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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

Chapter 1

Introducere

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 ODEs

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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?

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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
```

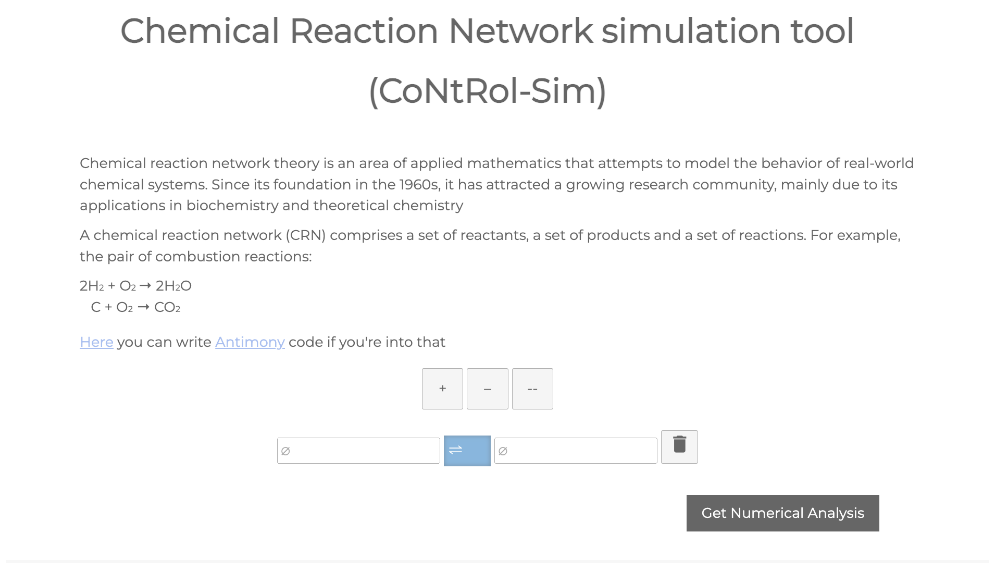
- give the `run_script.sh` execute permissions

```
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



Chemical Reaction Network simulation tool (CoNtRol-Sim)

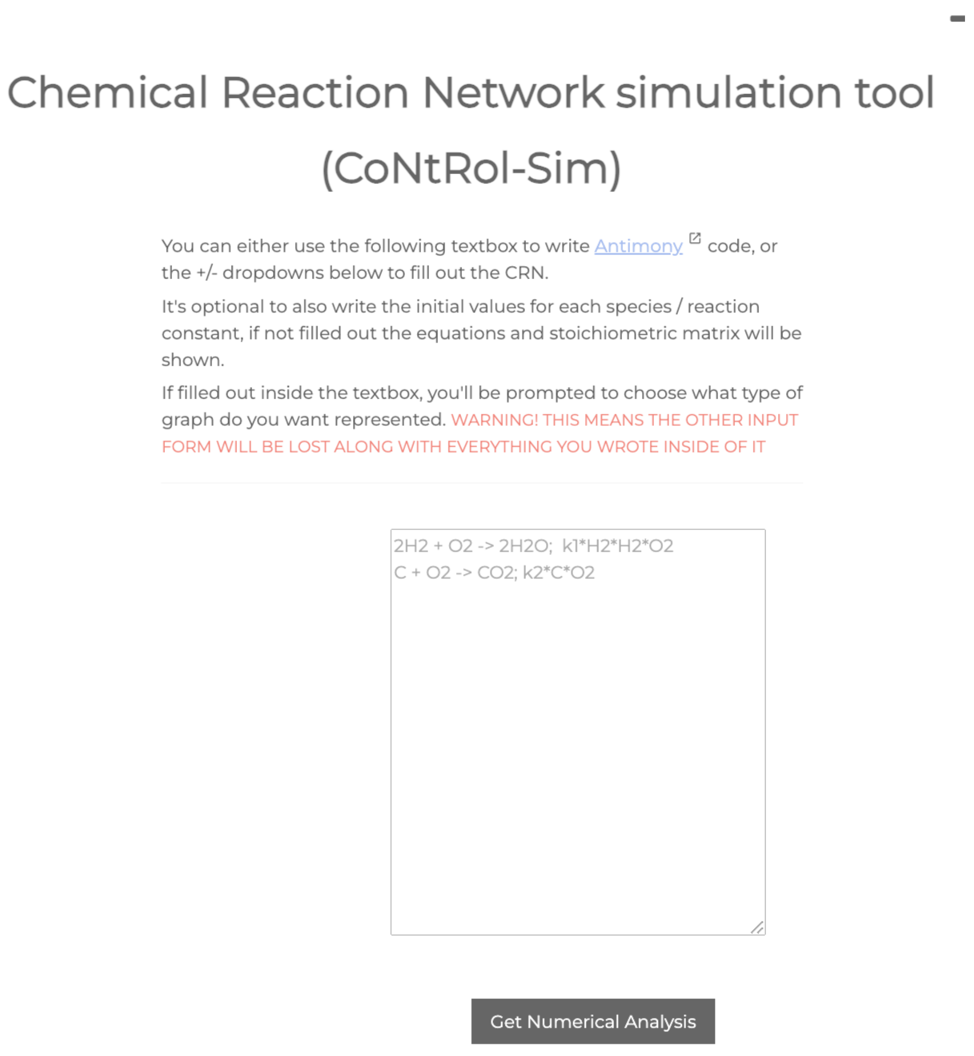
Chemical reaction network theory is an area of applied mathematics that attempts to model the behavior of real-world chemical systems. Since its foundation in the 1960s, it has attracted a growing research community, mainly due to its applications in biochemistry and theoretical chemistry

A chemical reaction network (CRN) comprises a set of reactants, a set of products and a set of reactions. For example, the pair of combustion reactions:

$2H_2 + O_2 \rightarrow 2H_2O$
$C + O_2 \rightarrow CO_2$

Here you can write Antimony code if you're into that

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


Chemical Reaction Network simulation tool (CoNtRol-Sim)

You can either use the following textbox to write Antimony code, or the +/- dropdowns below to fill out the CRN.

It's optional to also write the initial values for each species / reaction constant, if not filled out the equations and stoichiometric matrix will be shown.

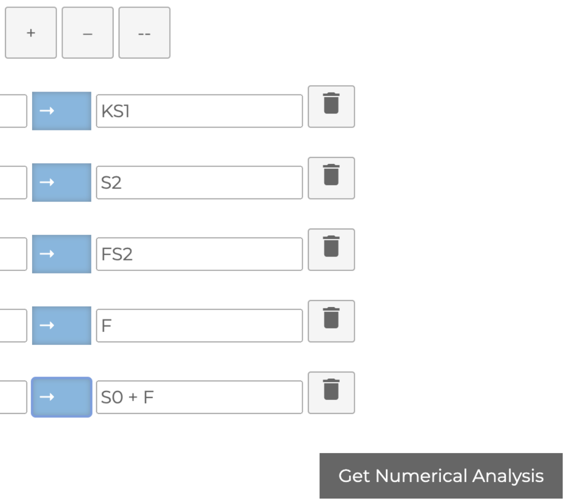
If filled out inside the textbox, you'll be prompted to choose what type of graph do you want represented. WARNING! THIS MEANS THE OTHER INPUT FORM WILL BE LOST ALONG WITH EVERYTHING YOU WROTE INSIDE OF IT

```
2H2 + O2 -> 2H2O;  k1*H2*H2*O2
C + O2 -> CO2; k2*C*O2
```

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

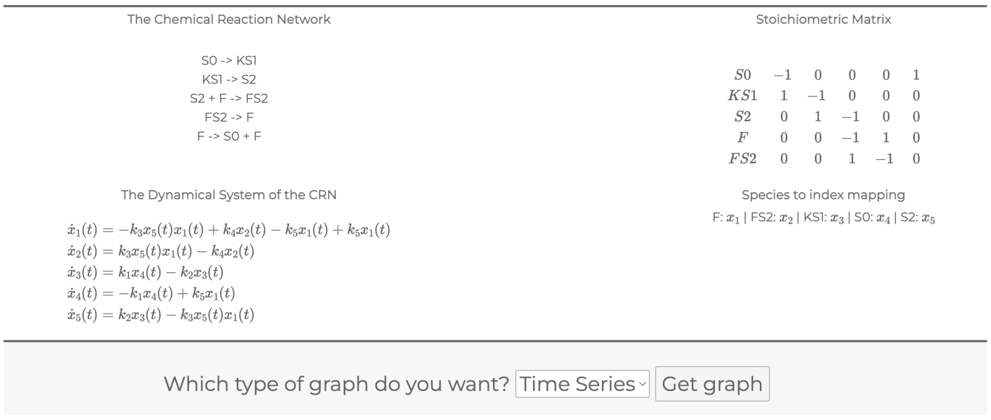
```
S0 -> KS1; k1*S0
KS1 -> S2; k2*KS1
S2 + F -> FS2; k3*S2*F
FS2 -> F; k4*FS2
F -> S0 + F; k5*F
```

and its longer to write alternative:



S0	KS1
KS1	S2
S2 + F	FS2
FS2	F
F	S0 + F

both yield the same numerical analysis results:



The Chemical Reaction Network

S0 -> KS1
KS1 -> S2
S2 + F -> FS2
FS2 -> F
F -> S0 + F

Stoichiometric Matrix

$$\begin{array}{cccccc} S0 & -1 & 0 & 0 & 0 & 1 \\ KS1 & 1 & -1 & 0 & 0 & 0 \\ S2 & 0 & 1 & -1 & 0 & 0 \\ F & 0 & 0 & -1 & 1 & 0 \\ FS2 & 0 & 0 & 1 & -1 & 0 \end{array}$$

The Dynamical System of the CRN

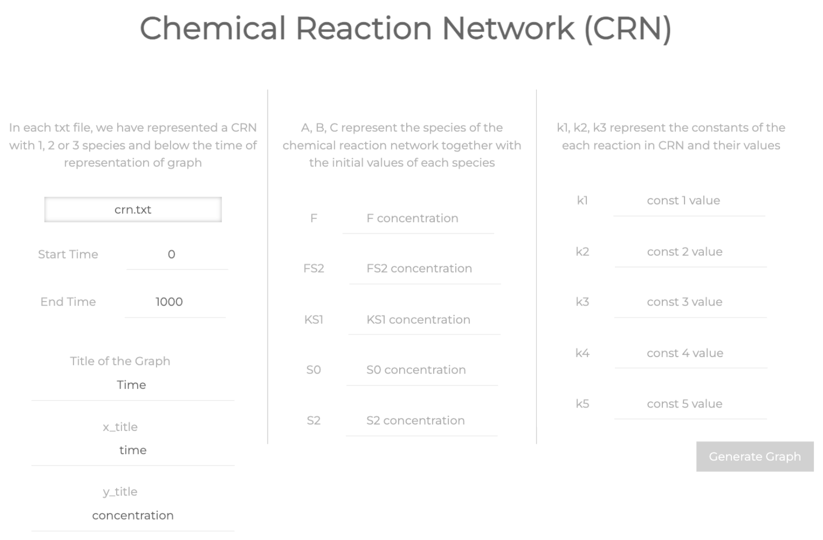
$$\dot{x}_1(t) = -k_3x_5(t)x_1(t) + k_4x_2(t) - k_5x_1(t) + k_5x_1(t)$$
$$\dot{x}_2(t) = k_3x_5(t)x_1(t) - k_4x_2(t)$$
$$\dot{x}_3(t) = k_1x_4(t) - k_2x_3(t)$$
$$\dot{x}_4(t) = -k_1x_4(t) + k_5x_1(t)$$
$$\dot{x}_5(t) = k_2x_3(t) - k_3x_5(t)x_1(t)$$

Species to index mapping

F: x_1 | FS2: x_2 | KS1: x_3 | S0: x_4 | S2: x_5

Which type of graph do you want? Time Series

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



Chemical Reaction Network (CRN)

In each txt file, we have represented a CRN with 1, 2 or 3 species and below the time of representation of graph

crn.txt

Start Time	0
End Time	1000

Title of the Graph
Time

x_title
time

y_title
concentration

A, B, C represent the species of the chemical reaction network together with the initial values of each species

F	F concentration
FS2	FS2 concentration
KS1	KS1 concentration
S0	S0 concentration
S2	S2 concentration

k1, k2, k3 represent the constants of the each reaction in CRN and their values

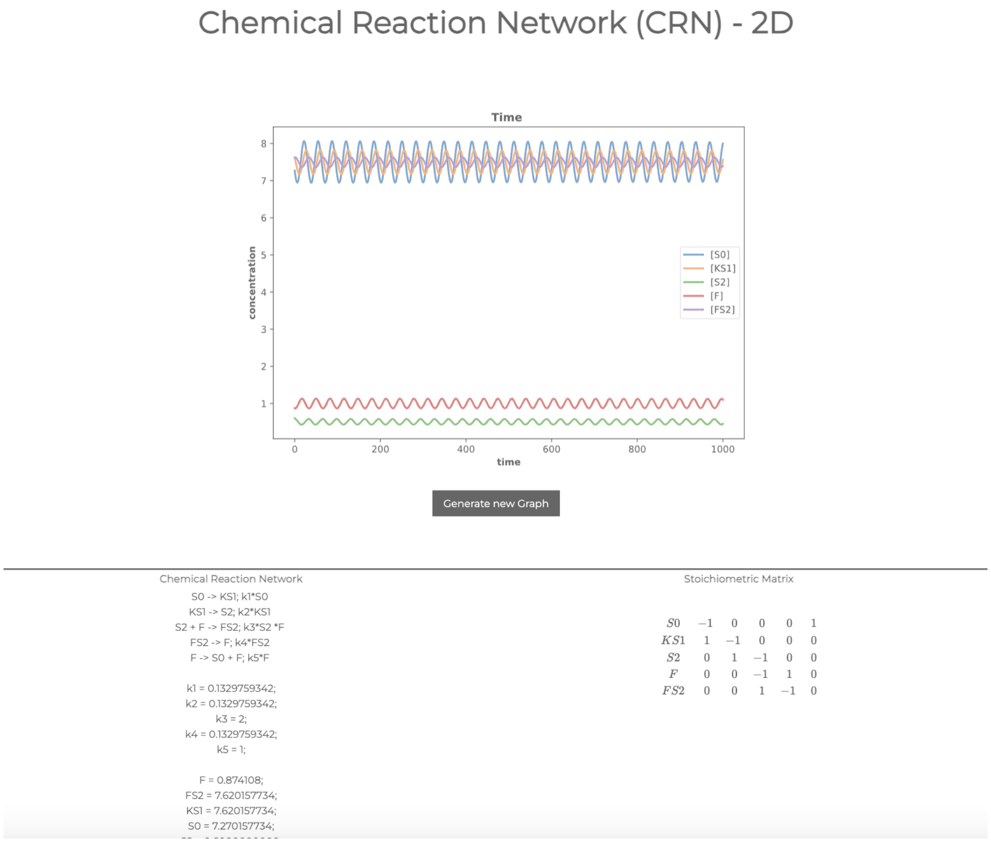
k1	const 1 value
k2	const 2 value
k3	const 3 value
k4	const 4 value
k5	const 5 value

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:



Chemical Reaction Network

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

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

F = 0.874108;
FS2 = 7.620157734;
KS1 = 7.620157734;
S0 = 7.270157734;
```

Stoichiometric Matrix

$$\begin{array}{cccccc} S0 & -1 & 0 & 0 & 0 & 1 \\ KS1 & 1 & -1 & 0 & 0 & 0 \\ S2 & 0 & 1 & -1 & 0 & 0 \\ F & 0 & 0 & -1 & 1 & 0 \\ FS2 & 0 & 0 & 1 & -1 & 0 \end{array}$$

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5.0.3 The bottom line

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

$$\begin{tikzcd} \textit{write out your system} \arrow[r] & \textit{get numerical analysis} \arrow[r] & \textit{choose your desired graph} \arrow[d, bend left, "\textit{fill out data values}"] \\ & & \textbf{Voilà} \end{tikzcd}$$

Bibliography