Solution to Exercise 7: Diffusion

Problem 1: Diffusion of neurotransmitters in the synaptic cleft

a) With cartesian coordinates the operator ∇^2 can be written as

$$\nabla^2 = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2} \quad . \tag{1}$$

Since the concentration c only depends on x, it follows directly that

$$\nabla^2 c = \frac{\partial^2 c}{\partial x^2}. \tag{2}$$

b) (1) The concentration on the postsynaptic side is according to the formula listed in the text given by

$$c(d,t) = \frac{N}{\sqrt{4\pi Dt}} e^{-d^2/4Dt} \quad . \tag{3}$$

<u>$t \to 0$:</u> In this limit both the term $\exp(-d^2/4Dt)$ in the nominator and the term $(4\pi Dt)^{1/2}$ in the denominator approaches zero, but the exponential approaches zero much faster than the square-root (or any polynomial function). Therefore the overall expression approaches zero.

<u>$t \to \infty$:</u> In this limit the term $\exp(-d^2/4Dt)$ in the nominator approaches 1 while the term $(4\pi Dt)^{1/2}$ in the denominator approaches "infinity". Therefore the overall expression approaches zero.

The "physical" reason for this is that (i) in the limit $t \to 0$ all the neurotransmitter molecules are located at the postsynaptic side ($x = 0$), and (ii) in the limit $t \to \infty$ the neurotransmitter molecules distribute equally throughout the available volume. Since the available volume is "infinite" in our free random walk, the concentration at each point goes to zero.

(2) To plot the postsynaptic concentration profile as a function of time it it useful to introduce, for example, the dimensionless time $\tau = Dt/d^2$. Using Eq. (3) the expression for the time-dependent postsynaptic concentration is found to be

$$c(d,\tau) = \frac{N}{\sqrt{4\pi}d} \frac{1}{\sqrt{\tau}} e^{-1/4\tau} \equiv \frac{N}{\sqrt{4\pi}d} f(\tau) \quad . \tag{4}$$

The function

$$f(\tau) = \frac{1}{\sqrt{\tau}}\, e^{-1/4\tau} \tag{5}$$

is shown in Fig.1.

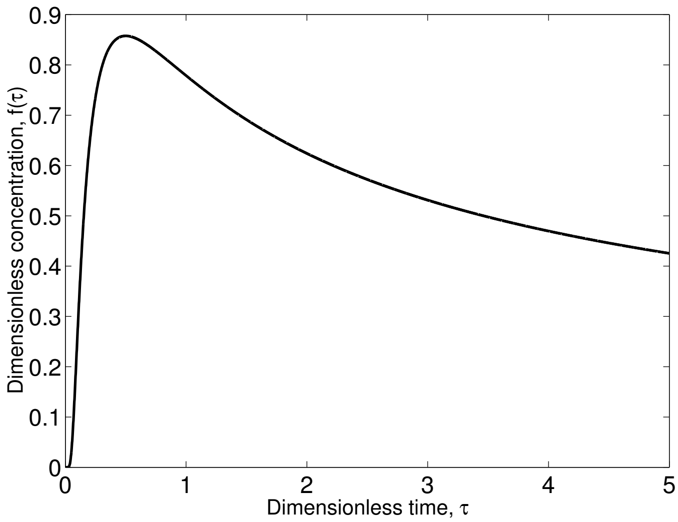

Figure 1: Plot of the function $f(\tau)$ in Eq.(5), corresponding to the "dimensionless concentration" at the postsynaptic side.

(3) To find an expression for t_{max} we find the maximum point of the function $f(\tau)$. This is found by finding the τ for which the the derivative of $f(\tau)$ is zero, i.e.,

$$\frac{df}{d\tau} = -\frac{1}{2}\tau^{-3/2}\, e^{-1/4\tau} + \tau^{-1/2} e^{-1/4\tau}\frac{1}{4}\tau^{-2} = 0 \tag{6}$$

This equality is fulfilled for $\tau = 1/2$, i.e., $\tau_{max} = 1/2$. This corresponds to $t_{max} = \tau_{max} d^2/D = d^2/2D$.

The corresponding maximum point in the postsynaptic concentration is given by

$$c(d, \tau_{max}) = \frac{N}{\sqrt{4\pi d}} f(1/2) = \frac{N}{\sqrt{4\pi d}}\sqrt{2}\, e^{-1/2} = \frac{N}{\sqrt{4\pi d}} \cdot 0.858\ldots \quad . \tag{7}$$

This is seen to qualitatively agree with Fig. 1.

With the parameter values $D = 8 \cdot 10^{-10}$ m^2/s and $d = 50$ Å $= 5 \cdot 10^{-9}$ m inserted into the formula for t_{max} we find

$$t_{max} = \frac{d^2}{2D} = \frac{(5 \cdot 10^{-9})^2}{2 \cdot 8 \cdot 10^{-10}}\mathrm{s} \approx 2 \cdot 10^{-8}\mathrm{s} \tag{8}$$

This is a negligible time delay compared to overall time delay of roughly 1 ms for the "signal" to move from the presynaptic to the postsynaptic side.

c) (1) For the steady-state situation the diffusion equation simplifies to

$$\frac{\partial^2 c}{\partial x^2} = 0 \quad . \tag{9}$$

The general solution to this is

$$c(x) = Ax + B \quad , \tag{10}$$

and the boundary conditions $c(0) = c_0$ and $c(d) = 0$ determine the coefficients to be $B = c_0$ and $A = -c_0/d$. The solution fulfilling our boundary conditions is thus

$$c(x) = c_0(1 - x/d) \quad , \tag{11}$$

which is a linearly decaying concentration profile from the presynaptic to the postsynaptic side.

The corresponding particle flux (which is the same everywhere in the synaptic cleft) is found to be

$$J_\infty = -D\frac{dc}{dx} = -Dc_0\Big(-\frac{1}{d}\Big) = \frac{Dc_0}{d} \quad , \tag{12}$$

We thus see that the steady-state particle flux is proportional to the diffusion constant D and the presynaptic concentration c_0, while it is inversely proportional to the width of the synaptic cleft.

(2) For the plotting of the particle flux it is convenient to use the dimensionless time $\tau = Dt/d^2$. Then the formula for the particle flux is given by

$$\frac{J(\tau)}{J_\infty} = 1 + 2\sum_{n=1}^{\infty}(-1)^n e^{-n^2\pi^2\tau}, \tag{13}$$

for all $\tau > 0$. This function is plotted in Fig.2.

If we (i) could measure the particle flux at the postsynaptic side as a function of time and (ii) knew the value of the width of the synaptic cleft d, we could rapidly find an estimate for D by using our theoretical expression in Eq. (13). For example, for $\tau = 1/6$ (i.e., $t = d^2/6D$) we find from Eq. (13) that $J(1/6) = 0.62J(\infty)$. Thus by reading of the time in our experiment for which $J(t) = 0.62J(\infty)$ (as shown in Fig. 2) we get the experimental value of $t_{1/6}$ and thus D.

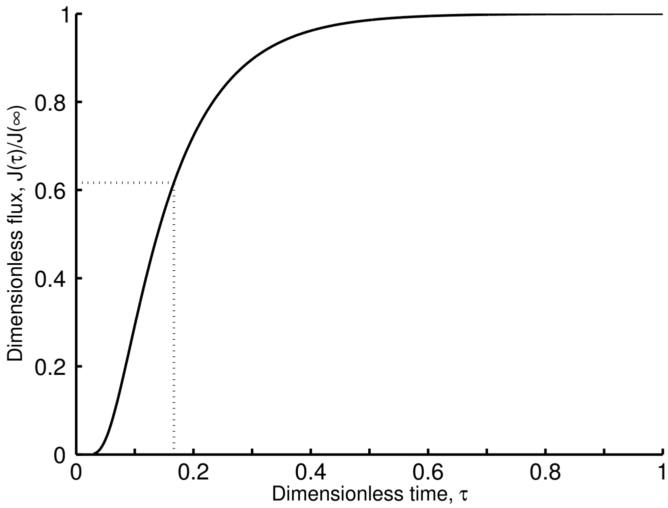

Figure 2: Plot of the particle flux $J(\tau)/J(\infty)$ (Eq. 13) at the postsynaptic side.

Problem 2: Diffusion of point source in 3D

The solution for the diffusion of a point source of a N particles is given by

$$c(\mathbf{r}, t) = \frac{N}{(4\pi Dt)^{3/2}} e^{-\mathbf{r}^2/4Dt} \quad . \tag{14}$$

To obtain the time at which the density wave peaks, set the time derivative to zero:

$$0 = \frac{\partial c}{\partial t} = \left[\frac{r^2}{4Dt^2} - \frac{3}{2t} \right] \frac{N}{(4\pi Dt)^{3/2}} e^{-r^2/4Dt} \tag{15}$$

Note that the notation $\partial/\partial t$ instead of d/dt signifies that r is kept constant when differentiating with respect to t. Note also that r^2 is the same as $\mathbf{r}^2$.

Solution of Eq. (15) gives the peak time t_p:

$$t_p = r^2/6D \tag{16}$$

Note that at the time t_p, the position r corresponds to the expected spatial deviation from the starting point.