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FACULTY OF MATHEMATICS AND COMPUTER SCIENCE
SPECIALIZATION [Secție]

DIPLOMA THESIS

[Titlu lucrare]

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ABSTRACT

Abstract: un abstract in engleza one in romanian un rezumat în limba engleză

cu prezentarea, pe scurt, a conținutului pe capitole, punând accent pe contribuțiile proprii și originalitate

Contents

1 Introduction **1**

2 Introduction to Chemical Reaction Networks **2**

3 Dynamical Systems **3**
3.1 Defining Ordinary Differential Equations 3
3.2 Forming Ordinary Differential Equation systems 4
3.3 Applications of dynamical systems and classifications 4

4 Existence and Absence of Hopf Bifurcation in Phosphorylation–Dephosphorylation CRN **5**
4.1 What is a Phosphorylation–Dephosphorylation CRN? 5
4.2 What is a Hopf Bifurcation? 5
4.3 Putting them together 5

5 CoNtRoL Simulations Web Application **6**
5.0.1 Overview of the technologies 6
5.0.2 Running it 6
5.0.3 The bottom line 11

Bibliography **12**

Chapter 1

Introduction

Introducere: obiectivele lucrării și descrierea succintă a capitolelor, prezentarea temei, prezentarea contribuției proprii, respectiv a rezultatelor originale și menționarea (dacă este cazul) a sesiunii de comunicări unde a fost prezentată sau a revistei unde a fost publicată.

Chapter 2

Introduction to Chemical Reaction Networks

Chapter 3

Dynamical Systems

3.1 Defining Ordinary Differential Equations

Definition 1. *An **ordinary differential equation** is an equation of an unknown function of one variable. This can be expressed as a function **of** this unknown function and its various derivatives.*

Its general form looks something like:

$$F(t, y(t), y'(t), ..., y^{(n)}(t)) = 0, \tag{3.1}$$

Where $y(t)$ is the unknown function of independent variable t and $F : \Omega \to \mathbb{R},\ \Omega \subseteq \mathbb{R}^{n+1}$.
This would be what's called the implicit form of the differential equation.

Definition 2. *The **order** of an ODE is the highest order of the derivative present in the equation.*

In our case, the order is n. If, however F satisfies the regularity condition **of the implicit function theorem** then the equation can be written in a much more digestible form.

The **implicit function theorem** allows one to convert a relation (implicit form) to functions of some variables. These functions may not be unique, but togather, their graph may locally satisfy the relation.
As an example: The relation for a cardiod cannot be expressed as a sole function, we'd instead need the union of the graph of two separate functions for expressing it. (si aici gen faci tu niste graphuri cu maple sau alte d-astea vezi cum faci virtual machineu ala sau mergi la faculta la un pc cu maple si iti faci lista cu ce vrei sa graphuiesti)

Reminder: A function $f(x)$ is continuously differentiable if $\exists f'(x)$ and $f'(x) \in C^n$ where $n >= 0$

Theorem 1. Let $F : D \subseteq \mathbb{R}^{n+1} \to \mathbb{R}$ be a continuously differentiale function with the relation that $F(t, y(t), y'(t), ..., y^{(n)}(t)) = 0$. Let us express a point in the set $\mathbb{R}^{n+1} = \mathbb{R} \times \mathbb{R}^n$ as (t, **Y**) = $(t, y, y', \ldots, y^{(n)})$ and fix one such point s.t. $F(t, \mathbf{Y}) = 0$. So $\exists \square_{(t,\mathbf{Y})} \ni U \times V \subseteq D$ s.t. $F \in C^1(U \times V)$ and $\frac{\partial F}{\partial y}(t, \mathbf{Y}) \neq 0$. Then this means $\exists \square_t \ni U_0 \subseteq U, \square_{\mathbf{Y}} \ni V_0 \subseteq V$ and a function $f : U_0 \to V_0$ s.t. $f(t) = \mathbf{Y}$ and $F(t, f(t)) = 0, \forall t \in U_0; f \in C^1(U_0)$ and $\frac{\partial f}{\partial t_i} = -\frac{\frac{\partial F}{\partial t_i}(t, f(t))}{\frac{\partial F}{\partial y}(t, f(t))}, \forall i = \overline{1, n}, \forall t \in U_0$ and $F \in C^1(U \times V), K \in N^* \Rightarrow f \in C^K(U_0)$.

So restricting the domain Ω to one that allows the implicit form to be represented as a function of the form

$$y^{(n)}(t) = f(t, y(t), y'(t), ..., y^{(n-1)}(t)) \tag{3.2}$$

would yield what's called the **explicit** form of the ODE.

A **solution** is an expression of the unknown function $y(t)$ which satisfies the relation $y^{(n)}(t) = f(t, y(t), y'(t), \ldots, y^{(n-1)}(t))$. A **general solution** includes all of these functions and usually has some constants of integration in the expression, while a **particular solution** doesn't have them. A particular solution is usually found if we also have some initial conditions given for the unknown function, like $y(a) = b, y'(a) = c$ for some $a, b, c \in \mathbb{R}$. Or, more formally:

Definition 3. A function $y : I \to \mathbb{R}$ is a solution of the equation 3.1 if the following conditions are met:

1. $I \subseteq \mathbb{R}$ is nondegeneate interval. ($|I| > 1$)
2. $y \in C^n(I)$ and $(t, y(t), y'(t), \ldots, y^{(n)}(t)) \in D_f, \forall t \in I$.
3. $y^{(n)}(t) = f(t, y(t), y'(t), \ldots, y^{(n-1)}(t)), \forall t \in I$. (3.2 is satisfied)

3.2 Forming Ordinary Differential Equation systems

We may take a sequence of such oradinary differential equationsin order to form a system:

$$\{ y'_1(t) = f_1(t, y_1(t), y_2(t), \ldots, y_n(t)) y'_2(t) = f_2(t, y_1(t), y_2(t), \ldots, y_n(t)) \vdots y'_n(t) = f_n(t, y_1(t), y_2(t), \ldots, y_n(t))$$

3.3 Applications of dynamical systems and classifications

Chapter 4

Existence and Absence of Hopf Bifurcation in Phosphorylation–Dephosphorylation CRN

4.1 What is a Phosphorylation–Dephosphorylation CRN?

4.2 What is a Hopf Bifurcation?

4.3 Putting them together

Chapter 5

CoNtRoL Simulations Web Application

Here we will present the open-source Web application developed for easing work involving chemical reaction networks, hopefully for students and researchers one day. It can be used for obtaining numerical analysis of chemical reaction networks, as well as plotting species against time, one another and so on. We'll present the technologies used throughout the project, how to run it locally and a couple of usage examples involving what we've presented in the previous chapters.

5.0.1 Overview of the technologies

The website is a back-end application built in **Python**, a programming language known for its use in basically every single science, including natural sciences so it's a no-brainer when in comes to plotting. The web server is built using **Flask**, a lightweight web app framework and the webpages served are server-side rendered by Flask's template engine depedency - **Jinja**.

The crux of the functionality is aided by the Python library **Tellurium**; which is, as their docs say; "A Python Environment for Reproducible Dynamical Modeling of Biological Networks". It uses a subset of the Systems Biology Markup Language (**SBML**) called **Antimony** which can be used in this app to create a Chemical Reaction Network, as well as the friendlier selects form. So the bits doing the magic are the calls to `road_runner.loada()` which are used to ***load*** **a**ntimony code into the model. the `road_runner..simulate()` function is then used for running and obtaining sumulation data, followed by `road_runner.plot()`, which in turn calls a `matplotlib` headless backend for writing the plotted results to a file.

5.0.2 Running it

As explained in the `README` of the project, running locally is done automatically by the `run_script.sh`, which figures out your machine's local IP, sets the required environment variables and runs `flask --debug run --host="$ip"`. Output regarding traffic to the server as well as internal workings of the app will now be redirected to `stdout` of the terminal.

All the user has to do beforehand is:

- clone the project

```
git clone https://github.com/viktorashi/Open-CoNtRol.git
```

- change **d**irectory into it.

```
cd Open-CoNtRol
```

- install the requirements

```
pip install -r requirements.txt
```

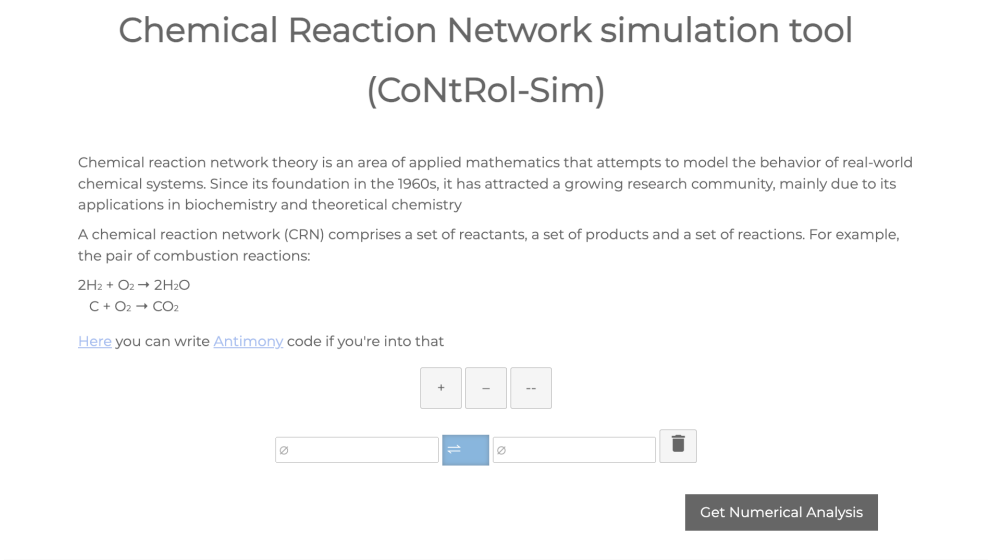
- give the `run_script.sh` execute permissions

```
chmod +x ./run_script.sh
```

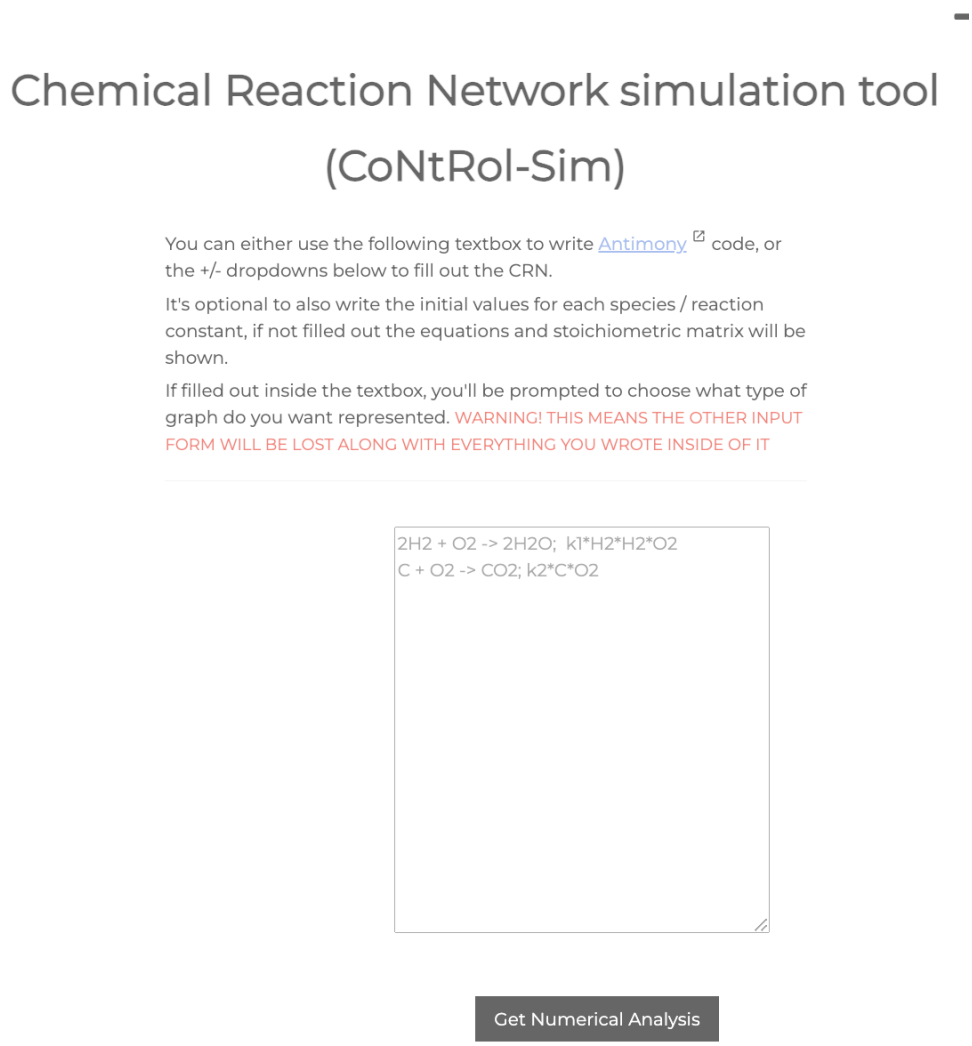
- and finally run it

```
./run_script.sh
```

Among the wall of output will also be the line showing the address your server is located at, for example: `* Running on http://192.168.0.94:5000`, address at which you'll be greeted with this screen



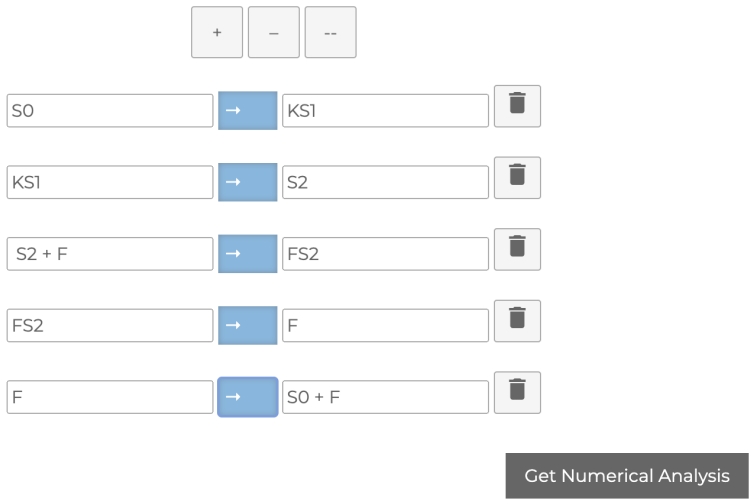
You can either use this as a starting point or the page located at the `/antimony` path:



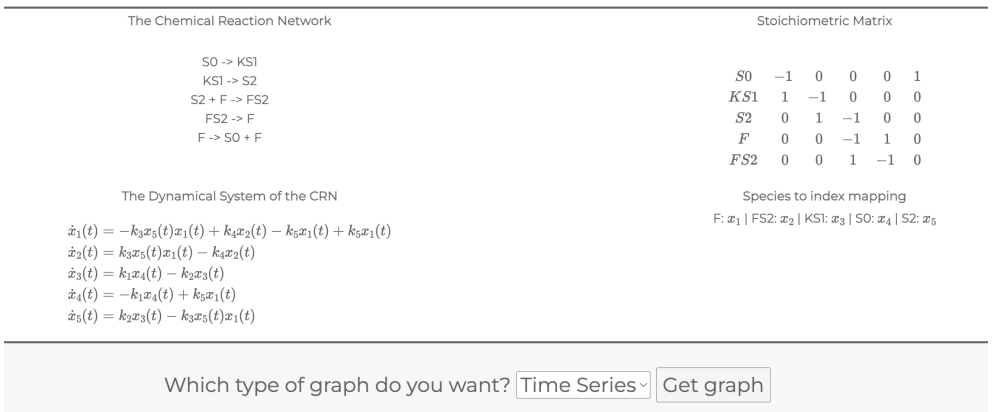
Both of these redirect to `/numerical_analysis` analysing the system ... well, numerically. As an example, this Antimony code:

```
S0 -> KS1; k1*S0
KS1 -> S2; k2*KS1
S2 + F -> FS2; k3*S2*F
FS2 -> F; k4*FS2
F -> S0 + F; k5*F
```

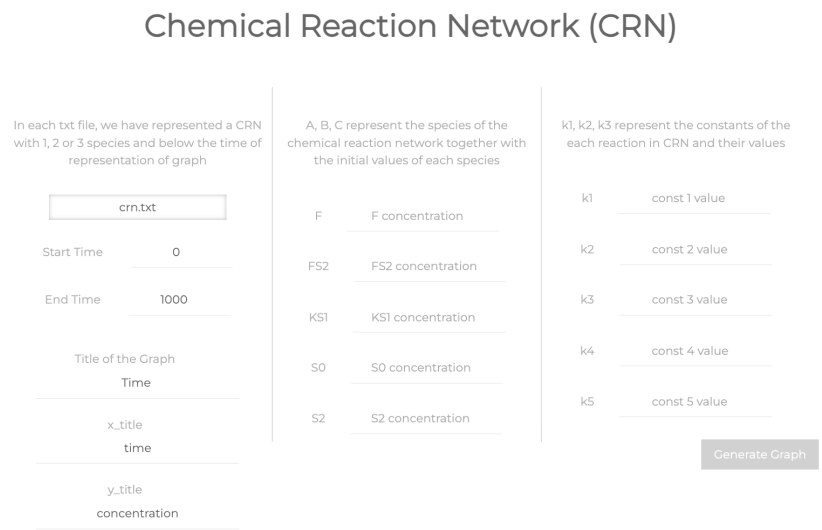
and its longer to write alternative:



both yield the same numerical analysis results:



from here, one can choose from a selection of graphs they can represent given this system, the default one being the time series representation:

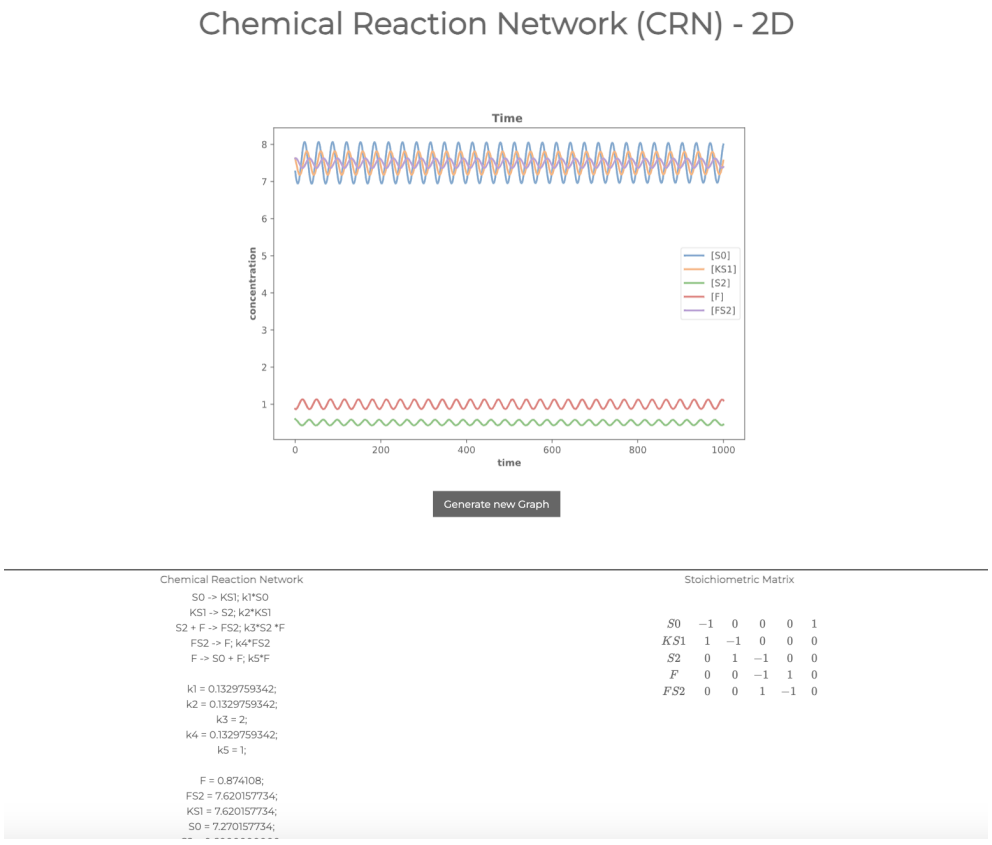


from which we fill out the initial values of the concentrations for each species as, well as the reaction rates. So given, for example the values:

```
F = 0.874108
FS2 = 7.620157734
KS1 = 7.620157734
S0 = 7.270157734
S2 = 0.6000000000

k1 = 0.1329759342
k2 = 0.1329759342
k3 = 2
k4 = 0.1329759342
k5 = 1
```

outcomes the graph:



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5.0.3 The bottom line

So this is how the workflow of the app typically goes.

write out your system → get numerical analysis → choose your desired graph *fill out data values*

Voilà

Bibliography