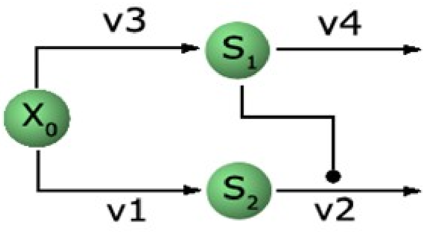
PROJECTS

Homeostasis

- A homeostatic system is one that resists internal change when external parameters are perturbed. We will illustrate two such networks: one that shows perfect adaptation and another that near adaptation.
- Perfect adaptation describes a system that recovers from a perturbation without any error (thus perfectly). There are a number of approaches to achieving perfect adaptation, one is via integral control and another, simpler approach, is via coordinate stimulation. In this tutorial we will illustrate perfect adaptation using coordinate stimulation.
- A simpler and perhaps more common method for achieving homeostasis is to use negative feedback to resist external perturbations. Unlike systems which show perfect adaptation, systems which employ negative feedback cannot completely restore a disturbance.

Homeostasis

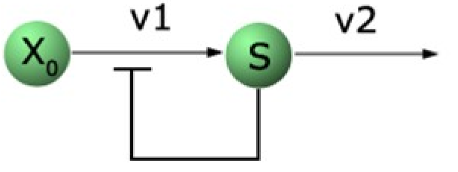
S_2 remains homeostatic



$$v1 = k_1 X_0 \qquad v2 = k_2 S_1 S_2$$

$$v3 = k_3 X_0 \qquad v4 = k_4 S_1$$

S remains homeostatic



$$v1 = \frac{X_0}{K_m + S^4} \qquad v2 = k_1 S$$

Perfect Adaptation

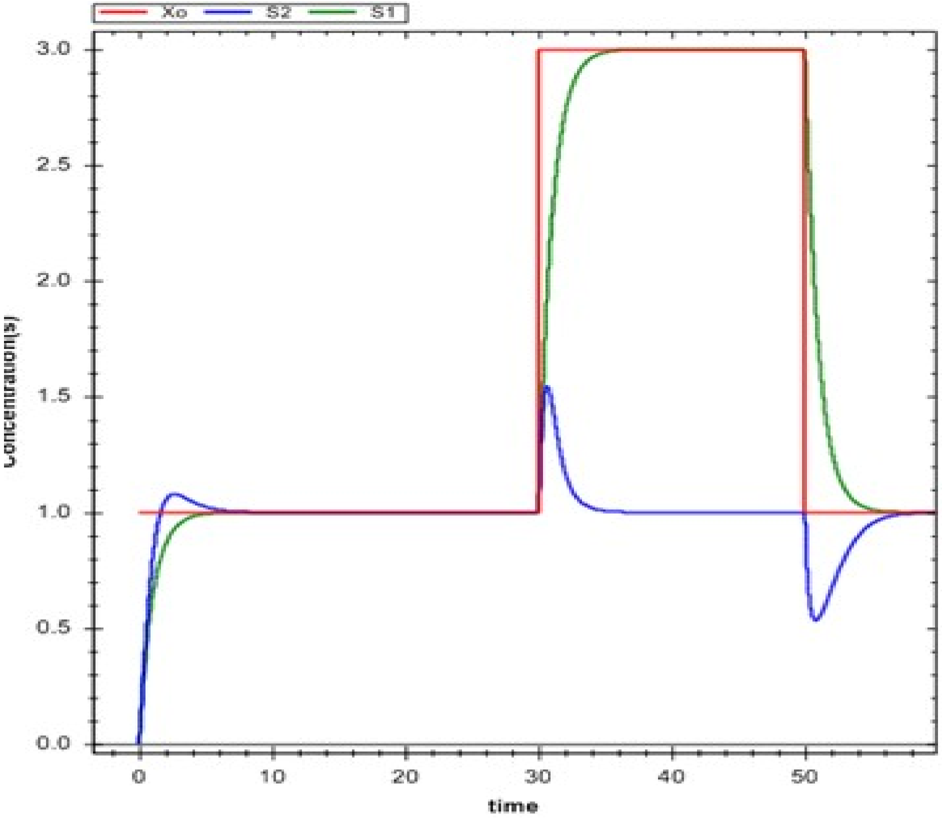
Negative Feedback

Perfect Adaptation

```
r = te.loada('''
    $Xo  -> S2;  k1*Xo;
     S2  -> $w;  k2*S1*S2;
      $Xo  -> S1;  k3*Xo;
     S1  -> $w;  k4*S1;
  at (time > 10): Xo = Xo * 2;
  at (time > 15): Xo = Xo/2;

  # initialize
  k1 = 1; k2 = 1;
  k3 = 1; k4 = 1;
  Xo = 1.0;
''')
```

Exercise: Build a model that shows perfect adaptation.



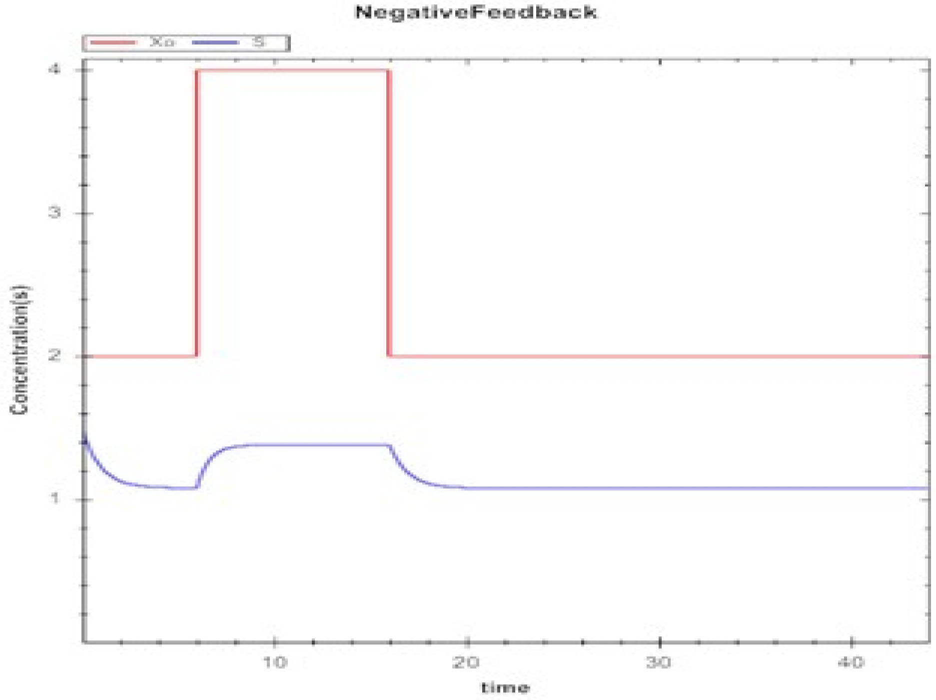
Negative Feedback

```
r = te.loada ('''
    $Xo   -> S;   Xo/(km + S^h);
       S  -> $w;  k1*S;

     # initialize
     h = 1;   # Hill coefficient
     k1 = 1;  km = 0.1;
     S = 1.5; Xo = 2

     at (time > 10): Xo = 5;
     at (time > 20): Xo = 2;
''')
```

Negative Feedback



Positive Feedback

Enter the following model:

```
r = te.loada ('''
     $Xo -> S1;
       1 + Xo*(32+(S1/0.75)^3.2)/(1 +(S1/4.3)^3.2);
     S1 -> $X1; k1*S1;

Xo = 0.09; X1 = 0.0;
S1 = 0.5; k1 = 3.2;
''')
```

Exercises

Carry out a time course scan on the positive feedback model.

Scan over different starting points for S1

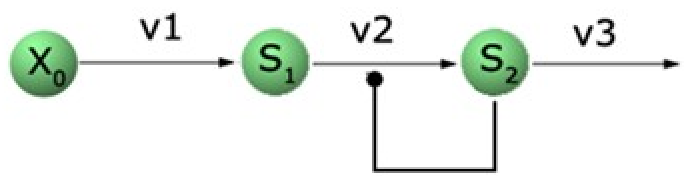
To help you get started:

Plot 12 time course curves, start S1 at 0.05 and incrementing S1 by 1.0 for each time course simulation.

What do you observe?

Relaxation Oscillator

- A relaxation oscillator utilizes a positive feedback coupled to a negative feedback loop.



$$v1 = k_1 X_0 \qquad v2 = \frac{k_2 S_1 S_2{}^h}{k_m + S_2{}^h} + k_3 S_1 \qquad v3 = k_4 S_2$$

Relaxation Oscillator

```
r = te.loada ('''
  v1: $Xo -> S1; k1*Xo;
  v2:  S1 -> S2; k2*S1*S2^h/(10 + S2^h) + k3*S1;
  v3:  S2 -> $w; k4*S2;

  # Initialize
  h  = 2; # Hill coefficient
  k1 = 1; k2 = 2; Xo = 1;
  k3 = 0.02; k4 = 1;
''')
```