X Diffusion

In the first part of this course we assumed that the state of a cell at a particular point in time could be described by the concentrations (or number of molecules in the stochastic case) of key components. These concentrations could change over time but we implicitly assumed that within the cell these concentrations do not vary as a function of position inside the cell. In other words, we considered the cell as a well-stirred biochemical reactor. For small cells such as *Escherichia coli* this is often a valid assumption particularly when we are interested in dynamical phenomena that occur at a much slower time-scale than the relatively fast random mixing by diffusion. However in larger cells such as eukaryotic cells and even sometimes in bacteria we cannot assume that the cell interior is well-stirred. As a starting point for building up the mathematical tools necessary to model spatial inhomogeneous system we use Fick’s laws:

*Fick’s first law*

Consider Fig. 24 illustrating particles moving along one dimension $x$. The particles are randomly moving. Assume there are $N(x)$ particles in the gray region on the left of area $A$ and $N(x+\Delta x)$ particles in the gray region on the right of area $A$. How many particles will
cross the area $A$ to the right? Since the probability to travel to right or the left is identical $0.5N(x)$ particles will travel to the right. However $0.5N(x+\Delta x)$ will travel to the left and cross area $A$. Therefore the net number of crossing to the right is:

$$-\frac{1}{2}(N(x+\Delta x) - N(x)).$$

The flux of molecules $J$ through the area $A$ during a short time interval $\tau$ is defined as:

$$J = -\frac{1}{2}(N(x+\Delta x) - N(x)) \quad \text{[X.1]}$$

rewriting [X.1] in terms of the concentration $C(x) \equiv \frac{N(x)}{A\Delta x}$ results in:

$$J = -\frac{(\Delta x)^2}{2\tau} \left( C(x+\Delta x) - C(x) \right) = -D \frac{\partial C(x)}{\partial x} \quad \text{[X.2]}$$

Therefore in the limit where $\Delta x \to 0$ the flux $J$ is proportional to the concentration gradient and to a constant we define as the diffusion constant. It is not a priori clear why the ratio $D \equiv \frac{(\Delta x)^2}{\tau}$ is a constant. This will become more clear later when we treat diffusion from a more microscopic viewpoint. Equation[X.2] is often called Fick’s first law.

![Figure 25. Derivation of Fick’s second law.](image-url)
**Fick’s second law**

Fick’s second law is a result of his first law and the assumption that the particles cannot be created or destroyed. Consider the volume $A\Delta x$ in Fig. 20. A flux $J(x)$ enters the box from the left and a flux $J(x+\Delta x)$ leaves the box to the right. Since there are no particles created or destroyed in the box the rate of change of the concentration in the box during a short time $\tau$ is given by:

$$\frac{C(t+\tau) - C(t)}{\tau} = \frac{1}{A\Delta x} \left( J(x) - J(x+\Delta x) \right) A\tau = -\left( \frac{J(x+\Delta x) - J(x)}{\Delta x} \right)$$  \[X.3\]

Taking the limit $\tau \to 0$ and $\Delta x \to 0$ results in:

$$\frac{\partial C(x)}{\partial t} = -\frac{\partial J(x)}{\partial x}$$  \[X.4\]

Combing [X.4] with [X.2] yields the second law of Fick:

$$\frac{\partial C(x,t)}{\partial t} = D \frac{\partial^2 C(x,t)}{\partial x^2}$$  \[X.5\]

This tells us that rate of change of the concentration at a specific time and position is proportional to the curvature (second derivative) of the concentration profile.

**Random walks**

Let us now consider a one-dimensional random walk of $N$ particles. A particle always takes a fixed step size $\Delta x$ towards the left or right with equal probability. The position of the particles is denoted by $x_i(n)$, where the subscript denotes which particles ($i=1...N$) and $n$ denotes the number of steps that particle $i$ took. All particles start their random walk at $x=0$: $x_i(0)=0$ for $i=1...N$. It is easy to show that the position averaged over all particles is always zero independent of how many steps were taken:
\[ \langle x(n) \rangle = \sum_{i=1}^{N} x_i(n) = \sum_{i=1}^{N} (x_i(n-1) \pm \Delta x) = \sum_{i=1}^{N} x_i(n-1) = \sum_{i=1}^{N} x_i(0) = 0 \] \hspace{1cm} [X.6]

However individual particles are spreading in both the positive and negative x direction. A convenient way to quantify the spreading is to calculate the variance of the distribution of positions. The variance is defined as

\[ \text{Var}(x(n)) = \langle x^2(n) \rangle - \langle x(n) \rangle^2 \]

\[ \text{Var}(x(n)) = \sum_{i=1}^{N} x_i^2(n) - \left( \sum_{i=1}^{N} x_i(n) \right)^2 = \langle x^2(n-1) \rangle + \Delta x^2 \] \hspace{1cm} [X.7]

As expected the variance is non-zero. For each extra step the variance grows by \( \Delta x^2 \) and since the variance is zero for \( n=0 \) we can write:

\[ \langle x^2(n) \rangle = n\Delta x^2 \] \hspace{1cm} [X.8]

During one step the particle moves at a constant velocity \( v = \Delta x/\tau \). This means that a time \( t \) the particle performed \( n=t/\tau \) steps, therefore the variance is proportional to \( t \):

\[ \langle x^2(n) \rangle = t\frac{\Delta x^2}{\tau} \equiv 2Dt \] \hspace{1cm} [X.9]

Here we used the definition that we introduced in equation [X.2].

**Further reading**