SysMIC Workshop: Working with Models

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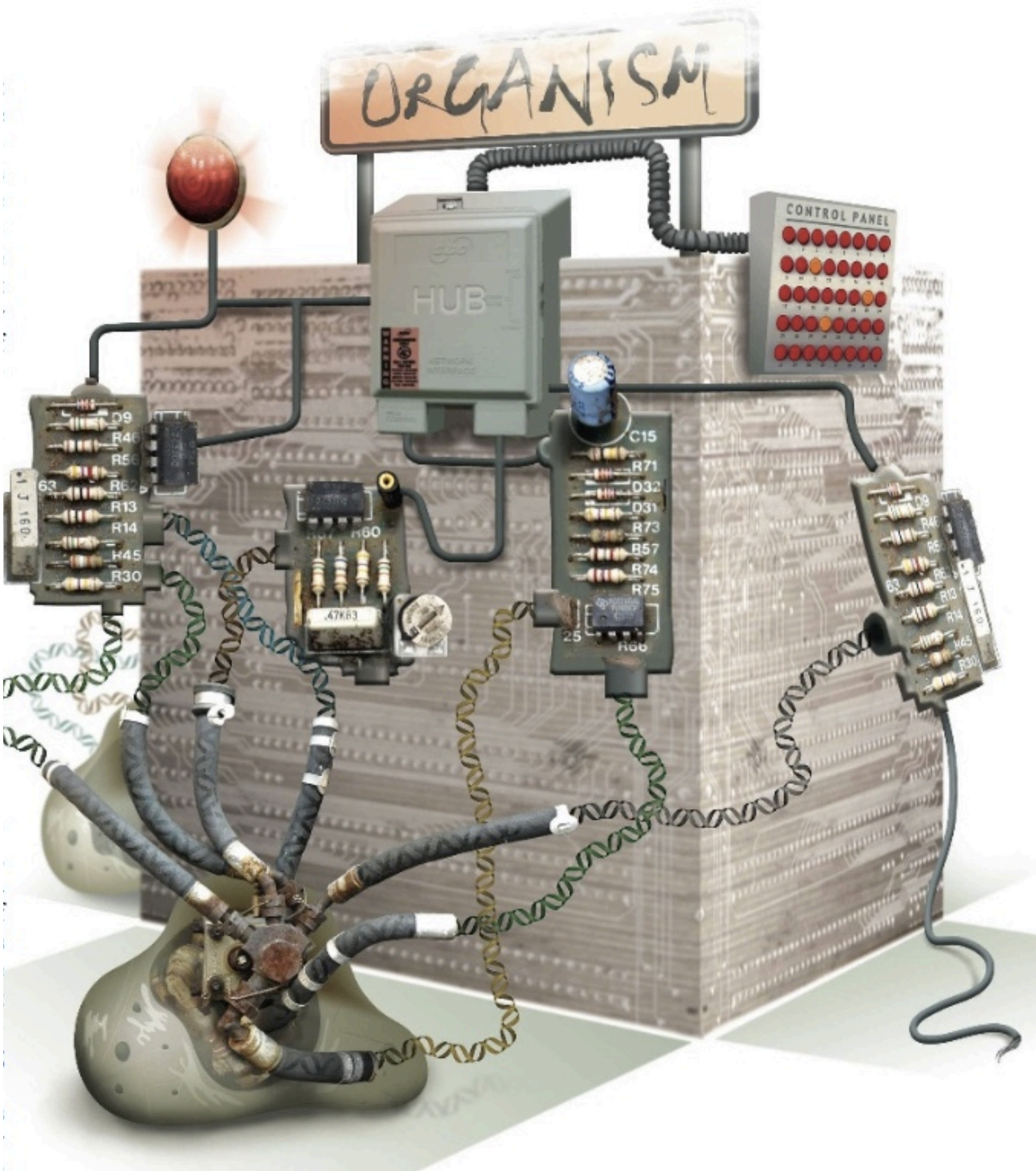
Activities	
Welcome	
Introduction:	**The Goodwin Model**
Exercise:	**Setting up a model of a linear chain or reaction without and with feedback**
Exercise:	**Numerical Simulations of a set of differential equations**
Tasks:	**- State Space** **- Parameter Space** **- Parameter Protocol**

Algorithms of Life

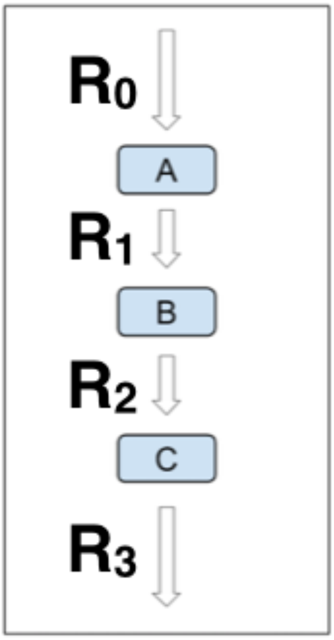


From: Paul Nurse: Life, Logic and Information.
Nature 454, 424-426 (24 July 2008)
http://www.nature.com/nature/journal/v454/n7203/full/454424a.html

Warm-up Exercises

1. Linear chain of reactions

We consider a chain of first order reactions expanded by one zero order influx:



Implement this model in a model function file.

There should be three variables with 4 reactions. Each reaction should get a rate constant. Assign k0 = k1 = k2 = k3 = 1.

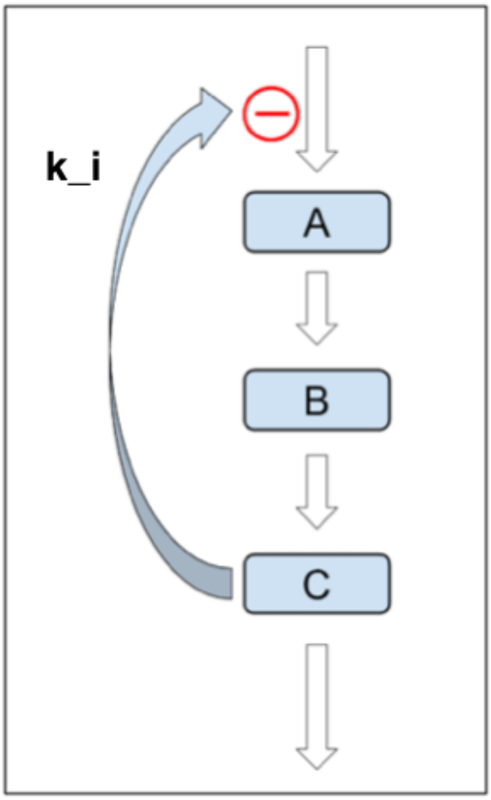
Use initial conditions A(0) = 5, B(0) = C(0) = 0.

Simulate the model using MATLAB's ode45 function for 10 time units.

Describe the time course of each of the variables.

2. Linear chain with negative feedback

Now expand the linear pathway model to include negative feedback.



The feedback function is implemented as: k0 / (Km + k_1*[C]^n)

What does this "network" look like when using MATLAB's biograph?

Assign k0 = k1 = k2 = k3 = 1, Km = k_i = 1, n=1.

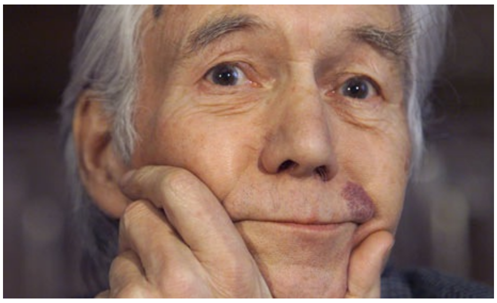
Use initial conditions A(0) = 5, B(0) = C(0) = 0.

Simulate the model using MATLAB's ode45 function for 10 time units.

Describe the time course of each of the variables.

Compare the result to the linear chain without feedback.

The Goodwin Model



$$
\begin{aligned}
dX_1/dt &= k0 / (K_M + k_i \cdot X_3^n) - k1*X_1 \\
dX_2/dt &= k1*X_1 - k2*X_2 \\
dX_3/dt &= k2*X_2 - k3*X_3
\end{aligned}
$$

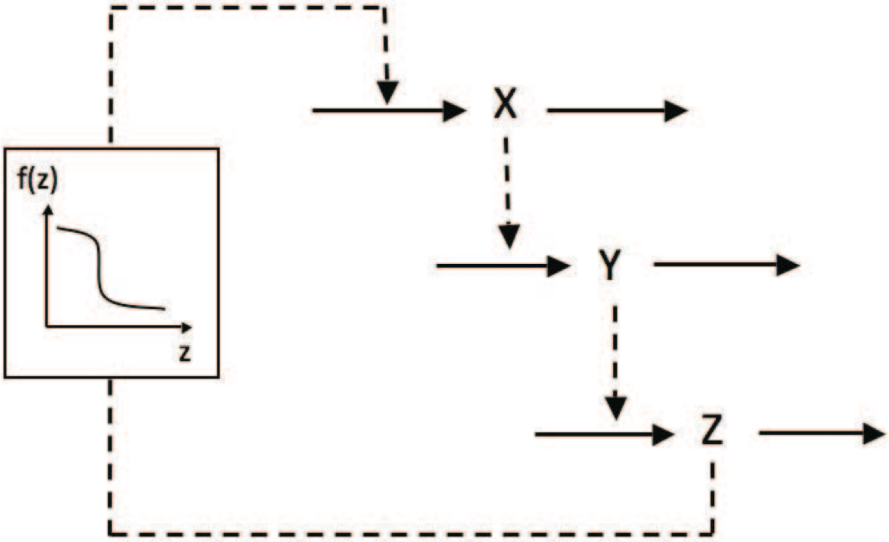


Figure 1. Scheme of the Goodwin model. In the original version of the model, the negative feedback exerted by Z on the synthesis of X is described by a non-linear Hill function.
doi:10.1371/journal.pone.0069573.g001

Goodwin, B. (1963). Temporal Organization in Cells. New York: Academic Press.
https://ia600407.us.archive.org/32/items/temporalorganiza00good/temporalorganiza00good.pdf

Goodwin Model with Negative Feedback

Model equations:

$$dX_1/dt = k0 / (K_M + k_i \cdot X_3^n) - k1*X_1$$
$$dX_2/dt = k1*X_1 - k2*X_2$$
$$dX_3/dt = k2*X_2 - k3*X_3$$

Parameters: k0 = 1; Km = 0.1; k_i = 0.1; n = 1 or 10;
k1 = k2 = k3 = 1;

Matlab Algebraic:

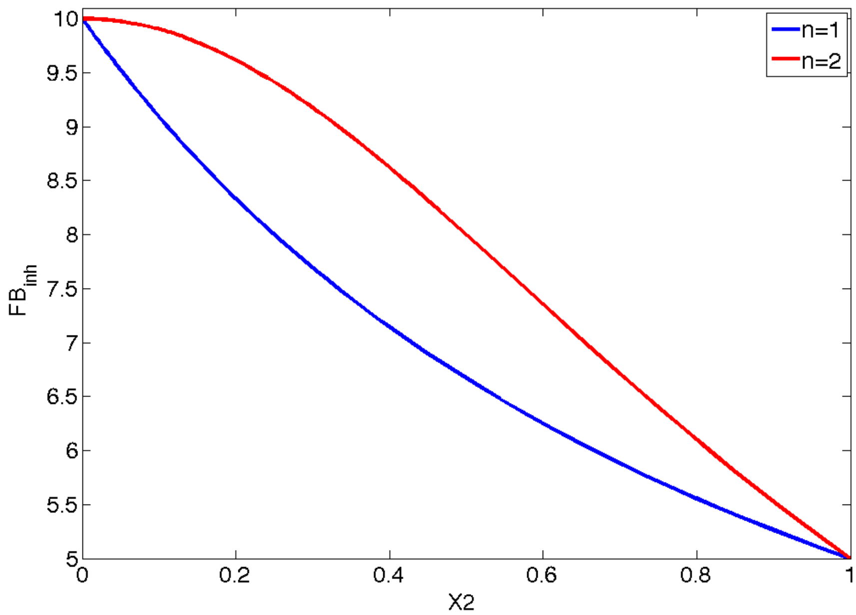
```
dxdt(1) =  k0 / ( Km1 + k_i*x(3)^n ) - k1*x(1);
dxdt(2) =                      k1*x(1)      - k2*x(2);
dxdt(3) =                      k2*x(2)      - k3*x(3);
```

Matlab Symbolic:

```
f1 =  1/(0.01+0.1*x3^1) - x1;
f2 =                   x1 - x2;
f3 =                   x2 - x3;
```

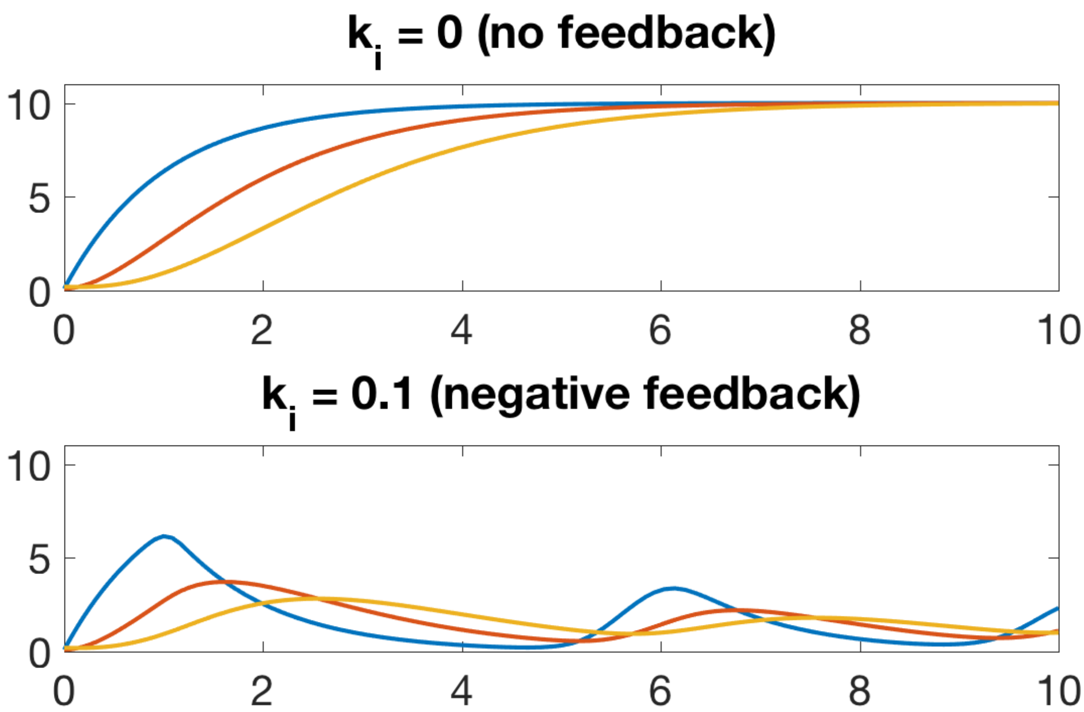
Feedback Inhibition

```
% Parameters
k0 = 1; Km = 0.1; k_i = 0.1;

% Define Function
FB_inh1 = @(X2) k0/(Km+k_i*X2^1);

% Plot Function
fplot(FB_inh1,[0,1]); hold on

% Re-Define Function
FB_inh2 = @(X2) k0/(Km+k_i*X2^2);

% Re-Plot Function
fplot(FB_inh2,[0,1],'r')
```



For n=1, the function decays with decreasing slope. For n=2, the decrease is sigmoidal: starting from zero the slope increase, goes through an inflection point, then slowing towards zero for large values of X2.

Exemplary Simulation Output:



For k_i=0, there is just an increase towards the steady state in all variables. For k_i=0.1, there is an increase followed by a maximum (overshoot) and then an oscillatory state.