BACKGROUND ON CELL MOTION

This lab module contains an introduction to the measurement of diffusive and directed motion of micron-size objects in water. The background material presented here deals with viscous drag and some general aspects of cell motion; this material is adapted from David Boal's PHYS 101 and PHYS 445 notes. The operation of the light microscope used in the lab module itself is described in the lab write-up.

I. CELL MOTION

Cells are more than just passive objects responding to external stresses: they can actively change shape or move with respect to their environment. A very familiar example of cellular shape change is the contraction of our muscle cells. Less familiar, but very important to our health, is the locomotion of cells such as macrophages, which work their way through our tissues to capture and remove hostile cells and material. Another example of cell movement is the rotation of flagella (Latin plural for the noun *whip*) that extend from some cells and provide them with propulsion in a fluid medium. Playing a similar role to the flagella of bacteria are cilia (Latin plural for *eyelash*), which occur on the surfaces of some cells and wave in synchrony like tall grass in the wind, creating currents in their fluid environment. For nucleus-bearing cells (eukaryotes) this motion involves, at least in part, two of the three common filaments in the cytoskeleton: *actin* filaments (8 nm diameter) and *microtubules* (25 nm diameter); flagella are composed of a different type of filamentous protein, namely *flagellin*.

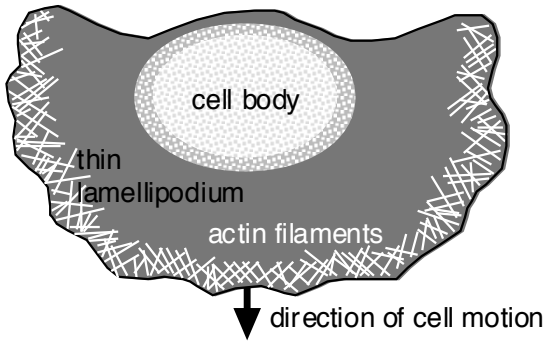


FIG. 1. The diagram shows a stylized view of a particular eukaryotic cell gliding on a substrate; the view is perpendicular to the plane of the substrate. Actin filaments occur at high density within several microns of the leading edge of the *lamellipodium* of the moving cell. In profile, the thin *lamellipodium* hugs the substrate, and only the cell body has an appreciable thickness.

Specialized proteins can slide along actin and tubulin filaments, the energy for their motion being provided by ATP hydrolysis. These so-called motor proteins can be grouped into three families: *myosins* associate with actin, while *kinesins* and *dyneins* associate with microtubules. Because actin filaments and microtubules have physically distinct plus and

minus ends, the motor proteins have a preferred direction to their movement. Kinesin and dynein together provide a mechanism for transport in either direction from the nucleus with modest speeds at cellular length scales. Motors on axonal microtubules can walk at speeds up to 2–5 microns per second towards the end of the axon, a rate which permits a chemical cargo of neurotransmitter, for example, to be transported in 2–6 days from a production site in the brain to the end of a motor neuron a meter away.

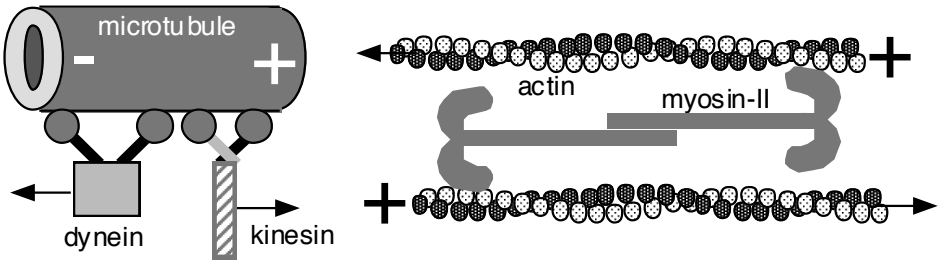


FIG. 2. Myosin walks towards the plus end of actin; with two myosins attached tail-to-tail, the minus ends of the actin filaments are pulled towards each other.

The relative speed of actin and myosin falls in a range from 10^{-2} to 1 μm/s, depending on conditions in the cell. If the myosin head in the cartoon above moves forward at about 5 nm per completed step, and if 10^1–10^2 steps can be completed per second then the motor protein can advance at a rate of 0.05 to 0.5 μm/s. Although this speed appears slow, our muscles employ actin/myosin bundles joined end-to-end to amplify this motion to reach centimeters per second. The force generated by a single myosin motor has been measured by several techniques, generally yielding values in the 3 to 8 pN range.

A common propulsion mechanism for swimming bacteria employs whiplike flagella, which can extend from both ends of a bacterium. Flagella have a typical length of 10 μm, although examples ten times this length are known, such that their length is usually several times that of the main body of the bacterium. Both torque and thrust are generated by a flagellum as it rotates about its axis, driven by a rotary motor. The filament executes a helical motion as it rotates, and acts like a propeller.

As illustrated in the cartoon below, the flagellar helix moves through a fluid at an angle with respect to the symmetry axis of the bacterium. The resistive force from the fluid can be resolved into two components: one generates a thrust along the symmetry axis while the other results in a torque around the axis. As shown, the rotation of the flagellum is balanced by the slower counter-rotation of the cell proper. The figure displays the rotation of *E. coli*: normally the filament rotates counter clockwise (CCW) as viewed looking along the axis towards the cell. When the appropriate flagella rotate CCW cooperatively, the cell can move forward at speeds of 20 μm/s in a mode of motion called a "run". However, the motor has a switch permitting it to run in reverse, or clockwise (CW); flagella rotate CW independently, resulting in no net thrust on the cell such that it "tumbles," losing its orientation. For *E. coli* under common conditions, a typical run lasts 1 second, and a typical tumble lasts 0.1 seconds, with much variation.

As a bacterium swims, its flagella may rotate at 100 revolutions per second (Hz) or more.

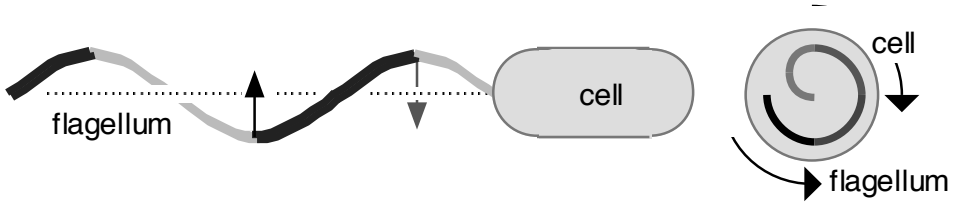


FIG. 3. Flagellum dynamics. (a) A flagellum adopts a helical shape as it rotates about the symmetry axis of a rod-shaped bacterium. (b) Looking along the axis towards the cell, the flagellum rotates counter clockwise to provide thrust, and the cell slowly rotates clockwise in response. Darker regions are closer to the viewer.

Such rotational rates are comparable to an automobile engine, which runs comfortably at 30 Hz (or 1800 rpm) and reaches its operating limit at ≈100 Hz; also like a car engine, flagellar motors fail catastrophically if driven too hard. A single flagellum attached to a fixed substrate can cause the cell body to rotate at 10 Hz, a lower rotation rate than the free flagellum because of viscous drag on the cell. Extensive measurements have been made of the torque generated by the *E. coli* flagellar motor; the torque decreases monotonically to zero at several hundred revolutions per second, depending on conditions. The magnitude of the torque lies in the range 2–6 $\times 10^{-18}$ N·m in a number of cells investigated to date.

II. BROWNIAN MOTION

Newton's first law of mechanics tells us that an object continues in its state of uniform motion in a straight line unless acted upon by an external force. So, an individual object, isolated in space with no forces acting on it, has a constant velocity v and kinetic energy K. The systems of interest to us in biophysics are far from this situation: we study macromolecules and cells in a liquid environment with which they constantly interact and exchange energy and materials. In such situations, even if the system were prepared such that all of its components had identical shape, composition and speed (but not identical velocity, which would just mean that the system as whole were translating), the components would exchange energy and momentum among each other. That is, an ensemble of interacting objects displays a distribution of speeds and kinetic energies such that there are few objects traveling at low speed and few at high speeds. The algebraic function governing the kinetic energies of classical objects (no quantum or relativistic effects) was derived in the 1800s and goes by the name of the Maxwell-Boltzmann distribution, and it has the important property that the mean kinetic energy of an object moving in one dimension is given by $\langle K \rangle = \frac{1}{2} k_B T$, where $\langle \cdots \rangle$ indicates an average taken over an ensemble of objects, k_B is Boltzmann's constant ($k_B = 1.38 \times 10^{-23}$ J/K) and T is the temperature in degrees Kelvin. In the three-dimensional world, this expression becomes

$$\langle K \rangle = \frac{3}{2} k_B T \,, \qquad \text{(translational motion)} \tag{1}$$

The mean total kinetic energy is higher if the object can rotate about an axis, but we will leave that consideration aside here. Note that Eq. (1) does not depend upon the mass m of the object, although the speed of the object will depend on m through

$$\langle v^2 \rangle = \frac{3k_B T}{m} \,. \tag{2}$$

Equations (1) and (2) apply to systems in thermal equilibrium. Note that $\langle K \rangle$ depends linearly on temperature.

Pre-lab question 1: Find the root mean square speed $\langle v^2 \rangle^{1/2}$ for a hydrogen molecule of mass 3.3×10^{-27} kg and for an *E. coli* bacterium of mass $\approx 10^{-15}$ kg, both at $T = 300$ K.

Now, the mean thermal speeds given by Eq. (2) are pretty impressive for molecules, as you have just shown in Question II. Even for cells, the root-mean-squared (rms) speed is of order 1 mm/s, or a few thousand cell-lengths per second. Does this mean that if we look at a cell under a microscope it will zip out of sight in less than a blink? No, because the cell interacts with its local environment, changing its direction incessantly, such that its mean displacement grows only like the square root of the elapsed time. This thermal motion is referred to as Brownian motion (discovered by botanist Robert Brown in 1827) and is one of the phenomena studied in this lab module.

III. RANDOM WALK

A discussion of statistical mechanics often starts with the behaviour of the so-called *random walk*. An anthropometric example of a random walk is the trajectory of a drunken sailor, to use a slightly derogatory description of sailors. We imagine the sailor starts off a lamppost at night and, being drunk, disoriented and walking in the dark, cannot see where he is going. He takes N steps, probably of slightly different length and certainly of varying direction. Now, if he were sober and walking along a street in the daylight, the length of his path would be N times the length of each step. At night, the distance that he walks is still governed by this rule (sum over the lengths of each step), but the end-to-end *displacement* of his trajectory is much less. That is, if each step has the same length b, then

$$[\text{distance}] = Nb \,, \qquad \text{(sober or drunk, it's just the path length)}$$

but

$$[\text{displacement}] \sim Nb \,, \qquad \text{(sober, straight line)}$$

or

$$[\text{displacement}] \ll Nb \,, \qquad \text{(drunk, random directions)}.$$

It's probably unfair to use a nineteenth century stereotype of sailors as an illustration, but one could also imagine random walks to be taken by animals and insects looking for food: a straight trajectory is followed for a short time and, if no food is found, the trajectory is randomly changed to a different direction.

Now, let's describe the random walk mathematically. Characterize each step of the walk by a vector $\mathbf{b}_i$, which has a magnitude and direction. The distance or contour length of the path, is the just the scalar sum over the individual steps:

$$[\text{contour length}] = L = \sum_{i=1}^{N} \mathbf{b}_i \,. \tag{3}$$

Equation (3) is a scalar equation—it is just a sum over the (scalar) lengths of each step. There is no direction dependence to Eq. (3) so that no matter how the path twists and turns, the contour length is always the same if the average step size is the same.

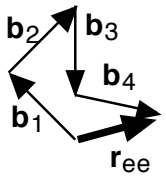
It's a different story for the displacement of the path, which is the distance from the start point to the stop point. Here, the end-to-end displacement is represented by the *vector* $\mathbf{r}_{ee}$. In the diagram below, it is easy to see that

$$L = b_1 + b_2 + b_3 + b_4 \,, \qquad \text{all scalars}$$

whereas

$$\mathbf{r}_{ee} = \mathbf{b}_1 + \mathbf{b}_2 + \mathbf{b}_3 + \mathbf{b}_4 \,, \qquad \text{all vectors} \,.$$

For this walk, the magnitude of the displace $\mathbf{r}_{ee}$ is much less than L. For N steps, the



summation for the displacement is

$$\mathbf{r}_{ee} = \sum_{i=1}^{N} \mathbf{b}_i \,. \tag{4}$$

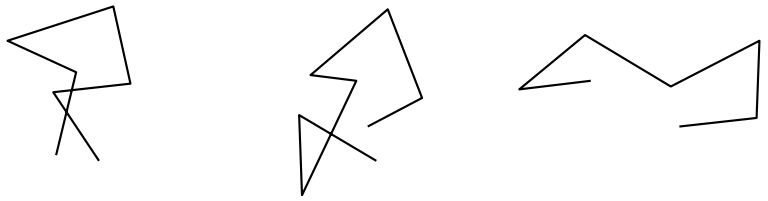
Even though each individual value of $\mathbf{r}_{ee}^2$ is different, it turns out that it is very easy to calculate the average value of $\mathbf{r}_{ee}^2$ when taken over a large number of different configurations. For now, each step is assumed to have the same unit length b, even though the directions are different from step to step. From Eq. (4), the general form of the dot product of $\mathbf{r}_{ee}$ with itself for a particular walk is

$$\mathbf{r}_{ee} \cdot \mathbf{r}_{ee} = \left(\sum_{i=1}^{N} \mathbf{b}_i \right) \cdot \left(\sum_{i=1}^{N} \mathbf{b}_i \right) \tag{5}$$

$$= (\mathbf{b}_1 + \mathbf{b}_2 + \mathbf{b}_3 + \cdots) \cdot (\mathbf{b}_1 + \mathbf{b}_2 + \mathbf{b}_3 + \cdots) \tag{6}$$

$$= \mathbf{b}_1^2 + \mathbf{b}_2^2 + \mathbf{b}_3^2 + \cdots + 2\mathbf{b}_1 \cdot \mathbf{b}_2 + 2\mathbf{b}_1 \cdot \mathbf{b}_3 + 2\mathbf{b}_1 \cdot \mathbf{b}_4 + \ldots + 2\mathbf{b}_2 \cdot \mathbf{b}_3 + \ldots \tag{7}$$

Equation (7) applies to each specific configuration. But there are an infinite number of random walks of N steps starting from the same origin:



We find the average value $\langle \mathbf{r}_{ee}^2 \rangle$ by summing over all these paths, a task that is simpler than it might seem. From Eq. (7), the mean value $\langle \mathbf{r}_{ee}^2 \rangle$ is

$$\langle \mathbf{r}_{ee}^2 \rangle = Nb^2 + 2\langle \mathbf{b}_1 \cdot \mathbf{b}_2 \rangle + 2\langle \mathbf{b}_1 \cdot \mathbf{b}_3 \rangle + 2\langle \mathbf{b}_1 \cdot \mathbf{b}_4 \rangle + \ldots + +2\langle \mathbf{b}_2 \cdot \mathbf{b}_3 \rangle + \ldots . \tag{8}$$

We now want to argue that the averages of the cross terms, for example $\langle \mathbf{b}_1 \cdot \mathbf{b}_2 \rangle$, are all equal to zero. To see this, we recall from the definition of the dot product that $\mathbf{b}_1 \cdot \mathbf{b}_2 = b^2 \cos\theta_{12}$, since all the vectors have the same magnitude, b. Here, θ_{12} is the angle between the vectors $\mathbf{b}_1$ and $\mathbf{b}_2$. Since the lengths b are constant, we have

$$\langle \mathbf{b}_1 \cdot \mathbf{b}_2 \rangle = b^2 \langle \cos\theta_{12} \rangle .$$

Now we argue that since any value of θ_{12} is equally likely to occur, the average of $\cos\theta_{12}$ must equal zero, since for every particular value, for example θ_{12}^* that you might encounter, you will also encounter the value $\theta_{12}^{**} = \theta_{12}^* + \pi$ (or 180°) equally often. But $\cos\theta_{12}^{**} = -\cos\theta_{12}^*$, and thus the two terms cancel out in the average. In other words, the dot product is positive as often as it is negative, and the ensemble average (the brackets $\langle \ldots \rangle$), is then $\langle \mathbf{b}_1 \cdot \mathbf{b}_2 \rangle = 0$. Since the same argument holds for all pairs of $\mathbf{b}_i$ and $\mathbf{b}_j$, we conclude that

$$\langle \mathbf{r}_{ee}^2 \rangle = Nb^2 \tag{9}$$

Pre-lab question 2: Construct a random walk in one dimension by flipping a coin—"heads" on a flip says take a step to the right along the x-axis, and "tails" says take a step to the left along the x-axis.[a] As a warm-up exercise, explicitly draw out all the configurations for a one-dimensional walk with 4 steps and evaluate $\langle r_x^2 \rangle$. Assuming $b = 1$, how close is your calculated $\langle r_x^2 \rangle$ to N? Now, flip a coin repeatedly to sample a few large random walks in one dimension. Determine r_x^2 for ten random flips, then repeat the sequence with another ten flips, starting each walk at $r_x = 0$. Do each set of ten flips a total of five times, so that you have constructed five independent walks. As averaged over the five walks, how close is your measured $\langle r_x^2 \rangle$ to the ideal limit $\langle r_x^2 \rangle = Nb^2$?

[a] The opening scene of Tom Stoppard's play *Rosencrantz and Guildenstern are Dead* gives an amusing twist to this thought experiment.

Pre-lab question 3: A protein is a linear sequence of amino acids, each of which contributes about 0.4 nm to the contour length of the string. But the amino acid backbone of a protein does not behave like a stiff rod; rather, it wiggles and sticks to itself at various locations. Calculate $\langle \mathbf{r}_{ee}^2 \rangle^{1/2}$ for an actin molecule assuming that its configurations obey a random walk; actin is 375 Å long. (Note that a filament of actin is composed of many individual molecules).

IV. DIFFUSION

The concept of a random walk applies easily to the process of diffusion, where a particle moves randomly due to its collision with other particles. Suppose that the diffusing particle makes one step of length b per unit time. Then the random walk of Eq. (9) tells us that the average end-to-end displacement of the walk is

$$\langle \mathbf{r}_{ee}^2 \rangle = b^2 t \,, \tag{10}$$

where t is the number of time steps. Now, the question is how big is b? For a gas molecule traveling fast in a dilute environment, b might be very large, but for a protein moving in a crowded cell, b is rather very small. We recognize this variation in b by writing $\langle \mathbf{r}_{ee}^2 \rangle$ as

$$\langle \mathbf{r}_{ee}^2 \rangle = 6Dt \,, \qquad \text{(diffusion in three dimensions)} \,. \tag{11}$$

The factor 6 depends on the dimension and equals $2d$, where d is the dimension of the space the particle moves in. Thus, for a particle on a line, $\langle \mathbf{r}_{ee}^2 \rangle = 2Dt$ and for a particle moving in a plane, $\langle \mathbf{r}_{ee}^2 \rangle = 4Dt$. In all of these cases, D has units of $[length^2]/[time]$.

For most fluids, D is in the range 10^{-14} to 10^{-10} m^2/s, depending on the size of the molecule. It is more convenient to measure lengths in microns. In that system of units, D is typically in the range of 0.01 to 100 μm^2/s. For the ATP molecule, which is the energy currency of the cell, $D \approx 300$ μm^2/s. For a bacterium, $D \approx 0.5$ μm^2/s.

Pre-lab question 4: How long does it take for a randomly moving protein to travel a distance equal to the diameter of a bacterium, say 2 μm, if its diffusion constant is 10 μm^2/s?

To analyze Brownian motion in more detail, there are two approaches. In the first, we focus on an individual particle that is subject to random thermal forces and to fluid drag. In Sec. V, we will see that the inertial term is negligible for a micron-scale particle in water (our typical object of interest). Thus, we write Newton's law of motion as

$$\gamma \dot{x} = \xi_F(t) \,, \tag{12}$$

where the drag force is $F = \gamma v = \gamma \dot{x}$ and where $\xi_F(t)$ is a random thermal force that results from the collision of water molecules with the larger particle of interest. In a formal sense, we can integrate Eq. (12), which is an example of a *Langevin equation*. The result is

$$x(t) = \frac{1}{\gamma} \int_0^t dt' \, \xi_F(t') \, . \tag{13}$$

Of course, the problem is that we do not know the function $\xi_F(t)$ so that we cannot naively carry out the integral. The usual way forward is to assume that we know something about the statistics of the force. In particular, let us assume that at any time t, the ensemble of possible forces is $\xi_F(t)$ obeys a Gaussian distribution, of mean 0 (otherwise the particle would drift in one direction) and variance ξ^2. In our bracket notation, we can write

$$\langle \xi_F(t) \rangle = 0 \, , \qquad \langle \xi_F(t) \, \xi_F(t') \rangle = \xi^2 \delta(t - t') \, . \tag{14}$$

The first part of Eq. (14) is the no-drift condition. The second part requires some explanation. Since the δ-function is 0 for $t \neq t'$, the statement is that the thermal shocks at time t are independent of those at time t'. Of course, if we look at very short times (e.g., the time between shocks, about 10^{-13} s, this statement is not true. Otherwise, it's a safe assumption. The amplitude at equal times is then the aforementioned variance ξ^2. Then, we can show that for $\Delta x = x(t) - x(0)$, we have $\langle \Delta x \rangle = 0$ and $\langle (\Delta x)^2 \rangle = 2Dt$. The above-mentioned result for $\mathbf{r}_{ee}$ then applies to the vector with components (Δx, Δy, Δz).

Another point of view is to track the probability distribution for the position of a particle. In one dimension, $P(x, t)$ is the probability to be between x and $x + dx$ and at times between t and $t + dt$. This probability obeys a diffusion equation,

$$\frac{\partial P}{\partial t} = D \frac{\partial^2 P}{\partial x^2} \, , \tag{15}$$

which again has higher-dimensional generalizations. The solution to Eq. (15) depends on the initial conditions, $P(x_0, t_0)$. If the initiation condition is that the position is known exactly at some initial time, then the subsequent evolution is given by

$$P(x, t) = \frac{1}{\sqrt{4\pi D t}} e^{-\frac{x^2}{4Dt}} \, , \tag{16}$$

which is a δ-function at $t = 0$ and a Gaussian of mean 0 and variance $2Dt$ at finite times. See Fig. 4.

V. VISCOSITY

If you were asked to develop a conceptual framework for mechanics, without knowing anything about Newton or Galileo, you might well adopt the same starting point as Aristotle: the natural mechanical state of things is that of rest, and every object stops unless acted upon by a force to keep it moving. This declaration seemed so obvious that Aristotle's approach to mechanics stood for about two millennia. Indeed, someone who has not taken a

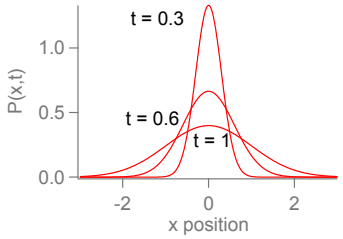


FIG. 4. Probability distribution for diffusion over time t, starting from initial conditions at $t = 0$, for which the particle position was known exactly over time.

physics course probably has an implicit picture of mechanics close to that of Aristotle. The problem with this picture is that it does not recognize the nature of drag forces and the idea of motion without friction.

Drag forces are speed dependent, in that the magnitude of the resistive force rises with the speed of the object. At high speeds, such as a car driving on a highway, the drag force from a fluid is quadratic in v as

$$F = \frac{1}{2}\rho A C_D v^2 \,, \qquad \text{(turbulence)} \,, \tag{17}$$

where ρ is the density of the fluid, A is the cross sectional area of the object in the direction of motion, and C_D is the drag coefficient (a dimensionless number of the order unity). Such motion is rarely, if ever, achieved in the cellular context. At low speed with no turbulence, the drag force exerted by a fluid is linear in speed, $F = \gamma v$, where the proportionality constant γ has different units from the k appearing in quadratic drag. For example, the Irish physicist George Stokes established that a sphere of radius R moving at speed v through a fluid experiences a drag force of

$$F = 6\pi\eta R v \,, \qquad \text{(smooth flow, no turbulence)} \,. \tag{18}$$

In Eq. (18), η represents the viscosity, a physical property of the fluid that can vary widely: Note that the viscosity depends strongly on temperature (compare honey at room temperature to heated honey). The viscosity of "thick" materials also decreases strongly when even a small amount of solvent (e.g., water) is mixed in.

Fluid	η (kg/m·s at 20 °C)
Air	1.8×10^{-5}
Water	1.0×10^{-3}
Olive oil	0.084
Glycerine	1.34
Glucose	10^{13}

For cells, typical values of η would be 10^{-3} to 10^{-2} kg/m·s, which is up to ten times the viscosity of water. The effective viscosity also depends on the size of the diffusing object if

other obstacles are present in the cell—for micron-size components, the apparent viscosity may be much larger than that of water.

Let's now solve the motion of an object subject only to linear drag in the horizontal direction—that is, omitting gravity. The initial speed of the object is v_o, and it obeys Newton's law with linear drag

$$F_{\text{drag}} = ma \quad \Longrightarrow \quad -\gamma v = m\frac{dv}{dt}\,, \tag{19}$$

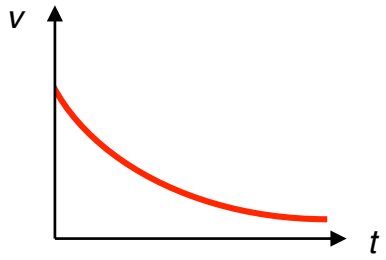
where the $-$ sign indicates that the force is in the opposite direction to the velocity. This equation relates a velocity to its rate of change: its solution is not a specific number like $v = 5$ m/s. Rather, its solution gives the form of the function $v(t)$. It is easy to see that the solution is exponential in form, because

$$\frac{d\,e^x}{dx} = e^x\,.$$

That is, the derivative of an exponential is an exponential, satisfying Eq. (19). Taking care of the constants, we can show using the chain rule that

$$v(t) = v_0\, e^{-\frac{\gamma t}{m}}\,. \tag{20}$$

Please confirm this form. The characteristic time scale for the velocity to decay is m/γ.



Even though the velocity goes to zero only in the limit of infinite time, the object reaches a maximum position of mv_o/γ, also at infinite time. The maximum distance can be found by integrating the v vs. t graph, yielding

$$\Delta x = \frac{mv_0}{\gamma}\left(1 - e^{-\frac{\gamma t}{m}}\right)\,, \qquad \text{linear drag, no } g\,. \tag{21}$$

Example: drag force on a bacterium in water

Let's calculate the drag force on an idealized spherical bacterium swimming in water. For ease of calculation, we assume:

- the bacterium is a sphere of radius $R = 1$ micron
- the fluid medium is water with $\eta = 10^{-3}$ kg / m·s.

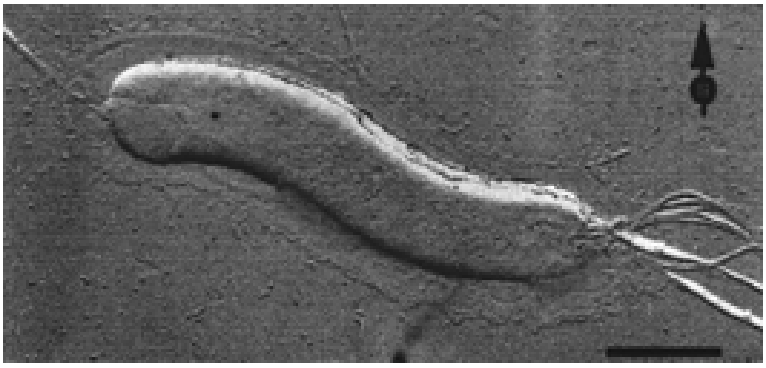


FIG. 5. TEM image of *Aquaspirillum metamorphum* taken by Terry Beveridge at the University of Guelph; scale bar is 0.5 μm.

- the density of the cell is that of water $\rho = 1.0 \times 10^3$ kg/m^3.
- the speed of the bacterium is $v = 2 \times 10^{-5}$ m/s.

As before, we need to know the mass of the cell, and the prefactor γ:

- mass of cell $= \frac{4\pi}{3}\rho R^3 = \frac{4\pi}{3}10^3(1 \times 10^{-6})^3 = 4.2 \times 10^{-15}$ kg.
- $\gamma = 6\pi\eta R = 6\pi \cdot 10^{-3} \cdot 1 \times 10^{-6} = 6\pi \cdot 10^{-9} = 1.9 \times 10^{-8}$ kg/s.

We're now set to determine the maximum distance that the bacterium can travel if its flagella stop operating:

$$x = \frac{mv_o}{\gamma} = \frac{4.2 \times 10^{-15} \cdot 2 \times 10^{-5}}{1.9 \times 10^{-8}} = 4.4 \times 10^{-12} \text{ m} = 0.04 \text{ Å}\,.$$

This is a small distance!

VI. STOKES-EINSTEIN EQUATION

The diffusion constant can be determined analytically for a few specific situations. One case is the random motion of a sphere of radius R moving in a fluid of viscosity η, which Einstein solved using Stokes' Law: $F = 6\pi\eta Rv$, from Eq. (18). The so-called Einstein relation is then

$$D = \frac{k_B T}{6\pi\eta R}\,. \tag{22}$$

Since $k_B T$ is close to the mean kinetic energy of a molecule, the Einstein equation implies that

- hotter objects or ones with more kinetic energy diffuse faster.

- large objects or ones in more viscous environments diffuse slower.

One subtle point is that Stokes' Law holds when the sphere is infinitely far from any wall. When a sphere is close to a wall, the drag increases, because there is more shear in the fluid. (The fluid velocity must match that of a bounding surface. Thus, it must be v at the surface of the sphere and 0 at any boundary.) This increase in drag *decreases* the diffusion coefficient. (It does NOT change the fluid viscosity η.) Thus, if a sphere is near a wall (or in a thin cell sandwiched between two surfaces), we expect to see a smaller diffusion coefficient than predicted by the Stokes-Einstein relation. The reduction can be by as much as a factor of three. Unfortunately, the exact value depends on a lot of details, including, for example, the relative position of the sphere with respect to the two walls (i.e., is it in the centre, near one wall, etc.). But, qualitatively, we expect to see a smaller horizontal diffusion constant, with the reduction factor reflecting how thin the sample is relative to the size of the sphere. For more details, see L. J. Faucheux and A. J. Libchaber, Phys. Rev. E 49, 5158 (1994).

Pre-lab question 5: A biological cell contains internal compartments with radii in the range 0.3 to 0.5 μm. Estimate their diffusion constant according to Eq. (22) if $\eta = 2 \times 10^{-3}$ kg / m·s and their motion is not hindered by other cellular components.

VII. REYNOLDS NUMBER

Equations (17) and (18) tell us that, no matter what the numerical values are assigned to the physical constants of the equations, there is always a low speed regime where the motion of the fluid relative to the object is smooth or laminar and there is always a high speed regime where the motion is turbulent. What the physical constants determine is the approximate boundary between these regimes. The ratio of Eq. (17) to Eq. (18) is necessarily dimensionless, since both quantities are forces, and indicates the transition point between laminar and turbulent flow. Now, because some of the quantities in these two equations depend upon the shape of the object moving through the fluid, or its orientation with respect to the direction of motion, it is conventional to drop dimensionless factors like 6π or the drag coefficient in taking the ratio of the forces, so that

$$[\text{turbulent force}]/[\text{laminar force}] \sim \frac{\rho A v^2}{\eta R v} .$$

Further, the cross sectional area A and radius R are replaced by just L^2 and L, respectively, where L is the relevant length scale of the object. This leaves a convenient dimensionless (but speed-dependent) parameter defined as the *Reynolds number* Re to characterize the motion:

$$Re = \frac{\rho L v}{\eta} . \tag{23}$$

In principle, a more accurate expression can be obtained for each fluid flow situation of interest, and $Re = 1$ would represent the rough boundary between flow regimes, a boundary

that is not discontinuous, as one can easily convince oneself by plotting the sum of Eqs. (17) and (18) for one's favourite sports car. A Mazda Miata has $C_D = 0.37$, for example. Nevertheless, values of Re two orders of magnitude or more are clearly in one domain or the other:

- $Re > 10^2$ turbulent
- $Re < 10^{-3}$ laminar.

Substitution of values for the parameters typical of the cellular environment, as done in the following question, show that cell motion is laminar in most cases. Thus, to understand the motion of cells in water, we must consider "life at low Reynolds number."

E. coli are approximately 1 μm in length and about half that in diameter. They are rod shaped, as shown in Fig. 3.

Pre-lab question 6: Calculate Re for a cell with $L = 1$ μm swimming at 20 μm/s in a fluid with viscosity 10^{-3} kg/m·s and density 10^3 kg/m^3. Is the cell undergoing laminar or turbulent motion?