"Kinetics: Simbiology (I)"

The purpose of this lab is to become familiar with SimBiology by modeling a simple ligand binding reaction. Consider a binding reaction where ligand (L) binds to a protein receptor (R) to form a loosely bound encounter complex (L·R), and finally a tightly bound product (P).

$$L + R \leftrightarrow L.R \rightarrow P$$

The SimBiology model of this receptor-ligand reaction looks like this (in MATLAB):

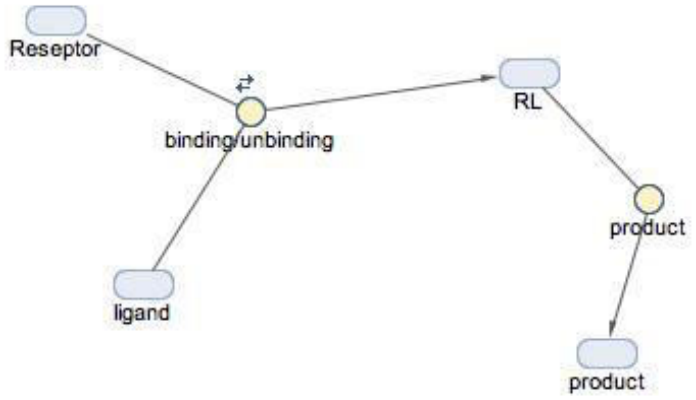

Fig.1. Simbiology Model for receptor-ligand reaction

Let's walk through the steps of how to build this model in SimBiology.

Procedure:

Part A— Receptor-Ligand Reaction:

1. Open Matlab and type simbiology at command window.
2. Go to Model tab in SimBiology window.
3. Home > add model > create new blank model
4. Rename window's name to Receptor-Ligand reaction by double clicking on window.
5. Drag and drop three species and one reaction to the window.
6. Double click on the name of the species and rename species to Ligand, Receptor and ligand-receptor respectively.
7. Rename reaction to binding/unbinding
8. Hold down control key and draw an arrow from Ligand and Receptor to binding/unbinding
9. Draw an arrow from binding/unbinding to ligand-receptor
10. Double click on Ligand and set initial amount to 10.0
11. Double click on Receptor and set initial amount to 5.0
12. Double click on binding/unbinding
    a. and check "reversible"
    b. select "MassAction" for KineticLaw
        i. set "Forward Rate Parameter" (Name "k_f") value to 0.02
        ii. set "Reverse Rate Parameter" (Name "k_r") value to 0.01

13. Add another “species” and “reaction”. Name the species product and reaction as k-prod.
14. Connect ligand-receptor to k-prod and k-prod to product.
15. Select MassAction for kinetic law of k-prod and set value to 0.05.
16. Go to “Add Task” > Simulate model > Run simulation.
    a. Does the reaction reach a steady state?
    b. If not, increase simulation time to 100 by going to “simulation setting”.
17. Repeat simulation for following values:
    a. “Forward Rate Parameter” : 0.01 , “Reverse Rate Parameter” : 0.02 , “k-prod” : 0.05
    b. “Forward Rate Parameter” : 0.02, “Reverse Rate Parameter” : 0.01 , “k-prod” : 0.5

18. Complete Table.1.

Part B—Enzyme-Substrate Reaction:

This same reaction can be used to describe Michaelis-Menten enzyme kinetics, in which substrate (S) binds a protein enzyme (E) to form an encounter complex (E·S), and then chemically converts to product (E + P).

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} E{\cdot}S \xrightarrow{k_{cat}} E + P$$

Suppose initial amounts for E and S are 10.0 and 5.0, respectively. Repeat the simulation for different values of k_1 , k_{-1} , and k_{cat} as specified in Table.2 and then complete this table.

Name: **TUID:**

Section:

Part A:

Table.1

Case#	K_f	K_r	K_{prod}	Δt(s) to reach steady state
#1	*0.02*	*0.01*	*0.05*	
#2	*0.01*	*0.02*	*0.05*	
#3	*0.02*	*0.01*	*0.5*	

Part B:

Table.2

Case#	K_1	K_{-1}	K_{cat}	Δt(s) to reach steady state
#1	1000	100	1	
#2	100	1000	1	
#3	100	1	1000	