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TURKU CENTRE *for* COMPUTER SCIENCE

TUCS Technical Report
No 1167, October 2016



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Abstract

Quantitative models may exhibit sophisticated behaviour that includes having multiple steady states, bistability, limit cycles, and period-doubling bifurcation. Such behaviour is typically driven by the numerical dynamics of the model, where the values of various numerical parameters play the crucial role. We demonstrate in this paper that such behaviour may also emerge in elementary set theoretical forbidding/enforcing-based models, rather than quantitative models, through the interplay of the interactions between the various components of the model. We demonstrate this for the first time using reaction systems as our modelling framework.

Keywords: Qualitative models; bistability; limit cycle; period-doubling bifurcation; reaction systems.

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1 Introduction

During the recent years a shift in the focus of molecular biology is observed. It is progressively moving from the determination of novel cellular components (e.g., transcription factors, genes, receptors) and the recognition of their individual functions, to the comprehension of how ensembles of cellular components operate in a concerted manner in order to receive, transmit, and process various stimuli into system-level, complex physiological responses, see, e.g., [21, 8, 26]. The molecular machinery that underlies the regulation of complex cellular phenomena such as proliferation, differentiation, and apoptosis, is being progressively uncovered and characterised, see, e.g., [22, 23, 31, 10]. As our knowledge about the components and modules necessary for proper functioning of a cell is constantly growing, the resulting biological models become increasingly complex. As a consequence, they become difficult or even impossible to intuit. Sketched-out drawings, flow charts, and other forms of static diagrams used sometimes by biologists become insufficient to identify and analyse system-level functionalities and their characteristics. They are undergoing a transformation from purely static representation of biological knowledge into dynamical computational models, which can provide insights into the functioning of the systems. Analytical and predictive power of computational modelling and formal reasoning becomes more and more essential for our understanding of biology, in particular the comprehension of how compositions of cellular components lead to various, common types of emergent behaviour.

Bistability is one example of a system-level characteristic property recurring in the description of various cellular systems ([1, 29]). Bistable systems are ones that toggle between two alternative stable states. They are considered to impose switch-like biochemical behaviour. There exists a number of reviews in the literature that present theoretical and experimental advances that cast light on what is needed for a biological system to exhibit bistability, e.g., [20, 30, 29].

Limit cycle oscillation is another system level behaviour of interest for this study. The usefulness of limit cycles in describing periodic biological and ecological phenomena (like the Lotka-Volterra system [18]) make them a compelling subject to study. In a dynamical system with limit cycle, all stable periodic trajectories are attracted to a unique unstable steady state [15].

Period-doubling bifurcation is another interesting system level behaviour which is well connected to chaotic behaviour in nature. This mode of deterministic chaos is a common pattern in living organisms, see [16]. In a system with a period-doubling bifurcation, a slight change in the system's parameters, makes an initially stable cycle of length k unstable, and produces a new stable cycle of length $2k$, see [27].

The analysis and understanding of these behaviours are typically performed in the realm of quantitative models, in particular models based on ordinary differential equations. In such models, the characteristics of a system are usually gen-

erated through a quantitative interplay between the well-chosen numerical values of the kinetic constants and of the initial concentrations of the variables. This is to some extent unsatisfactory, being governed by numerical setups that say nothing about the structure (nature) of the system under study. Therefore, our insight into the causes of and the mechanisms driving these behaviours remain on a very basic level of detail. In this study, we take a qualitative view to explore different behaviours of a dynamical system. By taking such an approach and removing all numerical dependent features and replacing them by the qualitative elements that the numbers are derived from, we aim to identify structural mechanisms that can lead to bistability, limit cycles, and bifurcations. Several studies have employed Boolean frameworks to demonstrate the above mentioned behaviours, see for example [2, 17, 24]. We address the problem on an elementary level here, by adopting *reaction systems* as our modeling framework. We show bistability, limit cycle oscillations and period-doubling bifurcation may emerge using only elementary set-theoretical operations.

The article is structured as follows. In Section 2 we introduce a few basic definitions of reaction systems. In Section 3 we describe the link between dynamical systems and reaction systems. In Section 4- 6 we introduce the notions of *multi-stable*, *mono-stable* and *periodic* reaction systems and provide some examples having these properties. We conclude with a brief discussion in Section 7.

2 Reaction systems

Reaction systems (RS), introduced in [12], is a qualitative framework inspired by the functioning of the living cells. There are only two main regulation mechanisms, *facilitation* and *inhibition*, in reaction systems, that drive the interactions between reactions. Intuitively a reaction is enabled when all components needed to facilitate the reaction are present and all components which inhibit such a facilitation are absent from the environment. Based on this intuition a reaction is formalised as a triplet: its reactants, its inhibitors, and its product set.

In the world of reaction systems, reactions are the pivotal ingredients and it is reactions that lead the transformation of the system from one state to the other. This modelling approach provides a causal insight for the modeller and facilitates a better understanding of the cause-effect relationships of the reactions and consequently of the model as a whole. In contrast, in traditional modelling approaches one mainly deals with the outcome of a process and not with the process itself. Another point that makes reaction systems an interesting tool for modelling is its qualitative nature and how it deals with the phenomena under study only through the facilitation and inhibition mechanisms. There are two main assumptions considered in the reaction systems framework:

- *The threshold assumption.* It is assumed that either an element is present in the environment in abundance or it is absent from it. This implies that

there is no counting in (the basic formulation of) the RS framework and as a result, reaction systems are qualitative, rather than quantitative;

- *The no permanency assumption.* It is assumed that an element vanishes from the environment if no reaction is triggered to preserve it. This follows the basic energetics of the living cells, where all the different components are actively supported through energy, i.e., through various cellular reactions.

The two main assumptions of the reaction systems framework yield a very different modelling framework than in traditional ODE-based modelling. For example, concurrency on resources between different reactions is described in reaction systems through facilitators and inhibitors, rather than through a competition driven by the numerical values of kinetic constants as in ODE-based model. This provides a deeper and more explicit understanding of the phenomenon under study. We refer to [5] and [6] for two biological models implemented in reaction systems including a comparison with the corresponding ODE-based models.

We recall some basic definitions of reaction systems. For details we refer to [12].

A *reaction* is a triplet of non-empty, finite sets: $a = (R_a, I_a, P_a)$, where $R_a \cap I_a = \emptyset$. The sets R_a, I_a, P_a stand for the set of *reactants*, *inhibitors*, *products* of a , respectively. Given a set S , if $R_a, I_a, P_a \subseteq S$, then a is a reaction in S . The set of reactions in S is denoted by $rac(S)$.

Let A be a finite set of reactions, T a finite set, and $a \in A$.

- (i) The *result* of a on T , denoted $res_a(T)$, is

$$res_a(T) = \begin{cases} P_a, & \text{if } R_a \subseteq T \text{ and } I_a \cap T = \emptyset \\ \emptyset, & \text{otherwise.} \end{cases}$$

- (ii) The *result* of A on T , denoted $res_A(T)$, is

$$res_A(T) = \bigcup_{a \in A} res_a(T).$$

A *reaction system* (RS in short) is defined as an ordered pair $\mathcal{A} = (S, A)$, where S is a finite set and $A \subseteq rac(S)$. The set S is called the *background* (set) of A .

Let \mathcal{A} be a reaction system. An *interactive process* in \mathcal{A} is a pair $\pi = (\gamma, \delta)$, where $\gamma = C_0, C_1, \dots, C_n, \delta = D_0, D_1, D_2, \dots, D_n \subseteq S$, $n \geq 1$, with $D_0 = \emptyset$ and, for each $1 \leq i \leq n$, $D_i = res_A(C_{i-1} \cup D_{i-1})$. The sequence γ is the *context sequence* of π . The *state sequence* of π is $\tau = W_0, W_1, \dots, W_n$, where $W_i = C_i \cup D_i$, for all $i \in \{0, \dots, n\}$. We denote the *final state* W_n by $\text{fst}(\pi)$; since W_n is completely defined by the context sequence γ , we also write $W_n = \text{fst}(\gamma)$.

Note that the dynamics of a reaction system can also be represented by a state transition diagram, where the nodes are the elements of the RS state space and the directed edges are labeled by the given context at each state.

We say that $D \subseteq S$ is a *steady state* of \mathcal{A} for context C if $\text{res}_{\mathcal{A}}(C \cup D) = D$. For details about this notion we refer to [5] and [3].

3 Dynamical Systems and Reaction Systems

In this section we briefly describe the link between dynamical systems and reaction systems; this was originally discussed in [7].

Dynamical systems (either continuous or discrete) are defined through their structures (e.g., ODEs, probabilistic transitions, etc.) and through their numerical setup (e.g., initial conditions, kinetic or stochastic constants). The structure of dynamical systems, together with their numerical setup, define the trajectories of the system. In this paper we are mirroring a dynamical system's trajectories through a reaction system's state transition diagram. To do this we fix the initial state of the RS to correspond to the initial conditions of the dynamical system. The numerical setup of the dynamical system is represented through a constant context sequence. In case we need to observe changes in the dynamical system as an effect of changing its numerical setup, we will consider a non-constant context sequence.

Note that, by applying a few changes in the set of reactions of an RS, a constant non-empty context sequence can be replaced with an empty context sequence, as shown in the next lemma.

Lemma 3.1. *Let $\mathcal{A} = (S, A)$ and $\gamma = C, C, \dots, C$ a constant context sequence. Let $\tau = W_0, W_1, \dots, W_n$ be the state sequence corresponding to γ in \mathcal{A} . There exists a reaction system $\mathcal{A}' = (S, A')$ such that $\tau = W_0, W_1, \dots, W_n$ is the state sequence corresponding to the empty context sequence.*

Proof. Let $\mathcal{A}' = (S \cup \{d_I\}, A')$ and $A' = A \cup \{(C, d_I, C)\}$, where d_I is a new symbol. The result easily follows. \square

4 Multi-stable Reaction Systems

In this section we introduce the notion of *multi-stable reaction systems* and then present some formal properties of such systems. We later provide an example of a bio-inspired dynamical system as a special case of multi-stable reaction systems.

Definition 1. *We say that $\mathcal{A} = (S, A)$ is a multi-stable reaction system if there are at least two different initial states such that with a constant context sequence, their corresponding interactive processes lead to distinct steady states.*

The following result proves the existence of reaction systems with any fixed number of steady states.

Lemma 4.1. *For any given set S of size n and any $0 \leq k \leq 2^n$, there exists a reaction system $\mathcal{A} = (S, A)$ with exactly k steady states.*

Proof. Let $S = \{s_1, \dots, s_n\}$ and $0 \leq k \leq 2^n$. Let T be a state transition diagram where the nodes are the 2^n subsets of S where there is a self loop on the nodes $\{s_1\}, \dots, \{s_k\}$ and the edges from all other nodes are directed to the node $\{s_1\}$. We label all the arcs with empty sets. It is shown in [7] that any finite state transition diagram can be translated to a reaction system; therefore the above mentioned diagram can be translated to a reaction system with S as its background set. Such a reaction system is a multi-stable reaction system with exactly k steady states. \square

Bistable systems, where the biological systems have the capacity to operate in two distinct modes, in a stable manner, are an example of multi-stable systems. Typically, the system can switch from one stable mode to the other in response to a specific external input. Mathematically, these bistable systems are usually described by models that exhibit two distinct stable steady states [9]. Bistability is a recurrent motif in biology, and there are many examples of systems which can operate, in a stable manner, in two very distinct modes. For instance, in the well known lac operon in the bacteria *Escherichia coli*, a group of genes are repressed in the presence of glucose and transcribed in the combined absence of glucose and presence of lactose [19, 28].

The smallest chemical reaction system with bistability is presented in [33]. It consists of the minimal number of reactants, reactions, and terms in the associated system of ordinary differential equations (ODEs). The reactions corresponding to the minimal bistable system of [33] and their corresponding ODEs are presented in Table 1. Fig. 1 illustrates the behaviour of the minimal bistable system of [33]. As it can be seen, for lower levels of the input signal S , the system has only one *base-level* steady state $x = 0$. As the level of S increases, the system undergoes a saddle-node bifurcation, which renders the system bistable. This behaviour is observable in Fig. 1 at $S = 4$: beyond that point the system has one more stable steady state in addition to $x = 0$ (as well as another unstable steady state).

The process can be reversed: for a high level of the signal strength, the system is bistable. As the signal decreases and reaches the lower saddle-node bifurcation point, the drastic jump to the lower steady-state will occur.

In this section we are proposing a counterpart in the reaction systems framework of the example in [33]. We discuss the qualitative behaviour of such a system.

We construct the RS model corresponding to the minimal reaction network of [33] by going through its reactions and introducing corresponding counterparts in the reaction system framework. We then check if this proposed model indeed exhibits a bistable behaviour. In the background set we introduce variables x ,

Table 1: The reactions and the ordinary differential equations corresponding to the minimal bistable system of [33].

Reaction	Ordinary differential equations
$S + y \xrightarrow{k_1} 2x$ (1)	$\frac{dx}{dt} = 2k_1Sy - k_x^2 - k_3xy - k_4x$
$2x \xrightarrow{k_2} x + y$ (2)	
$x + y \xrightarrow{k_3} y + P$ (3)	$\frac{dy}{dt} = k_2x^2 - k_1Sy$
$x \xrightarrow{k_4} P$ (4)	

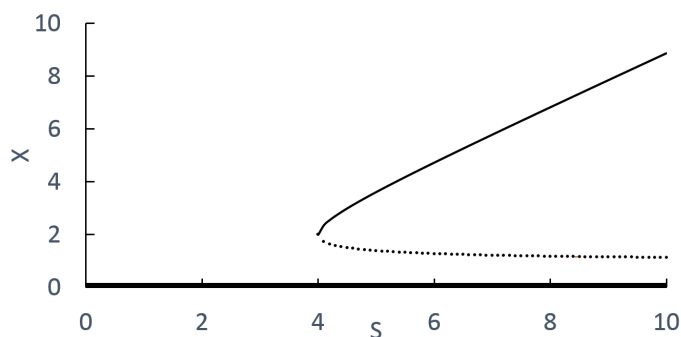


Figure 1: Minimal bistable system: The figure shows two stable steady states (solid lines) and one unstable state (dotted line).

y corresponding to the variables of the ODE-based model. We also introduce variables s , S to distinguish between low and high external signal, allowing for capturing the bistability switch. Finally, we also use (as usual in RS modeling) a dummy inhibitor variable d_I . We are ignoring variable P in our RS model. The RS reactions are presented in Table 2. A state transition diagram corresponding to this reaction system is given in Fig. 2.

Behaviour. The chemical reaction network of [33] has the following qualitative behaviour corresponding to its steady states:

- it has a single stable steady state for the small concentrations of substrate, and
- it has two stable steady states and one unstable steady state for large concentrations of substrate.

A steady state in reaction system is defined in correspondence with a specific

Table 2: The reactions in the reaction systems corresponding to the minimal bistable system of [33], the background set for the reaction systems is $\{s, S, x, y\}$.

Reactions in bistable reaction system
$(\{S, y\}, \{d_I\}, \{x\})$
$(\{x\}, \{d_I\}, \{y\})$
$(\{x, y\}, \{S\}, \{y\})$

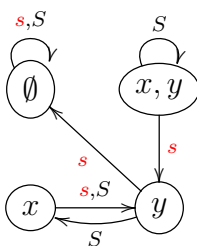


Figure 2: The state transition diagram of the RS corresponding to the minimal bistable system of [33].

context. We consider $\{s\}$ and $\{S\}$ to be two fixed contexts corresponding to the low signal and the high signal levels respectively. A state transition diagram corresponding to this reaction system is given in Fig. 2 where the labels on the arcs represent the fixed context that facilitates the transition. It is clear from the state transition diagram that a constant context sequence $\{s\}$ takes the system from any state to state \emptyset . It is also clear that under constant context sequence $\{S\}$ the system remains either in state \emptyset or in state $\{x, y\}$, showing that it has two stable steady states. As a side remark, note also that the system cycles between states $\{x\}$ and $\{y\}$ under constant context sequence $\{S\}$. This can be interpreted as correspondence to the third unstable steady state of the ODE-model under high external signal.

Lemma 4.2. *The reaction system built in this section is minimal in terms of the number of reactants needed for a multi-stable system.*

Proof. The result follows from the observation that any such system has at least two distinct steady states and consequently needs at least two distinct reactants. \square

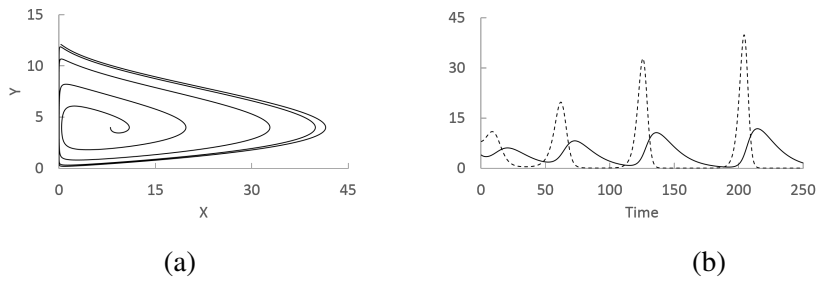


Figure 3: Limit cycle behaviour: (a) closed loop; (b) periodic oscillations.

5 Mono-stable Reaction Systems

In this section we introduce the notion of *mono-stable reaction system* and provide an example of a bio-inspired dynamical system with similar behaviour.

Definition 2. We say that $\mathcal{A} = (S, A)$ is a mono-stable reaction system if there is exactly one initial state such that for a constant context sequence, its corresponding interactive process leads to a steady state.

Note that any other initial state with a constant context sequence lead to a cycle of length greater than one. In the special cases where all these cycle are the same, the reaction system exhibits the behaviour similar to the biological systems with *limit cycle*. We formulate a definition for reaction systems with limit cycle as follows.

Definition 3. We say that $\mathcal{A} = (S, A)$ is a reaction system with limit cycle if there is exactly one initial state such that for a constant context sequence, its corresponding interactive processes leads to a steady state and all other initial states with a constant context lead to a unique cycle of length greater than one.

Being able to explain the oscillatory phenomena in biological systems makes the limit cycle one of the most interesting kinetic behaviours [11]. A cycle with length greater than one in the phase space is called a *limit cycle* (a cycle of length one is a steady state). It is known that in a dynamical system with limit cycle behaviour, there is a unique unstable steady state surrounded by stable periodic trajectories that converge to the steady state [15]. Limit cycles have proven to be useful in describing periodic processes in nature, e.g. the Lotka-Volterra system [18]. That is why finding such trajectories is an interesting subject to study [17].

Fig. 3(a) shows the typical behaviour of systems with limit cycle where all trajectories in the neighbourhood spiral towards the limit cycle. Fig. 3(b) a system with periodic behaviour.

It is known that a small modification of the numerical parameters of a dynamical system may make it switch from a bistable behaviour to one with a limit cycle,

Table 3: The reactions and the ordinary differential equations corresponding to the minimal chemical system with limit cycle of [33].

Reaction	Ordinary differential equations
$S + x \xrightarrow{k'_1} 2x$ (5)	$\frac{dx}{dt} = (k'_1 - k'_4)x - k'_2xy$
$x + y \xrightarrow{k'_2} y + P$ (6)	
$y \xrightarrow{k'_3} P$ (7)	$\frac{dy}{dt} = k'_5z - k'_3y$
$x \xrightarrow{k'_4} z$ (8)	$\frac{dz}{dt} = k'_4 - k'_5z$
$z \xrightarrow{k'_5} y$ (9)	

see [13]. Following this suggestion we build a reaction system corresponding to the chemical reaction network of Table 3 by tweaking the reaction system built in the previous section. We modify the reaction system of Table 2 by adding an inhibitor to its first reaction. The result is also presented in Table 4.

Similar to the previous section, we consider $\{s\}$ and $\{S\}$ to be two fixed contexts corresponding to the low and the high signal levels respectively. A state transition diagram corresponding to this reaction system is given in Fig. 4 where the labels on the arcs represent the fixed context that facilitates the transition. Similar to the behaviour of the chemical reaction networks with limit cycle, the constant context sequence $\{s\}$ leads to the steady state \emptyset . Under a constant context sequence $\{S\}$, our model may either end in steady state \emptyset or cycle between states $\{x\}$ and $\{y\}$.

Table 4: The reactions in the reaction systems corresponding to the minimal chemical system with limit cycle of [33], the background set for the reaction systems is $\{s, S, x, y\}$.

Reactions in reaction system with limited cycle
$(\{S, y\}, \{x\}, \{x\})$
$(\{x\}, \{d_1\}, \{y\})$
$(\{x, y\}, \{S\}, \{x\})$

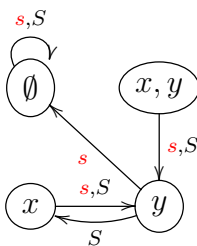


Figure 4: The state transition diagrams the RS corresponding to the minimal chemical system with limit cycle of [33].

6 Periodic Reaction Systems

In this section we introduce the notion of *periodic reaction system* and provide an example of a dynamical system with similar behaviour.

Definition 4. We say that $\mathcal{A} = (S, A)$ is a periodic reaction system if the corresponding interactive processes of all initial states for a constant context sequence lead to cycles of length equal or greater than one.

An example of periodic behaviour in nature is the period doubling bifurcation. A period-doubling is a bifurcation in which a minimal modification of a parameter value causes the system to switch to a new behaviour where the period of the system is twice as large as the original one. A period-doubling cascade is a sequence of doublings of the period, from one state to the other. For details on period-doubling bifurcation we refer to [27, 25]. Understanding the period-doubling behaviour is of utmost important since it facilitates the better explaining, and possibly controlling, the chaotic phenomena occurring in nature, see for example [14] and [32].

Fig. 5 illustrates a period-doubling bifurcation for the discrete dynamical system $x_{n+1} = r - x_n^2$ where x_0 and r belong to the intervals $[-2, 2]$ and $[0, 2]$ respectively.

The cascade of period-doubling can be viewed as a binary counter with adjustable length, i.e., for every $1 \leq i \leq n$, the period i is of length 2^i and each state of the period i is labeled with a binary number between 0 and 2^i as depicted in Fig. 6. We use this intuition in building a periodic reaction system corresponding to a dynamical system with period-doubling behaviour. In this model the change from period i to period j of the system is triggered by having trigger j introduced into the system by the context. A binary counter RS model has been introduced in [12] and our model is an extension of that model. We introduce a few new reactions to the system to have control over the length of the counter as well as to facilitate the transition from one period to the other.

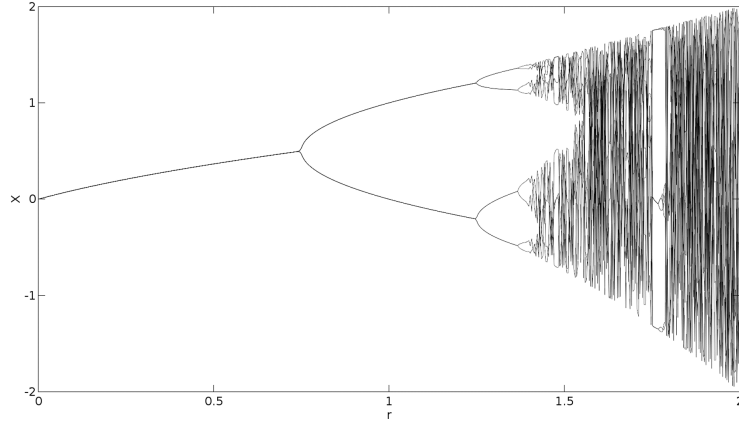


Figure 5: Period doubling cascade.

Definition 5. Let $\mathcal{A} = (S, A)$ be a reaction system such that $S = \{e_0, \dots, e_n, t, 1, \dots, n\}$, where e_0 denotes the start of the counting, e_i represents 1 on the i th position in the binary notation for some $0 \leq i \leq n$, t is the trigger for ending the counting process and $1 \leq i \leq n$ is the threshold for the binary counter. The set of reactions A is defined as:

- $a_{10} = (\{e_1\}, \{e_0, t\}, \{e_1\})$,
- $a_{ij} = (\{e_i\}, \{e_j, t, 1, \dots, i-1\}, \{e_i\})$, for all i, j such that $1 \leq j < i \leq n$,
- $b_1 = (\{e_0\}, \{e_1, t\}, \{e_1\})$,
- $b_i = (\{e_0, \dots, e_{i-1}\}, \{e_i, 1, \dots, i-1, t\}, \{e_i\})$, for all i such that $2 \leq i \leq n$,
- $r_1 = (\{e_0\}, \{t\}, \{e_0\})$,
- $r_2 = (\{e_0, t\}, \{e_1, \dots, e_n\}, \{e_0\})$,
- $l = (\{t\}, \{e_0\}, \{e_0\})$,
- $q_i = (\{e_0, \dots, e_i, i\}, \{t\}, \{t\})$, for all i such that $1 \leq i \leq n$,
- $s_i = (\{i\}, \{t, i+1, \dots, n\}, \{i\})$, for all i such that $1 \leq i \leq n$.

In the reaction system of Definition 5 reactions $a_{10}, a_{ij}, b_1, b_i, r_1, l$ and q_i for all i, j such that $1 \leq j < i \leq n$, are adopted from the reaction system of [12] with small modifications respecting the newly introduced counting upper bound in our study. This set of reactions is responsible for the binary counting as well as ending the process whenever trigger $\{t\}$ is introduced in the system.

Reaction a_{10} guarantees that if e_0 is not present, then the incrementing process is not performed, while it takes place otherwise.

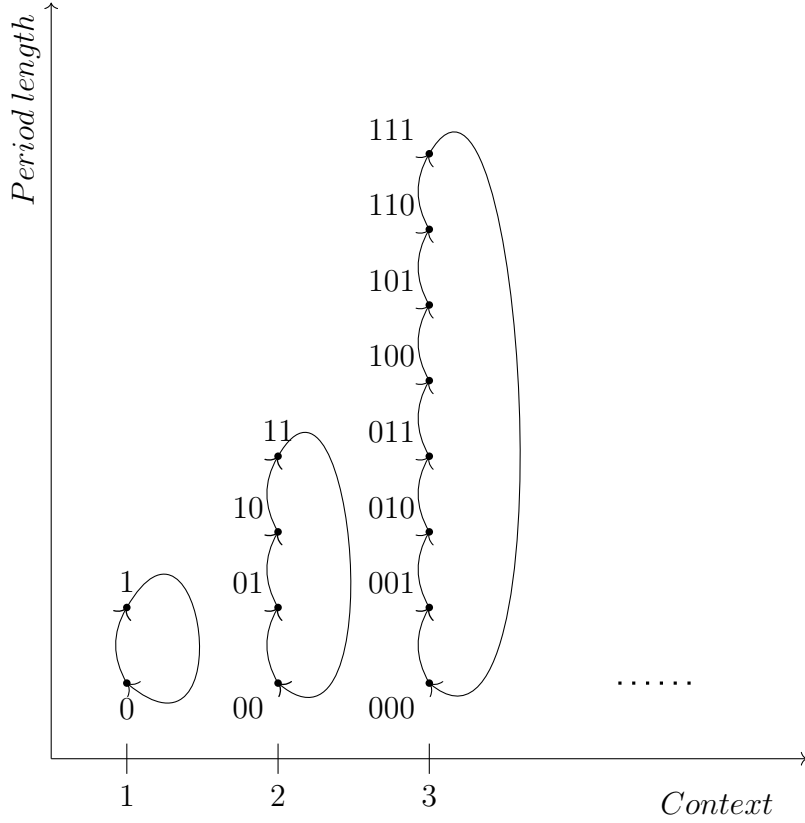


Figure 6: Period-doubling cascade illustrated as a binary counter.

For all $\{i, j\}$ such that $1 \leq j < i \leq n$, the reaction a_{ij} is defined by $a_{ij} = (\{e_i\}, \{e_j, t, 1, \dots, i-1\}, \{e_i\})$. Therefore, a_{ij} produces e_i as long as e_j and ending trigger t are not present and the counter threshold is greater than i . Thus, if a binary number has 1 on the i th position and 0 on the j th position, where $j < i$, its successor still has 1 on the i th position.

For each $2 \leq i \leq n$, the reaction b_i is defined by $b_i = (\{e_0, \dots, e_{i-1}\}, \{e_i, 1, \dots, i-1, t\}, \{e_i\})$ to produce e_i if e_i is not present while all of e_0, \dots, e_{i-1} are present. Thus, b_i inserts 1 to the i th position when 1 is added to a number that has 0 on position i and 1 on each position smaller than i , the ending trigger is not available and the counter threshold is greater than i .

Reaction l starts the counting by adding e_0 to the current state when the trigger t is introduced.

Reactions q_i , for all $1 \leq i \leq n$, stop the counter when the binary number has reached its threshold.

Reaction r_1 keeps e_0 in the system as long as t is not added to the system.

Reaction r_2 resets the system and reactions s_i , for all $1 \leq i \leq n$, are responsible for respecting the given counter upper bound as well as switching from one period to the other.

Note that for switching from one period to the other, the new upper bound (and new period) i needs to be introduced to the system through the context.

To better illustrate the behaviour of this reaction system, we provide an example here. The state sequence corresponding to the initial state $\{e_0, 3\}$ with an empty context sequence is: $\{e_0, 3\}, \{e_0, e_1, 3\}, \{3, e_0, e_2\}, \{3, e_0, e_1, e_2\}, \{3, e_0, e_3\}, \{3, e_0, e_1, e_3\}, \{3, e_0, e_2, e_3\}, \{3, e_0, e_1, e_2, e_3\}, \{3, e_0, t\}$, which, based on our defined notions, translates to the following binary sequence: 000, 001, 010, 011, 100, 101, 110, 111, 000. This sequence represents the period of length 2^3 in our period-doubling reaction system. Note that any other initial state $\{e_0, k\}$ would enter the period of length 2^k .

7 Discussion

We continued in this paper the line of research initiated in [5, 4, 3] to bring to the framework of reaction systems different modelling concepts such as mass-conservation, steady state, periodicity, elementary fluxes, invariants, stationary process, multi-stability, bifurcation. The aim of this line of research is two folded. On one hand, it aims to provide a biomodeller with a set of basic modelling tools and concepts to serve her in building and analysing a biomodel with reaction systems. There are clear advantages in using reaction systems as a modelling framework alongside traditional (both quantitative and qualitative) modelling frameworks; to mention only two: the transparent causality between events taking place in a system, and the explicit formulation of the mechanisms responsible for triggering a reaction, in terms of facilitation and inhibition. On the other hand, this line of research aims to demonstrate the surprising expressive power of reaction systems, given the elementary nature of the mathematical structures they are based on.

We demonstrated that sophisticated dynamical behaviours such as exhibiting arbitrarily many steady states, bistability, limit cycles, and period doubling can be reproduced in the reaction systems framework. Such behaviours are usually exhibited through quantitative mechanisms driven by well chosen numerical setups. We introduced in this paper natural correspondents of these concepts for reaction systems and showed that they can emerge as a result of simple reaction systems models. This is consistent with earlier results of [17, 24, 2] that such patterns may be obtained through Boolean algebra-based mechanisms. Instead we use in this paper the elementary set theoretical framework provided by reaction systems.

Acknowledgments

This work was partially funded by the Academy of Finland (project 267915), the Otto A. Malm foundation and the Oskar Öflunds stiftelse foundation.

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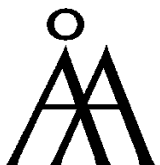
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ISBN XXX-XXX-XXX-X

ISSN 1239-1891