

Assignment 1: Modeling

Due: 24th October (Wednesday)

Build a series of gene regulatory networks of increasing length. Each network will have a negative feedback loop from the last gene to the first gene. **DO NOT** model mRNA. Each gene will produce protein directly.

The protein degradation rates should be modeled as first order mass-action kinetics, $k_2 \cdot P$.

The rate constant k_2 for all protein degradation steps should be set to 0.05

All genes other than the one with the negative feedback should be modeled using that rate law:

$$v = \frac{1}{k_1 + P_i}$$

k_1 should be set to 0.1

For the step with negative feedback us the following rate law:

$$v = \frac{1}{k_1 + P_i^h}$$

Where h is the Hill coefficient. The value of the Hill coefficient should range from 1 to 10 (can be a real number, eg 2.5). For testing you can set $h = 9$

Build the following sized networks (a. to f.) and answer the following questions:

- 1) Build each of the networks, you'll probably have to do this in a single file. Show a plot of the time evolution of each network using the default values given above.
- 2) **Some of the networks** can display oscillatory behavior. Investigate the onset of oscillations as a function of the Hill coefficient, h . You can monitor the last protein for oscillations (all proteins will oscillate but the last one is convenient)
- 3) Which network can oscillate and which cannot?
- 4) Create the following table:

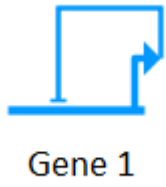
Number of genes in network	Value of h where we begin to see oscillation

- 5) Plot a bar graph of the data in the table above. For networks that don't oscillate, set the bar to zero to indicate no oscillations observed.

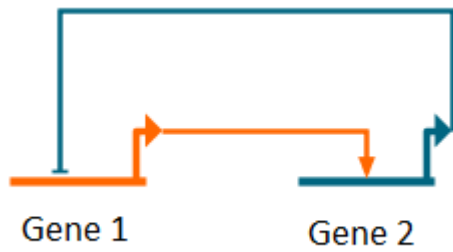
Extra points for automatic oscillation detection, rather than manually looking at the data.

One possibility: Compute the average of a signal, subtract this average from the signal. If the new data has negative values, then the data is likely to be oscillating. There may be other tricks one can use also. A full Fourier analysis seems overkill however.

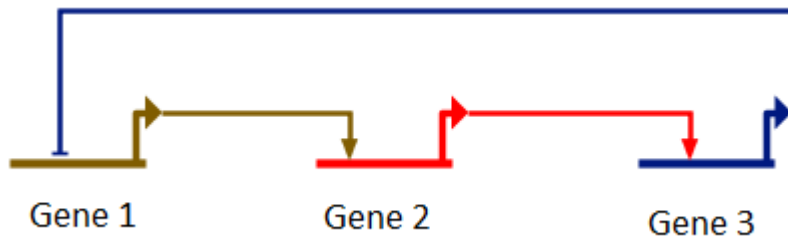
a) One gene



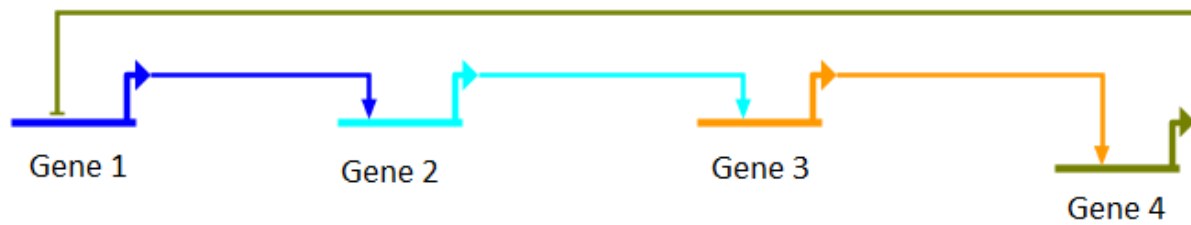
b) Two genes



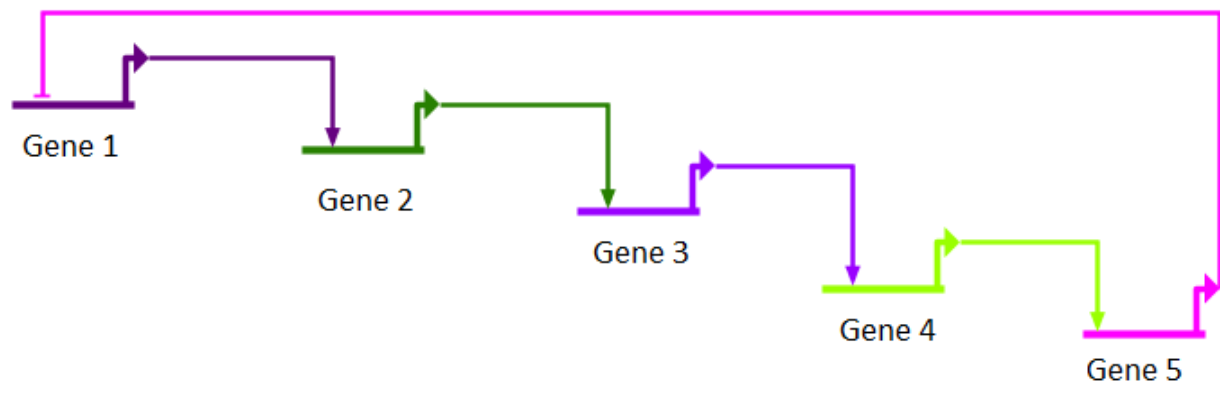
c) Three genes



d) Four genes



e) Five genes



f) And a final network with 10 genes (figure not shown)