Chapter 3.

The Brownian motion work theorem

3a) The general expression for Newton's second law for Brownian objects subject to fluctuating thermal forces, $\tilde{\mathbf{F}}(t)$, and secular forces, such as the swimming force, $\mathbf{F}_s$, is given by the Langevin equation

$$M\frac{d}{dt}\mathbf{v} = -6\pi\eta r K'\mathbf{v} + \tilde{\mathbf{F}}(t) + \mathbf{F}_S$$

where the shape factor for a prolate ellipsoid of revolution, K', has been included and is equal to one if the semi-major axis, R, and the semi-minor axis, r, are equal, as in the case of a sphere. The fluctuating force components are statistically determined by

$$< \tilde{F}_i(t)\tilde{F}_j(t') > = 2kT6\pi\eta r K'\,\delta_{ij}\,\delta(t-t')$$

This means that correlations last for an extremely short time, modeled here by a Dirac delta function of the time variables, are vanishing for different Cartesian components, modeled here by the Kronecker delta function of the Cartesian indices, proportional to temperature and also proportional to the drag coefficient of the drag force. This last factor is the substance of what is called the fluctuation-dissipation relation because it connects the strength of the fluctuations to the rate of dissipation. The fluctuating force is completely independent of the secular force, the swimming force, i.e.

$$< \tilde{\mathbf{F}}(t)\mathbf{F}_S > = 0$$

In appendix 3.1 the types of calculations producing results to be presented here are elucidated. In the appendix, the Brownian particle is assumed to be a sphere whereas here the shape factor, K', is included as well.

The relaxation time for the Langevin equation above is given by

$$\tau_R = \frac{M}{6\pi\eta r K'}$$

This permits rewriting the Langevin equation in the form

$$\frac{d}{dt}\mathbf{v} = -\frac{1}{\tau_R}\mathbf{v} + \frac{\tilde{\mathbf{F}}(t)}{M} + \frac{\mathbf{F}_\mathrm{s}}{M}$$

This equation has the formal solution

$$\mathbf{v}(t) = \mathbf{v}(0)\exp\left[-\frac{t}{\tau_R}\right] + \frac{1}{M}\int_0^t ds \exp\left[-\frac{(t-s)}{\tau_R}\right]\left(\mathbf{F}_\mathrm{s} + \tilde{\mathbf{F}}(s)\right)$$

$$= \mathbf{v}(0)\exp\left[-\frac{t}{\tau_R}\right] + \frac{1}{M}\mathbf{F}_\mathrm{s}\tau_R\left(1 - \exp\left[-\frac{t}{\tau_R}\right]\right) + \frac{1}{M}\int_0^t ds \exp\left[-\frac{(t-s)}{\tau_R}\right]\tilde{\mathbf{F}}(s)$$

The first term depends on the initial velocity that is given by a Maxwell distribution and which will ultimately be averaged over with respect to the Maxwell distribution. The second term results from the secular swimming force. Because the drag force is proportional to the velocity, the steady state result of the secular force is a constant velocity rather than a constant acceleration as would be the case in the absence of a drag force. The exponential time dependence in the first two terms decays to zero very quickly for very short relaxation times. Thus, in steady state the initial velocity term is absent and the secular force term is the constant $\frac{1}{M}\mathbf{F}_\mathrm{s}\tau_R$. The third term is of a different kind because it is never constant but instead fluctuates indefinitely. It represents the residual thermal fluctuations that accompany the secular motion. Only its statistical properties can be determined and this is done through averaging.

To determine the average work done by the three parts of the Langevin force it is necessary to perform double averages (see appendix 3.1) of products of the forces with the velocity. These averaged products yield the power, and their time integrals over a finite time interval yield the work done for that time interval. The secular force power is given by

$$\{<\mathbf{F}_s \cdot \mathbf{v}(t)>\} = \frac{1}{\mathrm{M}} F_S{}^2 \tau_R \left(1 - \exp\left[-\frac{t}{\tau_R} \right] \right)$$

The velocity contains an initial velocity term that does not survive the Maxwell averaging, and a fluctuating force term that does not survive the stochastic force averaging. Each of these terms vanishes because they are linear. The Brownian motion stochastic force power is given by

$$\{<\tilde{\mathbf{F}}(t) \cdot \mathbf{v}(\mathrm{t})>\} = \frac{1}{M} \int_0^t ds \exp\left[-\frac{(t-s)}{\tau_R} \right] <\tilde{\mathbf{F}}(t) \cdot \tilde{\mathbf{F}}(s)>$$

$$= \frac{1}{M} \int_0^t ds \exp\left[-\frac{(t-s)}{\tau_R} \right] 3 \times 2kT \times 6\pi\eta r K' \delta(t-s)$$

$$= \frac{1}{2M} 3 \times 2kT \times 6\pi\eta r K' = 3 \frac{kT}{\tau_R}$$

The factor of 3 is from the dimensionality of the description and the result is one thermal unit of energy, kT, per relaxation time. As will be seen below for ubiquinone, for which the relaxation time is very short, this is a very large power. Finally, the drag force power is given by

$$-6\pi\eta r K' \{<\mathbf{v}(t) \cdot \mathbf{v}(t)>\} = -6\pi\eta r K' \{\mathbf{v}(0) \cdot \mathbf{v}(0)\} \exp\left[-\frac{2t}{\tau_R} \right]$$

$$+\frac{-6\pi\eta rK'}{M^2}\int_0^t ds\int_0^t ds'\exp\left[-\frac{(t-s)+(t-s')}{\tau_R}\right]3\times 2kT\times 6\pi\eta rK'\,\delta(s-s')$$

$$=-6\pi\eta rK'\times 3\frac{kT}{M}\exp\left[-\frac{2t}{\tau_R}\right]+\frac{-6\pi\eta rK'}{M^2}\frac{\tau_R}{2}\left(1-\exp\left[-\frac{2t}{\tau_R}\right]\right)3\times 2kT\times 6\pi\eta rK'$$

$$=-3\frac{kT}{\tau_R}\exp\left[-\frac{2t}{\tau_R}\right]-3\frac{kT}{\tau_R}\left(1-\exp\left[-\frac{2t}{\tau_R}\right]\right)$$

$$-3\frac{kT}{\tau_R}$$

wherein the definition of the relaxation time has been substituted several times. Notice how the Maxwell average of the quadratic initial velocity term is cancelled by one of the terms in the quadratic fluctuating force term, yielding a constant final result. This fact is an aspect of what is called *stationarity* for this stochastic process.

Notice that the Brownian motion fluctuating force produces a positive power, i.e. the fluctuating force does work on the Brownian particle. In contrast, the drag force produces a negative power, that means the Brownian particle does work against viscosity. The magnitudes of these two powers is the same. The work done on the particle by the fluctuating force is precisely cancelled by the work done against viscosity. This is a manifestation of the fluctuation-dissipation relation.

3b) For the minnow, the secular force power is

$$\frac{1}{\mathrm{M}}F_S^{\,2}\tau_R\left(1-\exp\left[-\frac{t}{\tau_R}\right]\right)$$

in which $M = 134gm$, $\tau_R = 222s$ (recall from appendix 2.1 that $K' = 1.598$ and $r = 2\,cm$), and $F_S = 6\pi\eta r K' \mathrm{v}_{SS} = 60\,dynes$ ($\mathrm{v}_{SS} = 100cm/s$). Clearly, the relaxation time in this case is not small. The maximum power at times long compared to the relaxation time works out to be 5.96 x 10^{-4} Watts (W). This is barely more than ½ mW. While this may seem rather small it only means that the minnow's swimming involves a power about 100 times smaller than a 60 W light bulb. Since the Stokes drag force is really not valid for the minnow because it's secular motion is at such high Reynolds number, the actual power needed to swim is somewhat larger.

The thermal power, on the other hand, is given by

$$3\frac{kT}{\tau_R} = 3\frac{4.18\times10^{-14}ergs}{222s} = 5.7\times10^{-23}W$$

This is 19 orders of magnitude smaller than the secular power and again underscores the insignificance of the thermal fluctuations for the minnow's motion.

3c) The corresponding results for the E. Coli are more interesting. The relaxation time is 6.53 x 10^{-8} s, as was noted earlier. Therefore, the saturation formula for the secular force power may be used

$$\frac{1}{\mathrm{M}}F_S^{\;2}\tau_R = 1.23\times10^{-17}\,W$$

The values for the physical quantities introduced for E. Coli in chapter 2 were used to get this: $M = 2\times10^{-12}gm$, $\mathrm{v}_{SS} = 2\times10^{-3}cm/s$, $K' = 1.204$, $r = 0.5\times10^{-4}cm$, $\eta = 0.027\,poise$, and $F_S = 0.612\times10^{-7}\,dynes$ (this is equivalent to 0.612 picoNewtons (pN)). This is an incredibly small power compared with the minnow.

The thermal power, however, is given by

$$3\frac{kT}{\tau_R} = 3\frac{4.18\times10^{-14}\,ergs}{6.53\times10^{-8}\,s} = 1.92\times10^{-13}W$$

While this is a fraction of a picoWatt (pW) it is nevertheless four orders of magnitude larger than the secular power. The E. Coli's world is dominated by thermal energy. Recall that its thermal speed is 100 times larger than its maximum secular velocity. Nevertheless, through flagellar propulsion the E. Coli can produce a secular run for an average of one second using very low power (12 attoWatts). This highlights what can be done with low power by sustained secular motion in a background of vigorous thermal motion. As has been emphasized, the thermal motion is associated with very short mean free paths and mean free times so that at the end of a typical E. Coli run the thermal root-mean-square displacement is only 1/40 the length of the run.

3d) For ubiquinone the relaxation time is 4.07 x 10^{-15} s. This is so short a time that the damped exponential in the power formulas can be totally ignored. Ubiquinone does not swim inside the membrane lipid bilayer because it does not have fins nor a flagellum. For the sake of argument suppose that it did have some means of propulsion to secularly cross the 80 Angstrom membrane in the diffusion time 2.75 x 10^{-6} s. This corresponds to a hypothetical secular velocity of $\mathrm{v}_{SS} = 0.29\,cm/s$. Since the Stokes drag coefficient for ubiquinone is $6\pi\eta R = 3.5\times10^{-7}\,gm/s$, the hypothetical secular force required for this would be

$$F_S = 6\pi\eta R\,\mathrm{v}_{SS} = 1.02\times10^{-7}\,dynes$$

i.e. about one pN. This means that the saturated hypothetical secular force power is

$$\frac{1}{\mathrm{M}}F_S{}^2\tau_R = 2.94\times10^{-15}\,W$$

which is a few femtoWatts. While there is no known physical mechanism for such a secular motion for ubiquinone, this gives a value against which to compare the thermal power.

The thermal power for ubiquinone is given by

$$3\frac{kT}{\tau_R} = 3\frac{4.18\times 10^{-14} ergs}{4.07\times 10^{-15} s} = 3.08\times 10^{-6} W$$

This is nine orders of magnitude larger than the hypothetical secular power. While microWatts (μW) may sound small, it is enormous for a single molecule. The ubiquinone world is overwhelmingly dominated by thermal energy. How can this large thermal power be understood? It is a result of the erratic path taken by Brownian motion. As was discussed in chapter two, the actual path length is orders of magnitude greater than the thickness of the membrane. As the ubiquinone executes the Brownian motion it does work against the viscous Stokes drag force regardless of which direction it is moving. An estimate of this effect can be obtained as follows. The total thermal energy expended in crossing the membrane is the product of the diffusion time and the thermal power

$$work = 2.75\times 10^{-6} \times 3.08\times 10^{-6} \times 10^{7} ergs = 8.47\times 10^{-5} ergs$$

The average drag force is determined by the thermal speed multiplied by the Stokes drag coefficient. Since the thermal speed is 5.34 x 10^3 cm/s and the drag coefficient is 3.5 x 10^{-7} gm/s, the average drag force is 1.87 x 10^{-3} dynes. If this average drag force acts over the entire Brownian path length, L, then L must be equal to the thermal work done divided by the average force, which yields 4.5 x 10^{-2} cm. This is about 5 times longer than the estimate made in chapter 2 using a simpler argument. Part of this difference is that here the work was calculated for a three dimensional process whereas in chapter 2 the description was restricted to one dimension and this accounts for a factor of 3. Thus, the two estimates are very close after all. The important point is that a great deal of work must be done by Brownian motion the get the ubiquinone across the membrane and this amount of work dwarfs any metabolic energy magnitudes. Nevertheless, the Brownian fluctuating force provides just the required large amount of energy to the Brownian particle. The energy supplied precisely balances the energy dissipated by viscosity. Moreover, the diffusion time taken by Brownian motion to get ubiquinone across the membrane, a few μs, is very small on a metabolic process time scale that is typically ms. Also important is the fact that Brownian motion would not be able to accomplish the systematic transfer of ubiquinone across the membrane if it were not *rectified*. The rectification results from asymmetric boundary conditions caused by metabolically generated concentrations of electron donors and acceptors. Energies on the metabolic scale create enough asymmetry to do the trick. In chapter 2 it was shown that the redox potential difference between the electron donor and the electron acceptor for ubiquinone is about 0.32 x 10^{-12} ergs per molecule. This is much less than the nearly 10^{-4} ergs expended by rectified Brownian motion to effectuate the transport. If the hypothetical secular force computed above moved the ubiquinone across the membrane then the work done that way would be 1.02 x 10^{-7} dynes x 8 nm which equals 8.16 x 10^{-14} ergs. This is about a quarter of the redox energy difference. If the redox energy could be directly harnessed as a secular force on the ubiquinone, it would be adequate to do the job at reasonable efficiency (about 25%). However, this is not what happens. While with rectified Brownian motion as the mechanism, much much larger energy magnitudes are involved, the thermal energy of the cell is more than adequate to meet the needs.

Appendix 3.1 Double averaging for the Langevin equation

It took until 1908 for a mathematical description of Brownian motion to be formulated. This was done by Paul Langevin and the resulting equation is called the Langevin equation. It is given by

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

for a sphere in three dimensions. M is the Brownian particle's mass, η is the viscosity (in poise, gm/cm-s) of the fluid in which the particle is immersed, R is the particle's radius and $\tilde{\mathbf{F}}(t)$ is a fluctuating force. The term $-6\pi\eta R\mathbf{v}$ is called the drag force and is valid only for the linear $\mathbf{v}$ regime. At higher velocities, more complicated processes become possible. The specific form of the drag force given here is for a spherical particle and the drag coefficient, $-6\pi\eta R$, was originally calculated from the Navier-Stokes hydrodynamic equations by Stokes in 1851. While it was derived for a macroscopic sphere, it is known to be valid even for molecules. The fluctuating force is a phenomenological term designed to represent the effect of fluid molecules colliding with the Brownian particle. In liquid water, these collisions occur on a sub-picosecond time scale. The fluctuating force is characterized statistically and this makes the Langevin equation a *stochastic* differential equation.

The symbol $<...>$ will be used to denote averaging with respect to $\tilde{\mathbf{F}}(t)$. The first assumption about $\tilde{\mathbf{F}}(t)$ is that

$$<\tilde{\mathbf{F}}(t)> = 0$$

This means that the random force on the Brownian particle caused by the collisions with fluid molecules is equally likely to be from the left or the right, the top or the bottom or from in front or from behind. Even when the Brownian particle is moving with velocity $\mathbf{v}$, this is so as long as $\mathbf{v}$ is not too large. The second assumption about $\tilde{\mathbf{F}}(t)$ has to do with the fluctuating force's *two time* correlation function

$$<\tilde{F}_i(t)\tilde{F}_j(t')> = 2kT\lambda\ \delta_{ij}\ \delta(t-t')$$

Several points need to be emphasized about this expression. At this stage λ is just a parameter to be determined below. The factors of $2kT$, where k is Boltzmann's constant and T is the absolute temperature (in Kelvins), imply that the fluctuation strength increases with temperature. The Kronecker delta function implies that the different Cartesian components are statistically independent. The Dirac delta function of time implies that the value of $\tilde{\mathbf{F}}(t)$ from one instant to the next is totally uncorrelated. This is, of course, an approximation to reality but means that any real correlations in time are for such short times relative to all other time scales in the problem that they can be ignored.

The fact that we do not need any more assumptions about the statistics of $\tilde{\mathbf{F}}(t)$, such as higher order correlations, represents what is called the Gaussian property of $\tilde{\mathbf{F}}(t)$. This property reflects the fact that $\tilde{\mathbf{F}}(t)$ is caused by myriads of fluid molecules and their summation satisfies the *central limit theorem* of probability theory, thereby yielding a Gaussian process.

The Langevin equation is solved formally by

$$\mathbf{v}(t) = \mathbf{v}(0)\exp\left[-\frac{6\pi\eta R}{M}t\right] + \int_0^t ds\exp\left[-\frac{6\pi\eta R}{M}(t-s)\right]\frac{\tilde{\mathbf{F}}(s)}{M}$$

which can be verified by differentiation. It is now clear that a time scale for this description is given by the relaxation time, τ_R, given by

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

Thus the correlations in $<\tilde{F}_i(t)\tilde{F}_j(t')>$ above must exist for times $t - t' << \tau_R$. Using $<...>$, one obtains

$$<\mathbf{v}(t)> = \mathbf{v}(0)\exp\left[-\frac{t}{\tau_R}\right]$$

because

$$< \int_0^t ds \exp\left[-\frac{t-s}{\tau_R}\right]\frac{\tilde{\mathbf{F}}(s)}{M} > = \int_0^t ds \exp\left[-\frac{t-s}{\tau_R}\right]\frac{1}{M} < \tilde{\mathbf{F}}(s) > = 0$$

since averaging and integration are both *linear operations*. This means an integral is the limit of a sum, and the average of a sum is the sum of the averages. If $\mathbf{v}(0) \neq 0$, then $< \mathbf{v}(\mathrm{t}) >$ will decay to zero. However, one expects the Brownian particle to come to thermal equilibrium with the fluid at temperature T as $t \to \infty$. To see how this happens, one must look at the kinetic energy. This means that, aside from a factor of $M/2$, one needs the values of $< \mathbf{v}(t) \cdot \mathbf{v}(t) >$. From the formula for $\mathbf{v}(t)$ above the inner product can be formed. Note, however, that the cross terms are linear in $\tilde{\mathbf{F}}(t)$ and, therefore, will average to zero. Thus, one gets

$$< \mathbf{v}(t) \cdot \mathbf{v}(t) > = \mathbf{v}(0) \cdot \mathbf{v}(0) \exp\left[-\frac{2t}{\tau_R}\right] + \int_0^t ds \int_0^t ds' \exp\left[-\frac{t-s+t-s'}{\tau_R}\right]\frac{1}{M^2} < \tilde{\mathbf{F}}(s) \cdot \tilde{\mathbf{F}}(s') >$$

$$= \mathbf{v}(0) \cdot \mathbf{v}(0) \exp\left[-\frac{2t}{\tau_R}\right] + \frac{2k_B T\lambda}{M^2}\int_0^t ds \int_0^t ds' \exp\left[-\frac{t-s+t-s'}{\tau_R}\right] 3\delta(s-s')$$

$$= \mathbf{v}(0) \cdot \mathbf{v}(0) \exp\left[-\frac{2t}{\tau_R}\right] + \frac{6k_B T\lambda}{M^2}\int_0^t ds \exp\left[-\frac{2(t-s)}{\tau_R}\right]$$

$$= \mathbf{v}(0) \cdot \mathbf{v}(0) \exp\left[-\frac{2t}{\tau_R}\right] + \frac{3k_B T\lambda}{M^2}\tau_R\left(1-\exp\left[-\frac{2t}{\tau_R}\right]\right)$$

There are two ways to look at this. First one can let $t \to \infty$ and require thermal equilibrium.

$$\lim_{t \to \infty} < \mathbf{v}(t) \cdot \mathbf{v}(t) > = \frac{3k_B T\lambda\tau_R}{M^2} = \frac{3k_B T\lambda}{M 6\pi\eta R}$$

From statistical mechanics it is known that that $\frac{1}{2}M < \mathbf{v}\cdot\mathbf{v} > = \frac{3}{2}k_B T$. Therefore,

$$\frac{3k_B T\lambda}{M6\pi\eta R} = \frac{3k_B T}{M} \Rightarrow \lambda = 6\pi\eta R$$

This identity is called the *fluctuation-dissipation* relation since it connects the strength of the fluctuating force correlations, λ, with the drag coefficient, $6\pi\eta R$. With this result, one gets for finite t that

$$< \mathbf{v}(t)\cdot\mathbf{v}(t) > = \mathbf{v}(0)\cdot\mathbf{v}(0)\exp\left[-\frac{2t}{\tau_R}\right] + \frac{3k_B T}{M}\left(1-\exp\left[-\frac{2t}{\tau_R}\right]\right)$$

This sets the stage for the second perspective. The $\mathbf{v}(t)$ is determined by random force fluctuations on the Brownian particle. Even though the average velocity dies to zero, the random forces keep kicking the Brownian particle around. Thus $\mathbf{v}(0)$ should be determined by the Maxwell distribution

$$M(\mathbf{v}(0)) = \frac{1}{\sqrt{2\pi\frac{k_B T}{M}}}\exp\left[-\frac{M\mathbf{v}(0)\cdot\mathbf{v}(0)}{2k_B T}\right]$$

that is written in *normalized* form so that

$$\int_{-\infty}^{\infty} d^3\mathrm{v}(0)M(\mathbf{v}(0)) = 1$$

Averaging with respect to the Maxwell distribution is denoted by {…}. Thus

$$\{\mathbf{v}(0)\} = \int_{-\infty}^{\infty} d^3\mathrm{v}(0)\,\mathbf{v}(0)M(\mathbf{v}(0)) = 0$$

and

$$\{\mathbf{v}(0)\cdot\mathbf{v}(0)\} = \int_{-\infty}^{\infty} d^3\mathrm{v}(0)\,\mathbf{v}(0)\cdot\mathbf{v}(0) M(\mathbf{v}(0))) = \frac{3k_BT}{M}$$

Consequently, one obtains

$$\{<\mathbf{v}(t)>\} = 0$$

but

$$\{<\mathbf{v}(t)\cdot\mathbf{v}(t)>\} = \{\mathbf{v}(0)\cdot\mathbf{v}(0)\}\exp\left[-\frac{2t}{\tau_R}\right] + \frac{3k_BT}{M}\left(1-\exp\left[-\frac{2t}{\tau_R}\right]\right) = \frac{3k_BT}{M}$$

for all t by virtue of a cancellation. This last property exhibits the characteristic of the Langevin process called *stationarity* because it is independent of the absolute time t. A deeper exhibition of this property is the identity, not derived here,

$$\{<\mathbf{v}(t)\cdot\mathbf{v}(t')>\} = \frac{3k_BT}{M}\exp\left[-\frac{|t-t'|}{\tau_R}\right]$$

that shows a dependence on $|t-t'|$ and not on the absolute times t and t' separately. This sort of time dependence is an example of the *stationarity* property of this stochastic process. Note that even though $\tilde{\mathbf{F}}(t)$ has a Dirac delta function correlation, the driven process, $\mathbf{v}(t)$, has an exponentially decaying correlation with the characteristic time scale τ_R.

There are analogues to these results for voltage, or current, fluctuations and resistance, for reaction progress variable fluctuations and reaction rates, for flux fluctuations and the diffusion constant and for many other systems. In each of these, the strength of the two-time fluctuation correlations is proportional to the relaxation parameter.

References

[1] Fox, R.F., Gaussian Stochastic Processes in Physics, *Physics Reports C*, **48**, 179-283 (1978).