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Stochastic Simulation of Chemical Reactions

In this chapter we will introduce stochastic methods for modelling spatially homogeneous systems of chemical reactions, including the chemical master equation and the Gillespie SSA, where the acronym SSA stands for the term “stochastic simulation algorithm” in this book. We will also discuss the connection between stochastic and deterministic modelling approaches.

1.1 Stochastic Simulation of Degradation

We start with the simplest possible example, which is the single chemical reaction

$$A \xrightarrow{k} \emptyset, \tag{1.1}$$

where A is the chemical species of interest and k is the rate constant of the reaction. The symbol $\emptyset$ denotes chemical species that are of no further interest. The rate constant k in (1.1) is defined so that $k\,\mathrm{d}t$ gives the probability that a randomly chosen molecule of the chemical species A reacts (is degraded) during the time interval $[t, t + \mathrm{d}t)$ where t is time and $\mathrm{d}t$ an (infinitesimally) small time step.

Let us denote the number of molecules of chemical species A at time t by $A(t)$ (a convention that will be used throughout the book). Then, in the time interval $[t, t + \mathrm{d}t)$, a number of things may happen: none of the molecules may react, exactly one may react, or more than one may react. Assuming that each molecule acts independently, we may combine the individual probabilities of reaction to deduce that

$$\begin{array}{lll} \text{no reactions occur} & \text{with probability} & 1 - A(t)k\,\mathrm{d}t + O(\mathrm{d}t^2), \\ \text{exactly one reaction occurs} & \text{with probability} & A(t)k\,\mathrm{d}t + O(\mathrm{d}t^2), \\ \text{two or more reactions occur} & \text{with probability} & O(\mathrm{d}t^2), \end{array}$$

where $O(\mathrm{d}t^2)$ signifies terms proportional to $\mathrm{d}t^2$. If $\mathrm{d}t$ is small enough then the quadratic terms in $\mathrm{d}t$ are much smaller than the linear terms, and they may be safely neglected. Thus, in a small enough time interval, the chance of two or more reactions happening is negligible.

Let us assume that we have n_0 molecules of A in the system at time $t = 0$, i.e. $A(0) = n_0$. Our first goal is to compute the number of molecules $A(t)$ for times $t > 0$. The mathematical definition of the chemical reaction (1.1) can be directly used to design a "naive" stochastic simulation algorithm (SSA) for simulating it. We choose a small time step Δt, and compute the number of molecules $A(t)$ at times $t = i\Delta t$, $i = 1, 2, 3, \ldots$, by testing to see if a reaction occurs in each time interval and updating $A(t)$ accordingly.

To do that, we need a computer routine generating random numbers. Most modern programming languages contain a routine for generating random numbers uniformly distributed in the interval $(0, 1)$ (e.g. the function `rand` in Matlab). The routine will generate a number $r \in (0, 1)$, such that the probability that r is in a subinterval $(a, b) \subset (0, 1)$ is equal to $b - a$ for any $a, b \in (0, 1)$ with $a < b$. Using this routine we compute the number of molecules of $A(t)$ as follows. Starting with $t = 0$ and $A(0) = n_0$, we perform two steps at time t:

```
(a1) Generate a random number $r$ uniformly distributed in the interval
     $(0, 1)$.
(b1) If $r < A(t)k\,\Delta t$, then put $A(t + \Delta t) = A(t) - 1$;
     otherwise, put $A(t + \Delta t) = A(t)$.
     Then continue with step (a1) for time $t + \Delta t$.
```

Since r is a random number uniformly distributed in the interval $(0, 1)$, the probability that $r < A(t)k\,\Delta t$ is equal to $A(t)k\,\Delta t$. Consequently, step (b1) says that the probability that the chemical reaction (1.1) occurs in the time interval $[t, t+\Delta t)$ is equal to $A(t)k\,\Delta t$. Thus step (b1) correctly implements the definition of (1.1) provided that Δt is small. The time evolution of A obtained by the "naive" SSA (a1)–(b1) is given in Figure 1.1(a) for[*] $k = 0.1\,\mathrm{sec}^{-1}$, $A(0) = 20$ and $\Delta t = 0.005\,\mathrm{sec}$. We repeated the stochastic simulation twice and we plotted two realizations of the SSA (a1)–(b1). We see in Figure 1.1(a) that these two realizations of the SSA (a1)–(b1) give two different evolutions. Each time we run the algorithm, we obtain different results. This is generally true for any SSA. Therefore, one might reasonably ask what useful and reproducible

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[*] We use "sec" rather than "s" to denote seconds throughout the whole book. This is to avoid possible confusion with the use of lower case letter s to denote speed or other variables in later chapters of this book.

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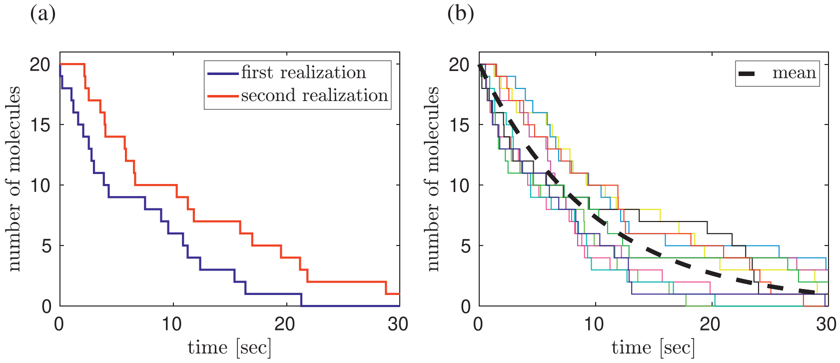

Figure 1.1 *Stochastic simulation of chemical reaction* (1.1) *for* $k = 0.1\,\text{sec}^{-1}$ *and* $A(0) = 20$. (a) *Number of molecules of A as a function of time for two realizations of the "naive" SSA (a1)–(b1) for* $\Delta t = 0.005$ *sec.* (b) *Results of ten realizations of the SSA (a2)–(c2) (solid lines; different colours show different realizations) and stochastic mean* (1.8) *plotted by the dashed line.*

information can be obtained from stochastic simulations? We will come back to this question later in this section.

The probability that exactly one reaction (1.1) occurs during the infinitesimal time interval $[t, t+\mathrm{d}t)$ is equal to $A(t)k\,\mathrm{d}t$. To design the SSA (a1)–(b1), we replaced $\mathrm{d}t$ by the finite time step Δt. In order to get reasonably accurate results, we must ensure that $A(t)k\,\Delta t \ll 1$. For our simulations we used $k = 0.1\,\text{sec}^{-1}$ and $\Delta t = 0.005\,\text{sec}$. Since $A(t) \le A(0) = 20$ for any $t \ge 0$, this gives $A(t)k\,\Delta t \in [0, 0.01]$ for any $t \ge 0$. Consequently, the condition $A(t)k\,\Delta t \ll 1$ is reasonably satisfied during the simulation. We might further increase the accuracy of the SSA (a1)–(b1) by decreasing Δt. However, decreasing Δt increases the computational intensity of the algorithm. The probability that the reaction (1.1) occurs during the time interval $[t, t+\Delta t)$ is less than or equal to 1% for our parameter values. Thus during most time steps we generate a random number r in step (a1) only to find out that no reaction occurs in step (b1): we need to generate a lot of random numbers before the reaction takes place. This naive SSA is extremely inefficient: we can do a lot better.

The key to improving the algorithm is a change in viewpoint. Instead of focusing on time we focus on events: rather than stepping forward in time and asking did a reaction take place, we ask at what time will the next reaction occur?

If the time is t now, our goal is to compute the time $t + \tau$ when the next reaction (1.1) takes place. Of course, τ is a random variable, so that what we need to calculate is its probability distribution function. Let us denote by

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$f(A(t), s)\,\mathrm{d}s$ the probability that, given $A(t)$ molecules at time t in the system, the next reaction occurs during the time interval $[t + s, t + s + \mathrm{d}s)$ where $\mathrm{d}s$ is an (infinitesimally) small time step. In order for this to happen, there must have been no reaction during the interval $[t, t + s)$, and then a reaction must have occurred during the interval $[t + s, t + s + \mathrm{d}s)$. Thus, if we let $g(A(t), s)$ be the probability that no reaction occurs in interval $[t, t + s)$, the probability $f(A(t), s)\,\mathrm{d}s$ can be computed as a product of $g(A(t), s)$ and $A(t + s)k\,\mathrm{d}s$:

$$f(A(t), s)\,\mathrm{d}s = g(A(t), s)A(t + s)k\,\mathrm{d}s.$$

Since no reaction occurs in $[t, t + s)$, we have $A(t + s) = A(t)$, so that in fact

$$f(A(t), s)\,\mathrm{d}s = g(A(t), s)A(t)k\,\mathrm{d}s. \tag{1.2}$$

It remains for us to calculate $g(A(t), s)$. For any $\sigma > 0$, the probability that no reaction occurs in the interval $[t, t + \sigma + \mathrm{d}\sigma)$ can be computed as the product of the probability that no reaction occurs in the interval $[t, t + \sigma)$ and the probability that no reaction occurs in the interval $[t + \sigma, t + \sigma + \mathrm{d}\sigma)$. Hence

$$g(A(t), \sigma + \mathrm{d}\sigma) = g(A(t), \sigma)[1 - A(t + \sigma)k\,\mathrm{d}\sigma].$$

Since no reaction occurs in the interval $[t, t + \sigma)$, we have $A(t + \sigma) = A(t)$. Consequently, after some rearrangement,

$$\frac{g(A(t), \sigma + \mathrm{d}\sigma) - g(A(t), \sigma)}{\mathrm{d}\sigma} = -A(t)k\,g(A(t), \sigma).$$

Passing to the limit $\mathrm{d}\sigma \to 0$, we obtain the ordinary differential equation (in the σ variable)

$$\frac{\mathrm{d}g(A(t), \sigma)}{\mathrm{d}\sigma} = -A(t)k\,g(A(t), \sigma).$$

Solving this equation with initial condition $g(A(t), 0) = 1$, we obtain

$$g(A(t), \sigma) = \exp[-A(t)k\sigma].$$

Now (1.2) can be written as

$$f(A(t), s)\,\mathrm{d}s = A(t)k\exp[-A(t)ks]\,\mathrm{d}s. \tag{1.3}$$

Thus we have found that the time interval to the next reaction, τ, is distributed according to the exponential distribution with mean $(A(t)k)^{-1}$. The exponential distribution is, together with other useful distributions, defined in the Appendix.

To use this in our simulation algorithm we need to generate random numbers τ distributed according to (1.3). The easiest way to accomplish this is to use the following auxiliary function:

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$$F(\tau) = \exp[-A(t)k\tau] = \int_\tau^\infty f(A(t), s)\,\mathrm{d}s. \tag{1.4}$$

The function $F(\tau)$ represents the probability that the time to the next reaction is greater than τ, and is monotone decreasing for $A(t) > 0$. For our present purposes what is important is that, if τ is a random number in the interval $(0, \infty)$, then $F(\tau)$ is a random number in the interval $(0, 1)$. Moreover, if τ is a random number distributed according to the probability density function (1.3), then $F(\tau)$ is a random number *uniformly* distributed in the interval $(0, 1)$. To show this let $0 < a < b < 1$ be chosen arbitrarily. The probability that $F(\tau) \in (a, b)$ is equal to the probability that $\tau \in (F^{-1}(b), F^{-1}(a))$, which is given by the integral of $f(A(t), s)$ over s from $F^{-1}(b)$ to $F^{-1}(a)$. Using (1.3) and (1.4) we obtain

$$\begin{aligned}\int_{F^{-1}(b)}^{F^{-1}(a)} f(A(t), s)\,\mathrm{d}s &= \int_{F^{-1}(b)}^{F^{-1}(a)} A(t)k\exp[-A(t)ks]\,\mathrm{d}s \\ &= -\int_{F^{-1}(b)}^{F^{-1}(a)} \frac{\mathrm{d}F}{\mathrm{d}s}\,\mathrm{d}s = -F[F^{-1}(a)] + F[F^{-1}(b)] = b - a.\end{aligned}$$

Thus, if we have an algorithm that generates a random number r uniformly distributed on $(0, 1)$, we can generate the time of the next reaction by setting

$$r = F(\tau) = \exp[-A(t)k\tau].$$

Solving for τ, we obtain the formula

$$\tau = \frac{1}{A(t)k} \ln\left[\frac{1}{r}\right]. \tag{1.5}$$

Consequently, the improved SSA for the chemical reaction (1.1) can be written as follows. Starting with $t = 0$ and $A(0) = n_0$, we perform three steps at time t:

(a2) Generate a random number r uniformly distributed in the interval $(0, 1)$.
(b2) Compute the time when the next reaction (1.1) occurs as $t + \tau$ where τ is given by (1.5).
(c2) Compute the number of molecules at time $t + \tau$ by $A(t + \tau) = A(t) - 1$. Then continue with step (a2) for time $t + \tau$.

Steps (a2)–(c2) are repeated until we reach the time when there is no molecule of A in the system, i.e. $A = 0$. The SSA (a2)–(c2) computes the time of the next reaction $t+\tau$ using formula (1.5) in step (b2) with the help of one random number only. Then the reaction is performed in step (c2) by decreasing the number of molecules of chemical species A by 1. The time evolution of A obtained

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by the SSA (a2)–(c2) is given in Figure 1.1(b). We plot ten realizations of the SSA (a2)–(c2) for $k = 0.1\,\mathrm{sec}^{-1}$ and $A(0) = 20$. Since the function $A(t)$ has only integer values $\{0, 1, 2, \ldots, 20\}$, it is not surprising that some of the computed curves $A(t)$ partially overlap. On the other hand, all ten realizations yield different functions $A(t)$. Even if we made millions of stochastic realizations, it would be very unlikely (with probability zero) that there would be two realizations giving exactly the same results. Therefore, the details of one realization $A(t)$ are of no special interest (they depend on the sequence of random numbers obtained from the random number generator). However, averaging values of A at time t over many realizations (that is, computing the stochastic mean of A), we obtain a reproducible characteristic of the system – see the dashed line in Figure 1.1(b). The mean of $A(t)$ over (infinitely) many realizations can be also computed theoretically as follows.

Let us denote by $p_n(t)$ the probability that there are n molecules of A at time t in the system, i.e. $A(t) = n$. Let us consider an (infinitesimally) small time step $\mathrm{d}t$ chosen such that the probability that two molecules are degraded during $[t, t + \mathrm{d}t)$ is negligible compared to the probability that only one molecule is degraded during $[t, t+\mathrm{d}t)$. Then there are two possible ways for $A(t+\mathrm{d}t)$ to take the value n: either $A(t) = n$ and no reaction occurred in $[t, t+\mathrm{d}t)$, or $A(t) = n+1$ and one molecule was degraded in $[t, t + \mathrm{d}t)$, i.e.

$$p_n(t + \mathrm{d}t) = p_n(t) \times (1 - kn\,\mathrm{d}t) + p_{n+1}(t) \times k(n + 1)\,\mathrm{d}t.$$

A simple algebraic manipulation yields

$$\frac{p_n(t + \mathrm{d}t) - p_n(t)}{\mathrm{d}t} = k(n + 1)\, p_{n+1}(t) - kn\, p_n(t).$$

Passing to the limit $\mathrm{d}t \to 0$, we obtain the so-called *chemical master equation* in the form

$$\frac{\mathrm{d}p_n}{\mathrm{d}t} = k(n + 1)\, p_{n+1} - kn\, p_n. \tag{1.6}$$

Equation (1.6) looks like an infinite system of ordinary differential equations (ODEs) for p_n, $n = 0, 1, 2, 3, \ldots$. However, our initial condition $A(0) = n_0$ implies that there are never more than n_0 molecules in the system, so that $p_n \equiv 0$ for $n > n_0$ and the system (1.6) reduces to a system of $(n_0 + 1)$ ODEs for $p_0, p_1, \ldots, p_{n_0}$. The equation for $n = n_0$ reads

$$\frac{\mathrm{d}p_{n_0}}{\mathrm{d}t} = -kn_0\, p_{n_0}.$$

Solving this equation with the initial condition $p_{n_0}(0) = 1$ (since we know with certainty that there are n_0 molecules of A at time $t = 0$), we find

$$p_{n_0}(t) = \exp[-kn_0 t].$$

Using this formula in the chemical master equation (1.6) for $p_{n_0-1}(t)$, we obtain

$$\frac{\mathrm{d}}{\mathrm{d}t}\, p_{n_0-1}(t) = kn_0 \exp[-kn_0 t] - k(n_0-1)\, p_{n_0-1}(t).$$

Solving this equation with initial condition $p_{n_0-1}(0) = 0$, we obtain

$$p_{n_0-1}(t) = \exp[-k(n_0-1)t]\, n_0 (1 - \exp[-kt]).$$

Using mathematical induction, it is possible to show that in general

$$p_n(t) = \exp[-knt] \binom{n_0}{n} \{1 - \exp[-kt]\}^{n_0-n}, \tag{1.7}$$

where

$$\binom{n_0}{n} = \frac{n_0!}{n!(n_0-n)!}$$

is the binomial coefficient. Looking at the Appendix, we can observe that the formula (1.7) is the probability mass function of the binomial distribution with parameter $\exp[-kt]$. It provides complete information about the stochastic process defined by (1.1) with the initial condition $A(0) = n_0$. We can never say for sure that $A(t) = n$; we can only say that $A(t) = n$ with probability $p_n(t)$. In particular, we can use (1.7) to derive a formula for the mean value of $A(t)$ over (infinitely) many realizations, which is defined by

$$M(t) = \sum_{n=0}^{n_0} n\, p_n(t).$$

Using (1.7), we deduce that

$$\begin{aligned} M(t) &= \sum_{n=0}^{n_0} n\, p_n(t) \\ &= \sum_{n=0}^{n_0} n \exp[-knt] \binom{n_0}{n} \{1 - \exp[-kt]\}^{n_0-n} \\ &= n_0 \exp[-kt] \sum_{n=1}^{n_0} \binom{n_0-1}{n-1} \{1 - \exp[-kt]\}^{(n_0-1)-(n-1)} \{\exp[-kt]\}^{n-1} \\ &= n_0 \exp[-kt]\,, \end{aligned} \tag{1.8}$$

where the last step follows from the binomial theorem applied to the identity $(\{1 - \exp[-kt]\} + \exp[-kt])^{n_0-1} = 1$. The chemical master equation (1.6) and its solution (1.7) can be also used to quantify the stochastic fluctuations around the mean value (1.8), i.e. how much an individual realization of the SSA (a2)–(c2) can differ from the mean value given by (1.8). We will present the corresponding theory and results on a more complicated illustrative example

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in Section 1.2. Finally, let us note that a classic deterministic description of the chemical reaction (1.1) is given by the ODE (see the Appendix)

$$\frac{\mathrm{d}a}{\mathrm{d}t} = -ka,$$

where $a(t) = A(t)/\nu$ is the concentration of chemical species A in a container of volume ν. Solving this equation with initial condition $a(0) = n_0/\nu$, we obtain the function (1.8) divided by volume ν, i.e. $a(t) = M(t)/\nu$. In other words, the stochastic mean can be obtained by solving the corresponding deterministic ODE. However, we should emphasize that this is not true for general systems of chemical reactions, as we will see in Section 1.4, Section 1.5 and Chapter 2.

1.2 Stochastic Simulation of Production and Degradation

The reaction (1.1) eventually leads to the elimination of all molecules of A. We now make it more interesting by adding also some production of A. Thus let us suppose that we have a chemical species A in a container of volume ν which is subject to the following two chemical reactions:

$$A \xrightarrow{k_1} \emptyset, \qquad \emptyset \xrightarrow{k_2} A. \tag{1.9}$$

The first reaction describes the degradation of chemical A with the rate constant k_1 previously studied. We couple it with the second reaction, which represents the production of chemical A with the rate constant k_2 per unit volume. The exact meaning of the second chemical reaction in (1.9) is that one molecule of A is created during the time interval $[t, t + \mathrm{d}t)$ with probability $k_2 \nu \, \mathrm{d}t$ where ν is the system volume. As before, the symbol $\emptyset$ denotes chemical species that are of no special interest to us, i.e. the second reaction does not mean that chemical A would be produced from empty space. Indeed, in Section 2.4, we revisit this example and present a slightly larger chemical system which has similar dynamics as (1.9) without using notation $\emptyset$ in its production reaction. In this section, the impact of other chemical species on the rate of production of A is assumed to be time-independent and is already incorporated in the rate constant k_2.

The rate constants k_1 and k_2 have different physical units. The rate constant k_1 is expressed in the units of [sec^{-1}]. The units of the rate constant k_2 are [$\mathrm{m}^{-3}\,\mathrm{sec}^{-1}$]. It is the production rate per unit of volume and per unit of time, so that the probability that one molecule of A is created during the time interval $[t, t+\mathrm{d}t)$ is equal to $k_2 \nu \, \mathrm{d}t$. The scaling with the volume ν is natural: if we divide the container into two equal parts, the production rate in each part will be half of the production rate in the whole container. In this section, the scaling with

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the system volume ν is not crucial: to simulate the production of molecules in a container of volume ν, we do not need to specify k_2 and ν individually but only the product $k_2\nu$, which is the global production rate (with units [sec^{-1}]). The scaling of the reaction rates with the volume ν will be more important in later chapters, when we consider spatially inhomogeneous systems.

To simulate the system of chemical reactions (1.9) we want again to think in terms of events by jumping forwards to the time that the next reaction happens. We can do this by performing the following four steps at time t (starting with $A(0) = n_0$ at time $t = 0$):

(a3) Generate two random numbers r_1, r_2 uniformly distributed in $(0, 1)$.
(b3) Compute $\alpha_0 = A(t)k_1 + k_2\nu$.
(c3) Compute the time when the next chemical reaction takes place as $t + \tau$ where

$$\tau = \frac{1}{\alpha_0} \ln\left[\frac{1}{r_1}\right]. \tag{1.10}$$

(d3) Compute the number of molecules at time $t + \tau$ by

$$A(t+\tau) = \begin{cases} A(t) + 1 & \text{if } r_2 < k_2\nu/\alpha_0, \\ A(t) - 1 & \text{if } r_2 \geq k_2\nu/\alpha_0. \end{cases}$$

Then continue with step (a3) for time $t + \tau$.

Let us examine this algorithm, to see why it correctly simulates (1.9). First we observe that the probability that both reactions in (1.9) occur in the time interval $[t, t+\mathrm{d}t)$ is quadratic in $\mathrm{d}t$, and so is negligible as before. Thus the probability that one of the reactions takes place in the time interval $[t, t+\mathrm{d}t)$ is equal to the probability that the first reaction occurs, $A(t)k_1\,\mathrm{d}t$, plus the probability that the second reaction occurs, $k_2\nu\,\mathrm{d}t$. We label this combined probability of some reaction occuring $\alpha_0\,\mathrm{d}t$, and calculate it in step (b3).

The formula (1.10) in step (c3) gives the time $t + \tau$ when the next reaction takes place; it can be justified using the same arguments as for the formula (1.5). Now that we know a reaction has taken place, the final step is to decide which reaction it was. Whether a molecule is produced or degraded depends on the relative probabilities of the two reactions: a molecule is produced with probability $k_2\nu/\alpha_0$; if a molecule is not produced then one must have been degraded. The decision as to which reaction takes place is given in step (d3) with the help of the second uniformly distributed random number r_2.

Five realizations of the SSA (a3)–(d3) are presented in Figure 1.2(a) as solid lines. We plot the number of molecules of A as a function of time for $A(0) = 0$, $k_1 = 0.1\ \text{sec}^{-1}$ and $k_2\nu = 1\ \text{sec}^{-1}$. We see that, after an initial transient, the

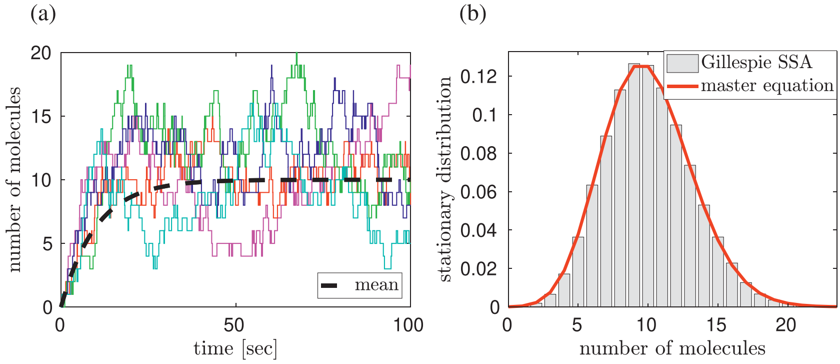

Figure 1.2 *Stochastic simulation of the system of chemical reactions* (1.9) *for* $A(0) = 0$, $k_1 = 0.1\,sec^{-1}$ *and* $k_2\nu = 1\,sec^{-1}$. (a) $A(t)$ *given by five realizations of the SSA (a3)–(d3) (solid lines) and stochastic mean (dashed line).* (b) *Stationary distribution* $\phi(n)$ *obtained by long-time simulation of the SSA (a3)–(d3) (grey histogram) and by formulae* (1.20)–(1.21) *(red solid line).*

number of molecules $A(t)$ fluctuates around its mean value. To compute the mean and quantify the stochastic fluctuations, we again use the chemical master equation. As before, let $p_n(t)$ denote the probability that $A(t) = n$ for $n = 0, 1, 2, 3, \dots$. This time there are three ways we can arrive at n molecules at time $t + \mathrm{d}t$: there could have been n molecules at time t and no reactions happened, or there could have been $n + 1$ molecules and one was degraded, or there could have been $n - 1$ molecules and one was produced. Thus

$$p_n(t + \mathrm{d}t) = p_n(t) \times (1 - k_1 n\,\mathrm{d}t - k_2\nu\,\mathrm{d}t) + p_{n+1}(t) \times k_1(n+1)\,\mathrm{d}t + p_{n-1}(t) \times k_2\nu\,\mathrm{d}t.$$

Rearranging and passing to the limit $\mathrm{d}t \to 0$ gives

$$\frac{\mathrm{d}p_n}{\mathrm{d}t} = k_1(n+1)\,p_{n+1} - k_1 n\,p_n + k_2\nu\,p_{n-1} - k_2\nu\,p_n. \tag{1.11}$$

Equation (1.11) needs to be slightly modified in the case $n = 0$: it is not possible to arrive at zero molecules at time $t + \mathrm{d}t$ by having -1 molecules at time t and producing one molecule! This means that the third term on the right-hand side of (1.11) is missing for $n = 0$. To save ourselves the bother of writing a separate equation for the $n = 0$ case we can continue to use (1.11) if we adopt the convention that $p_{-1} \equiv 0$.

Since one of the reactions (1.9) involves production of A, there is no maximum possible number of molecules of A, as there was in Section 1.1. Thus chemical master equation (1.11) does this time describe an infinite set of ODEs