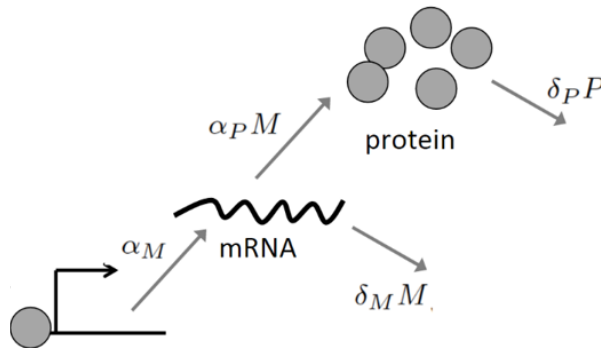


*Goals*

- To translate mathematical models into simulation code in Tellurium.
- To become familiar with basic programming procedures in Python/Tellurium: defining and manipulating variables, iterating using for loops, and plotting data

Consider the model of gene regulation presented in class:



- 1) Formulate a mathematical model for gene regulation in Tellurium, using the state variables and parameters described in class.
- 2) Simulate the system for these parameters:

$$\alpha_m = 10 \text{ copies/hr; } \alpha_p = 500/\text{hr; } \delta_m = 1/\text{hr; } \delta_p = 0.1/\text{hr;}$$

For initial conditions, assume that both mRNA and protein are absent. Plot simulation results then calculate from the data the steady-state protein level and the response time (i.e. the time needed for the system to reach half its steady state value). How do simulated values compare those from the analytical solutions?

- 3) Perform one-dimensional parameter scans of this system, varying these parameters from the following minimum to maximum values:
  - a)  $\alpha_m = 1$  to 50 copies/hr, and
  - b)  $\delta_m = 0.02$  to 1/hr.

For each parameter scan, plot on the same graph, (1) steady-state values, and (2) response times as a function of these parameters, both from simulation results, and from the analytical solution derived in class, obtained using the timescale separation assumption. How closely do simulations match analytical solutions?

- 4) *Optional.* Noise propagation in gene regulation. Convert the mathematical modeling you programmed in Tellurium into a Monte-Carlo simulation. Now run simulations of the system testing different parameter conditions to answer the following questions:

A measure of variability is the coefficient of variation (CV), defined as the standard deviation divided by the mean.

Perform stochastic simulations of the system, under the following parameter conditions:

$$\alpha_m = 10 \text{ copies/hr}; \alpha_p = 10/\text{hr}; \delta_m = 1/\text{hr}; \delta_p = 2/\text{hr};$$

- a) What is the CV of mRNA? How does it vary with the mean number of mRNA molecules at steady state?
- b) What is the CV of protein? Is the protein CV larger or smaller than the mRNA CV under the above parameter conditions?
- c) Run simulations of this system, testing different parameters to answer the following question: can the CV of protein be smaller than the CV of mRNA? If so, under what parameter conditions does this occur? HINT: *consider timescale separation.*