Ben Sauerwine
Biophysics Homework 2

4) <u>Diffusion cares about the dimension of space – sometimes!</u>
Assume that a particle initially localized at the origin of a d-dimensional homogeneous and isotropic space diffuses outward with diffusion constant D. We know that on average it will follow a "spreading Gaussian" probability density of the form:

$$p_{Gauss,d}(\vec{r},t) = \frac{1}{(4\pi Dt)^{\frac{d}{2}}}\exp\left\{-\frac{r^2}{4Dt}\right\}$$

Dimensionality does not seem to enter in any truly exciting way. The purpose of this exercise is to teach you that this is not so. We are interested in the return probability to the origin—or, precisely, in the probability of revisiting a small region of radius δ centered around the origin. The probability of being within that region at any given time t is obviously:

$$p_{back\ \ in\ \ \delta,d}(t) = \int\limits_{|\vec{r}|<\delta} d^d r p_{Gauss,d}(\vec{r},t) = \frac{1}{(4\pi Dt)^{\frac{d}{2}}}\int\limits_{|\vec{r}|<\delta} d^d r \exp\left\{-\frac{r^2}{4Dt}\right\}$$

For sufficiently large times and small δ the exponent will be close to zero and therefore $\exp\left\{-\frac{r^2}{4Dt}\right\} \approx 1$. How much time will the particle spend "close to home" during its "life time"? For this we need to work out

$$T_{\mathrm{Home},d} = \int_{\tau}^{\infty} dt p_{back\ \ in\ \ \delta,d}(t)$$

where τ is an extremely small time after $t = 0$, which we have to insert if we mess with the Gaussian to avoid the divergence at $t = 0$. All we now want to know is whether $T_{\mathrm{Home},d}$ is finite or not. You'll see that the answer depends on the space dimension (look at $d \in \{1,2,3\}$). Making reasonable assumptions about how such a diffusion process happens, what does this tell you about the return probability—or the question whether a particle will ultimately "leave home for good"?

For sufficiently large times t and sufficiently small δ, the probability of the particle being in its home region at this time will then be:

$$p_{back\ \ in\ \ \delta,d}(t) = \frac{1}{(4\pi Dt)^{\frac{d}{2}}} \int_{|\vec{r}|<\delta} d^d r \exp\left\{-\frac{r^2}{4Dt}\right\} \approx \frac{1}{(4\pi Dt)^{\frac{d}{2}}} \int_{|\vec{r}|<\delta} d^d r$$

$$p_{back\ \ in\ \ \delta,1}(t) = \frac{2\delta}{(4\pi Dt)^{\frac{1}{2}}} = \frac{1}{\sqrt{\pi D}} \frac{\delta}{t^{\frac{1}{2}}}$$

$$p_{back\ \ in\ \ \delta,2}(t) = \frac{\pi\delta^2}{(8\pi Dt)} = \frac{1}{8D} \frac{\delta^2}{t}$$

$$p_{back\ \ in\ \ \delta,3}(t) = \frac{4}{3} \frac{\pi\delta^3}{(12\pi Dt)^{\frac{3}{2}}} = \frac{1}{18D\sqrt{3\pi D}} \frac{\delta^3}{t^{\frac{3}{2}}}$$

Now I note that:

$$T_{\mathrm{Home},1} \propto \int_{\tau}^{\infty} \frac{dt}{\sqrt{t}} \to \infty$$

$$T_{\mathrm{Home},2} \propto \int_{\tau}^{\infty} \frac{dt}{t} \to \infty$$

$$T_{\mathrm{Home},3} \propto \int_{\tau}^{\infty} \frac{dt}{t^{\frac{3}{2}}} \to \frac{2}{\sqrt{\tau}}$$

So I see that in one or two dimensions, the particle under diffusion is likely to spend infinitely much time close to its starting point, whereas in more than two dimensions the particle will eventually migrate away from its neighborhood, never to return.

Thus, it appears that by virtue of the number of dimensions a particle may diffuse into, its long time behavior varies greatly.

5) **<u>The Stokes-Einstein Relation</u>**
The density $n(\vec{r},t)$ of particles that can neither be created nor destroyed evolves following the continuity equation $\dot{n} + \vec{\nabla} \cdot \vec{J} = 0$, where $\vec{J}$ is the particle current. For a purely diffusive process this current is $\vec{J}_{diffusion}(\vec{r},t) = -D\vec{\nabla}n(\vec{r},t)$, leading to the equation for free diffusion. However, if the particle is subject to external forces, other contributions to the current arise.

   1. **Say the particles are subject to an external force $\vec{F}$. In a viscous medium they acquire a velocity $\vec{v} = \frac{\vec{F}}{\zeta}$, where ζ is some friction constant. If $\vec{F}$ derives from a potential energy U, show that this drives an additional current given by**

$$\vec{J}_{potential}(\vec{r},t) = -\frac{n(\vec{r},t)}{\zeta}\vec{\nabla}U(\vec{r})$$

It is well-known that $\vec{J} = n\vec{v}$ and that $\vec{F} = -\vec{\nabla}U$. Combining these, then, I get:

$$\vec{J}_{potential}(\vec{r},t) = n(\vec{r},t)\vec{v}(\vec{r},t) = n(\vec{r},t)\frac{\vec{F}(\vec{r},t)}{\zeta} = -n(\vec{r},t)\frac{\vec{\nabla}U(\vec{r})}{\zeta}$$

2. **If the potential localizes the particles in a finite region of space, $n(\vec{r},t)$ will approach an equilibrium distribution $n_{eq}(\vec{r})$. From the condition that the total current $\vec{J} = \vec{J}_{potential} + \vec{J}_{diffusion} = 0$, find this distribution!**

Using $\vec{J} = \vec{J}_{potential} + \vec{J}_{diffusion} = 0$, I then have:

$$n_{eq}(\vec{r})\frac{\vec{\nabla}U(\vec{r})}{\zeta} = -D\vec{\nabla}n_{eq}(\vec{r})$$

or, more conveniently:

$$-n_{eq}(\vec{r})\frac{\vec{\nabla}U(\vec{r})}{D\zeta} = \vec{\nabla}n_{eq}(\vec{r})$$

I see that this first-order differential equation has a simple exponential solution:

$$n_{eq}(\vec{r}) = n_0 \exp\left\{-\frac{U(\vec{r})}{D\zeta}\right\}$$

Here, n_0 is chosen so that $\int n_{eq}(\vec{r})d^3r = N$, the total number of particles. I must obviously constrain that the potential at infinity grows very large, which is the same as saying that the potential localizes the particles to a finite region of space.

3. **Statistical Mechanics teaches us that the thermal equilibrium is the Boltzmann distribution. Comparing this with the result from the previous point, derive an equation between ζ, D, and the thermal energy k_BT. This is called the "Einstein Relation".**

Looking at the Boltzmann distribution,

$$\frac{N_i}{N} = \frac{g_i \exp\left\{-\frac{E_i}{k_B T}\right\}}{Z(T)}$$

I see the obvious analogy to my result from part (2):

$$\frac{N(\vec{r})}{N} = \frac{\exp\left\{-\frac{U(\vec{r})}{D\zeta}\right\}}{n_0}$$

Namely,

$$k_B T = D\zeta$$

The above is the Einstein Relation. I have checked my answer on Wikipedia, which uses instead of the frictional constant ζ a related mobility factor equal to its inverse.

4. **Rummage in your science attic and dig up the expression for ζ valid for spheres of radius R being dragged through a medium of viscosity η. Insert into the Einstein relation. You have arrived at the beautiful "Stokes-Einstein relation", which forms a connection between the thermal unit $k_B T$ and other observables that can be determined macroscopically.**

Take η to be in units $\frac{kg}{m \cdot s}$ and ζ to be in units $\frac{N \cdot s}{m}$.

Next, ignore all fluid-dynamic details. By virtue of the fact that I have only four quantities with distinct units to work with, I may infer that:

$$F \propto Rv\eta \propto m \cdot \frac{m}{s} \cdot \frac{kg}{m \cdot s} = N$$

Now using the same strategy of unit manipulation to infer ζ, I find that:

$$\zeta \propto \frac{F}{v} = R\eta \propto \frac{m \cdot kg}{m \cdot s} = \frac{N \cdot s}{m}$$

So I then conclude that, by substitution and insertion of some proportionality constant,

$$k_B T = DCR\eta$$

Here C is some hydrodynamic constant arising from a fluid flowing around this sphere, neglected since my calculation only looked at the units. Looking the Stokes-Einstein relation up on Wikipedia, I see that my unit-based approach got the appropriate general form and the appropriate constant was $C = 6\pi$.

6) **Partitioning of Hydrocarbons between Water and Oil**
In ideal-gas approximation the chemical potential of a solute molecule may be written as $\mu = \mu_{solvation} + k_B T \ln\left(n\lambda^3\right)$, where n is its number density and λ some length. Having, for instance, an oil and a water phase in contact, how does the density ratio of molecules solvated in them depend on the potential difference $\Delta\mu_{solvation}$? Consider an n-alkane and assume that upon transfer from oil into water each $-CH_2-$ unit in or $-CH_3$ end of the aliphatic chain increases the solvation energy by $\Delta\mu_{solvation} \approx 0.73\, {}^{kcal}\!/\!_{mol}$. Work out the concentration ratio for a chain of length 16 and one for length 32. Comment on the water-solubility of single-tailed surfactants versus two-tailed lipids. How would the hydrophilic head group change the situation? Considering all of this, would we expect to find free lipids inside the cell?

In equilibrium, the chemical potentials of the solute on either side of the boundary will be the same. Then, in equilibrium:

$$\mu_{water} = \mu_{oil}$$
$$l\mu_{solvation,water} + k_B T \ln\left(n_{water}\lambda^3\right) = l\mu_{solvation,oil} + k_B T \ln\left(n_{oil}\lambda^3\right)$$

Above, l indicates the length of the aliphatic chain.

Now, identifying $\Delta\mu_{solvation} \equiv \mu_{solvation,water} - \mu_{solvation,oil}$, I can solve:

$$\frac{l\Delta\mu_{solvation}}{k_B T} = \ln\left(\frac{n_{oil}}{n_{water}}\right)$$
$$\frac{n_{oil}}{n_{water}} = \exp\left\{\frac{l\Delta\mu_{solvation}}{k_B T}\right\}$$

Working out the exponential, I may take at room temperature: $k_B T = 4.1 \cdot 10^{-21} J$

$$\Delta\mu_{solvation} \approx 0.73\, {}^{kcal}\!/\!_{mol} = 3055\, {}^{J}\!/\!_{mol} = 5 \cdot 10^{-21}\, {}^{J}\!/\!_{particle}$$

Now I see straightforwardly that:

$$\frac{n_{oil}}{n_{water}} = \exp\left\{\frac{l\Delta\mu_{solvation}}{k_B T}\right\} \approx \exp\left\{\frac{5}{4}l\right\}$$

So now even for extremely short lipids, the amount of lipid in water is very small. Roughly speaking, $\frac{n_{water}}{n_{oil}} \approx 3.5^{-l}$ at room temperature, where l indicates the length of the aliphatic chain.

If these were double-tailed lipids, I might expect the lipid to be somewhat less than half as soluble than a single-tailed lipid of the same length (speaking in terms of length per tail, not in terms of total length of the two tails) since despite having twice the total hydrophobic chain length the double-tailed lipid may at least avoid water by pushing its tails together.

A hydrophilic head group would slightly increase solubility in water by somewhat by giving some mitigating factor to the entirely unfavorable solubility of the tail region.

At the end of the day, however, the $\frac{n_{water}}{n_{oil}} \approx 10^{-l}$ is the dominating effect, and free lipids will be extremely rare in the cell fluid.