## Problem Sheet 3

- 1. This is a warm-up problem. You are asked to verify a few results from the Lecture Notes. You do not need to write long derivations (a few lines for each point (a)–(f) will be enough).
  - (a) Show that the SSA (a8)-(c8) and the SSA (a9)-(c9) are equivalent.
  - (b) Derive the equation (9.9).
  - (c) Find the conditional probability that the trajectory of SDE (8.1) crosses the line x = 0 provided that it starts at  $X(t) = x_1 > 0$  and finishes at  $X(t + \Delta t) = x_2 > 0$ , i.e. verify the formula (10.2).
  - (d) Show that (10.4) is the solution of the diffusion equation (8.4) which satisfies the boundary conditions (10.3) and the initial condition  $p_x(x,0) \equiv p_{in}$  for  $x \in (0,\infty)$ .
  - (e) Verify that (10.9) is the solution of the Laplace equation (10.6) satisfying the boundary conditions (10.7)–(10.8).
  - (f) Derive the system of equations (11.5)–(11.8) for the mean vector  $\mathbf{M}(t)$ .
- 2. Consider the velocity jump process (9.17)-(9.18) with initial conditions X(0) = 0 and  $V(0) = v_0$ . In this question you are asked to analyze this velocity jump process in the limit  $\Delta t \to 0$ .
  - (a) Let  $t_1 > 0$  and  $t_2 > 0$ . Compute  $\langle V(t_1)V(t_2) \rangle$  where  $\langle \cdot \rangle$  denotes the average<sup>\*</sup>.
  - (b) Find  $\langle V(t) \rangle$ ,  $\langle V^2(t) \rangle$  and  $\langle V^3(t) \rangle$  as functions of time and  $v_0$ .
  - (c) Compute the mean square displacement  $\langle X^2(t) \rangle^{1/2}$ . Plot the mean square displacement as a function of time.
  - (d) Suppose that t is large. What is the probability that the velocity V(t) is greater than 1?
  - (e) Derive the position-velocity Fokker-Planck equation (9.20).
- **3.** Consider the velocity jump process given by the algorithm (a10)–(d10) in the interval [0, L] where the boundary condition at x = 0 in the step (c10) is modified as the following partially adsorbing boundary condition:

(c10)\* If  $X(t + \Delta t)$  computed by (9.3) is less than 0, then  $\begin{array}{c}
X(t + \Delta t) = -X(t) - V(t) \Delta t \\
V(t + \Delta t) = -V(t)
\end{array}$ with probability  $1 - \frac{2\sigma}{s}$ . Otherwise, the trajectory is terminated.

- (a) Consider this process in the limit  $\Delta t \to 0$ . Show that we can obtain the Robin boundary condition (10.20) in the limit  $s \to \infty$ .
- (b) Consider that the boundary condition at x = L is fully reflective. Implement this algorithm for the model presented in Figure 10.3. Compute the distribution of molecules at t = 10 minutes using this velocity jump process. Compare with the results obtained in Figure 10.3. If there are any differences, explain them.

<sup>\*</sup>In Lectures 1-8, we used notation V(t) to denote variances (see for example, the definitions (1.12), (5.10) and (8.26)). In Lectures 9 and 13, we will use the symbol V(t) to denote the velocity. To denote averages (expected values) like means and variances, we will make use of the notation  $\langle \cdot \rangle$  to avoid confusion. We have previously also used  $E[\cdot]$  to denote expected values.

- 4. Consider an adsorbing sphere with radius  $R_1$  centered at the origin. Let us assume that a molecule diffuses according to (5.18)–(5.20) in the exterior of this sphere, i.e. in the domain  $\{(x, y, z) | R_1^2 < x^2 + y^2 + z^2\}$ . Whenever the molecule hits the sphere, it is adsorbed.
  - (a) Consider that the initial position of the molecule is  $[X(0), Y(0), Z(0)] = (x_0, y_0, z_0)$ . What is the probability that the molecule will be adsorbed by the sphere rather than wander away for good?
  - (b) Assume that the adsorbing sphere is inside a larger sphere with radius  $R_2$  (where  $R_2 > R_1$ ) and the molecule can only diffuse according to (5.18)–(5.20) in the finite domain:

$$\left\{ (x, y, z) \, | \, R_1 < \sqrt{x^2 + y^2 + z^2} < R_2 \right\}.$$

Let us consider reflective boundary conditions on the larger sphere (with radius  $R_2$ ). Calculate the average time taken for the molecule to be adsorbed.

- (c) Suppose now that the sphere with radius  $R_2$  in part (b) is also adsorbing. If the initial position of the molecule is  $[X(0), Y(0), Z(0)] = (x_0, y_0, z_0)$ , what is the probability that it is eventually adsorbed by the inner sphere? By the outer sphere?
- 5. Consider the molecular-based approaches to reaction-diffusion modelling studied in Lecture 12.
  - (a) Derive the formula (12.9) relating the reaction rate constant k and the parameters of the  $\lambda \overline{\varrho}$  model.
  - (b) Consider the algorithm (a12)–(c12). The step (c12) requires that we choose the time step  $\Delta t$  small enough that  $k_2h^2L/5\Delta t \ll 1$ . Let us choose a larger time step  $\Delta t$  which satisfies  $k_2h^2L/5\Delta t \ge 1$ . Can you reformulate step (c12) so that it correctly implements the underlying biological model?
- 6. Consider that the domain [0, L] is divided into K compartments of the length h = L/K and that the diffusing molecule follows the molecular-based one-dimensional model (5.18), starting in the middle of the first compartment, i.e. X(0) = h/2. What is the average time for this molecule to arrive at the middle of the second compartment? Can you see any relation with the rate of jump in the compartment-based model?
- 7. Consider a dimer molecule, modelled as two monomers (balls with masses m) connected by a spring. We denote positions of the centres of the first (resp. second) monomer by  $\mathbf{X}_1 = [X_{1;1}, X_{1;2}, X_{1;3}]$  (resp.  $\mathbf{X}_2 = [X_{2;1}, X_{2;2}, X_{2;3}]$ ) and assume that each monomer has its diffusion constant D and friction coefficient  $\beta$ . Let  $\mathbf{r}$  be the vector describing the separation between monomers, that is,  $\mathbf{r} = \mathbf{X}_2 - \mathbf{X}_1$ . The interaction (force) between the monomers is given in terms of the potential  $\Phi \equiv \Phi(r) : [0, \infty) \rightarrow \mathbb{R}$ , where  $r = |\mathbf{r}|$ . This potential generates an equal and opposite force on each of the monomers with magnitude  $\Phi'(r)$ . Thus, the time evolution of the dimer molecule is described by the following system of SDEs

$$\mathbf{X}_{i}(t+\mathrm{d}t) = \mathbf{X}_{i}(t) + \mathbf{V}_{i}(t) \,\mathrm{d}t, \tag{1}$$

$$\mathbf{V}_{i}(t+\mathrm{d}t) = \mathbf{V}_{i}(t) + (-1)^{i+1} \frac{\Phi'(r)}{m} \frac{\mathbf{r}}{r} \mathrm{d}t - \beta \mathbf{V}_{i}(t) \mathrm{d}t + \beta \sqrt{2D} \mathrm{d}\mathbf{W}_{i}, \quad \text{for } i = 1, 2, \quad (2)$$

where  $\mathbf{V}_i = [V_{i;1}, V_{i;2}, V_{i;3}]$  are velocities of the first and second monomer, respectively, and  $d\mathbf{W}_i = [dW_{i;1}, dW_{i;2}, dW_{i;3}]$  are three-dimensional vectors of independent white noise terms.

What is the diffusion constant of the centre of mass  $(\mathbf{X}_1 + \mathbf{X}_2)/2$  of the dimer molecule?

NOTE: Your solution to Questions 6 and 7 can be shorter than the formulation of these questions.

## A couple of additional questions (OPTIONAL)

8. There is a computer-based exercise in Question 3(b). If you want to have additional practice in writing computer codes which would test the theory from our lectures, you could try the following four exercises. In each case, you are asked to obtain the results presented in the Lecture Notes by using a different computational approach to modelling reaction-diffusion processes.

Since your final goal is to get the same picture as in the Lecture Notes, you will work in the parameter regimes where different methods or different models are expected to give the same answer. Once you have a working code, you could also explore parameter regimes where different methods do not give the same answer, confirming the theoretical analysis from the Lecture Notes.

- (a) Use the velocity jump process (9.17)-(9.18) together with the reflective boundary conditions to design a SSA for the computation of the diffusion example studied in Figures 8.2, 8.3, 9.1(c) and 9.1(d). Plot ten illustrative trajectories and the distribution of 1000 molecules. You should obtain the same answer as in Figures 8.2, 8.3, 9.1(c) and 9.1(d).
- (b) Reformulate the SSA (a12)–(c12) in a way that it does not uses a finite time-step  $\Delta t$  in steps (b12) and (c12), but computes the times when the next production and degradation events happen using exponentially distributed random numbers. Verify your algorithm numerically by recomputing the results from Figures 11.1 and 12.1. Can you further modify this SSA to a fully event-based algorithm which does not use the finite time step at all ?
- (c) Design a SSA for modelling the reaction-diffusion system from Sections 11.1 and 12.1 which has the velocity-jump process (a8)–(c8) as the underlying diffusion model. That is, you are asked to modify the SSA (a12)–(c12) by replacing (a6)–(c6) in the step (a12) by the velocityjump process (a8)–(c8). Verify your algorithm numerically by recomputing the results from Figures 11.1 and 12.1.
- (d) Compute the results in Figure 12.3(b) by implementing the compartment-based model of the reversible reactive boundary condition. To do this, you need to generalize the compartment-based SSA from Section 10.2.
- **9.** Derive the system of equations (12.12)–(12.14) for  $P_{\lambda}$ .