1. Consider our standard model for the dynamics of a single mRNA species with copy number n, with transitions

$$\begin{aligned} n &\rightarrow n+1 \\ n &\rightarrow n-1 \end{aligned}$$

and corresponding rates β and αn. Use parameter values $\beta = 1/\text{min}$ and $\alpha = 0.1/\text{min}$.

   (a) What is average lifetime of a transcript in minutes? For stochastic dynamics at equilibrium, what are the theoretical values for the mean and variance of n?

   (b) Using the variable X to denote a continuous approximation to the particle number n, what is the ODE corresponding to the stochastic dynamics? What is the steady-state value of X, defined as $\langle X \rangle$?

   (c) Write a Gillespie simulation for this system and provide your source code. A code framework will be available as a starting point. Perform a stochastic simulation for the dynamics of n using your simulation software. Have the program output the value of n at regular intervals of 1 minute. This takes some care because the random transitions will not necessarily occur at these fixed intervals. You do not have to provide the trajectory, just the source code.

   (d) Start the simulation at n equal to the integer closest to $\langle X \rangle$. Calculate and report the mean μ and variance σ^2 of n over 10,000 minutes. Compare these to the theoretical values.

2. Now consider the approach to equilibrium. The dynamical systems are the same, but the initial conditions are $X = 0$ (ODE) and $n = 0$ (stochastic).

   (a) What is the solution for $X(t)$?

   (b) Run 1000 simulations (trajectories) of the first $T = 100$ minutes for the stochastic system. Calculate the mean $\langle n(t) \rangle$ and the variance $\text{Var}[n(t)]$ at 1 minute intervals. Note: The mean $\langle n(t) \rangle$ here depends on time; it is computed by averaging over the 1000 trajectories at each time point. Similarly, the variance $\langle n(t)^2 \rangle - \langle n(t) \rangle^2$ is evaluated at 1 minute intervals over the 1000 simulations, computed separately for each time t. It is not the variance over the 100 minute trajectory. You should find that $\langle n(0) \rangle = \text{Var}[n(0)] = 0$, $\langle n(T) \rangle = \mu$, and $\text{Var}[n(T)] = \sigma^2$, where μ and σ^2 are from the previous equilibrium simulation. Plot the mean (solid line) and $\pm$ one standard deviation error bars (dashed line, standard deviation computed simply as the square root of the variance) for the 1000 trajectories, together with the ODE results for $X(t)$ (thick line).

   (c) Can you suggest (or derive) an analytical expression for the variance as a function of time?

(d) Suppose that the initial conditions are that the initial number of particles is n_0 but that there is decay only, with the transition $n \to n-1$ having rate αn. The ODE solution is $n(t) = n_0 \exp^{-\alpha t}$. Suggest (or derive) an analytical solution for the variance $V(t)$ for the corresponding stochastic system in which $n(t)$ is a random variable and the time-dependent variance $V(t) = \langle n(t)^2 \rangle - [n_0 e^{-\alpha t}]^2$. Solve for the time t when the variance $V(t)$ has its maximum value.

3. Finally, consider a model with bursts of transcription with burst size 5. The stochastic transitions are

$$\begin{aligned} n &\to n+5 \\ n &\to n-1 \end{aligned}$$

with corresponding rates $\beta/5$ and α.

(a) What is the corresponding ODE model? Does the ODE model depend on the burst size?

(b) Start a stochastic simulation with n equal to the closest integer to the steady-state value for the ODE model, and generate a 10,000 minute trajectory, recording the state (the value of n) at 1-minute intervals. Calculate and report the mean μ and variance σ^2.

(c) How do the mean and variance compare to the results for the stochastic system with burst size of 1? Do larger bursts correspond to smaller, equal, or larger mean and variance? Can you provide a conjecture for the mathematical expression relating mean and variance for bursts of size b generated at rate β/b, together with the rates β and α?