Problem Sheet 1

1. This is a warm-up problem. You are asked to verify a few results from the Lecture Notes. This problem is here to encourage you to read the Lecture Notes which cover the first four lectures. You do not need to write long derivations (a few lines for each point (a)–(d) will be enough).

(a) Show that (1.23) satisfies the recurrence formula (1.20)–(1.21).

(b) Derive the chemical master equation (2.10).

(c) Consider the chemical system (3.1)–(3.2) for the chemical species B and C. Assume that the number of A molecules is given by (3.16). Show that the equations for the mean values of B and C are exactly given by the system of ODEs (3.17)–(3.18).

(d) Show that the maximum of (4.8) is attained at the point a_m given by (4.9).

2. Consider four chemical species A_1, A_2, A_3 and A_4 in a reactor of volume ν which are subject to the following system of four chemical reactions

$$A_1 \xrightarrow{k_1} A_2, \qquad A_2 \xrightarrow{k_2} A_3, \qquad A_3 \xrightarrow{k_3} A_4, \qquad \text{and} \qquad A_4 \xrightarrow{k_4} A_2.$$

Assume that there are initially 10 molecules of A_1, and no molecules of A_i, $i = 2, 3, 4$ in the system, i.e. $A_1(0) = 10$ and $A_2(0) = A_3(0) = A_4(0) = 0$.

(a) Denote by $p_1(n_1, t)$ the probability that $A_1(t) = n_1$. Find $p_1(n_1, t)$ as a function of rate constants.

(b) Denote by $p_2(n_2, t)$ the probability that $A_2(t) = n_2$. Denote by $\phi_2(n_2)$ the corresponding stationary distribution, i.e.

$$\phi_2(n_2) = \lim_{t\to\infty} p_2(n_2, t).$$

Find $\phi_2(n_2)$ as a function of rate constants k_i, $i = 2, 3, 4$.

(c) What is the average time taken to reach a state with $A_1 = 0$ (no molecules of A_1) ?

(d) Let $k_4 = 0$. Derive a system of ordinary differential equations which describes the time evolution of variances $V_1(t)$ and $V_2(t)$ defined by

$$V_i(t) = \sum_{n=0}^{\infty} \big(n_i - M(t)\big)^2 p_i(n_i, t), \qquad i = 1, 2.$$

(e) Find $V_1(t)$ as a function of time t and k_1.

3. Consider the production-degradation system (1.9) which is described by the chemical master equation (1.11). Denote by $p(n, t)$ the probability that $A(t) = n$. Let $\phi(n)$ be the corresponding stationary distribution defined by (1.19).

(a) Multiply the chemical master equation (1.11) by x^n and sum over n to derive a partial differential equation (PDE) for the probability-generating function $G(x, t)$ defined by (2.3).

(b) Write the ordinary differential equation (ODE) which is satisfied by the stationary probability-generating function, $G_s(x)$, defined by (2.4). Solve this ODE for $G_s(x)$.

(c) Use $G_s(x)$ obtained in part (b) to derive formula for $\phi(n)$. You should again obtain (1.23).

4. Consider a chemical species A in a container of volume ν which is subject to the following two chemical reactions

$$A + A \xrightarrow{k_1} \emptyset, \qquad\qquad \emptyset \xrightarrow{k_2} A.$$

Consider parameter values $k_1/\nu = 0.005\,\mathrm{sec}^{-1}$ and $k_2\nu = 1\,\mathrm{sec}^{-1}$. Denote by $p(n,t)$ the probability that $A(t) = n$. Let $\phi(n)$ be the corresponding stationary distribution defined by (1.19).

(a) Write a computer code which estimates the stationary distribution $\phi(n)$ using long-time simulation of the Gillespie SSA (a4)–(d4).

(b) Write the chemical master equation which is satisfied by $p(n,t)$.

(c) Multiply the chemical master equation by x^n and sum over n to derive a PDE for the probability-generating function $G(x,t)$, defined by (2.3).

(d) Define the corresponding stationary probability-generating function, $G_s(x)$, by (2.4). Show that it is a solution of the ODE

$$G_s''(x) = \frac{k_2\nu^2}{k_1}\frac{1}{1+x}\,G_s(x).$$

(e) Use (2.5) to solve this ODE as

$$G_s(x) = C\sqrt{1+x}\; I_1\left(2\sqrt{\frac{k_2\nu^2(1+x)}{k_1}}\right), \qquad \text{where} \quad C \text{ is a constant.}$$

(f) Use $G_s(x)$ to calculate the stationary distribution $\phi(n)$ and mean $M_s = G_s'(1)$. You can use the derivative formulae for the modified Bessel functions, namely $I_n'(z) = I_{n-1}(z) - n/z\, I_n(z) = I_{n+1}(z) + n/z\, I_n(z)$. Note that the corresponding deterministic ODE model $\mathrm{d}a/\mathrm{d}t = -2k_1a^2 + k_2$ would approximate the mean as 10, while we have $M_s \doteq 10.13$.

(g) Compare your results obtained in part (a) by the Gillespie SSA (a4)–(d4) with formula for $\phi(n)$ derived in part (f) using the probability-generating function.

5. Consider the chemical system (3.25), i.e.

$$3A \underset{k_2}{\overset{k_1}{\rightleftarrows}} 2A, \qquad\qquad A \underset{k_4}{\overset{k_3}{\rightleftarrows}} \emptyset, \tag{3.25}$$

with the values of (dimensionless) rate constants k_1, k_2 and k_3 given as

$$k_1/\nu^2 = 2.5 \times 10^{-4}, \qquad k_2/\nu = 0.18, \qquad k_3 = 37.5.$$

In this problem (and Problem 4 of Problem Sheet 2), we will vary the value of $k_4\nu$ in the interval $(1700, 2500)$ and study the dependence of the behaviour of the chemical system (3.25) on this parameter.

(a) Write the deterministic ODE model describing the system (3.25). Find all steady states of this ODE for (i) $k_4\nu = 1750$; (ii) $k_4\nu = 2100$; (iii) $k_4\nu = 2200$; and (iv) $k_4\nu = 2450$. Which of these steady states are stable?

(b) Plot the dependence of the steady states of the deterministic ODE model as a function of $k_4\nu$ for $k_4\nu \in (1700, 2500)$.

(c) Use the Gillespie SSA (a4)–(d4) to simulate the chemical system (3.25) for (i) $k_4\nu = 1750$; (ii) $k_4\nu = 2100$; (iii) $k_4\nu = 2200$ and (iv) $k_4\nu = 2450$. For each parameter value, plot the time evolution of $A(t)$ and estimate the stationary distribution using long time simulation of the Gillespie SSA (a4)–(d4). Compare with the stationary distribution obtained by the chemical master equation - formula (3.32). If there are any differences, explain them.

A couple of additional questions (OPTIONAL)

6. Consider the production-degradation system (1.9) which is described by the chemical master equation (1.11). Assume that there are initially 0 molecules in the system, i.e. $A(0) = 0$, as in Figure 1.2(a). In particular, we have $M(0) = V(0) = 0$.

(a) By considering (1.17), prove that $V(t) = M(t)$, where $M(t)$ is given by (1.25).

(b) Find solution $p_n(t)$ of (1.11).

(c) Estimate $p_n(t)$ at time $t = 10$ sec using multiple realizations of the SSA (a3)–(d3) for parameter values $k_1 = 0.1\,\text{sec}^{-1}$ and $k_2\nu = 1\,\text{sec}^{-1}$. Use the results of your computer code to verify your solution obtained in part (b).

7. Consider two chemical species A and B in a reactor of volume ν which are subject to the following two chemical reactions

$$A + A \xrightarrow{k_1} B, \qquad\qquad B \xrightarrow{k_2} A + A.$$

These two reactions can also be equivalently written as one reversible chemical reaction:

$$2A \underset{k_2}{\overset{k_1}{\rightleftarrows}} B.$$

Suppose there are initially 100 molecules of A and no molecules of B. Denote by $p(n,t)$ the probability that there are n molecules of B at time t, and by $\phi(n)$ the corresponding stationary probability distribution.

(a) Find $\phi(n)$ as a function of the rate constants k_1 and k_2.

(b) Verify your result in part (a) by using the long-time simulation of the Gillespie SSA (a4)–(d4) for parameter values $k_1/\nu = 0.3\,\text{sec}^{-1}$ and $k_2 = 8\,\text{sec}^{-1}$.