Protein Networks and Systems Biology
ELIXIR 2015, Bologna, Italy

Discrete Modelling
Boolean Networks

Alberto Calderone
sinnefa@gmail.com

Bioinformatics and Computational Biology Unit
Molecular Genetics Laboratory
University of Rome Tor Vergata, Italy

December 11, 2015

Introduction

This training session is focused on boolean networks, a kind of networks used to model systems through causal dependencies and dynamics. Differently from protein interactions, we are now going to stress the importance of building a model that represents your idea. Remember that modelling often implies scaling down reality to a simpler representation. You should become able to translate ideas into boolean logic and thus boolean networks and analyse the final dynamics.

Introduction to Discrete Modelling

In this training session we will work with discrete models and, in particular, we will use GINsim to create and analyse boolean network networks to understand what we can learn from them and the challenges of this kind of modelling.

1. Go to GINsim website: http://ginsim.org/home
2. In the "DOWNLOADS" section download and install the right version for your Operating System.
3. To start GINsim open the Terminal (Shell), go to the directory where you downloaded the executable file and type the command `java -jar GINsim-version.jar`
4. Create a new model clicking on "'New Model'
5. Create nodes (they can be proteins, genes or anything) and links them as shown in the following Figure 1. Node names are arbitrary, just be sure they are correct in the boolean functions you will specify afterwards.

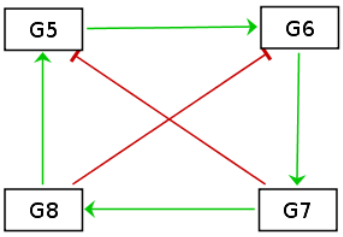

Figure 1:

Default editing mode:	allows to select and move objects.	
Insertion mode:	when selected, clicking on the graph panel adds a new element.	
Interaction insertion mode:	when selected, interactions are added by dragging from one gene to another. The interactions must be complemented by the definition of the logical parameters and functions for the target variable. These buttons allow to add different kinds of interactions: activation, inhibition, both.	

6. Assign to each node a boolean function. (Operators are & for "and", | for "or", ! for "not" and parenthesis "(" ")"). Select each node one by one and using the "Formulae" option in the bottom left corner of the window add the following functions.
   Please note: pay attention entities names, syntax and to incoming edges.

```
G5 = G8 & !G7
G6 = G5 & !G8
G7 = G6
G8 = G7
```

7. Under the menu "Tools" click "Run Simulation" and start a "Synchronous" simulation. Are there loops in the state diagram? Why do they occur? Comment with your partners and explore different formulae.

Ad this point you should be familiar with the basics of building a model with GINsim. Now you will create models that do what you would like them to do.

1. Create a model with two arbitrary nodes A and B where A is active when B is active, and vice-versa. Simulate.
2. Create a model with two arbitrary nodes A and B where A is active when B is inactive. Simulate.
3. Create a model with three arbitrary nodes A, B and C where A is active when B is active and C is inactive. Simulate.
4. Create an arbitrary model which has a simple attractor (It is a set of states in the state diagram that form a loop). Since you are going to do several attempts, instead of simulating each time, use the concept of "Circuits", GINsim allows you find Circuits and to see if they are Functional. Ideally your final model would have Positive and Negative Circuits, steady States and attractors.

Conclusions

In this session you became familiar with GINsim, a tool to assemble boolean networks and to simulate their dynamics. You should be able to translate your logic into formulas that govern the transitions of specific proteins or genes. According to your experimental data you should now be able to assemble a simple network and to analyse it, identifying steady-states and loops.