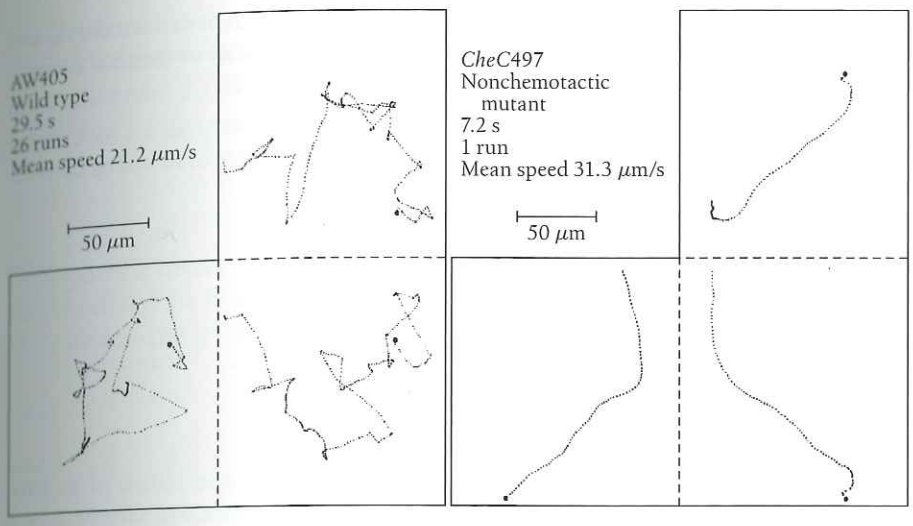

FIGURE 4.14

Two paths of *Escherichia coli* as seen in the original tracking microscope experiments. The three panels in each case are projections of the path onto the three orthogonal planes (imagine folding the paper into a cube along the dashed lines). At left, a wild type bacterium, showing the characteristic runs and tumbles. At right, a nonchemotactic mutant that never manages to tumble. Reprinted by permission from Macmillan Publishers, Ltd.: Brown and Berg (1972).

between the front and back of the bacterium is unlikely to be effective just on physical grounds, independent of biological mechanisms. To test for a time-domain mechanism, one can expose the bacteria to concentrations that are spatially uniform but varying in time; if the sign of the change corresponds to swimming up a positive gradient, runs should be prolonged. The first such experiment used very large, sudden changes in concentration and found that cells that experience large positive signals could became trapped in extremely long runs. A more sophisticated experiment used enzymes to synthesize attractants from inert precursors, exposing the cells to gradual changes more typical of those encountered while swimming. Purely time-domain stimuli were sufficient to generate modulations of run length that agree quantitatively with those observed for bacteria experiencing spatial gradients.

Problem 49: Chemotaxis in one dimension. To make the intuition of the previous paragraphs more rigorous, consider a simplified problem of chemotaxis in one dimension. There are then two populations of bacteria, the + population that moves to the right and the − population that moves to the left, each at speed v. Let the probability of finding a + [−] bacterium at position x be $P_+(x,t)$ $[P_-(x,t)]$. Assume that the rate of tumbling depends on the time derivative of the concentration along the bacterial trajectory as some function $r(\dot{c})$, where for the ± bacteria, we have $\dot{c} = \pm v dc/dx$, and that cells emerge from a tumble going randomly left or right.

(a) Show that the dynamics of the two probabilities obey

$$\frac{\partial P_+(x,t)}{\partial t} + v\frac{\partial P_+(x,t)}{\partial x} = -r\left(v\frac{dc}{dx}\right)P_+(x,t) + \frac{1}{2}\left[r\left(v\frac{dc}{dx}\right)P_+(x,t) + r\left(-v\frac{dc}{dx}\right)P_-(x,t)\right], \quad (4.45)$$

$$\frac{\partial P_-(x,t)}{\partial t} - v\frac{\partial P_-(x,t)}{\partial x} = -r\left(-v\frac{dc}{dx}\right)P_-(x,t) + \frac{1}{2}\left[r\left(v\frac{dc}{dx}\right)P_+(x,t) + r\left(-v\frac{dc}{dx}\right)P_-(x,t)\right]. \quad (4.46)$$

Explain the meaning of each of the terms in terms of what happens as cells enter ... emerge from tumbles. Note that in this approximation, tumbles themselves are instan... which is pretty reasonable (0.1 s versus the ~1–10 s for typical runs).

(b) To see whether the bacteria really migrate toward high concentrations, look ... steady state of these equations. If we simplify and assume that the rate of tumbling ... lated linearly by the time derivative of the concentration,

$$r(\dot{c}) \approx r(0) + \frac{\partial r}{\partial \dot{c}}\dot{c} + \cdots,$$

show that

$$P(x) = \frac{1}{Z}\exp\left[-\frac{\partial r}{\partial \dot{c}}c(x)\right].$$

Thus, in these approximations, chemotaxis leads to a Boltzmann distribution of ... in which the concentration acts as a potential. If the molecules are attractive, then ∂r ... and hence maxima of concentration are minima of the potential, conversely for repell... stronger the modulation of the tumbling rate is (as long as we stay in our linear approxim... the lower will be the effective temperature and the tighter the concentration of bacteria ... the local maxima of concentration.

Problem 50: Nonlinearities. In the simplified one-dimensional world of Problem ... you make progress without the approximation that $r(\dot{c})$ is linear? More specifically, ... the form of the stationary distribution $P(x)$ that solves Eq. (4.45) and Eq. (4.46) for no... $r(\dot{c})$? Can you show that there still is an effective potential with minima located at places ... the concentration is maximal?

Problem 51: A little more about the effectiveness of chemotaxis.

(a) In the one-dimensional model, what happens if the tumbling rate is modulated ... by the time derivative but also by the absolute concentration, so that the bacterium ... "currently good" for "getting better"?

(b) Can you generalize this discussion to three dimensions? Instead of having ... groups + and −, one now needs a continuous distribution $P(\Omega, x, t)$, where Ω ... the direction of swimming. Derive an equation for the dynamics of $P(\Omega, x, t)$ in the ... approximations used above, and see whether the Boltzmann-like solution obtains in the ... realistic case.

All this description so far is about the phenomenology of swimming. But how ... it actually work? The basic problem is that bacteria are too small to take adv... of inertia. When we swim, we can push off the wall of the pool and glide for ... distance, even without moving our arms or legs; this gliding distance is on the ... of one or two meters, roughly the length of our bodies. In contrast, if a bac... stops running its motors, it will glide for a distance comparable not to its body ...

Explain the meaning of each of the terms in terms of what happens as cells enter into and emerge from tumbles. Note that in this approximation, tumbles themselves are instantaneous, which is pretty reasonable (0.1 s versus the ~1–10 s for typical runs).

(b) To see whether the bacteria really migrate toward high concentrations, look for the steady state of these equations. If we simplify and assume that the rate of tumbling is modulated linearly by the time derivative of the concentration,

$$r(\dot{c}) \approx r(0) + \frac{\partial r}{\partial \dot{c}}\dot{c} + \cdots, \tag{4.47}$$

show that

$$P(x) = \frac{1}{Z}\exp\left[-\frac{\partial r}{\partial \dot{c}}c(x)\right]. \tag{4.48}$$

Thus, in these approximations, chemotaxis leads to a Boltzmann distribution of bacteria in which the concentration acts as a potential. If the molecules are attractive, then $\partial r/\partial \dot{c} < 0$ and hence maxima of concentration are minima of the potential, conversely for repellents. The stronger the modulation of the tumbling rate is (as long as we stay in our linear approximation) the lower will be the effective temperature and the tighter the concentration of bacteria around the local maxima of concentration.

Problem 50: Nonlinearities. In the simplified one-dimensional world of Problem 49, can you make progress without the approximation that $r(\dot{c})$ is linear? More specifically, what is the form of the stationary distribution $P(x)$ that solves Eq. (4.45) and Eq. (4.46) for nonlinear $r(\dot{c})$? Can you show that there still is an effective potential with minima located at places where the concentration is maximal?

Problem 51: A little more about the effectiveness of chemotaxis.

(a) In the one-dimensional model, what happens if the tumbling rate is modulated not just by the time derivative but also by the absolute concentration, so that the bacterium confuses "currently good" for "getting better"?

(b) Can you generalize this discussion to three dimensions? Instead of having just two groups + and −, one now needs a continuous distribution $P(\mathbf{\Omega}, x, t)$, where $\mathbf{\Omega}$ denotes the direction of swimming. Derive an equation for the dynamics of $P(\mathbf{\Omega}, x, t)$ in the same approximations used above, and see whether the Boltzmann-like solution obtains in this more realistic case.

All this description so far is about the phenomenology of swimming. But how does it actually work? The basic problem is that bacteria are too small to take advantage of inertia. When we swim, we can push off the wall of the pool and glide for some distance, even without moving our arms or legs; this gliding distance is on the order of one or two meters, roughly the length of our bodies. In contrast, if a bacterium stops running its motors, it will glide for a distance comparable not to its body length

(~1 μm) but to the diameter of an atom. To see this, think about a small particle moving through a fluid, subject only to drag forces (the motors are off). If the velocities are small, we know the drag will be proportional to the velocity, so Newton's equation is just

$$m\frac{dv}{dt} = -\gamma v. \tag{4.49}$$

For a spherical object of radius r, the Stokes formula tells us that $\gamma = 6\pi\eta r$, where η is the viscosity of the fluid, and we also know that $m = 4\pi\rho r^3/3$, where ρ is the density of the object. The result is that

$$v(t) = v(0)\exp(-t/\tau), \tag{4.50}$$

where

$$\tau = \frac{m}{\gamma} = \frac{2\rho r^2}{9\eta}. \tag{4.51}$$

If we assume that the density of bacteria is roughly that of water, then it is useful to recall that η/ρ has units of a diffusion constant, and for water $\eta/\rho = 0.01\ \text{cm}^2/\text{s}$. With $r \sim 1\ \mu\text{m} = 10^{-4}$ cm, this gives $\tau \sim 5 \times 10^{-7}$ s. If the initial velocity is $v(0) \sim 20\ \mu$m/s, the net displacement during this coasting is $\Delta x = v(0)\tau \sim 10^{-11}$ m; recall that a hydrogen atom has a diameter of ~ 1 Å $= 10^{-10}$ m.

The conclusion from such simple estimates is that bacteria can't coast. More generally, mechanics on the scale of bacteria is such that inertia is negligible, as if Aristotle (rather than Galileo and Newton) were right. This phenomenon really is about the nature of fluid flow on this scale. For an incompressible fluid (which is a good approximation here—surely the bacteria don't generate sound waves as they swim), the Navier-Stokes equations are

$$\rho\left[\frac{\partial \mathbf{v}}{\partial t} + \mathbf{v}\cdot\nabla\mathbf{v}\right] = -\nabla p + \eta\nabla^2\mathbf{v}, \tag{4.52}$$

where $\mathbf{v}$ is the local velocity of the fluid, p is the pressure, and as usual ρ is the density and η the viscosity. The pressure is not really an independent variable, but it needs to be there so we can enforce the condition of incompressibility,

$$\nabla\cdot\mathbf{v} = 0. \tag{4.53}$$

These equations need to be supplemented by boundary conditions, in particular, that the fluid moves with the same velocity as any object at the points where it touches that object. Thus, the velocity should be zero at a stationary wall and should be equal to the velocity of a swimmer at the swimmer's surface.

Problem 52: Understanding Navier-Stokes. This is not a fluid mechanics course, but you should be sure you understand what Eq. (4.52) is saying. In particular, it is nothing but Newton's $F = ma$. Explain.

Dimensional analysis is an enormously powerful tool in fluid mechanics. We are free to choose new units for length (ℓ) and time (t_0), and hence for velocity ($v_0 = \ell/t_0$), as well as for pressure p_0, and this gives us

$$\rho\left[\frac{v_0}{t_0}\frac{\partial\tilde{\mathbf{v}}}{\partial\tilde{t}} + \frac{v_0^2}{\ell}\tilde{\mathbf{v}}\cdot\tilde{\nabla}\tilde{\mathbf{v}}\right] = -\frac{p_0}{\ell}\tilde{\nabla}\tilde{p} + \eta\frac{v_0}{\ell^2}\tilde{\nabla}^2\tilde{\mathbf{v}}, \tag{4.54}$$

$$\frac{\rho\ell v_0}{\eta}\left[\frac{\partial\tilde{\mathbf{v}}}{\partial\tilde{t}} + \tilde{\mathbf{v}}\cdot\tilde{\nabla}\tilde{\mathbf{v}}\right] = -\frac{p_0\ell}{\eta v_0}\tilde{\nabla}\tilde{p} + \tilde{\nabla}^2\tilde{\mathbf{v}}, \tag{4.55}$$

where $\tilde{t} = t/t_0$, $\tilde{\mathbf{v}} = \mathbf{v}/v_0$, and $\tilde{p} = p/p_0$. Now we can set $p_0\ell/\eta v_0 = 1$, which gets rid of all the units, except we are left with a dimensionless combination

$$\mathrm{Re} \equiv \frac{\rho\ell v_0}{\eta}, \tag{4.56}$$

which is called the Reynolds number.[6] Notice that if we choose the unit of length to be the size of the objects that we are interested in, and v_0 to be the speed at which they are moving, then even the boundary conditions don't have any units, nor do they introduce any dimensionless factors that are far from unity. The conclusion is that all fluid mechanics problems with the same geometry (shapes) are the same if they have the same Reynolds number. In this sense, being smaller (reducing ℓ) is the same as living at increased viscosity.[7]

To make a long story short, we live at high Reynolds number, and bacteria live at low Reynolds number (Fig. 4.15), even though we are surrounded by the same fluid when we swim. To simulate the effect of being as small as bacteria on the human scale, we would have to swim through a fluid whose viscosity is roughly that of concrete just before it sets (!). Turbulence is a high–Reynolds number phenomenon, as is the more mundane gliding through the pool after we push off the wall. At low Reynolds number, life is very different. Inertia is absent, and so forces must balance at every instant of time. To say this more startlingly, if $\mathrm{Re} \to 0$, then time does not actually appear in the equations. Thus, as you swim, the distance that you move depends on the sequence of motions that you go through but not on the dynamics with which you execute them.

6. I admit that I was at first puzzled by the convention that this is "Reynolds number," not "Reynolds' number" (and certainly not "Reynold's number," although one sees this from time to time). The number is named after Osborne Reynolds (1842–1912), who emphasized its importance, although it had been introduced much earlier by Stokes. If it belongs to Reynolds, you might think it should be "Reynolds' number," but we also refer to "Bessel functions" and not "Bessel's functions." In a discussion that fascinated many of us in my student days, Jackson took the opportunity of a new edition of his *Classical Electrodynamics* to explain that, following this convention, we should talk about "Green functions" and not "Green's functions" (this "boggles some minds," he noted). The world of fluid mechanics abounds with such things—Prandtl number, Schmidt number, Nusselt number, Péclet number—all associated with proper names but not with the possessive construction.

7. It is worth reflecting on the level of universality that we have here. We could imagine starting with a molecular description of fluids, then figuring out that, on the relevant length and time scales, all we need to know are the density and viscosity. Now we see that even these quantities are tied up with our choice of units. If we want to know what happens in natural units (i.e., scaling to the size and speed of the objects of interest), then all that matters is a single dimensionless combination, Re.

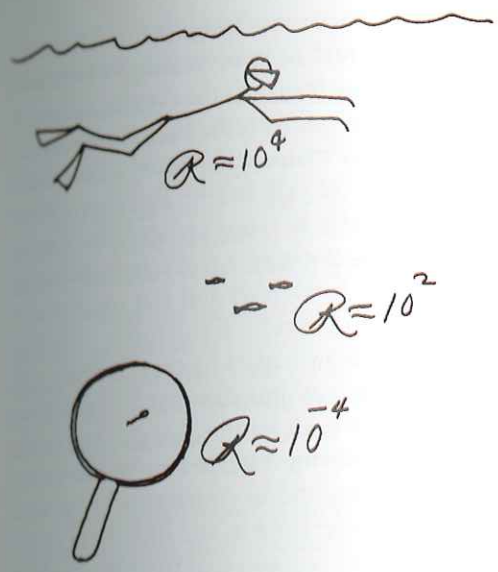

FIGURE 4.15

Purcell's delightful sketch, illustrating the range of Reynolds numbers relevant for swimming in humans, fish, and bacteria. Reprinted, with permission, from Purcell (1977). Copyright © 1977, American Association of Physics Teachers.

To use Purcell's evocative example, at high Reynolds number a scallop can propel itself by snapping shut, expelling a jet of water, and then opening slowly.[8] The jet will propel the scallop forward, and the drag of reopening can be made small by moving slowly. At low Reynolds number this strategy does not work, and the forward displacement generated by snapping shut will be exactly compensated by the drag on reopening. To have net movement from a cycle, the sequence of shapes that the swimmer goes through in the cycle must break time-reversal invariance, not just the trajectory.

So, how do bacteria evade the "scallop theorem"? If you watch them swimming, you can see that they have long filaments sticking out, and these seem to be waving. I emphasize that "see" is tough here. These filaments are very small, ~20 nm in diameter, much thinner than the wavelength of light. To see them, the easiest thing to do is to use dark-field microscopy, in which the sample is illuminated from the side and what you see is the light scattered by ~90°. These apparently waving appendages are called flagella, by analogy with the motile structures that project from eukaryotic cells, including some of the cells in our own bodies. The difference is that eukaryotic flagella are much thicker than bacterial flagella. If you slice through the tail of a sperm (a prime example of a eukaryotic flagellum) and take an electron micrograph, you find an enormously complex structure; if you analyze the system biochemically, you find it is made from many different proteins. Importantly, some of these proteins act as enzymes and eat ATP, which we know is a source of energy, for example, in our muscles. In contrast, the bacterial flagellum is small, with a relatively simple structure, and the biochemistry suggests that it is little more than a very long polymer made from one kind of protein; this protein is not an enzyme. How can this simple structure, with no ATPase activity, generate motions?

In experiments aimed at better ways to see the flagella, one can attach "flags" to them using viruses that would stick to the flagella by means of antibodies. Once in a

8. At least a hypothetical scallop. What real scallops do is less clear to me.