A Systems Biology Approach to Receptor-Ligand Interactions

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Abstract

We simulated receptor-ligand (RL) interactions using a systems biology approach. Utilizing versatile ODE equations, we were able to simulate a simplified, reversible receptor-ligand interaction pathway.

Introduction

A ligand is a molecule that forms a bond with a central metal atom in a complex compound, such as proteins, steroids, or gases like nitric oxide. A receptor is a molecule that responds to specific onsets such as neurotransmitters, antigens, and hormones. When a ligand binds to a receptor protein, this causes a response of a sort. Types of interactions include steroid hormones and their nuclear receptors, and polypeptide ligands and transmembrane receptors.

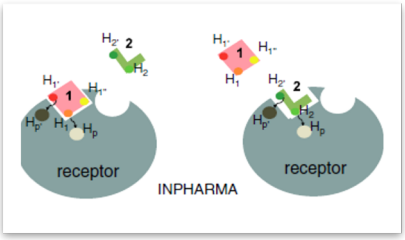

Fig 1: Basic receptor-ligand interaction (Yakimchuk, 2011)

Modelling

We simulated these interactions using the programming language Python, and the Python package *Tellurium*:

```
import tellurium as te
r = te.loada('''
model pathway()
   L + R -> A; k1*L*R
   A -> L + R; k2*A

   k1=0.25; k2=0.25;
   L=11; R=10; A=0;
end
''')
result = r.simulate(10, 100, 200)
r.plot(result, title="Receptor-Ligand interactions", xtitle="Time", ytitle="Concentration")
```

Fig 2: Python source code using the systems biology simulation package "Tellurium"

Methods

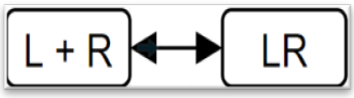

Fig 1: Basic RL interaction

We simplified RL relationships by breaking them down to a simple equilibrium reaction. A ligand (L) could be paired with the receptor (R) to create an activated receptor (LR or A).

This activated receptor could be reversed by separating the ligand from the receptor and into their two constituent parts.

We broke the equation up into these differential equations:

$$\frac{d[L]}{dt} = -k1[L][R] + k2[A]$$

$$\frac{d[R]}{dt} = -k1[L][R] + k2[A]$$

$$\frac{d[A]}{dt} = k1[L][R] - k2[A]$$

Where L = ligand, R = receptor, A = receptor by ligand interaction

We gave both L and R arbitrary numerical values for the sake of the simulation. To further analyze the LR interaction dynamic, we simulated the overabundance of ligands in the receptor environment by ensuring more L's were present than R's. The model was simulated for one minute and 30 seconds, and allowed us to analyze how the activation of ligand receptors changes over time.

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Simulation and Results

The simulation demonstrated that receptor activation is limited by the amount of available receptors in the environment.

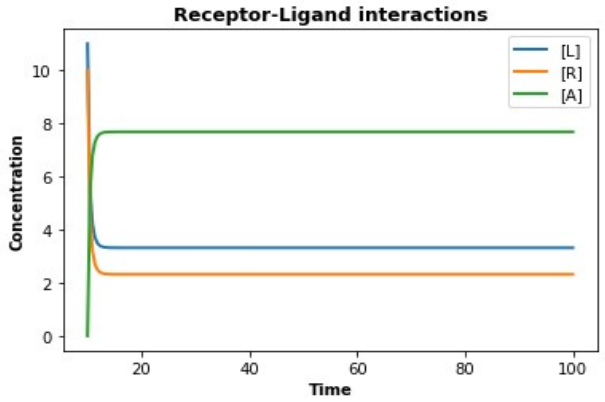

Fig 3: Receptor/Ligand interaction potential over time (in seconds)

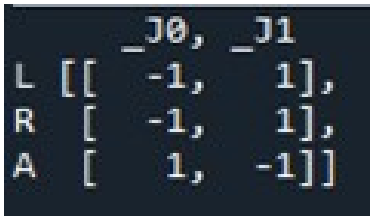

Fig 4: Receptor/Ligand reaction simulation stoichiometric matrix

References

http://groups.molbiosci.northwestern.edu/holmgren/Glossary/Definitions/Def-L/ligand-receptor_interact.html

Yakimchuk, K. "*Receptor-Ligand Binding Assays*". (2011 1-19). Mater Methods, //dx.doi.org/10.13070/mm.en.1.199