

Robustness of Dynamical Systems Attraction Basins Against State Perturbations: Theoretical Protocol and Application in Systems Biology

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Abstract. This paper aims at giving a general and precise method to achieve a good understanding of discrete dynamical systems by focusing on their attraction basins. This work is the result of a previous one which has permitted to show that the structural changes introduced by fixed boundary conditions on regulatory networks could directly and strongly influence the properties of their attraction basins. In this paper, we give an exhaustive stochastic study protocol to understand what happens on attraction basins of dynamical systems when the latter are subjected to state perturbations. Then, we give an application of this protocol by giving the results obtained on a specific system which is a model of the *Arabidopsis thaliana* flower's morphogenesis, depending on a specific boundary condition.

Keywords: Complex systems, robustness, boundary conditions, stochastic protocol.

1 Introduction

Questions on robustness of dynamical systems and more precisely of complex systems tend to become central in many disciplines. Intending to answer these questions seems to be crucial to understand the dynamical behaviour of such systems. Besides, relevant researches deployed on this thematic in various fields, attached to highlight the robustness of complex systems in different contexts, from the robustness as a consequence of the structural complexity of real networks to the robustness against updating iteration or topological perturbations, are numerous in the literature (see for example [1,2,3,4,5]).

In [6], the authors exposed three relevant kinds of robustness in the context of theoretical biology that seem to be of interest in more general frameworks, concerning the influence of changes in updating rules, architecture constraints or boundary conditions. In a previous work, we decided to focus on the last one and we argued that the dynamics of biological networks, and more generally of complex systems, is certainly regulated by fixed boundaries, illustrated for instance by external magnetic fields, chemical potentials or environmental

constraints. In [7], we focused on threshold Boolean networks and emphasised the influence of fixed boundary conditions on the attraction basins of a specific biological regulatory network describing the flower’s morphogenesis of the plant *Arabidopsis thaliana*. Indeed, we have mathematically pointed out the impact of the hormone Gibberellin on the size of attraction basins of this system but also on the distances separating them.

In this context of robustness in complex dynamical systems, we propose in this paper to go further by presenting a stochastic protocol giving the exact ability for a configuration of a certain attraction basin to fall into another basin when it is subjected to a state perturbation defined thanks to a parameter denoted by α and called the state perturbation rate. We show also that such an exhaustive study allows to obtain probabilities for a perturbed trajectory to keep or change its basin in an exact polynomial form which seems to be a good mathematical representation for the treated problem. Moreover, in a context of theoretical biology, we present an application of this protocol in order to characterise the influence of a fixed boundary on the dynamics of a genetic regulatory network modelling the flower’s morphogenesis of *Arabidopsis thaliana*.

In this paper, Section 2 will give the necessary definitions about dynamical systems and oriented graphs to broach the discussion on the notion of state perturbation and exhaustive protocol allowing to characterise the probabilities to go across the different basins of attraction exposed in Section 3. Then, Section 4 will expose the complementary results (from [7]) on the flower’s morphogenesis of *Arabidopsis thaliana* obtained thanks to this protocol before concluding and giving the main perspectives in Section 5.

2 Preliminary definitions

The systems ruled by interactions between elements taking place over time are called dynamical systems. In this work, we focus more precisely on dynamical systems whose underlying time is defined on a discrete space which are called *discrete dynamical systems*. 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 and
- f is the flow generated by a map $F : X \times T \mapsto X$ and satisfies $f(x, 0) = x$ and $f(f(x, t_1), t_2) = f(x, t_1 + t_2)$, where $f(x, t)$ denotes the state reached at time t on the orbit $f(x, T)$ starting in state x at time 0.

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*. As in [8], in this work, we do not impose the Poincaré's restriction defining a limit cycle as having inevitably a non empty attraction basin. These two particular kinds of configurations, resulting from successive applications of the flow f on a discrete dynamical system are called the *attractors* of the system.

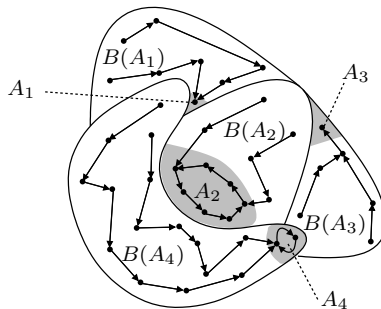


Fig. 1. Transitions in the space of configurations of a discrete dynamical system admitting four different attractors A_1 (a fixed point), A_2 (a limit cycle of length 7), A_3 (a fixed point) and A_4 (a limit cycle of length 2). The four corresponding attraction basins $B(A_1)$, $B(A_2)$, $B(A_3)$ and $B(A_4)$ are separated from each other by plain black lines (the basins frontiers), 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 .

A standard mathematical representation of a discrete dynamical system is by the use of a graph whose vertices (resp. edges) represent the components (resp. interactions) of the system; in the context of networks, we will speak about nodes (resp. bonds). Let us recall briefly the major graph definitions [9] used in this paper. Let be $G = (V, E)$ an oriented graph where V is the set of vertices and E is the set of edges.

Let v_i and v_j be two distinct nodes of V and P be a subset of E defined by $P = \{e_1, e_2, \dots, e_l\}$. 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 minimal 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*. As it is exposed in [7], the algorithm for the computation of the centre of an arbitrary graph is of important time complexity. In the general case, it needs $O(|V|^3)$ operations. In the case of sparse graphs, *i.e.*, where $|E|$ is significantly less than $|V|^2$, thanks to the algorithm of Johnson [10], this number of operations can be reduced to $O(|V|^2 \cdot \log|V| + |V| \cdot |E|)$.

In this work, we have decided to restrict our study to threshold Boolean networks following the Hopfield law [11] which are particular kinds of discrete dynamical systems. This choice comes from our wish to be clear enough in the explanation of the protocol exposed in Section 3 and its presentation will show that, despite this restriction, it is applicable in all kinds of either continuous or discrete dynamical systems because of the genericity of the notions used. So, let us consider such an arbitrary network represented by the oriented graph $G = (V, E)$ and composed hence by $|V|$ nodes and $|E|$ bonds between these nodes. Each node has two possible *activity states* defined by: $\forall i \in V, \sigma_i(t) = \begin{cases} 0 & \text{if } i \text{ is inactive} \\ 1 & \text{else} \end{cases}$, if $\sigma(t) = (\sigma_i(t))_{i \in V} \in \Omega = \{0, 1\}^{|V|}$ is the current configuration of the network G at time t .

The interactions between nodes are captured in an *interaction matrix* denoted by $W_{|V| \times |V|}$ in which the coefficient $w_{ij} \in \mathbb{R}$ represents the interaction weight that the node j has on the node i . If w_{ij} is negative (resp. positive), the node j is called an inhibitor (resp. activator) of the node i (if it is null, j does not act on i). Furthermore, \mathcal{N}_i represents the neighbourhood of the node i and is formally defined by: $i, j \in V; j \in \mathcal{N}_i \Leftrightarrow w_{ij} \neq 0$. 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 and $\theta_i \in \mathbb{R}$ is its activation threshold. Less formally, the state of the node i at time $t+1$ equals 1 if its activation potential at time t is greater than its activation threshold.

3 Protocol

The purpose of this section is to present a solution for measuring the ability of a discrete dynamical system to change its behaviour depending on state perturbations, *i.e.*, for measuring how its configurations can fall out their attraction basins due to these perturbations.

3.1 Known hypotheses

First, let us give the definitions and the hypotheses on which the protocol is based and conserve the notations given above. Consequently, let us consider an arbitrary threshold Boolean network denoted by $G = (V, E)$. We assume that the step of capture of the m attractors (and thus the one of the m attraction basins) has already been executed by simulating the dynamics of the network by successive applications of the given deterministic transition rule on all the $2^{|V|}$ possible initial configurations. So, we get a perfect knowledge of the m basins of attraction of G and we know for each possible initial configuration its corresponding attraction basin. We denote these m attraction basins by B_1, B_2, \dots, B_m . As we focus on the changes of behaviour of such a network depending on state perturbations, we define $\alpha = [0, 1]$ as the uniform probability for a node to change its state. We will call this probability the *state perturbation rate*.

Let $k \in \{0, \dots, |V|\}$ be the number of nodes changing their state during the state perturbation of a configuration. For a given configuration and a given value of k , the set K_k of all the possible state changes is the set of all the possible choices of k elements in a set of $|V|$ elements. The cardinal of this set is thus exactly the binomial coefficient:

$$|K_k| = \binom{|V|}{k}$$

3.2 Protocol core

With these first elements, we can define the probability for a configuration c to become the configuration c' differing from c only on a set of k nodes denoted by p_k . This probability is binary because the perturbation p_k makes the configuration c to become the configuration c' or not and is consequently given by:

$$P(c \rightarrow c' | p_k) = 0 \text{ or } 1$$

From this, it is easy to define the global probability for c to become c' if we consider all the possible state changes for a given value of k . This probability is computed by:

$$P(c \rightarrow c' | k) = \frac{\sum_{p_k \in K} P(c \rightarrow c' | p_k)}{\binom{|V|}{k}}$$

Furthermore, the probability to execute k state changes in a configuration c depending on the value of the state perturbation rate α is defined by:

$$P_\alpha(k) = \binom{|V|}{k} \cdot \alpha^k \cdot (1 - \alpha)^{n-k}$$

We can now define the probability depending on the state perturbation rate α for a configuration c to become the configuration c' . This probability is:

$$P_\alpha(c \rightarrow c') = \sum_{k=0}^{|V|} (P(c \rightarrow c' | k) \cdot P_\alpha(k))$$

The probability for the configuration c to become a configuration being a part of the attraction basin B_j is directly obtained from the previous one and is defined by:

$$P_\alpha(c \rightarrow B_j) = \sum_{c' \in B_j} P_\alpha(c \rightarrow c')$$

To finish, we easily obtain the probability to fall over from an attraction basin B_i to the one denoted by B_j by computing:

$$P_\alpha(B_i \rightarrow B_j) = \frac{\sum_{c \in B_i} P_\alpha(c \rightarrow B_j)}{|B_i|}$$

Thanks to this stochastic protocol allowing to compute these global probabilities, we can obtain the characteristic polynomials of the passage probabilities from an attraction basin B_i to another one B_j for $i, j \in \{1, \dots, m\}$ depending on the state perturbation rate α . Let us finally note that the form of these characteristic polynomials will be: $P_\alpha(B_i \rightarrow B_j) = z_{|V|} \cdot \alpha^{|V|} + z_{|V|-1} \cdot \alpha^{|V|-1} \cdot (1 - \alpha) + \dots + z_1 \cdot \alpha \cdot (1 - \alpha)^{|V|-1} + z_0 \cdot (1 - \alpha)^{|V|}$.

3.3 Discussion

We have just presented an exhaustive stochastic protocol bringing a new knowledge about discrete dynamical systems and their robustness against state perturbations. Numerous perturbations such as synchrony perturbation [3] or topology perturbation [12] have already been studied to achieve a better understanding of specific discrete dynamical systems. The idea to focus also on state perturbations comes from previous studies about the influence of fixed boundary conditions on which we are going to say some words in the next section.

However, although the interest of such a protocol is obvious, it is necessary to speak about a negative underlying point, its complexity. The algorithm implementing this protocol is indeed of time complexity $O(2^{3|V|})$, which consequently avoids its use on threshold Boolean networks composed by more than about twenty nodes. Nevertheless, we think that its implementation by a Monte Carlo method could be a good approximation in the context of large discrete dynamical systems and could even give optimal results in the computation of characteristic polynomials depending on the state perturbation rate α .

4 Application to the flower's morphogenesis of *Ara-bidopsis thaliana*

The objective of this section is to present some new results about the influence of a hormone exerting a constant exogenous inhibiting control on a particular boundary condition of the dynamical system modelling flower's morphogenesis of the plant *Arabidopsis thaliana*. To do that, we are going to briefly expose general information on the model of this biological process and the results obtained in previous studies. After this brief introduction, we will present new results emphasising and characterising the impact of the hormone at stake.

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

Fig. 2. Interaction matrix and threshold vector of the flower’s morphogenesis network where lines and columns are ordered by the following sequence of nodes: RGA, EMF1, TFL1, LFY, AP1, CAL, LUG, UFO, BFU, AG, AP3, PI, SUP.

4.1 Network and previous results

In [7], we have presented a variation around the Mendoza network [13], composed by thirteen nodes and thirty-three bonds, that points out the new relations between the genes revealed by experimental biological researches since 1998 (cf. Figures 2). The values given to the added interactions weights are minimal (*i.e.*, their absolute value are equal to 1). That is the result of our wish to focus on the structure of the network rather than on specific values that would have few chances to be realistic whatever they would be. The diameter (resp. the radius) of this network is 4 (resp. 1). Its boundary (resp. centre) is {LUG, RGA} (resp. {LFY}). Let us note that the results exposed in the sequel are based on the study of one of these two boundary nodes: RGA. Moreover, AP3, PI and BFU are not considered as boundary nodes as a consequence of the particular nature of their inter-connections (BFU is a “virtual” node allowing to model the real interactions occurring between AP3 and PI).

Thanks to the exact knowledge about the dynamics of this network, we have shown that the fixed inactive state of the node RGA has a direct influence on the relative size of the basins of attraction and also on the distance separating them from each others. Indeed, the effect of this fixed boundary node strongly affects the absolute size of two attraction basins (the one corresponding to configurations of sepal lineage and the other to configurations of inflorescence lineage), significantly enlarges the relative size of three floral basins (petal, carpel and stamen lineage) and thus causes an increase of the probabilities to choose an initial configuration in one of these three basins (cf. [7]). This corresponds to a first mathematical interpretation of the necessity of the RGA inactivation for the plant to develop normally.

To go further in studying the influence of this fixed boundary condition on the development of the *Arabidopsis* flower, we are now going to characterise the

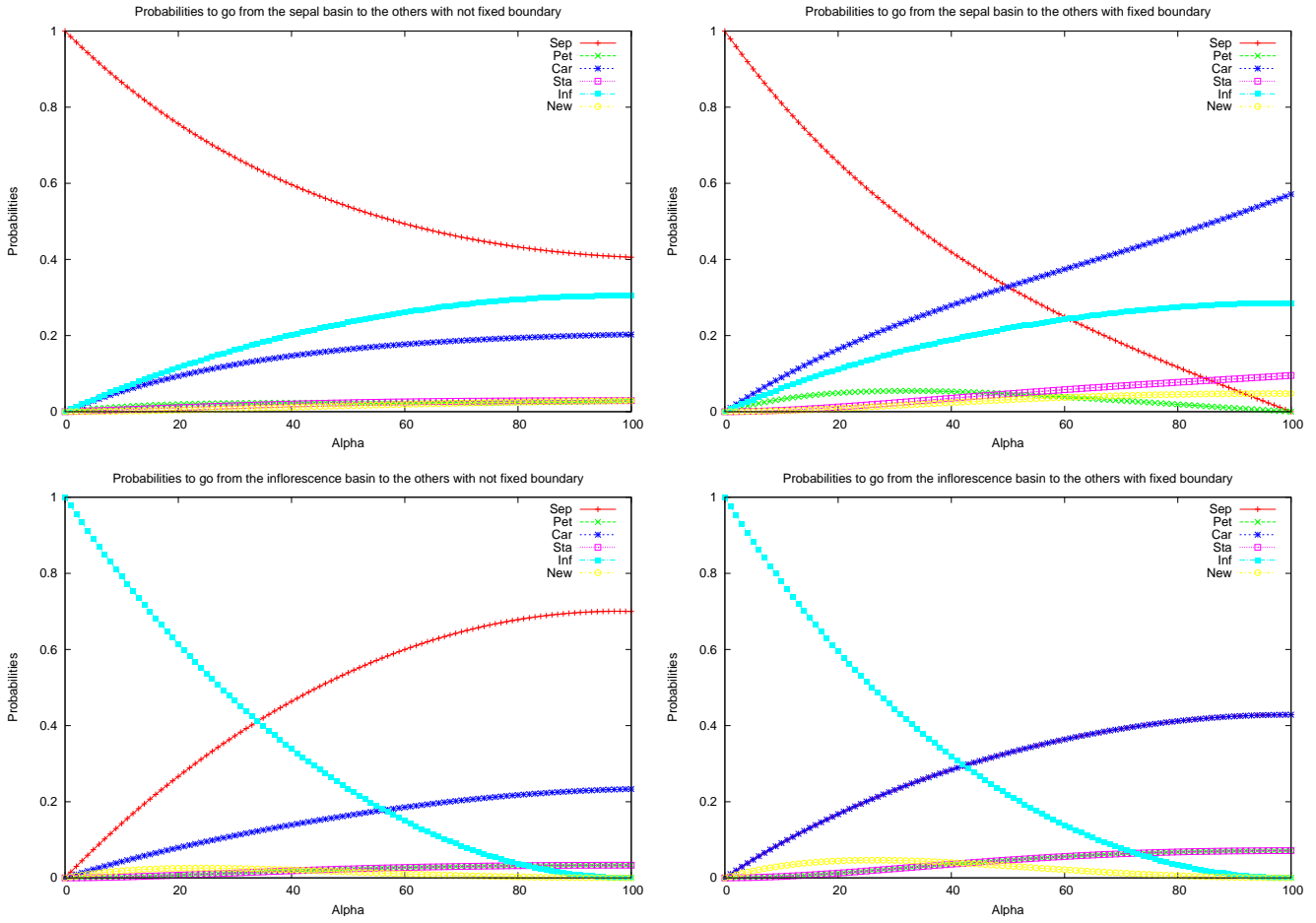


Fig. 3. Graphic representations of the characteristic polynomials of the probabilities, depending on the state perturbation rate α (indicated in percentage), to fall over from the sepal (resp. inflorescence) lineage basin to the others on the top (resp. the bottom) of the figure. The graphics on the left (resp. right) illustrate the results obtained in the case of not fixed boundary (resp. fixed boundary). In these representations, the name of the sepal (resp. petal, carpel, stamen, inflorescence, new) lineage basin is abbreviated by Sep (resp. Pet, Car, Sta, Inf, New).

robustness against state perturbations in two different cases (case 1: with not fixed boundary; case 2: with fixed boundary) thanks to the proposed protocol.

4.2 New results

The results of [7], briefly exposed above, have shown that the global behaviour of the floral morphogenesis of *Arabidopsis thaliana* is strongly affected by the fixed inactive state of the considered boundary which even so locally changes only two of the six attraction basins. Consequently, the sequel will particularly present the results (illustrated in Figure 3) obtained on the probabilities to go across the basins frontiers when the origin of the changeover is either the sepal lineage basin or the inflorescence lineage basin.

The validation of the proposed protocol is composed by two properties:

- the sum of the conditional probabilities to change from an attraction basin B_i to all the others (including itself) is equal to 1 and
- the one unit decreasing of the degree of the characteristic polynomials with the forced inactivation of RGA.

These two properties have been verified and the protocol has been consequently validated. For instance, let us present two polynomials representing the same probability but in the two different cases. In the case 1, the probability to go from the sepal lineage basin to the carpel lineage basin is given by: $P_\alpha^{(1)}(\text{Sep} \rightarrow \text{Car}) = \frac{1}{69}\alpha^7 - \frac{2}{23}\alpha^6 + \frac{17}{69}\alpha^5 - \frac{34}{69}\alpha^4 + \frac{52}{69}\alpha^3 - \frac{58}{69}\alpha^2 + \frac{14}{23}\alpha$ whereas it is in the case 2 equal to: $P_\alpha^{(2)}(\text{Sep} \rightarrow \text{Car}) = -\frac{1}{21}\alpha^6 + \frac{5}{21}\alpha^5 - \frac{4}{7}\alpha^4 + \frac{22}{21}\alpha^3 - \frac{23}{21}\alpha^2 + \alpha$.

Let us consider now the chances, depending on the state perturbation rate, to pass through the frontier of the sepal lineage basin when coming from this basin. One can remark that the increase of the state perturbation rate brings to significant changes (of different orders of magnitude) in the behaviour of the system. Indeed, in the case 1, even with a state perturbation rate equal to 1, some components ($\approx 40\%$) of the sepal lineage basin conserve their property to evolve towards configurations corresponding to the sepal tissue, which is not the case with the fixed boundary. Indeed, in the case 2, these components tend to reach the carpel lineage basin. The highlighting of this phenomenon is a first step that emphasises a strong link existing between the sepal and carpel lineage basins. Moreover, one can also remark that the polynomial characterising the changeover into the inflorescence lineage basin is inferior in the case 2 than in the case 1 and that, globally, the state perturbations balance the chances for the system to evolve towards floral attractors (sepal, petal, carpel and stamen) in the case 2.

Before focusing on the results obtained for the inflorescence lineage basin, let us note that, in the bottom right graphical representation of the figure 3, the red curve for the sepal destination is hidden by the blue one representing the results obtained for the carpel destination.

When the origin is the inflorescence lineage basin, the first interesting point to be underlined is that, despite the difference between their degree, the polynomials characterising the probability to not leave the origin basin are very close contrary to the ones that have been observed when the considered origin was the sepal lineage basin. One of the most interesting element here is that the influence

introduced by the inactive fixed boundary is expressed by a re-equilibrium of the high probability to go on the sepal lineage basin in the case 1 between the lineage basins corresponding to floral tissues in the case 2.

To finish, if we consider the obtained results on the other attraction basins that could not have been presented in this paper, we have noticed that, globally, the initial configurations tend to disperse more in the space of configurations, and specifically in the attraction basins corresponding to floral tissues, when the boundary is fixed. Consequently, we think that what should be retained in the context of the floral morphogenesis of the plant *Arabidopsis thaliana* is that the presence of the fixed inactive boundary condition is a necessary condition for the plant to develop normally. In other terms, the robustness of the flower's morphogenesis process against state perturbations is consolidated by the presence of the fixed boundary.

5 Conclusion and Perspectives

After having emphasised in a previous paper that it was relevant to focus on the links existing between boundary conditions and basins of attraction in discrete dynamical systems, we have proposed in this paper a complex stochastic protocol evaluating the probabilities to go through the attraction basins when their initial configurations are subjected to state perturbations. This protocol has allowed to demonstrate that the presence of an inactive boundary condition in the network of the flower's morphogenesis of *Arabidopsis thaliana* was a necessary condition for the plant to develop normally and to be robust to some kinds of perturbations.

So, because we think that the boundary of a system is the principal target of exogenous controls, such as flows of morphogenes in biology or magnetic fields in physics, this study has confirmed that their consideration was a fundamental point for the comprehension of the robustness of dynamical systems. This is particularly true in biological frameworks. As we know, from the biological point of view, the relevance of this kind of study is obvious because of the not infinitely expandable nature of vegetal or animal beings.

However, as we have discussed, the exponential complexity of the proposed protocol make it unusable to study large dynamical systems. Consequently, the major perspective of this work is to implement this protocol with a Monte Carlo method in order to launch new researches in the context of robustness and the importance to take into account the potential influence of boundary conditions in larger systems such as large grids on \mathbb{Z}^d or other regulatory networks. Next papers will focus on these perspectives, in a theoretical way as well as in more applied contexts.

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