Theoretical Computer Science ••• (••••) •••–•••

Contents lists available at ScienceDirect

Theoretical Computer Science

www.elsevier.com/locate/tcs

Steady states of constrained reaction systems

Sepinoud Azimi

Computational Biomodelling Laboratory, Åbo Akademi University and Turku Centre for Computer Science (TUCS), Turku, Finland

ARTICLE INFO

Article history:
Received 23 November 2016
Received in revised form 20 March 2017
Accepted 24 March 2017
Available online xxxx

Keywords:
Reaction system
Steady states
Constrained reaction systems
Reactant minimal
Inhibitor minimal
Product minimal
Maximally inhibited

ABSTRACT

Reaction systems, a mathematical formalism inspired by the mechanisms within a biological cell, focuses on an abstract set-based representation of chemical reactions via facilitation and inhibition. The simple yet elegant nature of reaction systems makes them ideal tools for analysing qualitatively the phenomena which typically are dealt with quantitatively. Steady states are one of the well studied and important subjects across various fields of science ranging from biology, to chemistry, to engineering and economics. Finding all steady states of an arbitrary reaction system has been shown to be an NP-complete problem. We study reaction systems with a small number of reactants and inhibitors and we propose an algorithm to list all steady states of such reaction systems. We also show that the complexity of such an algorithm is polynomial. This reduction in complexity opens a door to transform modelling with reaction systems from an abstract concept to a tool that can be used on real-life case studies.

1. Introduction

Reaction systems, first introduced in [16], is a qualitative framework inspired by the two main cellular regulation mechanisms, *facilitation* and *inhibition* which control the interaction between biochemical 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 $a = (R_a, I_a, P_a)$ where R_a represents the set of reactants, I_a the set of inhibitors and P_a the set of products corresponding to reaction a. This definition is well supported by how a biochemical reaction functions, i.e. when all reactants are available to facilitate triggering a reaction and there is nothing in the environment to inhibit such a triggering, the reaction transforms its set of reactants to the corresponding set of products.

The two main assumptions considered in reaction systems framework are as follows:

- *Threshold assumption:* indicates 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 reaction systems framework and as a result reaction systems are qualitatively analysed rather than quantitatively.
- *No permanency assumption:* assumes that an element vanishes from the environment if no reaction is triggered to preserve it.

Research done in the field of reaction systems has proven to be very versatile and promising, see for example [9,14,15,17,10,11,6,25]. The simple, yet expressive nature of this framework has attracted researchers from both theoretical and practical

E-mail address: sazimi@abo.fi.

http://dx.doi.org/10.1016/j.tcs.2017.03.047
0304-3975/

Please cite this article in press as: S. Azimi, Steady states of constrained reaction systems, Theoret. Comput. Sci. (2017), http://dx.doi.org/10.1016/j.tcs.2017.03.047

areas of science to focus on studying and analysing reaction systems. One of the main lines of such efforts focuses on laying a theoretical ground for the application of reaction systems to real world problems. A series of studies was initiated to formalise several properties of central interest in biomodelling and to study the computational complexity of deciding those properties, such as mass conservation, invariants, steady states, stationary processes, elementary fluxes, and periodicity, for more information see [5,4,3,7].

A system is said to be in a steady state if it does not experience any changes over time when in that state [19]. Studying steady states is a relevant topic in many fields of science ranging from biology (e.g., steady-state cancer treatment [21]), to chemistry (e.g., calculating the critical load of acidity for forest soils [26]), to electrical and mechanical engineering (e.g., voltage stability analysis [2]) to physiology (e.g., plant stress physiology [20]) and economics (e.g., stock market studies [1]).

In [3] it is shown that for a given reaction system, the complexity of deciding if there exists a non-empty steady state is an NP-complete problem. This property holds for reactions systems with an arbitrary number of reactions, however, in real life case-studies the number of reactants and reactions of a system is very often limited. This paper focuses on studying reaction systems with some level of constraints. We study the reaction systems with a small number of reactants and inhibitors. This is motivated by kinetical considerations of biochemical reactions suggesting that reactions typically have only a small number of reactants and inhibitors. Moreover, this constraint reduces complexity of deciding the existence of steady states.

This paper is structured as follows. In Section 2 we introduce some basic definitions of reaction systems. In Section 3 we introduce constrained reaction systems and discuss results related to the steady states of such systems. We summarise our result in Section 4.

2. Preliminaries

In this section we recall some of the basic definitions of reaction systems and introduce some new ones that we need throughout the paper. We denote sets with capital letters, the operation of set difference with $-$ and the cardinality of any set A with $|A|$.

Reactions are the building blocks of a reaction system. Intuitively, a reaction is triggered if all reactants needed for the reaction are available in the environment and there exist no reactants that inhibit the reaction. In this case, the reaction transforms the set of reactants to the set of products. This intuition is formally captured in the definition of a reaction in the reaction systems framework as follows, see [16,8] for more details.

Definition 2.1 *(Reactions).* [16] A *reaction* is a tuple $a = (R_a, I_a, P_a)$, where R_a, I_a and P_a are finite, non-empty sets and $R_a \cap I_a = \emptyset$. The sets R_a, I_a and P_a are called the set of *reactants*, *inhibitors* and *products* of a, respectively. We say a is a reaction over set S, if $R_a, I_a, P_a \subseteq S$. We denote the set of reactions in S by $\mathrm{rac}(S)$.

We next define the result of applying a reaction and a set of reactions on a given set. In this definition the result of applying a number of reactions to a set is the collective result of applying each reaction to the set independently. Indeed this is true because by the *threshold assumption* there is no competition for resources between different reactions and hence running a reaction does not prevent the application of any other one.

Definition 2.2 *(Reaction systems).* [16] Let A be a set of reactions, $a \in A$ and W a set.

(i) The *result* of a on W, denoted by $\mathrm{res}_a(W)$, is

$$\mathrm{res}_a(W) = \begin{cases} P_a, & \text{if } R_a \subseteq W \text{ and } I_a \cap W = \emptyset \\ \emptyset, & \text{otherwise.} \end{cases}$$

(ii) The *result of A on W*, denoted by $\mathrm{res}_A(W)$, is

$$\mathrm{res}_A(W) = \bigcup_{a \in A} \mathrm{res}_a(W).$$

A reaction a is *enabled* by W if $R_a \subseteq W$ and $I_a \cap W = \emptyset$, a is not enabled by W otherwise.

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

To capture the dynamics of a given reaction system the notion of *interactive process* has been introduced in [16]. In this study we are interested in the sequences such processes produce, i.e., *state sequences*. In what follows we present the formal definitions of interactive processes, state sequences and *context sequences*. Intuitively context sequences represent the changes enforced by the environment on a biochemical system.

Please cite this article in press as: S. Azimi, Steady states of constrained reaction systems, Theoret. Comput. Sci. (2017), http://dx.doi.org/10.1016/j.tcs.2017.03.047