CHEM-LV03 Analysis and Simulation of Stochastic Reaction-diffusion Systems
Department of Chemical and Metallurgical Engineering
Aalto University
Summer 2022 Exercise 1

Stochastic simulation of elementary chemical reactions

Classroom problems

Problem 1. *(Generating exponentially distributed random variables).*
Let $U \sim \mathcal{U}(0,1), \lambda > 0$, *and let* $g : (0,1] \to \mathbb{R}$ *be*

$$g(y) = -\frac{\ln(y)}{\lambda} = \frac{\ln(1/y)}{\lambda}.$$

Draw 10^5 *realizations of* $g(U)$ *when* $\lambda = 10$. *Next, plot a normalized histogram of your realizations together with the evaluation of the probability density function of an exponential distribution with parameter* λ.

Hint: When $X \sim Exp(\lambda)$, *we can use Julia's function pdf(*$Exp(1/\lambda), x$*) from package Distributions.jl. It is enough to plot it for* $x \in [0,1]$.

Problem 2. *(Gillespie Algorithm - naive formulation). Consider the chemical reaction*

$$\mathcal{A} \xrightarrow{\kappa} \emptyset,$$

where $\mathcal{A}$ *is the chemical species of interest and* κ *is the rate constant of the reaction. Obtain an evolution of* $(N_{\mathcal{A}}(t))_{t\geq 0}$ *for the first 30 seconds by stochastic simulation, given the following parameter values*

$$\begin{aligned} \kappa &= 0.1 sec^{-1} \\ N_{\mathcal{A}}(0) &= n_{\mathcal{A}}(0) \\ &= 20 \\ \Delta t &= 0.001 sec. \end{aligned}$$

Step 1. Compute the propensity function $\nu(t) = n_{\mathcal{A}}(t)\kappa\Delta t$.

Step 2- Generate a random number u uniformly distributed in the interval [0,1].

Step 2. Update the number of molecules if $u < n_{\mathcal{A}}(t_k)\kappa\Delta t$. *Continue with step 1 until stopping time* T *or other stopping criteria.*

Problem 3. *(Gillespie Algorithm).*

Step 1. Compute the propensity function $\nu_{n_r}(t)$ *for each of the* N_r *reactions. Then compute*

$$\alpha = \sum_{n_r}^{N_r} \nu_{n_r}(t).$$

Step 2. Compute the time when the next chemical reaction takes place as $t+\tau$, where τ is sampled from the exponential distribution with parameter α (Problem 1).

Step 3. Find out which reaction occurs at time $t+\tau$, that is, find j such that

$$u \geq \frac{1}{\alpha}\sum_{n_r=1}^{j-1}\nu_{n_r}(t) \quad \textit{and} \quad u < \frac{1}{\alpha}\sum_{n_r=1}^{j}\nu_{n_r}(t), \quad u \sim \mathcal{U}(0,1),$$

or sample j from the multinomial distribution with probability vector $\alpha^{-1}[\nu_1(t), \nu_2(t)\ldots, \nu_{N_r}(t)]$. Then the jth reaction takes place. Update numbers of reactants and products of the jth reaction. Continue with step 1 for time $t+\tau$.

(a) (Stochastic Simulation of Degradation) consider again the chemical reaction

$$\mathcal{A} \xrightarrow{\kappa} \emptyset,$$

where $\mathcal{A}$ is the chemical species of interest and κ is the rate constant of the reaction. Draw 10 realizations of $(N_{\mathcal{A}}(t))_{t\geq 0}$ for the first 100 seconds using the Gillespie algorithm above. Consider $n_{\mathcal{A}}(0) = 20$ as the initial condition on the number of molecules and $\kappa = 0.1 sec^{-1}$ as the rate of the reaction. Plot a time-series of your realizations.

(b) (Stochastic Simulation of Production and Degradation) consider now the chemical reactions

$$\mathcal{A} \xrightarrow{\kappa_1} \emptyset$$
$$\emptyset \xrightarrow{\kappa_2} \mathcal{A},$$

where $\mathcal{A}$ is the chemical species of interest and κ_1, κ_2 are the rate constants of the reactions. Draw 10 realizations of $(N_{\mathcal{A}}(t))_{t\geq 0}$ for the first 30 seconds. Consider $n_{\mathcal{A}}(0) = 0$ as the initial condition on the number of molecules, $\kappa_1 = 0.1 sec^{-1}$ and $\kappa_2 = 1\times 10^3 sec^{-1}m^{-3}$ as the reaction rates, and $V = 10^{-3}m^3$ as the volume of the vessel where the reactions take place. Plot a time-series of your realizations, as well as the evolution of the stochastic mean $M(t)$ given by

$$M(t) = \frac{\kappa_2 V}{\kappa_1} + \left(M(0) - \frac{\kappa_2 V}{\kappa_1}\right)\exp(-\kappa_1 t).$$

Hint: reactions of the type $\emptyset \xrightarrow{\kappa} \mathcal{A}$ have propensity function of the form $\nu(t) = \kappa V$.

(c) draw 10^6 realizations of the setup in (b) during the first 100 seconds of the reaction and plot a normalized histogram of your realizations at the stopping time $T = 100$ sec. Compare the histogram with the solution to the steady-state version of the chemical master equation, $\phi(\cdot)$, given by

$$\begin{aligned}
\phi(0) &= 1,\\
\phi(1) &= \frac{\kappa_2 V}{\kappa_1}\phi(0),\\
\phi(n+1) &= \frac{1}{\kappa_1(n+1)}[\kappa_1 n\phi(n) + \kappa_2 V\phi(n) - \kappa_2 V\phi(n-1)], \quad \textit{for } n \geq 1.
\end{aligned}$$

Homework

Problem 4. *Consider a model of transcription and translation consisting of three species $(\mathcal{G}, \mathcal{M}, \mathcal{P})$, representing Gene, mRNA, and Protein, respectively. We suppose that there are four possible transitions in our model:*

R1) $\emptyset \xrightarrow{\kappa_1} \emptyset + \mathcal{M}$ *(translation)*

R2) $\mathcal{M} \xrightarrow{\kappa_2} \mathcal{M} + \mathcal{P}$ *(transcription)*

R3) $\mathcal{M} \xrightarrow{d_M} \emptyset$ *(degradation)*

R4) $\mathcal{P} \xrightarrow{d_P} \emptyset$ *(degradation)*

Consider a volume V of size one and assume that we always have one Gene, that is $N_{\mathcal{G}}(t) \equiv 1, t \geq 0$. With the choice of rate constants $\kappa_1 = 200$, $\kappa_2 = 10$, $d_M = 25$, and $d_P = 1$, and of initial quantities $n_{\mathcal{M}}(0) = 50$ and $n_{\mathcal{P}}(0) = 8$:

(a) draw a realization of the stochastic model up to time $t = 8$.

(b) allow for the possibility that the protein dimerizes via the reaction $2\mathcal{P} \xrightarrow{\kappa_3} \mathcal{D}$, and that the degradation of the dimer is allowed by the reaction $\mathcal{D} \xrightarrow{d_d} \emptyset$. With the new set of species $(\mathcal{G}, \mathcal{M}, \mathcal{P}, \mathcal{D})$, draw a realization of the stochastic model when $\kappa_3 = 0.01$, $d_d = 1$ and $n_{\mathcal{D}}(0) = 0$. Hint: reactions of the type $2\mathcal{A} \xrightarrow{\kappa} \mathcal{B}$ have propensity function of the form $\nu(t) = \frac{\kappa}{V^2} N_{\mathcal{A}}(t)(N_{\mathcal{A}}(t) - 1)$.