions may have on the dynamics of real biological networks. More precisely, we have presented some elements about the

| | $d_H = 1$ | $d_H = 2$ | $d_H = 3$ | $d_H = 4$ | $d_H = 5$ | $d_H = 6$ |
|---|---|---|---|---|---|---|
| $\text{Pet}_1$ | 17.39 | 30.43 | 30.43 | 17.39 | 4.36 | 0.00 |
| $\text{Pet}_2$ | 42.86 | 42.86 | 14.28 | 0.00 | 0.00 | 0.00 |
| $\text{Car}_1$ | 60.87 | 34.78 | 4.35 | 0.00 | 0.00 | 0.00 |
| $\text{Car}_2$ | 100.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| $\text{Sta}_1$ | 4.35 | 30.43 | 39.13 | 21.74 | 4.35 | 0.00 |
| $\text{Sta}_2$ | 0.00 | 42.86 | 42.86 | 14.28 | 0.00 | 0.00 |
| $\text{Inf}_1$ | 66.66 | 33.33 | 0.00 | 0.00 | 0.00 | 0.00 |
| $\text{Inf}_2$ | 66.66 | 33.33 | 0.00 | 0.00 | 0.00 | 0.00 |
| $\text{New}_1$ | 0.00 | 14.49 | 33.33 | 33.33 | 15.94 | 2.90 |
| $\text{New}_2$ | 0.00 | 28.57 | 42.86 | 23.81 | 4.76 | 0.00 |

**Table 2.** Probabilities (in percentage) distribution of the distances between the sepal basin to the other basins of attraction. The index 1 (resp. 2) corresponds to the not fixed (resp. fixed) boundary case.

| | $d_H = 1$ | $d_H = 2$ | $d_H = 3$ | $d_H = 4$ | $d_H = 5$ | $d_H = 6$ |
|---|---|---|---|---|---|---|
| $\text{Sep}_1$ | 76.67 | 23.33 | 0.00 | 0.00 | 0.00 | 0.00 |
| $\text{Sep}_2$ | 50.00 | 50.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| $\text{Pet}_1$ | 0.00 | 13.33 | 33.33 | 33.33 | 16.67 | 3.33 |
| $\text{Pet}_2$ | 0.00 | 21.43 | 42.86 | 28.57 | 7.14 | 0.00 |
| $\text{Car}_1$ | 23.33 | 46.67 | 26.67 | 3.33 | 0.00 | 0.00 |
| $\text{Car}_2$ | 50.00 | 50.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| $\text{Sta}_1$ | 0.00 | 13.33 | 33.33 | 33.33 | 16.67 | 3.33 |
| $\text{Sta}_2$ | 0.00 | 21.43 | 42.86 | 28.57 | 7.14 | 0.00 |
| $\text{New}_1$ | 26.67 | 40.00 | 26.67 | 6.66 | 0.00 | 0.00 |
| $\text{New}_2$ | 42.86 | 42.86 | 14.28 | 0.00 | 0.00 | 0.00 |

**Table 3.** Probabilities (in percentage) distribution of the distances between the inflorescence basin to the other basins of attraction. The index 1 (resp. 2) corresponds to the not fixed (resp. fixed) boundary case.

links existing between boundary conditions and the basins of attraction of a specific genetic regulatory network. Indeed, we have not only emphasised that fixed boundary conditions can highly change the relative sizes of basins of attraction but also that they get some reduction properties which have been highlighted with the notion of distance between basins.

So, this study has shown that it seems judicious to generalise this approach to wider studies on discrete dynamical systems in order to go further in the comprehension of their robustness face to environmental constraints and to find generic rules available for a large class of such systems. According to us, the boundary of a network is the principal target of exogeneous controls, such as flows of morphogenes in biology or magnetic fields in physics.

The perspectives of this work are numerous and we are thus only going to expose two of them which seem to be among the most interesting from our point of view.

In order to realise a link between our theoretical studies on stochastic neural networks and this study showing both of them an important impact of boundary conditions, it would be relevant to choose a standard theoretical framework such as lattices on $\mathbb{Z}^d$ and to apply to them the deterministic transition rule presented in this paper. The objective would evidently be to compare the results obtained with this deterministic rule to a stochastic one parameterised to be close to the latter (the reaching of a limit value of this parameter allowing for example to get the deterministic rule from the stochastic one).

Another perspective has been slightly introduced in the Section 3 of this paper. It would consist in the creation and the application of an exhaustive protocol computing the probabilities to go from basins to others in function of a parameter $\alpha$ representing the probability for a node of the network to change its state. Next papers will focus on these perspectives.

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## References

1. Albert, R., Barabási, A.L.: Statistical Mechanics of Complex Networks. Reviews of Modern Physics **74** (2002) 47–97
2. Kitano, H.: Biological Robustness. Nature Reviews Genetic **5** (2004) 826–837
3. Demongeot, J., Jézéquel, C., Sené, S.: Boundary Conditions and Phase Transitions in Neural Networks. Theoretical Results. Neural Networks (Submitted in 2007)
4. Demongeot, J., Sené, S.: Boundary Conditions and Phase Transitions in Neural Networks. Simulation Results. Neural Networks (Submitted in 2007)
5. Cosnard, M., Demongeot, J.: Attracteurs : une approche déterministe. C.R. Acad. Sc. Maths. Série I **300** (1985) 551–556
6. Cosnard, M., Demongeot, J.: On the Definitions of Attractors. Lecture Notes in Computer Science **1163** (1985) 23–31
7. Harary, F.: Graph Theory. Addison-Wesley (1969)
8. Dijkstra, E.W.: A Note on Two Problems in Connexion with Graphs. Numerische Mathematik **1** (1959) 269–271
9. Johnson, D.B.: Efficient Algorithms for Shortest Paths in Sparse Networks. Journal of the Association for Computing Machinery (ACM) **24** (1977) 1–13
10. Hopfield, J.J.: Neural Networks and Physical Systems with Emergent Collective Computational Abilities. Proceedings of the National Academy of Sciences of the USA **79** (1982) 2554–2558
11. Koiran, P.: Computational Power of Artificial Neural Networks. PhD thesis, École Normale Supérieure de Lyon (1993) In French.
12. Kauffman, S.A.: The Origins of Order: Self-Organization and Selection in Evolution. Oxford University Press (1993)

13. Demongeot, J., Elena, A., Sené, S.: Robustness in Regulatory Networks: a Multi-Disciplinary Approach. Acta Biotheoretica (In press)
14. Mendoza, L., Alvarez-Buylla, E.: Dynamics of the Genetic Regulatory Network for *Arabidopsis thaliana* Flower Morphogenesis. Journal of Theoretical Biology **193** (1998) 307–319
15. Espinosa-Soto, C., Padilla-Longoria, P., Alvarez-Buylla, E.R.: A Gene Regulatory Network Model for Cell-Fate Determination during *Arabidopsis thaliana* Flower Development that is Robust and Recovers Experimental Gene Expression Profiles. The Plant Cell **16** (2004) 2923–2939
16. Yu, H., Ito, T., Zhao, Y., Peng, J., Kumar, P., Meyerowitz, E.M.: Floral Homeotic Genes are Targets of Gibberellin Signaling in Flower Development. Proceedings of the National Academy of Science of the USA **101** (2004) 7827–7832