Systems Biology Tutorial 6: The kinetic model

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1. Chemical equilibrium (closed system)

1. Select the lin3 model in the Model Database and open it in the Model Builder to edit. Click on Create Derivative to make your own editable copy.
   (a) Remove the fixed metabolites $s1$ and $p1$. Also remove the reactions that connected these to the model. Set the initial concentrations of $x2$ and $x3$ to 1 and 0 respectively.
   (b) Simulate the timecourse until the system reaches equilibrium and note the concentrations for $x2$ and $x3$.
   (c) Calculate the equilibrium constant for the reaction. Does it match the parameter value in the reversible MM kinetics?
   (d) Are there dependent metabolites in this model? Write down the conservation equation.
2. Select the lin3 model in the Model Database and open it in the Model Builder to edit. Click on Create Derivative to make your own editable copy.
   (a) Reload the model and turn $s1$ and $p1$ into time-varying metabolites. Set the initial concentrations of $s1$, $x2$, $x3$ and $p1$ to 1, 0, 0 and 0 respectively. Set the equilibrium constants $Keq1$, $Keq2$ and $Keq3$ to 1, 2 and 3 respectively.
   (b) Determine the concentrations at equilibrium for the individual metabolites.
   (c) Show how the Keq values of the individual steps can be used to predict the equilibrium constant of the pathway as a whole.
   (d) Determine the values of the rates at equilibrium. Is this what you would expect?

2. Steady state (open system)

Select the lin3 model in the Model Database and open it in the Simulator.

1. Set the equilibrium constants $Keq1$, $Keq2$ and $Keq3$ to 1, 2 and 3 respectively and set $s1$ and $p1$ to 2 and 1 respectively. $s1$ and $p1$ should remain fixed now as we are simulating an open system.
2. Simulate the system from initial conditions to steady state (find a suitable end time). Plot the simulation for both the species and the rates.
3. Show that the mass-action ratio of the pathway equals the product of the mass action ratios of the individual steps.
4. Determine the value of the flux. How does this compare to the rates of the closed system?

3. Published model of glycolysis in *Plasmodium falciparum*.

Select the penkler1 model in the Model Database and proceed to the Simulator.

1. Are there any dependent metabolites in this model? Write down the conservation equations for these metabolites.
2. How many independent fluxes are there?
3. Which reactions have the most control on the production of lactate?
4. Which reactions have the most control on the parasite glucose?