Assignment # **5**   Due: **11/7/25**

Drift, Diffusion, and Dynamic Instability

1. *Treadmilling Actin:* Actin filaments are long, asymmetric, polymers involved in a variety of cellular functions. In some cases the filaments are in a dynamic state in which monomers are removed from one end and added to the other. (The two ends are called minus and plus respectively, and this process is known as treadmilling.)

(a) Assume that monomers are added to the plus-end at rate a, and removed from the minus end at rate b. Write down the equations governing the rate of change of the probabilities $\{p(\ell, t)\}$, for finding a filament of length ℓ at time t. Note that $\ell = 1, 2, , 3, \cdots$, and that the equation of $p(1, t)$ is different from the rest.

(b) It is possible to have a dynamic steady state with probabilities $p^*(\ell)$ that do not change with time. Find the (properly normalized) distribution $p^*(\ell)$ in such a case.

(c) What is the condition for the existence of a time independent steady state, and the mean length of the filament in such a case?

(d) For $a > b$, what is the average length of a filament at time t, starting from individual monomers at time $t = 0$? Calculate the fluctuations (variance) in length, and write down an approximate probability distribution $p(\ell, t)$ with the correct first and second moment.

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2. *Growing/shrinking microtubules:* Consider a slightly generalized model of microtubule growth and shrinkage [M. Dogterom and S. Leibler, Phys. Rev. Lett. **70**, 1347 (1993)], described by the equations

$$\partial_t p_+(x, t) = -f_{+-}p_+ + f_{-+}p_- - \partial_x (v_+ p_+) + d \, \partial_x^2 p_+$$
$$\partial_t p_-(x, t) = +f_{+-}p_+ - f_{-+}p_- + \partial_x (v_- p_-) + d \, \partial_x^2 p_-$$

(a) Such coupled linear equations are usually solved by first Fourier transforming to $\tilde{p}(k, \omega) = \int dx dt e^{i(kx - \omega t)} p(x, t)$. Find the dispersion relations for allowed $\omega(k)$.

(b) Expand the 'slowly varying' mode as $\omega(k) = vk + iDk^2 + \mathcal{O}(k^3)$, and hence obtain the dependence of the drift velocity and diffusion coefficient of the microtubule length on the parameters describing the growing and shrinking states.

(c) Typical values of parameters for microtubules growing in a tubulin solution of concentration $c \approx 10\mu M$ are $v_+ \approx 2\mu m/min$, $v_- \approx 20\mu m/min$, $f_{+-} \approx 0.004s^{-1}$, $f_{-+} \approx 0.05s^{-1}$. Use these parameters (along with $d = 0$) to estimate a time scale τ beyond which diffusion effects are less important than the average drift. (Hence microtubules that have survived to a time τ are unlikely to be completely eliminated by catastrophes.)

(d) Let us assume a microscopic model in which growth occurs by addition of discrete molecules of size a at rates r_+ to the growing state, and detachment at rate r_- shrinking state. Write the corresponding Master equations and construct their continuum limit.

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3. *Internal states:* Consider a molecular motor modeled by an asymmetric hopping model with m internal states. Assume equal forward rates and no backward rates; i.e. $u_i = u$ and $w_i = 0$ for $i = 1, \cdots, m$. Visscher *et al.*, in Nature **400**, 184 (1999), use such a model to estimate the number of (rate limiting) internal states from observations of motion of kinesin on microtubules. In particular, they measure a 'randomness parameter' defined by

$$r \equiv \lim_{t \to \infty} \frac{\langle x^2(t) \rangle - \langle x(t) \rangle^2}{d \, \langle x(t) \rangle},$$

where $x(t)$ is the displacement of the motor after a time t, and d is the step size of kinesin along the microtubule. r measures how regular or noisy the stepping is; $r = 1$ for a pure Poisson process, smaller r indicates internal substeps.

(a) Relate r defined above to the parameters v and D of a drift–diffusion equation.

(b) Obtain v and D in terms of the parameters u, d, and m of the model.

(c) The experimental data (Fig. 4b of the above reference) indicate $r \approx 1/2$ at small force, and $r \approx 1$ at large force. What does this imply about the internal states of the motor?

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4. *Two state motor:* Let us examine the two-state motor (with step length d) in more detail. At each site the motor can be in one of two states, indicated by n or n' for the nth site. The forward transition rates are u_1 (for internal state change from n to n') and u_2 (for hopping from n' to $n+1$), and the corresponding backward transition rates are w_1 and w_2.

(a) Write down the master equations governing the time evolution of the probabilities $p(n, t)$ and $p(n', t)$.

(b) Use Fourier transforms to obtain the dispersion relation $\omega(k)$ for the slowly varying mode.

(c) Calculate the drift velocity v, the diffusion coefficient D, and the Einstein force f_E, as a function of u_1, u_2, w_1, and w_2.

(d) Assume that under an external load F, the forward hopping rate changes as $u_2 \to u_2 \exp\left(-\frac{fd}{k_B T}\right)$, while all the other rates remain unchanged. Calculate $v(f)$, and obtain the stalling force f_s.

(e) Direct observation of kinesin motors moving along microtubules (by Block's group at Stanford using in vitro solution of [ATP]=2mM) indicate $v \approx 670$nm/s, $D \approx 1400$nm^2/s, and $f_s \approx 5$pN. Data from chemical analysis suggest that forward state changes occur at rates of $u_1 \sim 2 \times 10^3\text{s}^{-1}$ and $u_2 \sim 50\text{s}^{-1}$. The backward rates are harder to measure- assume values of $w_1 \sim u_1/100$ and $w_2 \sim u_2/100$. How consistent are these results with a two state model?

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5. (Optional) *Entropy increase* is related to irreversibility. Consider a motor (or any other random walker), whose stochastic motion at long times can be described by a drift velocity v and diffusion constant D.

(a) What is the probability that the walker starting at the origin arrives to a position x after time t; and what is the probability of a reverse path from x to 0 in the same time?

(b) The increase in entropy is quantitatively related to the ratio of forward and backward probabilities as $\Delta S = k_B \ln \left[p_{\text{forward}}/p_{\text{backward}} \right]$. Compute the entropy increase for the random walker described above.

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6. (Optional) *Chemotaxis:* The motion of *E. Coli* in a solution of nutrients consists of an *alternating* sequence of *runs* and *tumbles*. During a run the bacterium proceeds along a straight line for a time t_r with a velocity v. It then tumbles for a time t_t, after which it randomly chooses a new direction $\hat{n}$ to run along. Let us assume that the times t_r and t_t are independently selected from probability distributions

$$p_r\left(t_r\right) = \frac{4t_r}{\tau_r^2} \exp\left(-\frac{2t_r}{\tau_r}\right) \quad , \quad \text{and} \quad p_t\left(t_t\right) = \frac{4t_t}{\tau_t^2} \exp\left(-\frac{2t_t}{\tau_t}\right) \quad .$$

(a) Assuming values of $\tau_r \approx 2\text{s}$, $\tau_t \approx 0.2\text{s}$, and $v \approx 30\mu\text{ms}^{-1}$, calculate the diffusion coefficient D for the bacterium at long times.

(b) In the presence of a chemical gradient the run times become orientation dependent, and are longer when moving in a favorable direction. For preferred motion up the z axis, let us assume that the average run time depends on its orientation $\hat{n}$ according to $\tau_r\left(\hat{n}\right) = \tau_0 + g\hat{n}\cdot\hat{z}$. Calculate the average drift velocity at long times.

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