Chapter 2.

Thermal energy: a minnow, an E. Coli and ubiquinone

2a) Consider a minnow using its fins to swim around in water. The minnow must do work against the viscosity of the water in order to make progress. The water's viscosity creates a drag force on the minnow that dissipates its energy. For a sphere moving through water the drag force was derived from hydrodynamics by George Stokes in 1851 [1]. The formula for this force is

$$F_d = -6\pi\eta R\mathrm{v}$$

where η is the viscosity of the water, typically one centipoise (0.01 gm/cm-s), R is the radius of the sphere and v is the sphere's secular velocity. The minus sign reflects the fact that this force opposes the motion and decreases the velocity as is seen with Newton's second law that reads:

$$M\frac{d}{dt}\mathrm{v} = F_d = -6\pi\eta R\mathrm{v}$$

in which M is the mass of the sphere. This simple equation has an exponentially decaying solution with a relaxation time, τ_R, given by

$$\tau_R = \frac{M}{6\pi\eta R}$$

For the minnow these formulas must be modified because the minnow is not a sphere. The minnow will instead be modeled as a prolate ellipsoid of revolution with semi-major axis R and semi-minor axis r. The drag force in this case is

$$F_d = -6\pi\eta rK'\mathrm{v}$$

where K' is given by [2]

$$K' = \frac{\frac{4}{3}\left(\beta^2 - 1\right)}{\frac{\left(2\beta^2 - 1\right)}{\sqrt{\beta^2 - 1}} \ln\left[\beta + \sqrt{\beta^2 - 1}\right] - \beta}$$

in which β is given by

$$\beta = \frac{R}{r}$$

which is greater than one for a prolate ellipsoid. In the appendix, two limits of this formula are discussed. When $\beta = 1$ it can be shown that $K' = 1$, and when $\beta >> 1$, it can be shown that

$$6\pi\eta r K' \cong \frac{4\pi\eta R}{\ln\left[\frac{2R}{r}\right] - \frac{1}{2}}$$

The first formula agrees with the drag force for a sphere, as it should, and the second agrees with an expression that can be found in a book by Howard Berg [3], and is applicable to something cigar shaped, like a minnow.

The drag force given above for a prolate ellipsoid of revolution is for motion parallel to the major axis as would be the case for the swimming minnow. The minnow's fins create a swimming force, F_S, that works against the drag force. Newton's second law for the swimming minnow is

$$M\frac{d}{dt}\mathrm{v} = -6\pi\eta r K'\mathrm{v} + F_S$$

If the swimming is steady, the swimming force will be constant and the minnow will achieve a steady state constant velocity given by

$$v_{SS} = \frac{F_S}{6\pi\eta r K'}$$

In this book, this steady state velocity is what is referred to as *secular* motion.

The importance of viscosity in a hydrodynamic context is determined by a dimensionless parameter called the Reynolds number, R_e [4]. It is defined in the present context by

$$R_e = \frac{R\, v_{SS}}{\nu}$$

where ν is the viscous diffusivity and is defined by

$$\nu = \frac{\eta}{\rho}$$

in which ρ is the mass density of the water. Clearly, the units for the viscous diffusivity are cm^2/s, the same as for the numerator of the Reynolds number. Water has a density close to 1.0 gm/cm^3. Thus the viscous diffusivity is approximately 0.01 cm^2/s. Assume that R is about 8 cm and that the steady state velocity is about 100 cm/s. This is about 2 ¼ miles per hour. Together, these quantities yield a Reynolds number of 80,000. This is a very high Reynolds number (common usage is to speak of high and low Reynolds numbers rather than of large and small ones).

Another important quantity to consider is the thermal speed of the center of mass of the minnow. As will be shown, this is a negligible speed for the minnow, but for the E. Coli and the ubiquinone it will be much larger. The thermal speed (in one dimension), v_T, is defined by

$$v_T = \sqrt{\frac{kT}{M}}$$

The fact that the water in which the minnow swims is warm means that there are thermal fluctuations that perturb the motion of the minnow's center of mass. On the average this motion is characterized by the thermal speed. The volume, V, of the minnow, treated as a prolate ellipsoid of revolution, is

$$V = \frac{4}{3}\pi R r^2$$

Above, R was taken to be 8 cm and r will be taken to be 2 cm. This makes the volume equal to 134 cm^3. The minnow is at neutral density relative to the water which implies that its mass, M, is 134 gm. This makes the thermal speed for a temperature of 25 ^oC (we choose this temperature, equivalent to 298.15 K, throughout as characteristic unless specified otherwise) equal to 1.75×10^{-8} cm/s. This is not quite 2 Angstroms per second and should be compared with the secular velocity of 100 cm/s. The thermal speed is ten orders of magnitude slower than the secular velocity.

The secular velocity is sustained by swimming and can be maintained in a straight line for at least several seconds. The thermal speed, on the other hand, is produced by myriads of collisions between the minnow and the water molecules that surround it. An individual water molecule experiences collisions on a time scale of order 10^{-14} s. Thus the minnow, in contact with huge numbers of water molecules, experiences collisions even more frequently. Since these collisions are from all directions and are uncorrelated the thermal speed does not persist in a given direction for even a time as long as 10^{-14} s. This phenomenon gives rise to the concept of a *mean free time*, the time between collisions. The *mean free path* is the product of the mean free time and the thermal speed and in this case is incredibly short, less than 10^{-22} cm. The thermal speed should be thought of as a magnitude, i.e. a *speed*, and not as a *velocity*, i.e. a vector with direction since the direction does not persist for times of any consequence as far as the minnow is concerned. The extreme values reported here are the reason why the thermal motion of the minnow's center of mass is almost never mentioned and is of no consequence in any case. It is mentioned here for purposes of comparison with the other cases to be described later in this chapter.

The consequences of a short mean free path and a small mean free time can be captured by the concept of *diffusion*. For times long compared to the Langevin relaxation time, the Brownian motion can be described by diffusion [5]. The diffusion equation in one spatial dimension associated with the Langevin equation is given by

$$\frac{\partial}{\partial t} f(x,t) = D \frac{\partial^2}{\partial x^2} f(x,t)$$

where $f(x,t)\,dx$ denotes the probability for finding the Brownian particle between x and $x+dx$ at time t, and D is the diffusion constant with the units cm^2/s and is given by Einstein's formula

$$D = \frac{kT}{6\pi\eta r K'}$$

This result is derived in appendix 2.2. It may be shown that the mean square deviation of a Brownian particle in time t is given by

$$<\Delta x^2> = 2Dt$$

For the minnow the value of the diffusion constant is $D = 6.8 \times 10^{-14} cm^2/s$. Thus the root-mean-square displacement in one second, given by $\sqrt{2Dt}$, is 3.7 x 10^{-7} cm (3.7 nm). In one second the secular displacement is 100 cm. The diffusion of the minnow's center of mass is entirely negligible compared to its secular motion. Because the thermal displacement depends on the square-root of time and the secular displacement depends on time linearly, there is a time for which both are equal. This time works out to be 1.36 x 10^{-17} s. For all longer times the secular displacement is larger and for one second it is 15 orders of magnitude larger, as was just shown above.

A Reynolds number can be associated with the thermal motion of the minnow as well as with the secular motion. Instead of using the steady state

secular velocity in the numerator of the Reynolds number ratio, use the thermal velocity. This gives a Reynolds number of

$$R_e = \frac{R\,\mathrm{v}_T}{\nu} = 1.4\times 10^{-6}$$

which is a very low Reynolds number. In describing the secular motion of the swimming minnow the Stokes formula for the drag force on a prolate ellipsoid was used. This formula is valid only for sufficiently slow motions. The first order Oseen correction to the Stokes formula for a sphere is [6]

$$F_d = -6\pi\eta R\mathrm{v}\left(1+\frac{3}{8}R_e\right)$$

which implies that the simple Stokes formula, without the 3/8 Re correction, only works for low Reynolds number. For the secular motion of the minnow for which the Reynolds number is 80,000, the true drag force is much more complicated, is nonlinear in the velocity and involves a turbulent wake behind the minnow. However, for the thermal motion the Oseen correction is completely ignorable since the thermal Reynolds number is so low. For all of the other cases treated in this book, both for secular and for thermal motion, the Reynolds number is low and the Oseen correction is not needed.

2b) An E. Coli is a small cylindrical bacterium about 2 microns (μm) (2 x 10^{-4} cm) long and with a cross-sectional diameter of about 1 μm. Its mass is about $M = 2\times 10^{-12}\,gm$. In the environment in which it typically swims the viscosity is $\eta = 0.027$ poise (0.027 gm/cm-s). The E. Coli is able to swim because it usually has six flagellar filaments that emanate from random positions on its body and extend into the surrounding medium about three body lengths [7]. Viewing the E. Coli from behind as it swims away the flagellar filaments rotate counter-clockwise and form a synchronous bundle that propels the cell body forward. This bundle can rotate up to 40 times per second. Since the rotation is in a viscous medium there is a reaction torque on the E. Coli body that causes a clockwise rotation of the body, but at a

much slower rate than the rate for the flagellar bundle. This is because the E. Coli moment of inertia is much larger than that of the flagellar bundle. The E. Coli can continue its secular "run" for an average time of 1 second. It then stops, reverses the flagellar filament rotation direction and reorients its direction. When the filaments are rotated in reverse, i.e. clockwise, they do not form a single bundle but instead stick out in different directions and the effect of their rotation is to reorient the direction of the E. Coli in an essentially random way. This motion is called a "tumble". The tumbles take, on average, about 0.1 s. The runs are the secular motion of the E. Coli and provide it with an average speed of $\mathrm{v} = 2 \times 10^{-3}$ cm/s. Therefore, the Reynolds number for the secular motion is

$$R_e = \frac{\mathrm{v}R}{\nu} = \frac{2 \times 10^{-3} \times 10^{-4}}{0.027} = 7.4 \times 10^{-6}$$

which is a very low Reynolds number. In this calculation the semi-major axis is $R = 10^{-4} cm$ and the fluid medium mass density is 1.0 gm/cm^3. Note that this secular Reynolds number is 10 orders of magnitude smaller than that for the minnow. This means that the motion of the E. Coli is dominated by viscosity whereas that of the fish is dominated by inertia. Using the Stokes drag force with the prolate ellipsoid of revolution correction, Newton's second law for the E. Coli is given by

$$M \frac{d\mathrm{v}}{dt} = -6\pi\eta r K' \mathrm{v} + F_S$$

where $r = 0.5 \times 10^{-4} cm$ is the semi-minor axis and for $\beta = 2$ the value of the correction factor is $K' = 1.204$ (the Berg approximation given in the appendix yields 1.504 for this case). This means that the relaxation time for the E. Coli motion is

$$\tau_R = \frac{M}{6\pi\eta r K'} = 6.53 \times 10^{-8} s$$

Therefore, if the E. Coli stops swimming while moving with a velocity of $\mathrm{v}_0 = 2\times10^{-3} cm/s$, then it travels a distance of

$$d = \int_0^\infty dt\ \mathrm{v}_0 \exp\left[-\frac{t}{\tau_R}\right] = \mathrm{v}_0\tau_R = 1.3\times10^{-10} cm$$

before it stops [7]. This is much less than an Angstrom!! This result emphasizes the meaning of viscosity dominating motion for low Reynolds number. However, it is not the whole story because of the Brownian motion that adds a random motion to this secular behavior.

The thermal speed for the E. Coli is given by

$$\mathrm{v}_T = \sqrt{3\frac{kT}{M}} = 0.24\, cm/s$$

This is a hundred times bigger than the secular velocity!! However, the secular velocity is maintained in virtually a straight line for up to a second whereas the thermal speed is maintained in a given direction for much less than 10^{-14} s. Another way to see this to look at the root-mean square deviation, as was done for the minnow. This requires the diffusion constant, D, given by

$$D = \frac{kT}{6\pi\eta rK'} = 1.36\times10^{-9}\,\frac{cm^2}{s}$$

Thus, the root-mean-square deviation, give by $\sqrt{2Dt}$, equals 5 x 10^{-5} cm for a time of one second. The secular displacement in a second is 2 x 10^{-3} cm given the average speed for a run and the fact that runs last on average a second. The secular displacement is 40 times the thermal displacement. While this is a large ratio it is not enormous like it was for the minnow. The time for which these two displacements are equal is 0.68 x 10^{-3} s. For times longer than this the secular displacement dominates. However, this result shows that thermal motions are significant at the ms time scale, the time

scale for many chemical processes in the E. Coli's metabolism. Note also that even though the thermal speed is larger than the secular velocity, the thermal Reynolds number is still much less than one.

2c) Ubiquinone is a ubiquitous component of electron transport chains in aerobic bacteria, mitochondria and chloroplasts. It is also called coenzyme Q, or CoQ for short. Below the notation UQ will be used for the generic quinone. Its ubiquity in aerobic organisms gives it the name ubiquinone. In the most common form in mammalian mitochondria the quinone ring is attached to a tail containing ten isoprene units. This tail facilitates the solubility of UQ in the mitochondrial membrane's lipid interior where UQ carries out its function. In chloroplasts it is called plastoquinone and the isoprene tail may contain 6-10 units. UQ's role is as an intermediary of redox reactions in the electron transport chain. In this role in undergoes a redox cycle in which the two carbonyl oxygens of the quinone ring become successively reduced (to hydroxyls) and oxidized. These oxidation-reductions involve whole hydrogen atoms, i.e. an electron and a proton for each oxygen. Thus the molecular weight of the oxidized form is 862 and that of the reduced form is 864. This makes the mass of UQ or UQH_2 1.44×10^{-21} gm. This is nine orders of magnitude smaller than the mass of the E. Coli, and 23 orders of magnitude smaller than the mass of the minnow.

The electron transport chains are the means by which carbohydrate substrates are oxidized by oxygen in metabolism. Some energy harvesting takes place during glycolysis and during the citric acid cycle, but the majority of the harvested energy is extracted by the electron transport chain through a combination of chemiosmosis and membrane assisted ATP synthesis. This is managed by a series of oxidation-reduction reactions involving iron-sulfur proteins, cytochromes, a few other coenzymes and UQ/UQH_2. While the details of these processes are fascinating, they take us beyond the scope of this chapter. What is important here is the fact that all of these components, except for UQ/UQH_2, are embedded in the membrane by a process of self-assembly and maintain their relative positions to each other and with respect to the inner and outer surfaces of the membrane. The terminology, inner and outer membrane surfaces refers to the lipid bilayer

that makes up the membrane. Since the intact membrane is a closed surface, it separates an interior region from an exterior region. Thus, the membrane's *inner surface* is adjacent to the interior of the membrane surrounded compartment, and the membrane's *outer surface* is adjacent to the external environment surrounded the membrane compartment. In addition, the lipid interior of the membrane bilayer itself will be referred to as well. This is where the enzyme complexes are embedded as well as where UQ/UQH_2 moves about. Only the UQ/UQH_2 are freely mobile species that diffuse back and forth between electron donors at the membrane interior interface and electron acceptors at the membrane exterior interface. Two types of complexes are present. The first is largely made up of iron-sulfur proteins and process reduced $NADH_2$ that is the electron donor supplied primarily by the citric acid cycle. This complex is called NADH-Q reductase. The second is largely made up of cytochromes and has molecular oxygen as its ultimate electron acceptor. It is really two complexes, called cytochrome reductase and cytochrome oxidase. Many replicas of these enzyme complexes exist in a given membrane and many UQ/UQH_2's are also present to connect the two segments of the transport chains. The focus here is the mechanism by which UQ/UQH_2 perform their function. This mechanism will serve as a paradigm for rectified Brownian motion as a general mechanism in subcellular biology.

[See pp. 30-32 of: Lipids, membranes and chemiosmosis]

The carbonyl oxygens of the quinone ring are polar groups, both when oxidized and when reduced to hydroxyl groups. As such they would not be very soluble in the interior of the membrane lipid bilayer. The isoprene tail, however, is lipophilic and flexible. It is reasonable to assume that the tail wraps around the quinone ring and shields the polar groups from the lipid environment in which UQ/UQH_2 move. This means that UQ/UQH_2, whether oxidized or reduced, may be modeled as a sphere of radius 7.5 Angstroms, or 0.75 nm given its mass. Membranes of the lipid bilayer structure are between 60 and 100 Angstroms thick. Since the UQ/UQH_2 has a radius its center's motion across the membrane will be assumed to cover about 80 Angstroms, if a membrane thickness of 95 Angstroms is assumed and room

is left for the size of the UQ/UQH_2. The redox potential change from the electron donor side to the electron acceptor side for UQ is of the order of 0.1V (Volts) during steady state metabolism. Since UQ is reduced by two electrons (and two protons) the change in Gibbs free energy is given by -0.1 x 2 x 1.6 x 10^{-19} J per molecule. Converting to Kcal requires multiplication by $10^{-3}/4.18$, yielding a final result of 7.7 x 10^{-24} Kcal. To get this in Kcal per mol requires a factor of 6 x 10^{23}, yielding 4.6 Kcal/mol. This is not very much energy and as will be seen it has nothing directly to do with the energetics of actually getting the UQ across the membrane.

Picture a cut through the membrane oriented so that the interior compartment is on the left and the external environment is on the right. UQ is reduced near the left side of the membrane by electron donors and is called UQH_2. Near the right side of the membrane, electron acceptors oxidize UQH_2 back into UQ, the oxidized form. These quinone species move in between through the lipid bilayer interior of the membrane. This interior has a viscosity of about 25 cp (0.25 gm/cm-s). Their dynamic motion is governed by the Langevin equation with Stokes drag force given for a sphere.

$$M\frac{d}{dt}\mathbf{v} = -6\pi\eta R\mathbf{v} + \tilde{\mathbf{F}}(t)$$

wherein the mass, radius and viscosity are given above and the fluctuating force satisfies the fluctuation-dissipation relation given in appendix 2.2. For this case the Langevin relaxation time is given by

$$\tau_R = \frac{M}{6\pi\eta R} = 4.07\times10^{-15}s$$

This is a very short relaxation time and if it is much shorter than the time for UQ/UQH_2 to cross the membrane then the Langevin description of the motion can be replaced by diffusion in accord with appendix 2.2. This condition can be determined self-consistently by assuming that diffusion is a satisfactory description and computing the root-mean-square displacement

formula to get the average time of transit across the membrane. The Einstein formula for the diffusion constant is

$$D = \frac{kT}{6\pi\eta R} = 1.16 \times 10^{-7} \frac{cm^2}{s}$$

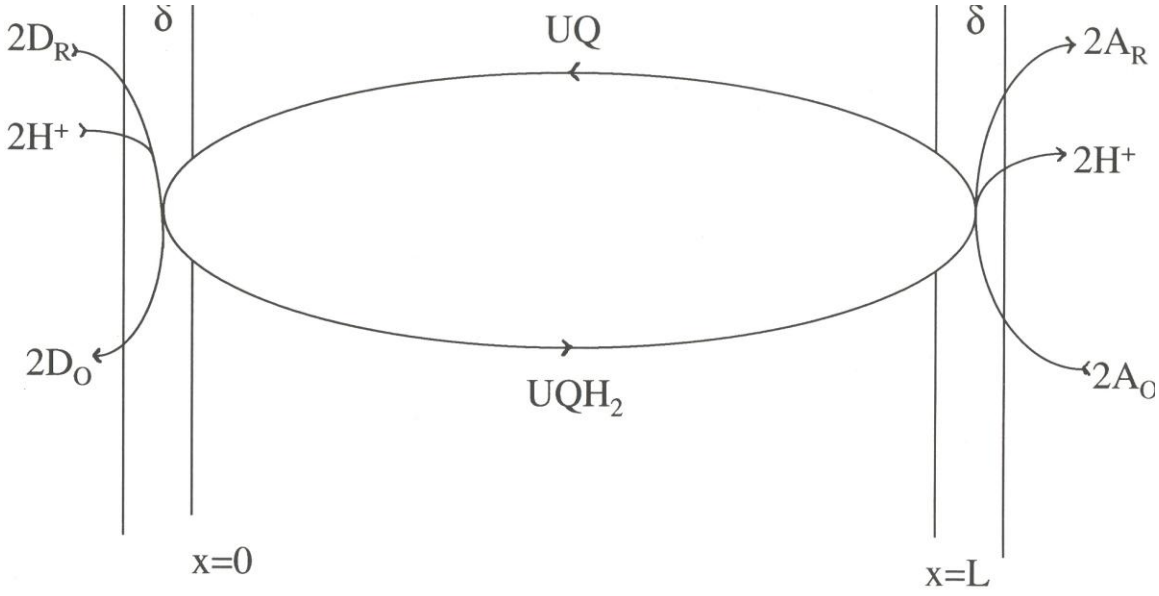
Assuming that UQ/UQH_2 travel a distance $d = 8\,nm$, the diffusion time, t_D, for membrane crossing is given by

$$t_D = \frac{d^2}{2D} = 2.75 \times 10^{-6} s$$

Since this is 9 orders of magnitudes longer than the Langevin relaxation time, the description is in the extreme diffusion limit of the Langevin equation. While this may seem surprising for such a small distance as 8 nm, it is a result of looking at a molecule rather than at some macroscopic object. The Langevin relaxation time is so short because the mass is so small. A better approach to this issue is to calculate the so-called mean first passage time (MFPT) for the quinone to go across the membrane. In this instance the result is precisely the same as given above.

The stage is now set to consider rectified Brownian motion for the quinone shuttle. Ubiquinone (UQ) receives a pair of electrons from FeS-proteins situated near the inside surface of the bacterial membrane at the same time that it receives a pair of protons from the cytosol of the bacterium. These two pairs reduce UQ to UQH_2. This reduced species of quinone is free to diffuse inside the lipid bilayer interior of the bacterial membrane. Eventually, in a few microseconds as was computed above, it arrives near the outside surface of the bacterial membrane where it gives up its electrons to cytochromes and its protons to the external milieu in which the bacterium lives. Having done so, the quinone is re-oxidized and UQH_2 becomes UQ again. This species is free to diffuse inside the lipid interior of the bacterial membrane and eventually makes its way back to near the inside surface for another round of reduction and oxidation. As long as there are electron donors near the inside surface and electron acceptors near the outside surface

there will appear, on the average, to be a steady cycle of UQH_2 moving from inside to outside and UQ moving from outside to inside while shuttling both electrons and protons. The electrons travel down the electron transport chain and the protons traverse the membrane from inside to outside. Thus, the electron donors and acceptors create asymmetric boundary conditions for the quinone diffusion by changing the identity of ubiquinone from reduced to oxidized to reduced *etcetera*. This is the essence of rectified Brownian motion.



This description can be made quantitative by explicitly using the diffusion equation. Let $f(x,t)$ denote the probability density at time t for reduced UQH_2 and let $g(x,t)$ denote the probability density at time t for oxidized UQ. The inside surface of the membrane is located at $x=0$ and the outside surface is located at $x=d$ (in the figure x = L is used). In steady state it is expected that the probability density for UQH_2 at the inside surface, denoted by Q_{in}^{r}, and the probability density for UQH_2 at the outside surface, denoted by Q_{out}^{r}, satisfy $Q_{in}^{r} > Q_{out}^{r}$, because UQH_2 is produced at the inside surface and is converted at the outside surface. Similarly, in steady

state it is expected that the probability density for UQ at the inside surface, denoted by Q_{in}^{o}, and the probability density for UQ at the outside surface, denoted by Q_{out}^{o}, satisfy $Q_{out}^{o} > Q_{in}^{o}$, because UQ is produced at the outside surface and is converted at the inside surface. The reduced species satisfies the diffusion equation

$$\frac{\partial}{\partial t} f(x,t) = D \frac{\partial^2}{\partial x^2} f(x,t)$$

with the boundary conditions at steady state given by

$$f_{SS}(0) = Q_{in}^{r} \quad and \quad f_{SS}(d) = Q_{out}^{r}$$

where the subscript SS denotes the steady state values. Similarly, the oxidized species satisfies the diffusion equation

$$\frac{\partial}{\partial t} g(x,t) = D \frac{\partial^2}{\partial x^2} g(x,t)$$

with the boundary conditions at steady state given by

$$g_{SS}(0) = Q_{in}^{o} \quad and \quad g_{SS}(d) = Q_{out}^{o}$$

These equations are easily solved and have the steady state solutions

$$f_{SS}(x) = f_{SS}(0) - \frac{x}{d}\left(f_{SS}(0) - f_{SS}(d)\right)$$

$$g_{SS}(x) = g_{SS}(0) - \frac{x}{d}\left(g_{SS}(0) - g_{SS}(d)\right)$$

The probability currents, or fluxes, are defined by

$$-D\frac{\partial}{\partial x}f_{ss}(x)=\frac{D}{d}\left(f_{ss}(0)-f_{ss}(d)\right)>0$$
$$-D\frac{\partial}{\partial x}g_{ss}(x)=\frac{D}{d}\left(g_{ss}(0)-g_{ss}(d)\right)<0$$

wherein the left-hand sides define the fluxes in the manner that is standard for diffusion (see appendix 1.1), and the right-hand sides are the results for the particular steady state solutions given above. The inequalities result from the boundary conditions. The meaning of these fluxes is simple, the reduced species goes from 0 to d and the oxidized species goes from d to 0. The flux magnitude is determined by

$$\frac{D}{d}=\frac{1.16\times10^{-7}}{8\times10^{-7}}\frac{cm}{s}=0.145\frac{cm}{s}$$

Note that the same D is used for both UQ and UQH_2 because they are of only slightly different radii, differing in mass by only 2 daltons out of 862. As long as energy metabolism is functioning so that the electron donors and acceptors maintain the asymmetric boundary conditions for reduced and oxidized quinone species, these non-zero fluxes are unchanged. If metabolism is shut down, then the boundary conditions become symmetric and the fluxes vanish.

Consider the thermal speed of the quinones. It is given by

$$\mathrm{v}_T=\sqrt{\frac{kT}{M}}=5.34\times10^{3}\ \frac{cm}{s}$$

This is equivalent to 120 miles per hour. If the quinones could move in a straight line at this speed, they would cross the 8 nm membrane in 1.5 x 10^{-10} s. This is four orders of magnitude faster than the diffusion time calculated above. The difference is accounted for by the fact that the Brownian motion is not sustained in a straight line for even as long as 10^{-14} s since the mean free time is less than this. Brownian motion is an erratic back and forth motion over very short steps. Thus, the path from one side of the membrane to the other by Brownian motion is not a straight path but is instead made up

of very many short back and forth steps so that the total Brownian path length actually traversed by the quinones is, on the average, of order 80 μm. Unlike the minnow or the E. Coli, the quinones have no other means for motion than Brownian motion. There are no fins nor flagella for the quinones. Since the redox states of UQ and UQH_2 are both electrically neutral, there is no electrical force caused by the electrical potential difference across the membrane created by chemiosmosis in actively metabolizing cells and organelles. This means that at the subcellular molecular level, rectified Brownian motion is perhaps the only source of effectively secular motion.

Appendix 2.1: Drag force correction formula

For $\beta = 1$ the prolate ellipsoid of revolution is simply a sphere after all and the correction factor, K', should equal 1. To see that this is so, replace β by $1+\Delta$ where $\Delta > 0$ for the prolate case. The desired limit is the limit $\Delta \to 0^+$. In this limit, replace β^2 by $1+2\Delta$ everywhere in K'. The key step in taking the limit is in properly expanding the logarithm term to third order:

$$\ln\left[1+\Delta+\sqrt{2\Delta}\right] \cong \Delta+\sqrt{2\Delta}-\frac{1}{2}\left(2\Delta+2\Delta\sqrt{2\Delta}\right)+\frac{1}{3}\left(\sqrt{2\Delta}^{3}\right)$$
$$=\sqrt{2\Delta}\left(1-\Delta+\frac{2}{3}\Delta\right)=\sqrt{2\Delta}\left(1-\frac{1}{3}\Delta\right)$$

When this is combined with the other factors in the denominator, both the denominator and the numerator become $\frac{8}{3}\Delta$ as $\Delta \to 0^+$.

The other limit is the highly prolate limit for which $\beta >> 1$. In this case it is easier to work with $\theta = \beta^{-1}$, in which case $\theta << 1$. K' can now be written in the form

$$K' = \frac{\frac{4}{3}\left(1-\theta^2\right)}{\frac{\theta\left(2-\theta^2\right)}{\sqrt{1-\theta^2}}\ln\left[\frac{1+\sqrt{1-\theta^2}}{\theta}\right]-\theta}$$

For small θ it follows that

$$\ln\left[\frac{1+\sqrt{1-\theta^2}}{\theta}\right] \cong \ln 2 - \frac{1}{4}\theta^2 - \ln\theta = \ln\left[\frac{2}{\theta}\right] - \frac{1}{4}\theta^2$$

Combining this with the other factors and dropping all θ^2 terms yields

$$K' \cong \frac{2}{3\theta}\left(\frac{1}{\ln\left[\frac{2}{\theta}\right]-\frac{1}{2}}\right)$$

This verifies the drag formula quoted from Berg in the text above. For a value of $\theta = 0.25$ which will be used for the minnow, the exact formula for K' gives 1.598 whereas the approximation gives 1.688. This is not too bad since θ is not really much less than 1.0. Thus the exact formula will be used. In the E. Coli case, $\theta = 0.5$ is used and the approximation is quite bad.

Appendix 2.2: derivation of the diffusion equation

Start from the generic Langevin equation for a sphere of radius R

$$M\frac{d}{dt}\mathbf{v} = -6\pi\eta R\mathbf{v} + \tilde{\mathbf{F}}(t)$$

in which $\tilde{\mathbf{F}}(t)$ is a fluctuating force that represents the statistical properties of the myriads of collisions between the water molecules and the Brownian particle. An exact dynamical solution to the problem of the motion of the Brownian particle and all of the fluid molecules by Newton's laws is simply intractable. By introducing a fluctuating, or *stochastic* force, Langevin was

able to capture the essential statistical properties in a phenomenological equation. The statistical properties for $\tilde{\mathbf{F}}(t)$ are that it is a Gaussian process with first and second moments given by

$$<\tilde{\mathbf{F}}(t)> = 0$$
$$<\tilde{F}_i(t)\tilde{F}_j(t')> = 2kT\times 6\pi\eta R\,\delta_{ij}\;\delta(t-t')$$

The first moment equation implies that on the average the fluctuating force has no effect since collisions are equally likely from all directions. The second moment equation is more complicated in meaning. The force subscripts denote the Cartesian components and the Knonecker delta of these subscripts implies that the different Cartesian component fluctuate independently of each other. The Dirac delta function of time means that the correlations are very short lived. The correlation coefficient contains two types of terms. The first term is the thermal factor, kT, that implies that the amplitude of the fluctuations increases with temperature. The second factor is identical to the Stokes drag coefficient and is the basis for what is called the fluctuation –dissipation relation that intimately connects the fluctuation strength with the secular relaxation parameter. When the relaxation time is very short, or when the dynamics is at very low Reynolds number, then the inertial term in the Langevin equation can be neglected and the equation becomes

$$0 = -6\pi\eta R\mathbf{v} + \tilde{\mathbf{F}}(t)$$

and since

$$\mathbf{v} = \frac{d\mathbf{x}}{dt}$$

this reduced equation is equivalent to

$$\frac{d\mathbf{x}}{dt} = \frac{\tilde{\mathbf{F}}(t)}{6\pi\eta R}$$

This stochastic differential equation can be written as

$$\frac{d\mathbf{x}}{dt} = \tilde{\mathbf{g}}(t)$$

in which $\tilde{\mathbf{g}}(t)$ inherits statistical properties from $\tilde{\mathbf{F}}(t)$ given by

$$< \tilde{\mathbf{g}}(t) > = 0$$
$$< \tilde{g}_i(t)\tilde{g}_j(t') > = \frac{2kT}{6\pi\eta R}\ \delta_{ij}\ \delta(t-t')$$

To every such stochastic differential equation there is associated a Fokker-Planck equation [8] that in this case reads

$$\frac{\partial}{\partial t}P(\mathbf{x},t) = \frac{kT}{6\pi\eta R}\nabla^2 P(\mathbf{x},t)$$

This is clearly a diffusion equation with a diffusion constant given by Einstein's formula. When it is restricted to one dimension the Laplace operator is replaced by a second order derivative in x.

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