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CS 6760 Project Intermediate Report #2

Rule Based Models

Since the last report I have made some progress but nothing earth shattering. My GitHub is <https://github.com/s-n-p/RuleBasedModels> and it contains many of the files and programs I am using. At the last report I was having trouble producing a valid sbml file that libSBML could read. With help from Jim I have solved that problem and have a correctly formatted sbml file. Using libSBML I have been able to validate the model and also get some basic information. It has taken some time to understand the methods and classes of libSBML but I finally have some output. I have printed the list of species for the MM model:

<Species S1 "E(s)">

<Species S2 "S(Y~0)">

<Species S3 "E(s!1).S(Y~0!1)">

<Species S4 "S(Y~P)">

I also have a list of rules and reactions:

Rule 1, formula: SU = 0 + S2

Rule 2, formula: SP = 0 + S4

Rule 3, formula: ES = 0 + S3

Rule 4, formula: Etot = S1 + S3

Reaction 1, formula: kp1 \* S1 \* S2

Reaction 2, formula: ksyn

Reaction 3, formula: kdeg \* S1

Reaction 4, formula: km1 \* S3

Reaction 5, formula: k2 \* S3

As well as parameters of the model:

<Parameter NA>

<Parameter V>

<Parameter km1>

<Parameter k2>

<Parameter kdeg>

<Parameter kp1>

<Parameter ksyn>

<Parameter E0>

<Parameter S0>

<Parameter SU>

<Parameter SP>

<Parameter ES>

<Parameter Etot>

The next steps I am working on are to extract the stoichiometry and parameter values. After that I hope to be able to start coding the mathematics of the model. I will likely need to meet with you to discuss the best options for the modeling. The Markovian models we have been discussing recently in class might work well.

The combinatorial complexity of some biological circuits can become intractable. One method that has been presented to solve this synthetic biology problem is rule-based modeling. A rule based model defines a set of rules for the molecules within the biological system. For example, a molecule X could have two different binding sites with rules defining how and when it is able to bind with other molecules. The rule will define what conditions are necessary for a molecule to bind with X and at what rate the reaction happens. For example, X might bind with Y if phosphorous is present but will bind with Z when phosphorous is not present. In this way a rule-based model defines rules for how each molecule in a system interacts with other molecules. In this framework it is possible to keep track of the state of the molecule.

The ultimate goal of my project is to create software to analyze and simulate a rule-based biological model. This is an ambitious project so some time will be necessary to understanding the SBML of rule-based models and learning the Libsbml python package in addition to the coding of the model simulation. I will use the following steps to guide me:

Step 1 – Try to create a simple rule-based model using current software such as BioNetGen or Kappa. Use the softwre to simulate the biological circuit to understand how it works.

Step 2 – Export the SBML file and import it into python using the libsbml python library.

Step 3 – Become familiar with the internal libsbml methods and how to use them. One example of this is to iterate through the rules and molecules of the model and print them out.

Step 4 – This step is to implement the necessary algorithms for analysis and simulation of the model. Ideally there will be graphs produced to visualize the circuit and the activity of the molecules, similar to what we have done before. This step will become more defined as I learn more about libsbml and the sbml for rule-based models.