1 Frictional coefficients

Consider a particle moving with velocity $v$ under the influence of some external force $F$ (say a gravitational or electrostatic external force). In addition to the external force, there is a viscous drag inhibiting the motion, which is proportional to the velocity:

$$F - fv = m\frac{dv}{dt}$$

If the velocity at time 0, $v_0$ is parallel to the applied force $F$ (here assumed to be constant), then the linear differential equation is easy to solve:

$$v(t) = \frac{F}{f} + [v_0 - \frac{F}{f}]e^{-ft/m}$$

The velocity decays (quickly, if you plug in numbers) to a final value $F/f$ which is linear in the applied force.

2 Relation between friction and molecular size and viscosity

The frictional drag must depend on particle size, and on the viscosity of the medium (typically water, which has a viscosity $\eta$ of about 0.01 poise = 0.01 g cm$^{-1}$ s$^{-1}$). Dimensional analysis can help here: suppose for a sphere of radius $r$:

$$f \propto \eta^x r^y$$

Now $f$ has units of g s$^{-1}$. The only possible values for $x$ and $y$ are 1, so that $f \propto \eta r$. For a sphere, where the molecules of the solvent “stick” to the surface, messy algebra can find Stokes law:

$$f_{sph} = 6\pi\eta r$$

3 Size and shape dependence of friction coefficients

It is common to compare the frictional coefficients of other simple shapes to that of a sphere of the same volume:
Table 1: Translational and rotational frictional coefficients of ellipsoids and cylindrical rods relative to spheres of the same volume [7–11]

<table>
<thead>
<tr>
<th></th>
<th>Prolate ellipsoid</th>
<th>Oblate ellipsoid</th>
<th>Cylinder</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R_e$</td>
<td>$(a b^2)^{1/3}$</td>
<td>$(a b^2)^{1/3}$</td>
<td>$(3/2p^3)^{1/3}(L/2)$</td>
</tr>
<tr>
<td>$F_t$</td>
<td>$q^{2/3} \ln \frac{1 + \sqrt{1 - q^2}}{q^2-1}$</td>
<td>$q^{3/3} \cdot \arctan \sqrt{q^2-1}$</td>
<td>$(2p^2/3)^{1/3}/(\ln p+\gamma)$, $\gamma = 0.312 + \frac{0.565}{p} + \frac{0.100}{p^2}$</td>
</tr>
<tr>
<td>$F_t(a)$</td>
<td>$\frac{4(1-q^2)}{3(2-2q^2)^{3/2} F_t}$</td>
<td>$\frac{4(1-q^2)}{3(2-2q^2)^{3/2} F_t}$</td>
<td>$0.64 \left(1 + \frac{0.077}{p} - \frac{0.183}{p^2}\right)$</td>
</tr>
<tr>
<td>$F_t(b)$</td>
<td>$\frac{3q^2 [2q^{2/3}(2-q^2)/F_t-2]}{3q^2 [2q^{2/3}(2-q^2)/F_t-2]}$</td>
<td>$\frac{3q^2 [2q^{2/3}(2-q^2)/F_t-2]}{3q^2 [2q^{2/3}(2-q^2)/F_t-2]}$</td>
<td>$2q^2 [9(\ln p+\delta), \delta = -0.662 + \frac{0.917}{p} - \frac{0.050}{p^2}$</td>
</tr>
</tbody>
</table>

Note: macromolecules always show a little more friction than they “should”, based on their size and shape. This is because (roughly speaking!) they drag along a certain amount of water with them (a “hydration layer”).

4 (Ultra)centrifuge: simplest idea

The centrifugal force on the particles is $m \omega^2 x$, where $\omega$ is the rotor speed and $x$ is the distance from the center of the rotor. The terminal velocity should equal this force divided by the friction coefficient. It is typical in the literature to report the Svedberg coefficient $s = v/(\omega^2 x)$, which has units of time. Measurements are reported in Svedberg units, where $1S = 10^{-13}$ s. Hence the Svedberg coefficient is proportional to the mass of the particle.

In simple terms, you can just measure the velocity, and compare $s$ of the sample to that for standards of known molecular weight. However, realistically, the particles in the sample cell are experiencing both driven motion (because of the rotor speed), frictional forces, and diffusion (natural spreading because of concentration gradients. We need to examine diffusion first, then come back to the centrifuge problem later.

5 Fick’s first and second laws of diffusion

(Definition The flux $J$ is the mass transported across a boundary per second, divided by the area of the boundary. In the figure, the mass in the little box is $c A dx$ (concentration times volume). Flux $J$ is this mass divided by $A dt$; hence $J = c(dx/dt) = cv$, where $v$ is the velocity of the flow.)

Consider the tiny volume shown in the figure. The rate of mass transport from left to right through the zone must be proportional to the concentration at the left, $c(x)$, and inversely proportional to the thickness of the zone, $dx$. Transport in the opposite direction is proportion to $c(x + dx)/dx$. The net rate is given by Fick’s first law of diffusion:

$$J = [D c(x) - D c(x + dx)]/dx = -D(\partial c/\partial x)_t$$  \hspace{1cm} (1)
Now, consider the change in mass inside the volume. This is just \( dm/dt = J(x) - J(x + dx) \). In terms of concentrations, this is \( dc/dt = (1/V)(dm/dt) = (1/dx)(dm/dt) \), where we have taken \( A \) to be a unit area. Combining these:

\[
(dc/dt)_x = [J(x) - J(x + dx)]/dx = -(\partial J/\partial x) t
\]  \hspace{1cm} (2)

Combining with Fick’s first law, we get **Fick’s second law of diffusion**:

\[
(dc/dt)_x = -\partial \left( -D(\partial c/\partial x)/dx \right) = D \left( \partial^2 c/\partial x^2 \right) t
\]  \hspace{1cm} (3)

### 6 Solution to the diffusion equations

![Graph showing diffusion over time](image)

If you start with a spike (Dirac delta function) of material, it will spread by diffusion according to \( c(x, t) = W_0 \exp(-x^2/4Dt)/\sqrt{4\pi Dt} \), where \( W_0 \) is the total mass.

### 7 Diffusion in the presence of an external force

Remember that a low Reynolds number, and accelerations caused by external forces are short-lived, and one quickly comes to a terminal velocity \( v = F/f \), where \( F \) is the external force and \( f \) is the friction coefficient. In the presence of both an external force and diffusion (Fick’s first law):

\[
J = -D (\partial c/\partial x) + cF/f
\]  \hspace{1cm} (4)

By virtue of Eq. 2, we get the **Smoluchowski equation**:

\[
(\partial c/\partial t) = D \left( \partial^2 c/\partial x^2 \right) - (F/f) (\partial c/\partial x)
\]  \hspace{1cm} (5)

Now, suppose you come to equilibrium \( (J = 0) \) where diffusion matches the external force (sedimentation equilibrium, say). Here gravity (or centrifugal force) is pulling particles down, creating a concentration gradient (higher concentration at the bottom). But diffusion works in the opposite direction, trying to equalize concentrations, and hence pulling particles up.

Rearranging Eq. 4 with \( J = 0 \) gives

\[
D \frac{dc}{c} = \frac{F}{f} dx
\]
Integrate both sides of this equation from \( x = 0 \) (top of the beaker) to position \( x \), and set

\[
 w = - \int F \, dx
\]

where \( w \) is the (reversible) work, minus sign because gravity pulls downward. Then

\[
 D \ln \frac{c(x)}{c(0)} = \frac{-w}{f}, \quad \text{or} \quad c(x) = c(0) \exp(-w(x)/fD)
\]

But at equilibrium we must also have the Boltzmann distribution law, so \( fD = kT \), or \( D = kT/f \), which is the Einstein-Smoluchowski equation. It is an example of a fluctuation-dissipation relation, connecting fluctuations \( (D) \) with friction, \( (\text{dissipation}, f) \).

### 8 Measuring sedimentation velocities

The graph shows scans across the centrifuge cell, recording the absorbance at 280 nm versus position within the cell. These scans were taken starting at 13 minutes after initiating a run at 45,000 rpm (the black data set in the graph), and then every ~12 minutes thereafter (red, green, cyan, etc.). In the first data set the sedimentation of the antibody has already depleted its concentration at the left and formed a sedimentation boundary.

At later times in the run the depleted region expands and the boundary moves away from the center of the rotor, until by the time of the last data set the concentration of antibody has dropped to essentially zero throughout the upper half of the cell.

What we often want to know is how much material is sedimenting at various sedimentation coefficients. By taking many scans close together in time, subtracting them in pairs, and doing some mathematical manipulation these data can be transformed into the sedimentation coefficient distribution, \( g(s^*) \), which is shown at the right.

This distribution resembles a chromatogram, and the area under each peak gives the total amount of that species. For this antibody sample we see only one distinct peak, centered at a sedimentation coefficient of \( \sim 6.5 \) S, which corresponds to the native antibody ‘monomer’. A sedimentation coefficient of 6.5 S is actually rather low for a 150 kDa species, which is consistent with high hydrodynamic friction from its highly asymmetric, non-globular ‘Y’ shape. The red curve is a fit of these data as a single species. This fit clearly fails to account for the data over the region from 8-12 S, indicating the presence of some dimer and possibly also some trimer.

Figure 2: sedimentation velocities

Figure 3: distribution of sizes
This example illustrates some of the main ideas of Sedfit: loading data from the entire sedimentation process, use of systematic noise decomposition (and subtraction), modeling with finite element solutions of the Lamm equation. If we expand the scale of the continuous sedimentation distribution $c(s)$ with maximum entropy regularization shown above, it can be seen that the $c(s)$ analysis reveals the presence of several oligomeric species and a smaller species. See http://www.analyticalultracentrifugation.com