

CS6280 Special Topics in Computer Science: Computational Systems Biology

A Very Brief SimBiology Primer

SimBiology

SimBiology is an integrated environment for modeling biological processes, and analyzing the models with simulation and experimental data. It is a toolbox add-on to MaATLAB, and hence is able to use other tools provided by MATLAB.

SimBiology has its own graphical user interface (GUI), allowing users to add biochemical reactions and species into their pathways easily. It can also import and export models specified using SBML [1] – an information standard for sharing, evaluating, and developing systems biology models cooperatively.

Biological models in SimBiology can be created in 2 ways, either using the graphical user interface, or using the command line interface for model creation.

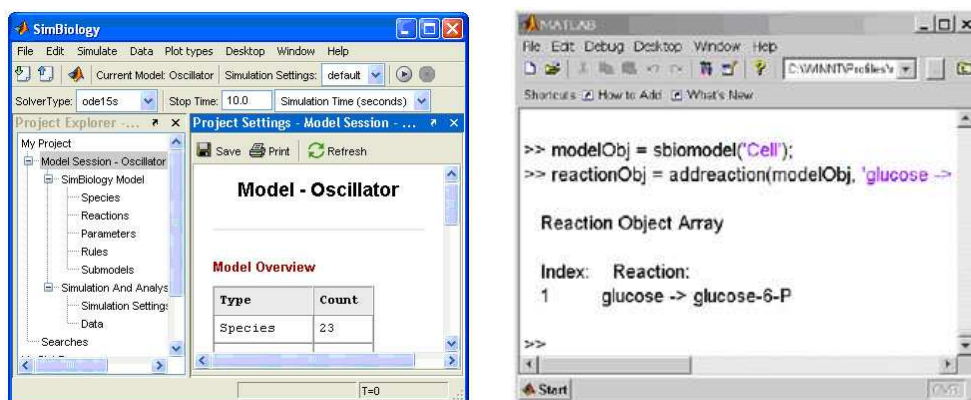


Figure 1 – The Graphical User Interface and command line for model creation

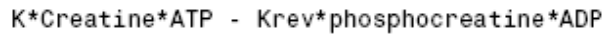
Modeling

SimBiology is organized as a hierarchical list of objects under one root object. The root is a model, which essentially is a collection of interrelated reactions and rules that acts on species (biological entities such as proteins, mRNA, ligands etc.). The models can be divided into different modules in a hierarchical manner.

A reaction describes a transformation, transport, or binding process that changes the concentration of one or more species, such as the reaction shown below.



Each of these reactions has a rate equation that is a mathematical expression that describes the rate at which the reactants combine to form products. For example, the rate equation for the above reaction can be expressed as below.



Where K and Krev are the rate parameters that will affect how fast the reaction will run. In the next section, we will model a simple network using the graphical user interface.

Gene Regulation Model

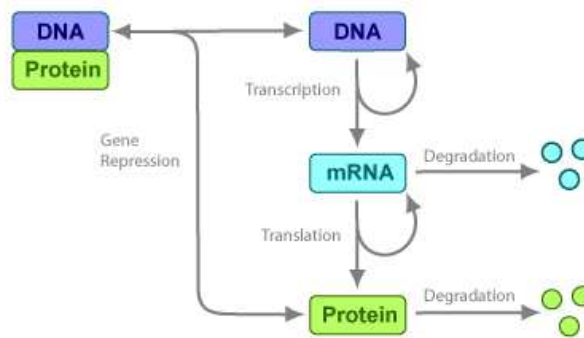


Figure 2 – Simple gene regulation model

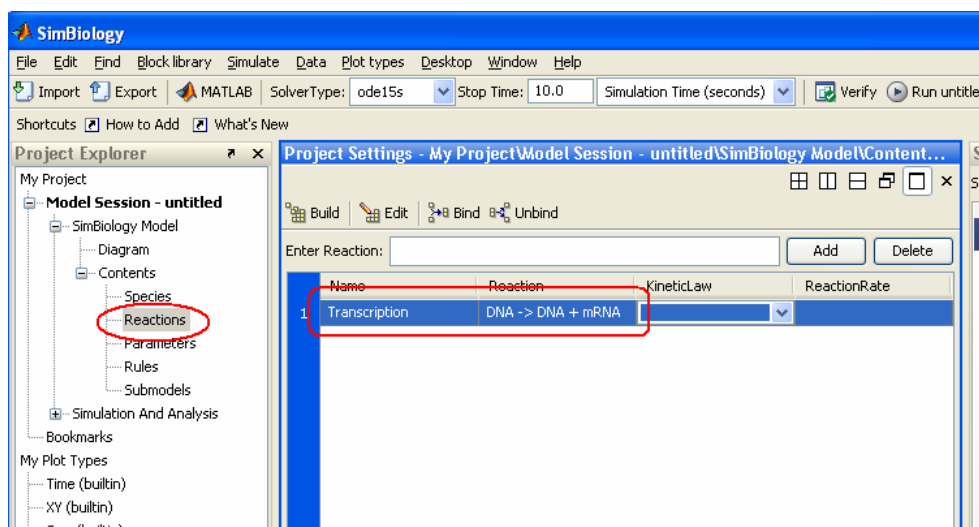
- 1 Open the SimBiology desktop window by typing in the following command in the MATLAB Command Window

```
>> sbiodesktop
```

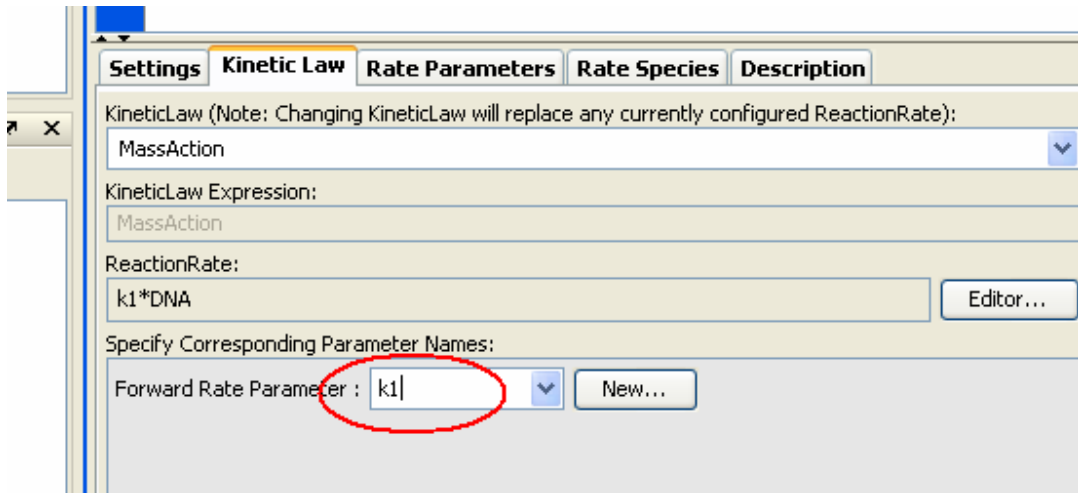
- 2 In the **Project Explorer**, double click the **Reactions** to open the Reactions pane. Enter in the following reaction in the **Enter Reaction** box, click **Add**

DNA -> DNA + mRNA

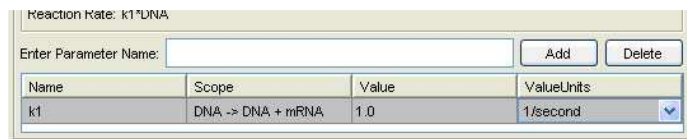
Double click the Name box and name it “**Transcription**”.



Select **MassAction** from the Kinetic Law drop down list. Under the **Kinetic Law** tab, enter **k1** as the **Forward rate parameter**, press Enter. Note that SimBiology updates the Reaction Rate to show $k_1 * \text{DNA}$



- Click on the Rate Parameters tab. Notice that SimBiology lists k1 with a default value of 1.0 for the parameter. Change the **ValueUnits** to 1/second (You may have to type it in if it's not present in the drop down list) and the value to be 0.2.



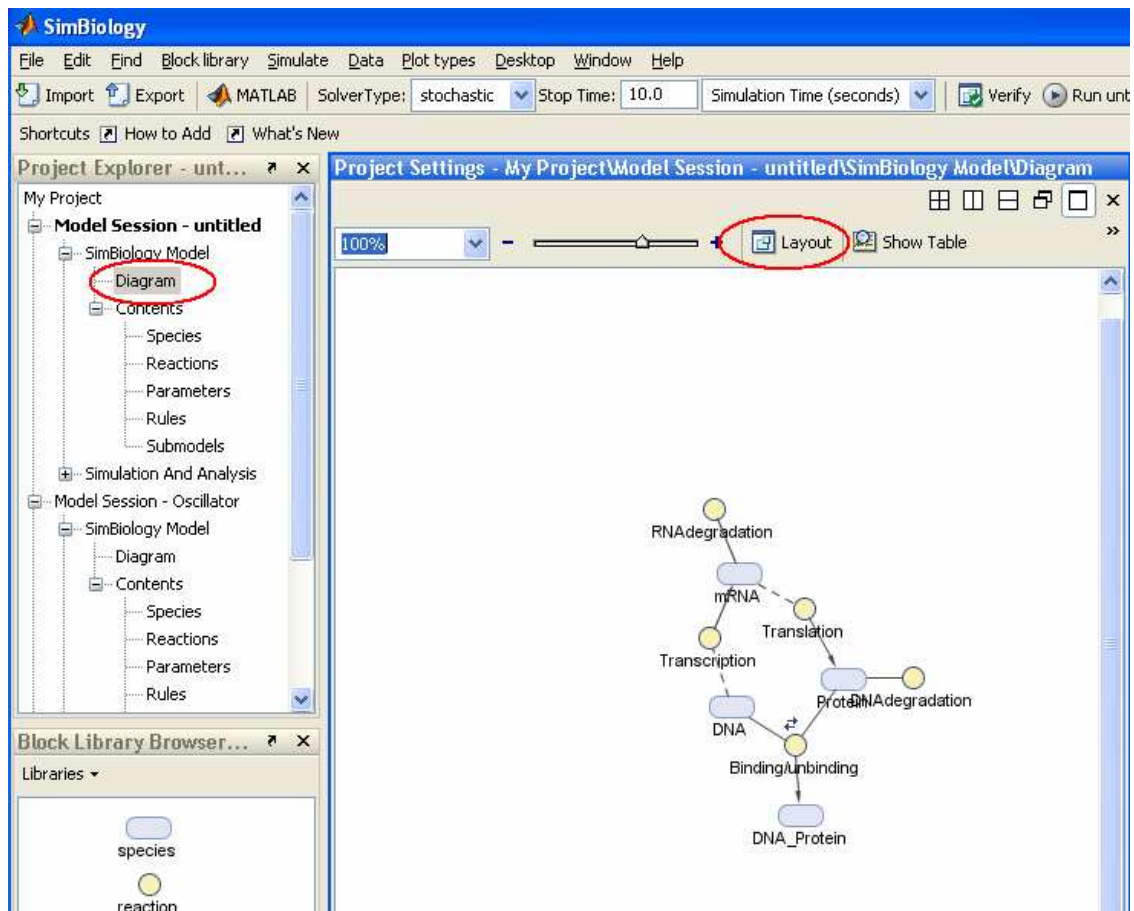
- Repeat until you get the below reactions, species and parameters.

Name	Reaction	KineticLaw	ReactionRate
Transcription	DNA -> DNA + mRNA	MassAction	$k_1 * \text{DNA}$
Translation	mRNA -> mRNA + protein	MassAction	$k_2 * \text{mRNA}$
Binding/Unbinding	DNA + protein <-> DNA_protein	MassAction	$k_3 * \text{DNA} * \text{protein} - k_{3r} * \text{DNA_protein}$
mRNA Degradation	mRNA -> null	MassAction	$k_4 * \text{mRNA}$
Protein Degradation	protein -> null	MassAction	$k_5 * \text{protein}$

Name	InitialAmount	InitialAmountUnits
DNA	50.0	molecule
mRNA	0.0	molecule
protein	0.0	molecule
DNA_protein	0.0	molecule

Name	Scope	Value	ValueUnits
k1	DNA -> DNA + mRNA	0.2	1/second
k2	mRNA -> mRNA + protein	20.0	1/second
k3	DNA + protein <-> DNA_protein	0.2	1/(molecule*second)
k3r	DNA + protein <-> DNA_protein	1.0	1/second
k4	mRNA -> null	1.5	1/second
k5	protein -> null	1.0	1/second

- 6 Double click **Diagram** in **Project Explorer**. Click **Layout**. You should be able to see the following graph.



Note that instead of step 2-5, you can construct this graph directly by drag and drop species and reactions from **Block Library Browser** and connect them by holding down the Ctrl key while clicking a Species or Reaction block.

- 7 These are the basics of creating a model using SimBiology. There are other reactions, rules and parameter types. For more details, please refer to the SimBiology User's Guide that comes together with SimBiology.

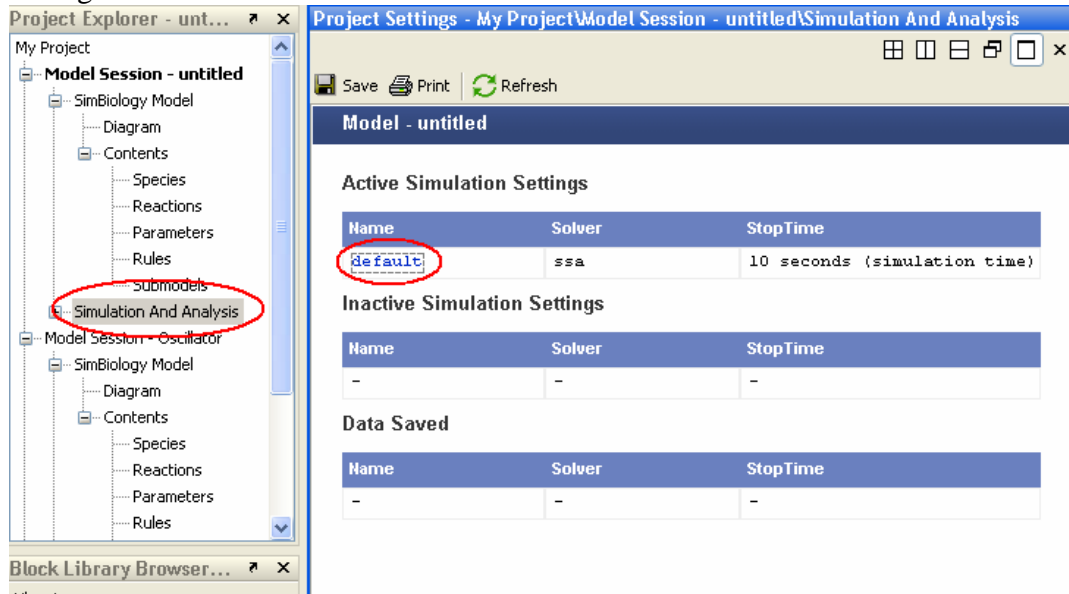
Simulation


After building the model, one can simulate it using the many solvers provided by SimBiology. Depending on the model complexity, one can choose the stiff solvers for more accuracy, or the non-stiff solvers for faster simulations [2].

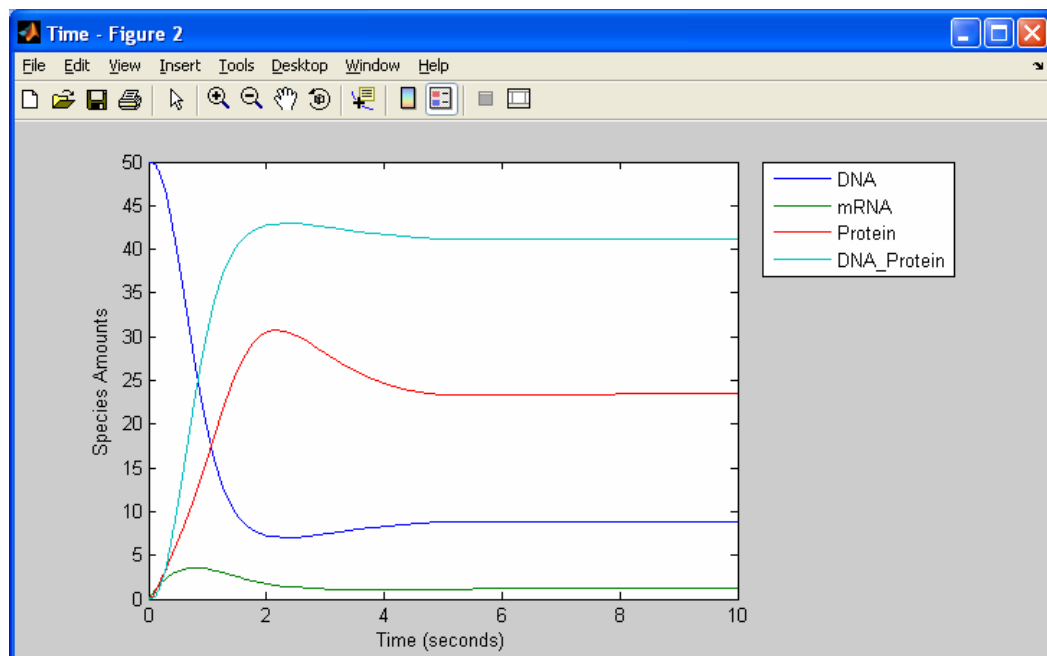
To simulate the model in the previous section, follow the steps below.

- 1 From the Project Explorer, click on **Simulation And Analysis** to bring up the

settings box.



- 2 Click **default** and set the **simulation time** to **10.0** seconds and choose **ode15s** as the **solverType**. Leave the rest of the settings as they are and click **Run** 
- 3 The simulation will run to completion and draws the result in a figure window.



- 4 Try another simulation, but this time with “**stochastic**” as the solver. What do you observe?

There are a lot more functionality provided by SimBiology and some of them can be used together with other toolboxes provided by MATLAB. The various tutorials in SimBiology can also be a good source for familiarizing yourself with the modeling process itself.

References

[1] Systems Biology Markup Language. www.sbml.org

[2] Higham, D. J. and Trefethen, L. N, “Stiffness of ODEs”, BIT Numerical Mathematics, 33 (2). pp. 285-303, 1993