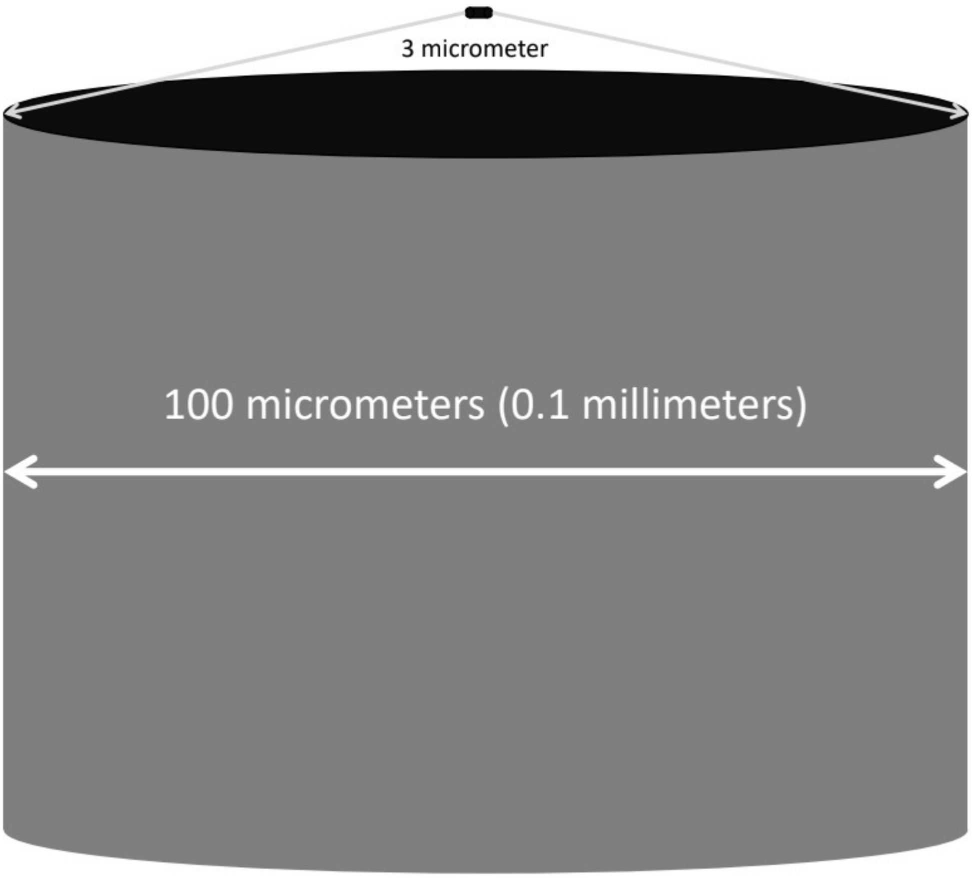
What it is like to be very small



Comparison of the size of an average *E. coli* bacterium to a human hair, drawn to scale. Only a very short section of the hair is shown. An average human hair is 0.1 millimeter (100 micrometers) in diameter. An average *E. coli* cell halfway between two cell divisions is 3 micrometers long and less than 1 micrometer in diameter.

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Storyline

Microbes are very small, and this has important consequences for them and their lifestyles. For one thing, it enables them to grow very fast and reach very high populations in a small space. They weigh almost nothing, so they are barely affected by gravity. They float in the air, and, unlike us when we are standing, they do not need to use energy to counteract the force of gravity. They normally live in water, not air, but even in water they are not like us, or even a fish. They do not need to move to get food, because food comes to them through diffusion. However, diffusion only works over short distances, so food gets depleted locally. Then the bacteria have to swim to new places where there is more food. But they do not swim like us, either. Because they have almost no **mass**, they also have almost no **momentum** so, unlike us, when they stop swimming, they stop immediately instead of gliding. They have solved this problem in a remarkable way.

What it is like to be very small: the Microbiology

1. ***Microbes are very small.*** Microbiology is the study of microscopic living organisms. These organisms are too small to examine with the naked eye, either to be seen at all or seen as more than a tiny particle. Not only are they minute, they are very diverse. There are far more fundamental differences in the organization, anatomy, physiology, and molecular mechanisms supporting life in microorganisms than in all the macroscopic life that we can visualize without the aid of microscopes. Microorganisms show greater variety than all the organisms with which we are familiar: animals, plants, and fungi. They inhabit more diverse and extreme environments, including deep sea vents, hot acid springs, nuclear reactor cooling pools, and on and in us.

Other Topic Frameworks (TFs) in this Section will deal with many of the ways in which microorganisms carry on their lives. Their enormous diversity includes all three of the domains of life: **Bacteria**, **Archaea**, and **Eukaryota**, the last of which is represented by the very large and diverse group called **Protozoa**. Bacteria and archaea lack what we thought was an essential feature of cells: a nucleus – a membrane bound **organelle** containing the genetic information of the cell, the **chromosomes**, which are made up of molecules of **DNA**. Bacterial chromosomes are single circular molecules of DNA that are exposed to the rest of the cell without a surrounding nuclear membrane. Protozoa are usually single-cells, but these cells are more like those of other Eukaryotes - they have a nucleus and multiple chromosomes. For most of evolutionary time, all eukaryotes were protozoa until they finally got together and started forming multicellular organisms about a billion years ago. Bacteria and Archaea have been around for a much longer time, at least 3.5 billion years, appearing within a billion years after the earth formed 4.6 billion years ago and finally became compatible with life.

This TF will focus on one characteristic feature of microorganisms: they are very small. Protozoa are relatively large, some being visible with the naked eye, if you squint and look closely. They are fairly large as cells go, bigger than most cells of multicellular organisms, so I am not going to discuss them. I am also not going to discuss Archaea, which are the same size as bacteria and look a lot like them but have very different ways of doing things at the molecular level. As a side note, microbiologists think that the first protozoa arose when a relatively large **anaerobic** archaeal cell swallowed a small **aerobic** bacterium that, instead of being digested, started living within the archaea. The swallowed bacteria evolved to become **mitochondria**, the energy power plants in our cells that allow the chemical energy in sugars to be captured in order to make **ATP**, the energy currency of the cell. **Chloroplasts**, which plants use to harvest sunlight and create sugar from the carbon dioxide in air, probably evolved in a similar way from a swallowed bacterium that could carry out **photosynthesis**. All eukaryotic cells have features derived from Archaea and Bacteria. Many genes got transferred from the mitochondria and chloroplasts to the nucleus. Thus, all eukaryotes, including us, are fusions of the other two basic domains of life.

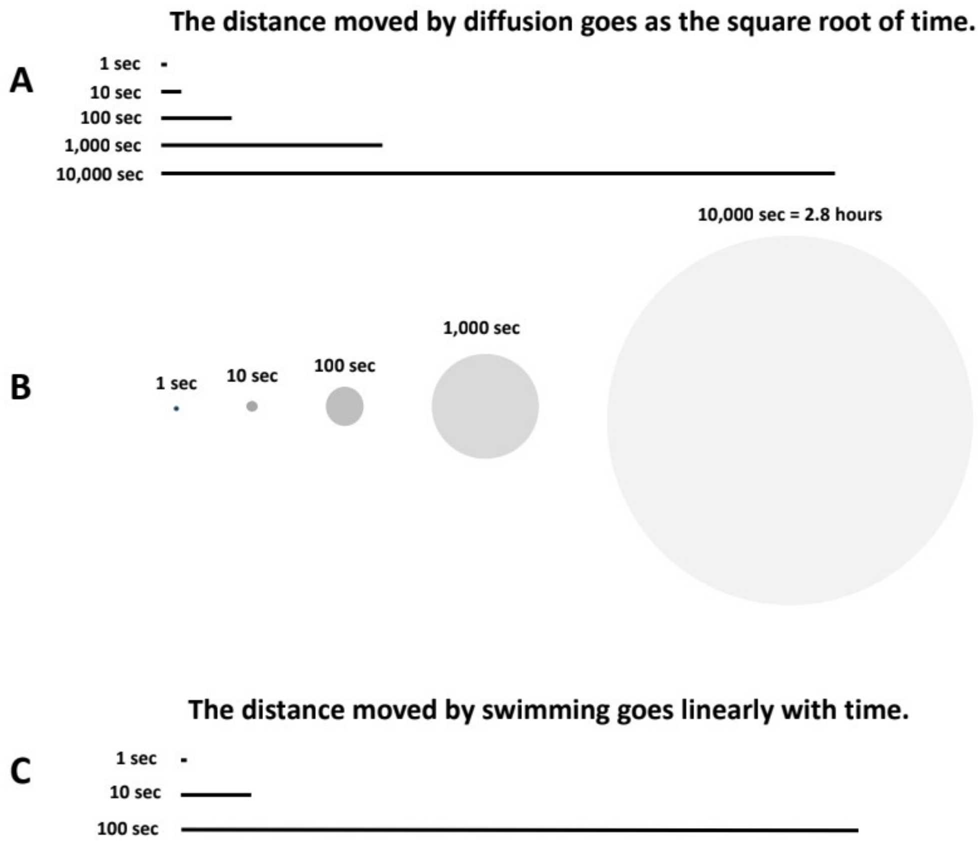
2. ***Microbes, being small, have different physical properties than we do.*** A quick word of caution is in order at the outset. Many things we take for granted based on the observation of life at our scale - which broadly means things we can easily see, from tiny insects to whales or dinosaurs - do not apply to bacteria. An ant can fall a great distance and not get hurt, and that is relatively easy to understand. But gravity is still important to an ant. Gravity means almost nothing to bacteria. Forces that we take for granted in our lives do not scale to things the size of bacteria. It is those differences we will be discussing in this chapter.

3. ***What do we mean by small when we talk about bacteria?*** Really small, although still much bigger than a virus. *Escherichia coli*, *E. coli* for short, is a bacterium that many people know. It is rod shaped with two rounded ends. It is two to four micrometers long and less than one micrometer in diameter. A millimeter is one thousandth as long as a meter, which is about forty inches. A micrometer is one thousandth of a millimeter, which makes it one millionth of a meter. You know from a ruler how small a millimeter is. A human hair is about a tenth of a millimeter, or 100 micrometers, wide. So, a human hair is twenty-five to fifty times as wide as an *E. coli* cell is long, and one hundred times as wide as an *E. coli* cell is wide (see cover image). That is very small, far below the ability of our eyes to resolve. Because of their small size, many bacteria fit into a very small space. In liquid medium in a test tube, *E. coli* can easily grow to one billion (10^9) cells per milliliter. There are one thousand milliliters in a liter, which is about a quart. In 10 milliliters, the total population can be ten billion, which is greater than the eight billion human beings on earth, all in one test tube. Each bacterium has a mass of about 1 picogram. There are a trillion picograms in a gram. Thus, the mass of ten billion bacteria is 10 milligrams, which is the mass of four average-sized snowflakes.

4. ***Bacteria can grow very rapidly.*** Cells of *E. coli* grow by doubling in length and then dividing to produce two daughter cells. In a nutrient-rich medium, they can double in length and divide within 20 minutes. So, they can reach a very high number very quickly. If their growth were unchecked, in a day a single *E. coli* cell could undergo 72 generations. 2^{72} is 4.7×10^{23}, which is half a trillion trillion cells. Even at only one picogram per cell, that is 470 billion grams, over 16 billion ounces, and over a billion pounds. In one day! In two days the total mass would be a billion billion pounds, or 1×10^{18} pounds, in three days it would be 1×10^{27} pounds, and in four days 1×10^{36} pounds. For comparison, the mass of the earth is about 6×10^{27} grams or 1.32×10^{25} pounds, and the mass of the sun is about 2×10^{33} grams or 4.4×10^{30} pounds. In three days a single *E. coli* cell could grow to a mass almost 200 times larger than the mass of the earth, and in four days could grow to a mass more than 200,000 times the mass of the sun. Of course, no such thing happens. *E. coli* runs out of space and food, and they pollute their surroundings. Just like any other organism, they reach the carrying capacity of their environment, and when they do, they first stop growing, and then they start dying.

5. ***The issue of diffusion.*** A concept that is very important to understand at a small size scale is diffusion. **Diffusion** is the random motion of molecules. What looks like a glass of still water is really an incredibly active space. The individual water molecules, and any molecules dissolved in the water, like salt or sugar, move very rapidly on a small length scale. The higher the temperature, the faster the molecules move. Sometimes a water molecule moves so fast that it escapes into the air. We call that evaporation. The reason water evaporates faster at higher temperature is because water molecules move faster, and therefore more of them escape.

The movement of diffusing molecules is a random walk in three dimensions. Molecules do not travel straight for long because they bump into each other. Imagine those bouncing balls on a screen saver. They keep colliding and heading off in new directions, like diffusion, except that, on their size scale, water molecules move very much faster than the balls, and in three dimensions. The distance a diffusing molecule moves is proportional to the **square root** of time. A diffusing molecule moves only 10 times as far in 100 seconds as it does in 1 second, and 100 times as far in 10,000 seconds (almost three hours) as it does in 1 second.



A) The top panel shows how a molecule would diffuse from its starting point with time. A molecule would diffuse in all three dimensions, but the distance it moves in any one dimension, shown as a line, increases as the square root of time, as does diffusion in two or three dimensions. Thus, the diffusing molecule will move 10 times as far in 100 seconds as in 1 second, and 100 times as far in 10,000 seconds. (**B**) Diffusion in two dimensions. The decreasing intensity of the shading shows that the concentration of the molecules will decrease from that in the original drop as they diffuse away from the original drop. The relative distance scale is as above. (**C**) A bacterium swimming in a straight line at a constant speed will move a distance that is directly proportional to time. Thus, it will move 10 times as far in ten seconds as it does in one second, and 100 times as far in 100 seconds as it does in 1 second. That means that, even though the instantaneous speed of a diffusing molecule may be faster than the instantaneous speed at which the bacterium swims, over a longer time the swimming bacterium will go farther than the diffusing molecule.

Molecules are much smaller than bacteria. An average-sized *E. coli* cell, which is 70% water, contains about 30 million water molecules. Those water molecules, and everything dissolved in water, diffuse inside the cell like crazy. Bacteria are much bigger than molecules, and they diffuse much slower. In a microscope you can watch the motion of a non-swimming bacterium suspended in water. Diffusing water molecules hit the cell unequally from different sides, and that causes the cell to jiggle. That random jiggling is called **Brownian motion**.

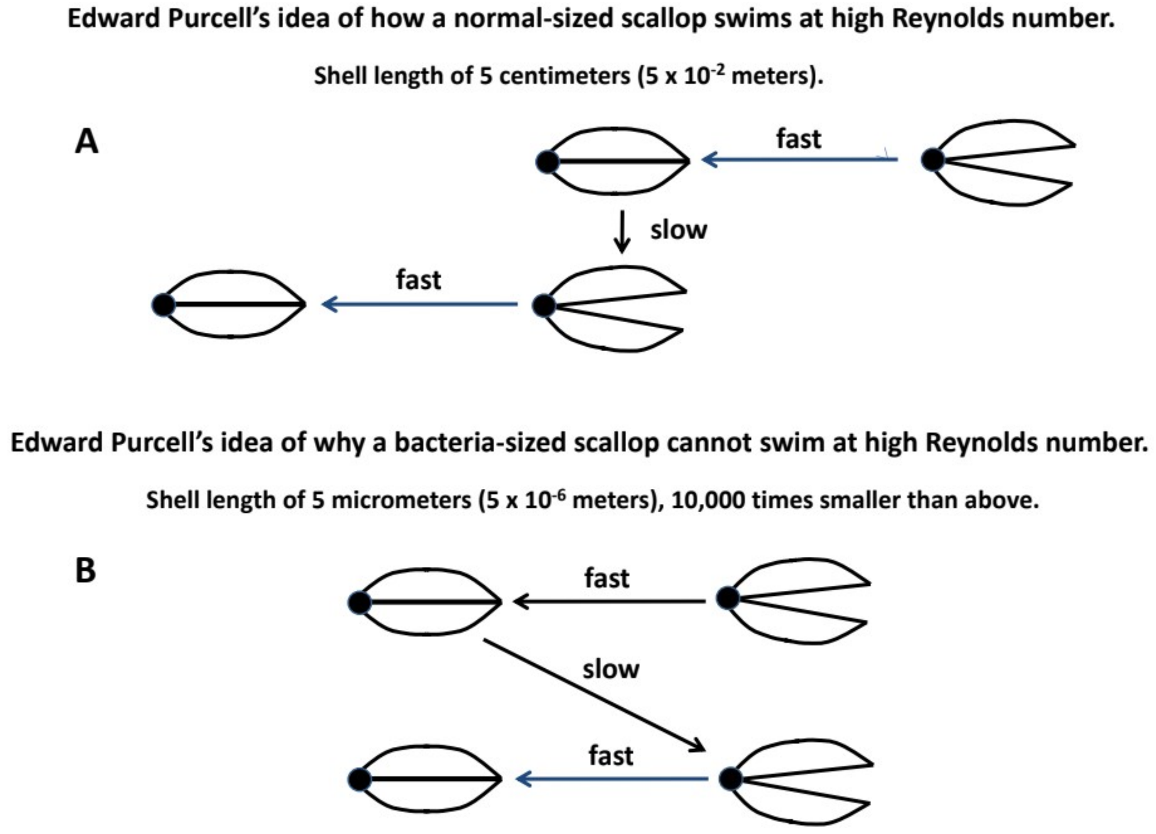
Because of their small size and the rapid motion of molecules over short distances, bacteria do not need an active process to move molecules around inside them. Much bigger eukaryotic cells have networks of fibers along which mobile motor proteins carry cargoes to different parts of the cell. Because of their small size, bacteria do not need such machinery. Diffusion is rapid enough to distribute things very quickly inside them.

6. ***Reynolds number is an important concept.*** The Reynolds number, simply stated, is the ratio of inertial forces to viscous forces. Inertial forces describe the tendency of something that is in motion to keep moving in the same direction. Viscous forces are the frictional resistance offered by a fluid to an object moving through it. We live at high Reynolds number, that is: we are big and heavy and the frictional resistance of air and water do not slow us down very much. For us, **inertia** is very important. Think of pushing off from the side of a swimming pool. After your feet leave the edge of the pool, you glide for a long distance, and the harder you push, the farther you glide. At an even higher Reynolds number, think how far an ocean liner or aircraft carrier will glide after it stops rotating its propellers. Of course, the **viscosity** of air is much lower than that of water, so an airplane that turns off its propeller can glide for a very long distance indeed.

Inertia means nothing to *E. coli*: it is so small and light that the frictional resistance of air and water is enormous, and moving is like us walking through deep mud. Like a fish, *E. coli* lives in a watery environment, unless it is growing on a surface in a collection of cells called a colony, which you can see with the naked eye, because it contains many millions of bacteria. For a bacterial cell, water is a very different environment than it is for you, or even than it is for a guppy or a goldfish. Humans and fish swim at high Reynolds number, and they can glide. If an *E. coli* cell stops actively swimming, it stops dead within one thousandth of its body length, which means a distance of a few nanometers. (A nanometer is one-millionth of a millimeter.) That is because of viscosity, which is friction in a liquid. For *E. coli*, water is like molasses or quick sand would be for you. Imagine trying to swim in quick sand. Like *E. coli*, you would be at low Reynolds number.

7. **E. coli** ***swims differently than we do.*** Here comes the non-intuitive part. If inertia means nothing, then how fast something happens becomes irrelevant in the sense that how far something moves no longer depends on how fast it moves. From experience, you know that when you do the breast stroke, if you pull your arms back very rapidly and then, without bending them at all, move them forward very slowly to where you started the stroke, you would still move forward. (Of course, you would move faster if you bend your arms on the return stroke, but you would still move forward if you did not.) If you were the size of *E. coli*, you would move forward the distance of the length of your stroke, and then, on the return stroke, you would move backward the same distance, even if the backward stroke were very fast and the return stroke very slow.

The Nobel Prize-winning Physicist Edward Purcell, in his memorable essay “Life at Low Reynolds Number,” proposed what came to be called The Scallop Theorem. A scallop is like a clam, with an upper and lower shell joined by a hinge. (That is why clams and scallops are called bivalves.) Purcell thought that a scallop moves by pushing itself backward when it closes its two shells quickly, then opens its shells slowly without moving backward much at all. At high Reynolds number that would work to swim because how fast something happens matters. If a scallop were the size of *E. coli*, that mechanism would not work. The scallop would move fast in one direction when it closes its shells quickly, then it would pull back exactly the same distance when it opens its shells slowly. **Reciprocal**, back-and-forth motion at one hinge does not work at low Reynolds number even when the motion is fast in one direction and slow in the other. Only the actual distance moved counts.

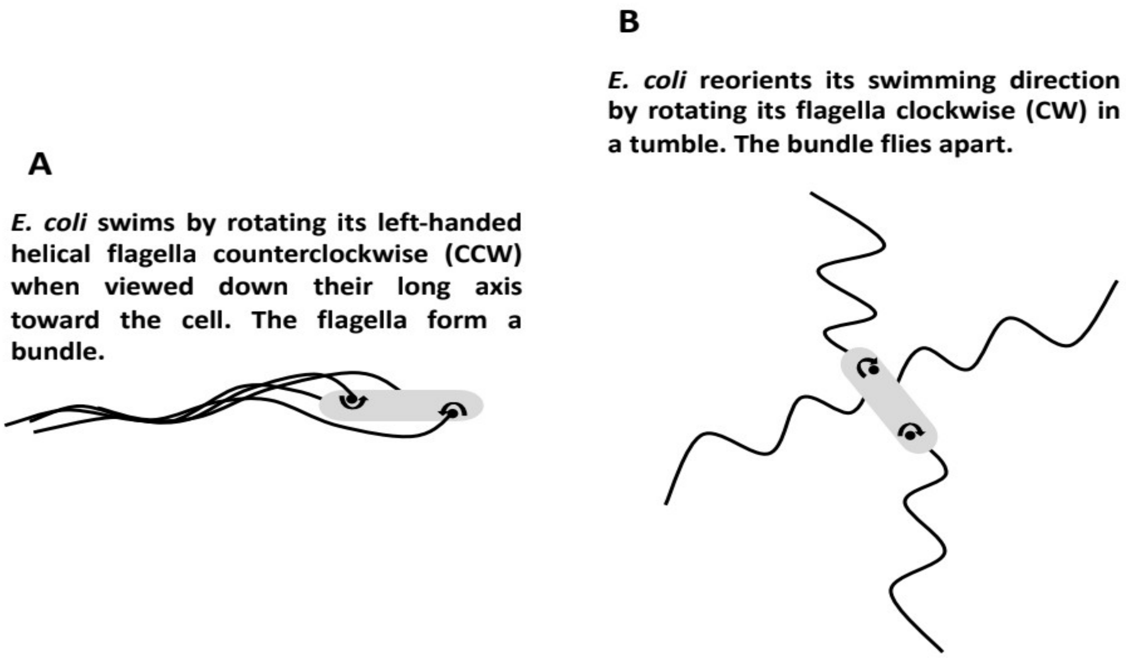


Edward Purcell’s example of a normal-sized scallop and a bacteria-sized scallop trying to swim. The normal-sized scallop (**A**), with a shell about five centimeters (two inches) in diameter, would swim at high Reynolds number by closing it shell rapidly and then opening it slowly. It moves when it closes its shell quickly, but it hardly moves in the other direction at all when it reopens its shell slowly. Thus, it can actually get somewhere. The bacteria-sized scallop (**B**), 10,000 times smaller with a shell about five micrometers in diameter, would swim forward at low Reynolds number when it closes its shell quickly, but it would move backward the same distance when it reopens its shell slowly. It would get nowhere, just move forward and back over the same path. That is because, at low Reynolds number, the distance moved is proportional only to the distance of the movement, not to the speed of the movement. (Purcell was a physicist, not a biologist, and Charles McCutcheon pointed out that he got the biology wrong. Scallops actually swim, at up to 5 body lengths per second, by squirting water out of vents near where the two shells join, so they swim in the direction to which the shells open. They likely could do that if they were the size of bacteria because it does not involve reciprocal motion. But that would spoil Purcell’s theorem.)

But, you can look in a microscope and see *E. coli* cells swimming at more twenty of their body lengths per second. This is as fast or faster than any fish can swim relative to its body size. Swimming bacteria look like they are really zipping along. Some marine bacteria that live in the ocean can swim ten times faster than that. How in the world do they do it?

8. ***One thing that does work at low Reynolds number is rotation, which is not reciprocal.*** It goes steadily in one direction. You might think a submarine scaled down to the size of a bacterial cell could swim in water, but it could not. A ship moves forward in response to the water its propellers, or jets, push backward, because of conservation of momentum, and that involves inertia. A submicroscopic sub could spin its propellers at fast as it wanted, but it would go virtually nowhere.

9. ***Flagella are the rotating propellers of bacteria***. Rotating a propeller is the strategy that bacteria use to swim, but with a critical difference compared to a ship. Their propellers are called flagella, because when they are not turning and are examined at high magnification in an electron microscope, they look like a wavy and very thin line, like a beating whip frozen in time. These flagella are huge relative to the size of the bacterial cell. They are helical, or spiral, and they can be many times longer than the length of the cell body. The width of the **helix**, called the amplitude, can also be about the same as the diameter of the cell.



The flagellar filaments of *E. coli* are left-handed helices. Imagine holding your left hand with the thumb pointed at you. Your thumb is the long axis of the helix. Your fingers curl in the same direction as a left-handed helix. When you point your thumb toward you and turn your hand counterclockwise (CCW), you will notice that your fingers tend to curl more tightly. The same thing happens with left-handed helical filaments. Each bacterium as 3 to 5 flagella. When each flagellum turns CCW, the filaments come together and form a bundle that pushes the cell forward (**A**). If you point your left thumb toward you and turn your hand clockwise (CW), your fingers are going to tend to uncurl. The same thing happens with left-handed helical filaments. When the flagella turn CW, the bundle flies apart and the cell goes through a chaotic motion (**B**), called a tumble, that reorients the cell. When the flagella turn CCW again, the flagellar bundle reforms, and the cell swims in a new direction.

10. Flagella rotate very fast. You may think there are two things wrong with this picture. First, how can anything in a living organism rotate? If we, or any animal with which we are familiar, would try to rotate its arms, legs, or wings, the muscles, nerves, bones, tendons, and ligaments would get all twisted up. So, we do not see rotating arms, legs, or wings in animals. But, what if you are very small and do not have any muscles, nerves, bones, tendons, and ligaments? You can have a rotary motor made up of protein molecules, some of which remain stationary like the stator of a machined rotary motor, and some of which, connected to the helical filaments of the flagella, rotate. In *E. coli* they rotate at several hundred times per second (20,000 rpm), and up to 1,500 times per second (100,000 rpm) in those very fast swimming marine bacteria.

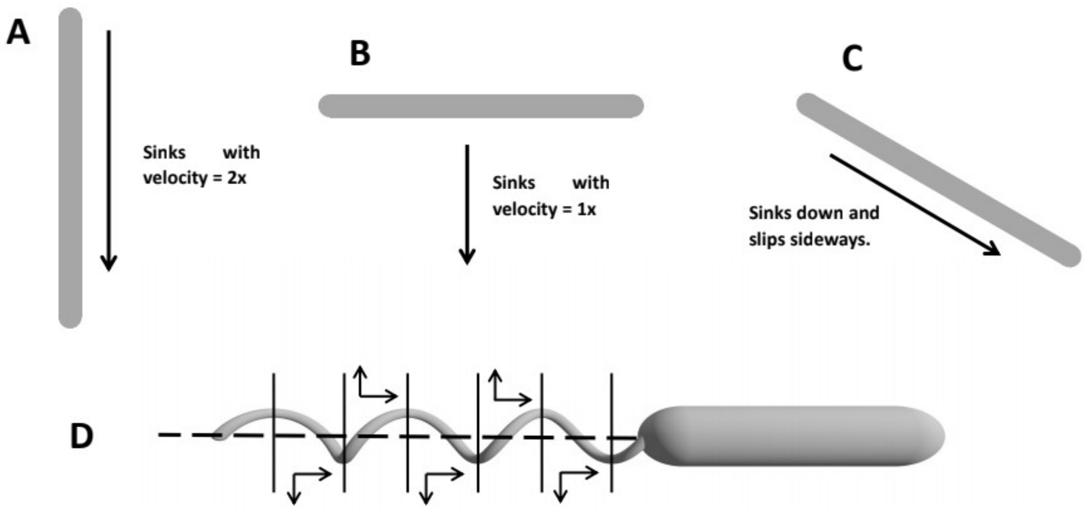
The motors that drive this incredibly fast rotation are truly tiny, with a diameter of about 50 nanometers (one-twentieth of a micrometer, or about one-fiftieth the length of a typical bacterial cell). And, they are electrical, not driven by a current of electrons like we are used to but driven by the flow of ions, either hydrogen (H^+) in *E. coli* or sodium (Na^+) in those marine bacteria. The ions pass through the motor in going from the outside of the cell to the inside. The energy for many, many things in bacteria, including the synthesis of the very important molecule ATP is driven by such inward ion currents. Like us, bacteria use ATP to drive most of the energy-requiring processes in the cell. The mitochondria in our cells, which a very long time ago (over a billion years) were bacteria captured by an Archaeal cell, make ATP the same way.

11. Flagella create a corkscrew movement. To visualize the way rotating flagella propel a cell, think of a long, straight rod placed very carefully in a very viscous liquid, like corn syrup. If you drop it vertically, it will sink straight down. If you drop it absolutely flat, perpendicular to the pull of gravity, it will also sink straight down, but at only half the speed that it does when it is placed vertically. If you place it at angle, it will both sink down and slide sideways. That is what happens with bacterial flagella. They are not sinking, but they are rotating through what is, to them, a very viscous medium - water. Therefore, they move through the water much like a corkscrew moves through a cork. They basically screw their way through the water, and because they are attached to the bacterial cell, they push it forward. Because they rotate very fast, their rotation can make the cell swim fast.

12. Why do bacteria bother to swim at all? Remember, at small distances, diffusion is very fast. A cell just floating in place will be bombarded by all of the dissolved nutrients - sugars, amino acids, vitamins, ions - that it needs. But wait. Diffusion is fast only over small distances. A bacterial cell soon takes up all the nutrients in its near vicinity. Pretty soon it will have depleted its local environment of nutrients, and it will take a long time for nutrients from farther away to diffuse to where the cell is located.

A cell cannot outswim diffusion over a short distance, but a cell can swim in one direction, unlike a diffusing molecule, so it can move long distances faster than a diffusing molecule, as shown in Figure 2. As an analogy, consider a sheep in a small pasture. Grass does not diffuse, but a sheep grazing randomly in a small pasture is doing the equivalent of diffusing. That works fine for the sheep until most of the grass in the pasture is eaten. Then, the sheep has to move, non-randomly, to a new pasture. Bacteria swim for the same reason - to find greener pastures.

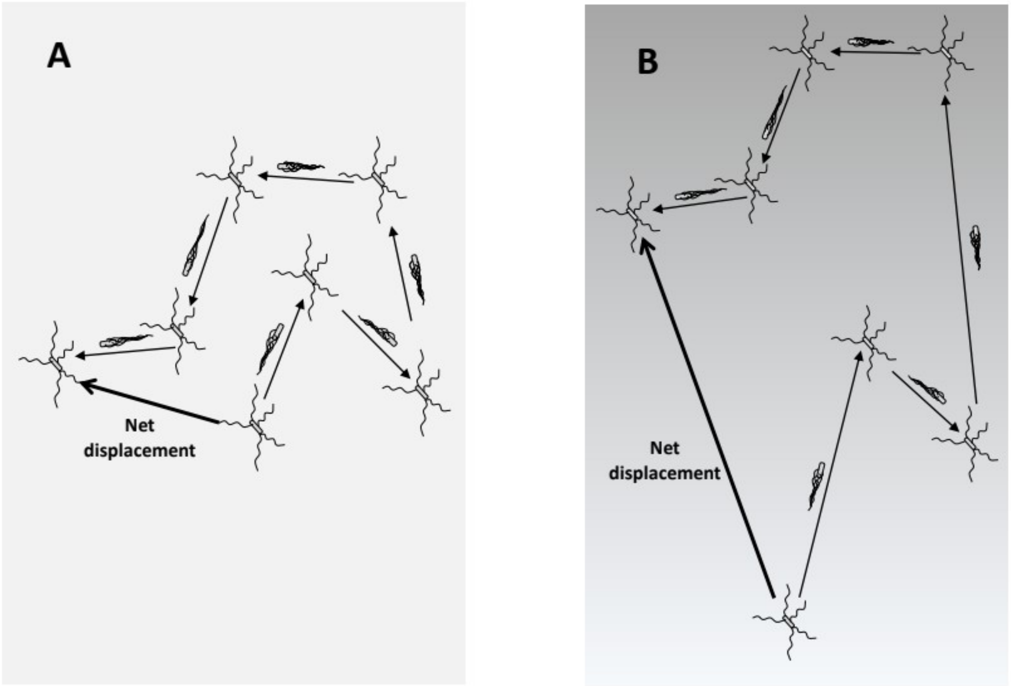
A rod sinking at low Reynolds number in a viscous liquid illustrates how a rotating helix propels a bacterium at low Reynolds number.



A helical bacterial flagellar filament can be viewed as a rod that is sinking or rising at an angle to the direction of swimming. When the left-handed helix turns CCW, alternating half helical turns move down and to the right or up and to the right, as shown by the arrows. The up and down components are equal and opposite and cancel each other out. The rightward components are additive and push the cell to the right.

How a rotating helix can propel something a low Reynolds number. Low Reynolds number at a non-microscopic scale can be generated by using a viscous liquid, like corn syrup. If you place a long thin rod exactly vertically (parallel to the pull of gravity) in the corn syrup, it will sink straight down (**A**). If you place the rod exactly horizontally (perpendicular to the pull of gravity), it will sink straight down at half the speed as when it was vertical (**B**). It goes slower because there is more surface area in the direction it is sinking. If you place it at an angle, it will both sink and slide sideways (**C**). When a bacterial flagellum rotates, half of the helix moves "up" and the other half moves "down" (**D**). This is equivalent to saying that the two halves are sinking in opposite directions. The forces acting up and down are equal and opposite, and they cancel. (Up and down are arbitrary conventions here, as the cell does not feel gravity and can swim up, down, or sideways equally well.) However, the slippage in the "upward" and "downward" halves is in the same direction, and so the forces on the long axis of the flagellar filament (the dashed line) add and propel the cell in that direction.

13. To find those greener pastures, bacteria swim in a purposeful manner. Migration in response to chemical gradients is called **chemotaxis**. **Photosynthetic** bacteria can do something similar with light, called **phototaxis**. The basic idea is simple. Just swim for a longer time in the direction in which things are getting better: higher concentrations of nutrients or other useful chemicals or beneficial wavelengths of light. When things are no longer getting better, change direction. In this way, bacteria can migrate up concentration gradients of chemicals or intensities of wavelengths of light that are beneficial, collectively called attractants, and down gradients of chemicals or intensities of wavelengths of light that are harmful, called repellents.



A 3D random walk.

A 3D biased random walk.
Swims are longer up the gradient.
The cell moves toward chemical.

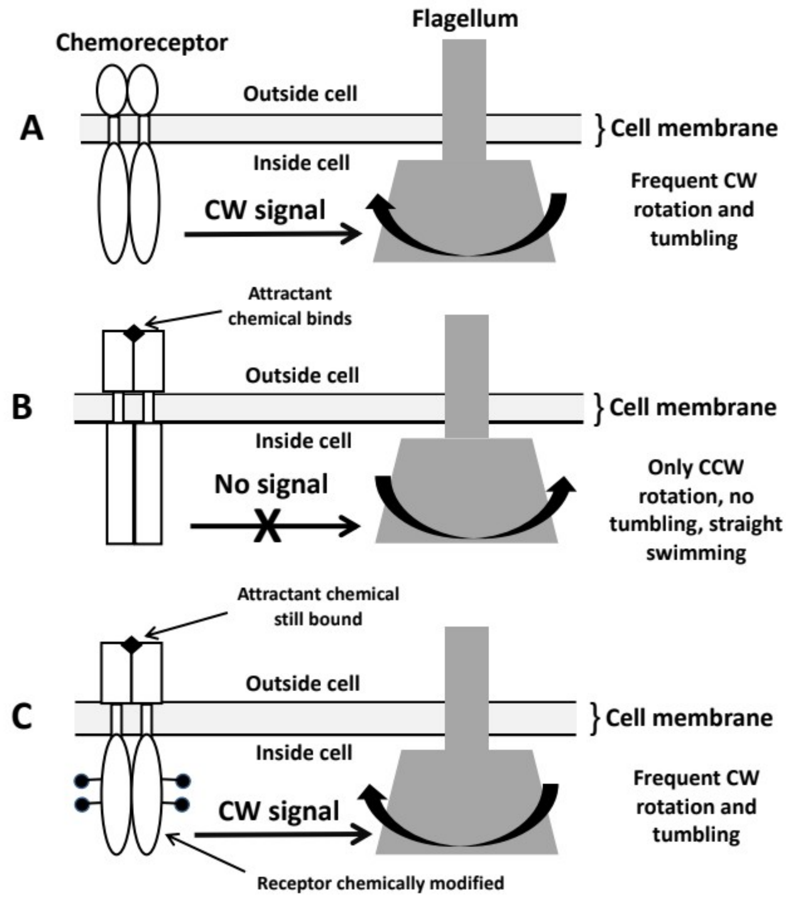
An *E. coli* cell migrates in a gradient of an attractant chemical by biasing a 3-dimensional random walk. (**A**) In the absence of a gradient, indicated by the uniform gray shading, an *E. coli* cell executes a 3-dimenionsal random walk, like a very drunk person might do in two dimensions. It swims straight for a short time when its flagella turn CCW, like a drunk taking a few steps in one direction. Then it rotates its flagella CW and tumbles to reorient itself, like a drunk staggering. It then starts rotating its flagella CCW, reforms the flagellar bundle, and takes off in a new, random direction. (**B**) In the presence of an attractant gradient, with the higher concentration at the top indicated by the darker gray shading, the cell still does a random walk, but it is biased in the direction toward higher concentrations of attractant. This is accomplished by extending the swims in the favorable direction by increasing the time between the periods of CW flagellar rotation that cause a reorienting tumble. The cell senses the attractant concentration increasing with time as it swims up the gradient, and that inhibits the signal for CW flagellar rotation. The cell progresses up the attractant gradient by biasing its random walk (swim). If the cell is in a repellent gradient, the swims become longer when the cell moves toward a lower concentration of the repellent.

14. Chemotaxis involves short-term memory. The small size of bacteria means that the concentration of a chemical, or the intensity of light, is very nearly the same at its front and its rear end, far too small a difference to detect reliably. So how can they sense a gradient? They compare the concentrations or intensities at different times along their swimming paths. To do so, they must do two things. First, they have to measure the concentration of a chemical or the intensity of light very accurately. They have **chemoreceptors** or **photoreceptors** that do that. Second, they have to remember the concentration they measured a short time previously. In this case, a short time means a few seconds. They must have a very short-term memory.

Remember that bacteria can swim at twenty to one hundred body lengths per second. That is a long enough distance for the concentration of a chemical or the intensity of light to change enough to be reliably measured. The very short term of the memory is crucial, because bacteria cannot swim in one direction for more than a few seconds because of Brownian motion. Remembering what the concentration was a minute ago, or even ten seconds ago, would be useless. But if the concentration or intensity of an attractant is increasing, it pays to keep swimming in that direction for a few seconds more. The same goes for a situation in which a repellent is decreasing in concentration or intensity. If there is no change, or if the change is in the wrong direction, the receptors signal the flagella to rotate in the opposite direction. They either reverse course or, as *E. coli* does, randomly reorient in a new direction.

15. Bacteria have no brains or nerves. The receptors communicate with the flagella by sending a chemical signal that diffuses through the cell. Recall that diffusion is very rapid at small distances, so the signals from the receptors are received at the flagellar motors in less than a tenth of a second. The memory is a chemical modification of the receptors that resets them to the signaling state they were in before they sensed the attractant or repellent.

We now know a great deal about all of the biochemistry and molecular biology that makes these remarkably sophisticated behaviors possible in bacteria. But that is not the point of this TF. The take-home message is that, if small size presents limitations to the way a cell utilizes and navigates its environment, evolution will find a way for them to do it. Bacteria have been doing it for a much longer time than Eukaryotes, not to mention multicellular Eukaryotes, and for many thousands of times longer than humans have been doing it. There is a magnificent microscopic world all around us, and within us, too.



A simplified view of the signaling pathway that generates the biased random walk. (**A**) A membrane-spanning chemoreceptor is shown to the left as an extended protein dimer with two identical subunits. The part of the receptor that binds attractants is outside the cell membrane, and the part that activates the signaling protein is inside the cell. With no attractant present, an active receptor (shown by the ovals) produces a signaling protein that rapidly diffuses through the cell to the flagellar motor. When the signaling protein binds to the motor, it causes the motor to turn CW. Another enzyme inactivates the signaling protein, so its concentration is maintained at a level that allows the motor sometimes to turn CCW and sometimes to turn CW. This allows the cell to carry out a random walk, as shown in **Figure 6**. (**B**) When an attractant molecule binds to the external part of the receptor, the ability of the intracellular part of the receptor to activate the signaling protein is blocked (shown by the conversion of the ovals to rectangles). As a result, the concentration of the signaling protein falls, the flagellar motor turns only CCW, and the cell keeps swimming straight. (**C**) The intracellular part of the receptor in its inactive state becomes a target for chemical modification by an adaptation protein. The modifications are shown as lollipops. Although the attractant is still bound, the intracellular part of the receptor can now activate the signaling protein again, and the flagellar motor can go back to alternating between CCW and CW rotation. To sense a higher concentration of attractant, another receptor molecule has to bind an attractant. Because there are thousands of receptors for each attractant, this sequence of events allows a cell to continue to move toward a higher concentration of attractant by repeating this process. There are different receptors for different attractants. In *E. coli*, there are four receptors, and each one senses several different attractants. Most attractants are nutrients, primarily amino acids and sugars.

The Evidence Base, Further Reading and Teaching Aids

Articles worth reading, some more technical than others

1) Purcell, EM. 1977. Life at low Reynolds number. *American Journal of Physics*, vol. 45, pp. 3-11.
2) Berg, HC, Anderson, RA. 1973. Bacteria swim by rotating their flagellar filaments. *Nature*, vol. 245, pp. 380-382.
3) Berg, HC. 1975. How bacteria swim. *Scientific American,* August issue.
4) Turner, L, Ryu, WS, Berg, HC. 2000. Real-time imaging of fluorescent flagellar filaments. *Journal of Bacteriology*, vol. 182, pp. 2793-2801. (with video)
5) Beeby, M, Ferreira, JL, Tripp, P, Albers, S-V. Mitchell, DR. 2020. Propulsive nanomachines: the convergent evolution of archaella, flagella and cilia. *FEMS Microbiology Reviews*, vol 44, pp. 253-304.

Videos available online

1) Howard Berg: Marvels of Bacterial Behavior, Part 1 https://www.youtube.com/watch?v=ioA1yuIA-t8

2) Howard Berg: Marvels of Bacterial Behavior, Part 2. https://www.youtube.com/watch?v=_cJ6k5R5RjU

3) http://www.rowland.harvard.edu/labs/bacteria/movies/synecho.php Various bacteria swimming

Glossary

aerobic: capable of using oxygen from the air or water to carry out respiration.
anaerobic: unable to use oxygen to carry out respiration. Oxygen is even poisonous to some anaerobic organisms, which are called strict anaerobes.
Archaea: archaea are organisms in one of the three domains of cellular life, the Archaea. They are usually single-celled, very small, and have circular chromosomes. They appear similar to bacteria in the microscope. They and the bacteria evolved much earlier in the history of the earth than did eukaryotes. However, they are very different from bacteria in structure and in the way they carry out some biochemical reactions.
ATP: adenosine triphosphate. Adenosine is an adenine molecule with a ribose sugar attached. Three phosphate groups (PO_4) are attached to the ribose, and very high energy bonds connect the phosphate groups. When ATP splits into ADP (adenosine diphosphate) and a free phosphate, a large amount of energy is released, and that energy drives energy-requiring activities in the cell.
Bacteria: bacteria are organisms in one of the three domains of cellular life, the Bacteria. They are usually single-celled, very small, and have circular chromosomes. They and the archaea evolved much earlier in the history of the earth than did the eukaryotes.
Brownian motion: the erratic random movement of microscopic particles in a fluid cause by continuous bombardment from molecules of the surrounding medium.
chemoreceptor: a protein found in the cell membrane that binds an attractant or repellent chemical and generates a signal inside the cell. In bacteria, the chemoreceptor sends a signal to the flagellar motor that tells the motor whether to rotate clockwise or counterclockwise.
chemotaxis: the ability of an organism to sense and migrate in a gradient of a chemical. A chemical that causes the organism to move to a higher concentration is called an attractant. A chemical that causes the organism to move to a lower concentration is called a repellent.
chloroplast: The organelle in a plant cell that absorbs light and uses its energy to drive the fixation of carbon dioxide from the air or water into sugar.
chromosome: an enormous single molecule of DNA that contain the genes of an organism. Bacteria and archaea typically have one circular chromosome per cell. Eukaryotes typically have multiple (two to several hundred) linear chromosomes that are contained within the nucleus, which is separated from the rest of the cell by a double membrane.
diffusion: a process resulting from the random motion of molecules. Diffusion will create a net flow of matter from a region of high concentration to a region of low concentration.
DNA: deoxyribonucleic acid. The famous double-helix that contains the four-letter code that provides the instructions for making almost all of the proteins in the cell. Different sequences of adenine, cytosine, guanine, and thymine (ACGT) encode the sequences of the 20 different amino acids that make up proteins. A pairs with T and G pairs with C in the double helix. When the helix zips open, a new strand can be made by the enzyme (a protein) DNA polymerase. It pairs every A,C,G, or T in each original strand with T,G,C, or A in the new strand, so two identical copies of the double-helix DNA are made. That is the way chromosomes replicate.
Eukaryota: eukaryotes are organisms in one of the three domains of cellular life, the Eukaryota, Eukaryotes include such familiar multicellular organisms as animals, plants, and fungi. Humans are eukaryotes. Single-celled protozoa are also eukaryotes. All eukaryotes have complex cells like ours with a nucleus containing multiple linear chromosomes.
helix: a shape like a corkscrew or a spiral staircase. Another name for helix is coil. The mathematical definition is a smooth curve in space with tangent lines at a constant angle. A

helix can have either a right-handed or left-handed twist. DNA is a right-handed helix. The *E, coli* flagellar filament is a left-handed helix.

inertia: the resistance of an object to a change in its state of motion, including being stationary.

mass: an intrinsic property of matter. Mass is independent of gravity, whereas weight depends on gravity. A human has the same mass on the moon, the earth, or Jupiter. However, the same human weighs less on the moon and more on Jupiter, because the moon has lower mass and less gravity than the earth and Jupiter has a greater mass and much higher gravity than earth. In an extreme case, in outer space, with almost no gravity, a human has the same mass but is almost weightless.

mitochondrion (plural mitochondria): the organelle in almost all eukaryotic cells that enables them to use oxygen and the energy derived from breaking down sugars and other nutrients to make ATP.

momentum: the mass of an object times its velocity. Physicists call momentum p, so p = mv.

organelle: a structure within a cell that has a particular function, like an organ in our body. The organelles with which most people are familiar in eukaryotic cells are the nucleus, mitochondria, chloroplasts, ribosomes, and cilia. The bacterial flagellum is also an organelle.

photoreceptor: a protein found in the cell membrane that absorbs light of a specific wavelength and generates a signal inside the cell. In bacteria, the photoreceptor sends a signal to the flagellar motor that tells the motor whether to rotate clockwise or counterclockwise.

photosynthesis: the ability of plants and certain bacteria to use the energy from light to power the fixation of carbon dioxide from the air or water into sugar.

phototaxis: the ability of an organism to sense and migrate toward different intensities of light. A higher intensity of a certain wavelength of light can either attract the organism or repel the organism, so there are both attractant and repellent forms of phototaxis.

Protozoa: one group of eukaryotes. They are typically single-celled, but they have a nucleus with multiple chromosomes. The individual cells can be quite large compared to most cells of animals, plants and fungi, although they are still microscopic. Some of them crawl and some of them swim, but they swim very differently than bacteria using beating organelles called cilia. Many think the first protozoa evolved when a large anaerobic archaea swallowed an oxygen-respiring bacteria.

reciprocal: in this context, something that is an exact reverse movement of a rigid object.

square root; the square root of a number is a value that, when multiplied by itself, gives the number. For example, the square root of 16 is 4, because 4 x 4 = 16.

velocity: the rate an object is moving in one direction. It is different than speed. Speed has no direction; it is just how fast something is moving.

viscosity: the quantity that describes the resistance of a fluid to flow.