Biol 002: Cellular Basis of Life

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Welcome to Biol 002 Lecture!

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Time: MWF 5:00pm-5:50pm

Classroom: Bournes Hall B118

Office Hours: TBD

Figure 1: Death And Life (1908) by Gustav Klimt

For all of our differences, we have so much in common. We are all human beings. We are all made up of the same proteins, our genes constructed with the same DNA. We are all together on this rock hurtling through space, and we are all powered by energy from the same star. But where did this rock come from? Why are we hurtling around it? How did life originate? What does it mean to be "alive"? In this course, we will wrestle with these and other questions, exploring the answers we've uncovered and the ones that we still seek.

This is our informal course textbook, **online** or in **PDF**. You can access the materials for class on **the website**, or through **Canvas**. Unit material—including the reading and slides—will be available the week before we begin the unit. Check out the **syllabus** for more details.

Unit 1

The Birth of the Universe

> In the beginning the Universe was created. This has made a lot of people very angry and been widely regarded as a bad move.
> *Douglas Adams, The Restaurant at the End of the Universe*

[**ACCESS UNIT 1 LECTURE MATERIALS**]

A classic question in philosophy is as follows: Why is there something rather than nothing? Which is to say, why is there a universe, and why is it full of stuff? Wouldn't it be just as easy—maybe easier!—for there to be simply nothing at all? What even is the universe? How did it originate? *When* did it originate? How did it develop? Common wisdom tells us that the universe is constantly expanding—but into *what* is it expanding? And why do we care?

Why we care is a complicated question with no singular answer, but I think we ought to care because life exists today as we know it because of the events that birthed and shaped the universe. Understanding life requires that we understand the physical laws that govern its construction. In fact, all of us here on Earth are really products of just one event that occurred nearly 14 billion years ago. In all the time and space of the universe, we only know of a single planet capable of supporting complex biological life. Our singular example suggests that a lot of very specific things were necessary for the formation of life, and that the life we know is irrevocably tied to the planet on which it formed.

1: The Big Bang

Let's start with the what. The **universe** is all of space and time and all matter and energy contained within it. Us humans usually care most about the planets, galaxies, stars, nebulae, and comets—because that's the stuff we can see. But this matter—which we call **ordinary matter**—actually represents only five percent of the matter contained in the universe. We know the most about this kind of matter, because, well, we can see it, and touch it, and also we *are* it. Yet nearly 85 percent of the matter in the universe is invisible to the entire electromagnetic spectrum, including all of human visible light. We call this matter **dark matter**, because, well, we can't see it, we can't touch it, and we decidedly are *not* it. We're not even exactly sure what it is although we do know it's there.[1]

Figure 1.1: M81 spiral galaxy image from **NASA**, an example of "ordinary matter."

We have a few good ideas about the birth of the universe and its age, and we call these ideas the **Big Bang Theory**. In regular speech, we might use the word theory to mean that we have a half-baked idea—*I have a theory that my television is brainwashing me with special light pulses.* But a **scientific theory** is something very different. It's usually a principle that has been tested repeatedly from many angles, over many years, often centuries. It's something that we can use to make accurate predictions about the future behavior of specific phenomena. Here is a comprehensive definition from **Wikipedia**:

[1] We won't touch on how we know it's there in class, but you can always **check out YouTube**.

> A scientific theory is an **explanation** of an aspect of the natural world and universe that has been **repeatedly tested** and **corroborated** in accordance with the scientific method, using accepted protocols of observation, measurement, and evaluation of results. Where possible, theories are tested under controlled conditions in an experiment. In circumstances not amenable to experimental testing, theories are evaluated through principles of abductive reasoning. **Established scientific theories have withstood rigorous scrutiny and embody scientific knowledge.**

Here are just a few scientific theories you may have heard about: **The Theory of Gravity**, **The Theory of Relativity**, **The Theory of Evolution By Natural Selection**, and **The Laws of Thermodynamics**. But let's get back to the theory of the day, the Big Bang.

The uncertainty in the beginning

My favorite part about the Big Bang Theory is that the "big bang" didn't start out big at all, and there was no bang. (There is no sound in space.) For those reasons, I've read that cosmologists actually hate the term "big bang," but unfortunately for them it's super catchy so it stuck. Over the thousands of years of recorded human history, human beings have put forth countless stories—creation stories—that attempt to explain the birth of the universe. I'm partial to the Finnish diving duck, whose egg fragments on the knee of the goddess of air gave birth to the world.

The goal of science is to systematically test explanations and predictions in an effort to build and organize human knowledge. This goal is sometimes analogous to our goals in storytelling and sometimes not. In the case of creation stories, I think the goal is the same—we want to know where we came from and why we are here. We search for meaning in the fact of our existence. But despite the decades of research there is still a lot of uncertainty surrounding the birth of the universe. The fact is, we still are not entirely sure *where* the universe came from or *why* it was suddenly there.

Part of the problem is that the universe is said to have started with a **singularity**. A singularity happens when gravity is so intense that all known physical laws of space and time completely break down. In our universe, predictable physical laws governing space and time (or, "spacetime") allow us to understand the behavior of matter and energy. But when these laws break down we have no language for that—what is "time," before time existed? And really, who's to say that a singularity isn't just a fancy name for a great cosmic egg? Because it is this singularity that gives birth to the universe.

All we know is that at some instance all the matter and energy that would ever be *in the entire universe* was condensed into a single point: the singularity. The conditions of this single point are so extreme that physical laws break down, so it's impossible to say what occurred during the earliest moments of the Big Bang. The temperature is so high in the early stages of the universe that atoms, the stuff that makes up all ordinary matter, cannot form. The four fundamental forces that govern everything in the universe—gravitation, electromagnetism, the weak nuclear force, and the strong nuclear force—did not exist at all as separate forces but were unified as one.

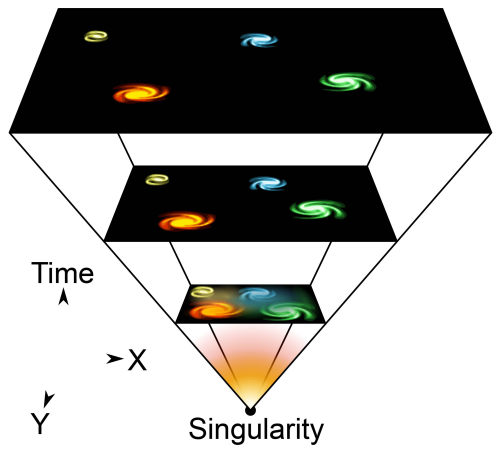


Figure 1.2: The universe begins with a singularity. (Photo from **Wikipedia**.)

But from this singularity the universe begins to expand.

Inflation and the four fundamental forces

As the universe expands, it cools. Between 10^{-36} seconds and 10^{-32} seconds after the singularity begins to expand, this single unified force governing all interaction begins to split into two forces that will eventually become four. But first. An event occurs that should be impossible based on everything we know about science and the universe: in barely a fraction of a second, the universe expands from roughly the size of a three-story building to something 62,100,000,000,000,000 miles across. This event is known as **inflation**.

In our knowable universe, nothing can travel faster than the speed of light. Rather than suggesting that the universe expanded faster than the speed of light, scientists say that the metric that governs the geometry of spacetime changed in scale. Basically, and I'm no physicist, the entire scale of the universe changed, like zooming in really close on a picture. The picture itself did not change but the scale did.

Through this expansion, the universe can continue to cool. The entire universe is completely filled **quark-gluon plasma**, a hot, dense collection of particles that will ultimately condense to form matter but hasn't yet. The universe is still too hot for that. But those four fundamental forces that constrain the behavior of all matter in the universe—gravity, electromagnetism, and the strong and weak nuclear force—now exist in the form we know them today.

Matter and antimatter

It's actually not clear why there is any matter in the universe at all. In the hot mess of the early universe, both matter particles and antimatter particles are created together in pairs. These are similar particles but with opposite charges, and when they come into contact they destroy ("annihilate") each other. Because they are created in pairs, that means that ultimately every matter particle should eventually destroy every antimatter particle and there would be nothing left except pure energy. But this is not a universe of pure energy. For all the "stuff" we see in the universe,

Table 1.1: A description of the four fundamental forces. These four types of interactions are not reducible to more basic interactions.

Forces	Description
Gravity	All things with mass or energy are attracted to (or gravitate toward) one another.
Electromagnetism	A type of physical interaction that occurs between electrically charged particles, carried by electromagnetic fields composed of electric fields and magnetic fields.
Strong Nuclear Force	An interaction that keeps the particles that make protons and neutrons together, and binds protons and neutrons into atomic nuclei.
Weak Nuclear Force	An interaction between the components of atoms that is responsible for the decay of atoms.
Electroweak Force	At extremely high temperatures, the electromagnetic force and weak force merge into a combined electroweak force.

from every nebula to every comet, from every planet in our solar system to every human-made artifact on Earth: *something* is there. Something is there because for every billion pairs of matter and antimatter created in the early universe, two matter particles were not annihilated. Two matter particles remained.

And we are the remnants of that great cosmic imbalance.

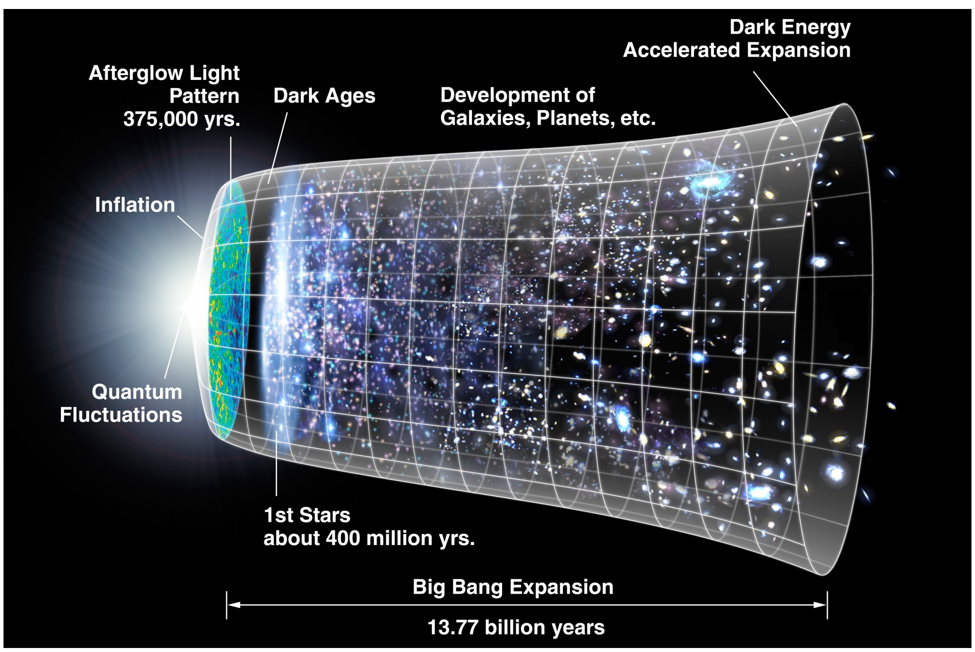


Figure 1.3: So far, we have discussed the first second of the history of the universe following the Big Bang. (Photo from **Wikipedia**.)

2: The Formation of Matter

I've spent a lot of time talking about mass, and atoms, and parts of atoms. But what actually is all that stuff? When we hold something in our hands, what is it that we are holding? Pinch your skin—something is there… but what? It's ordinary matter, which is simply anything that takes up space and has **mass**[2]. But wait, you say, skin is mostly made up of proteins. That's true. But what makes up proteins? Maybe you already know that proteins are made of amino acids. Okay, what makes up an amino acid? Mostly carbon, nitrogen, oxygen, hydrogen. Now we're getting somewhere. But what makes up carbon? Oxygen? Nitrogen?

Recall that at some point very soon after the Big Bang, the entire universe is filled with a substance we called "quark-gluon plasma." We will get into the states in which ordinary matter can exist (solid, liquid, gas, and plasma), but first let's talk about quarks and gluons. A **quark**[3] is one type of **elementary particle**, or, in other words, a particle that is not composed of any other particles—it is irreducible. A **gluon** is another kind of elementary particle. You don't need to know about their properties, just that they are two important elementary particles.

Figure 1.4: Mmm, let's construct a pie from scratch. Starting with an atom.

Why are the starting ingredients quarks and gluons? Because we want to build an **atom** from scratch, like a delicious apple pie. All ordinary matter is made up of different types of atoms that we call **elements**—we know about 116 of them which you can find on the periodic table. An atom is essentially the smallest bit of an element that you can get while still retaining the "special properties" of that particular element. What are the "special properties" of an element? What makes "oxygen" so "specially oxygen"? We'll get to that, but we'll start first with how atoms were built. Because there was a time when there weren't any atoms at all!

Making the atomic nucleus

Okay, so let's return to the early universe. The *very* early universe. A whole second hasn't even passed yet. Energy is too high for any meaningful interaction between quarks and gluons; it's just too dang hot. Hence the plasma. But as

[2] Mass versus weight: https://sciencenotes.org/mass-vs-weight-the-difference-between-mass-and-weight/

[3] There are six kinds of quarks, called "flavors." You don't need to know that, but I think it's funny. The quarks come in the flavors of up, down, charm, strange, top, and bottom.

the universe continues to expand and cool, quarks can now interact with gluons. When quarks and gluons are finally able to bind together, they create something called a **hadron**—there are a few kinds of hadrons, but the ones will focus on are called **protons** and **neutrons**. These particles are important because they will ultimately make up most of the ordinary matter in the universe as they bind together and form an **atomic nucleus**. Protons have a positive charge and neutrons have a neutral charge.

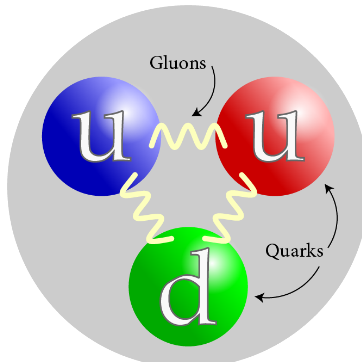


Figure 1.5: A depiction of a proton, a positively charged subatomic particle, made up of three quarks and the gluons that mediate their interaction. The strong nuclear force holds these particles together. (Diagram from **Wikipedia**.)

Between 10-20 seconds following the Big Bang, protons and neutrons are finally able to bind together. We call protons and neutrons **subatomic particles**, because they are two of the three main components of an atom. Now, the first element on the periodic table is one that we call hydrogen. Hydrogen is first on the periodic table and it has a little "1" next to it, which is its **atomic number**. The atomic number tells us how many protons an element contains, so in this case, one proton. We know that protons are positively charged, and the very first elements created in the universe were made up of only protons and neutrons: hence, they were positively charged. When an element has a charge we call it an **ion**. Positively charged hydrogen ions dominated the early universe, and even today, hydrogen makes up 75% of all ordinary matter *in the whole universe*.

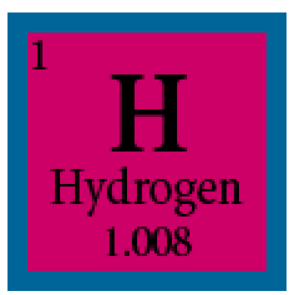


Figure 1.6: The element hydrogen on the periodic table. Hydrogen's atomic number is one, meaning it has one proton.

Making the whole atom

In the early universe, we form a few elements with only protons and neutrons. These are ions because they are all positively charged, including helium-4 (four protons and four neutrons), and lithium-7 (seven protons and seven neutrons). But for the next 370,000 years, the universe is still too hot and too dense to form a bona-fide atom. And we have no "neutral" elements; every element has a positive charge. What are we missing to make a real atom? We're missing something called an **electron**. Electrons are the third subatomic particle: they are tiny as hell and they are negatively charged. The reason why all the elements on the periodic table are depicted without a charge (neutral) is because they have the same number of electrons as protons, so neutral hydrogen has one electron and one proton. But the universe still needs to cool for this to happen.

Finally, sometime about 300,000-400,000 years after the Big Bang, we see a period called "Recombination." Finally, electrons bind with protons and neutrons and we form the first neutral atoms.

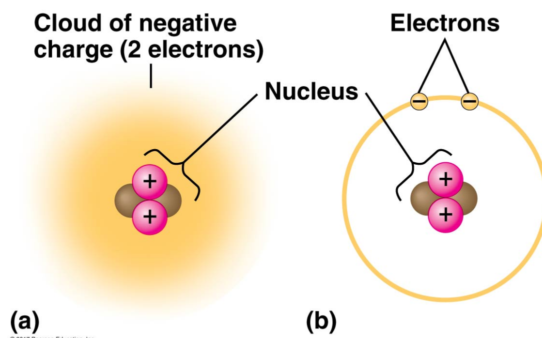


Figure 1.7: The element helium, which contains two protons and two neutrons in the atomic nucleus, also held together by the strong nuclear force. Surrounding the atomic nucleus is an "electron cloud" with two electrons.

Making more elements

Hydrogen, helium, and a smattering of lithium are formed as the universe continues to cool. For millions of years, the universe is simply dark. There are few photons and no stars. And there are no elements heavier than lithium in the universe. You see, to make an element heavier than lithium requires something called **nuclear fusion**. Basically, if we "fuse" the atomic nuclei of two helium elements, we can make beryllium—we added two protons and two neutrons to make an element with four protons and four neutrons. But this process requires wicked force.

There is only one thing that we know of that carries out the process of fusion naturally, and that is stars. Our sun is a star, and it's constantly fusing hydrogen atoms to make helium, which lets off such explosive force that it holds the entire solar system in place and powers the existence of all life that has ever been on Earth. In fact, the sun accounts for 99.86 percent of the total mass of the entire Solar System: so you, and me, and everything and everyone we know, and all the crap we made on Earth, and Earth, and all the other planets, and comets, and meteors, all that stuff is just the 0.14 percent matter leftovers.

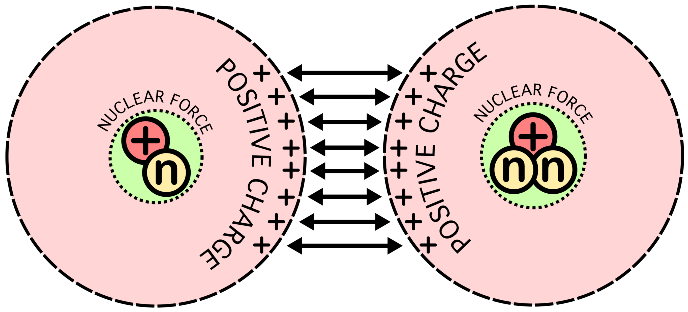


Figure 1.8: Positively charged atomic nuclei repel each other, and it takes a lot to overcome the energy barrier of these forces. (Image from **Wikipedia**.)

Eventually, all stars exhaust their supply of hydrogen.[4] Depending on the size of the star, things can start to get crazy. We will focus on stars whose mass is very large (not our sun, which is comparatively smaller). Once hydrogen supply is exhausted the star will start fusing other stuff, like helium to make beryllium, beryllium to make oxygen, and so forth. Stars can use atomic nuclei to power fusion all the way up until the element iron (26 on the periodic table).

Figure 1.9: A supernova in the M82 galaxy. (Image from **NASA**.)

One of the awesome things about fusion is that it helps maintain a star's shape and size by providing a constant outward pressure that exists in tandem with the inward gravitational pull exerted by the star's mass. Remember, stars are very, very, very large. This perfect balance exists until fusion starts to slow. As fusion slows, the outer pressure exerted by it abates, and now the core begins to condense. Eventually as a last gasp the star attempts fusion

[4]Not every star runs on hydrogen, but ours does, and the stars of the early universe did, so we'll focus on that.

with iron. (Whoa, buddy!) Repulsion of iron atoms' nuclei crushed closely together would create an implosion as the star collapses under it's own weight—but instead neutrons halt the implosion, matter bounces off the hard iron core, and BOOOOOOOM! A gigantic, superhot shockwave catapults its way through the cosmos jettisoning matter at 9000-250000 miles per second.

Why do we care about this? We care because the fusion reactions in stars cannot create anything heavier than iron. That means the heavier elements—especially the metallic ones that make up, say, a terrestrial planet like Earth—only come from these explosions. And in their wake, they leave nurseries where new stars may form, different stars made of different kinds of elements, and planets may form from the leftovers that surround them.

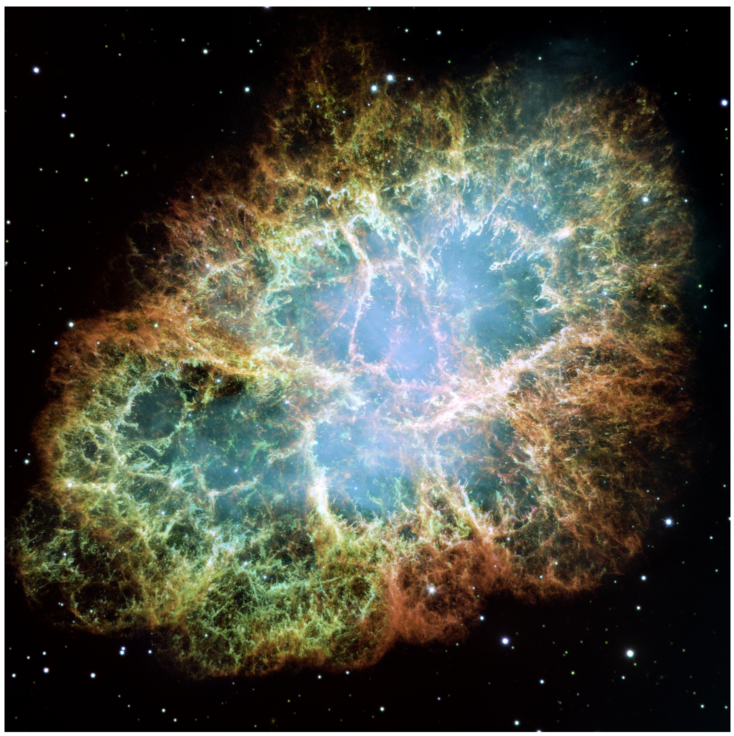


Figure 1.10: The Crab Nebula is the result of a supernova that occurred in 1084 A.D. that was documented by humans. (Image from **NASA**.)

Combining elements together

Protons are what determines what an element is—if you change the number of protons, you change the element. But you can change the number of neutrons or electrons and the element stays the same. If we have an atom of helium with two protons, two electrons, and two neutrons, it's neutral. But we can change the number of electrons and it will become a positively or negatively charged ion. Or, we can change the number of neutrons, and it becomes an **isotope**. So we would say that the proton is what determines the element's identity.

But the electron is what determines it's chemistry. The reason is that when elements bind together to form **molecules**, it's the electrons that are doing the binding part. Surrounding the atomic nucleus are **electron orbitals** that contain

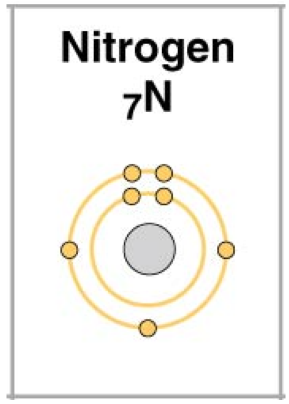


Figure 1.11: An electron distribution diagram for the element nitorgen. The first shell contains two electrons and the second shell contains five electrons. But the second shell can hold eight!

specific numbers of electrons. The first **shell** contains two electrons, and the next shells all contain eight. But take the element nitrogen: it has seven electrons, and we would depict it in a diagram above.

But we know that every shell after the first shell can hold *eight* electrons, and there are only five here. Nitrogen is not very happy like this. Atoms are most stable when their orbitals are filled. So what's a lonely nitrogen to do? Well, it can *share* electrons with another atom, called a **covalent bond**. Nitrogen is happy when it's triple-bonded to itself in the form of N_2. But, it can also bind with three hydrogen atoms and form NH_3.

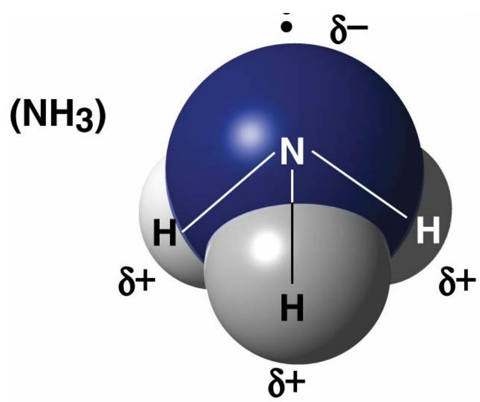


Figure 1.12: Nitrogen has greater electronegativity than hydrogen, so it pulls electrons closer to itself. This gives nitrogen a slightly negative charge and hydrogen a slightly positive charge.

Some atoms pull electrons toward themselves more than other atoms, a property called **electronegativity**. If one atom is more electronegative than another atom, it will pull the electrons they share closer and have a slightly negative charge. This is called **polarity**, and it will soon become very important.

3: Our Pale Blue Dot

The Milky Way Galaxy is old. Very, very old. Its estimated age makes it among the first galaxies to form 13 billion years ago. How did galaxies even form? The leading theory is that tiny quantum fluctuations[5] that existed when the universe inflated created unevenness in the resulting distribution of matter in the universe. These pockets of matter will eventually form **galaxies**, which are a group of stars, planets, stellar remnants, gas, dust, and dark matter that are gravitationally bound to one another. As galaxies grow in size, pockets of hydrogen may form that will ultimately collapse and form a **protostar**, a very young star that is still accumulating mass. It can take up to half a billion years for fusion to begin in the star's core and the protostar to become an actual star. A star typically has such a high mass that its gravitational pull on surrounding objects is very large.

Figure 1.13: The Milky Way Galaxy is nearly 200,000 light years across, so we are not totally sure of its shape. But we think it looks like this galaxy, UGC 12158. If the solar system were the size of a quarter, the Milky Way would be the size of the United States (Image from **Wikipedia**.)

The birth of the solar system

Several billion years after the Milky Way forms, about four and a half billion years ago, a large pocket of hydrogen gas, more than 25,000 light-years from galactic center, begins to collapse. Because only giant and short-lived stars produce the supernovic explosions we learned about previously, we know that the sun probably formed in a region where massive stars form and ultimately explode. We know that the sun formed from the remnants of an earlier star, because the elements contained within the solar system could not have existed without a supernova creating them.

The sun, like other stars, emerges when the outward pressure exerted by the gas pocket is overwhelmed by the inward pressure of gravity and a protostar is produced. Around this protostar a disk of particles starts to spin and condense,

[5] Quantum fluctuations are basically randomness in the energy distribution of particles.

and the atoms contained within it collide with greater and greater frequency. This makes things very hot. But it takes about 50 million years for the sun to transform from a protostar to a **main sequence star**, where it is stable and powered by nuclear fusion at its core.

Figure 1.14: A star-forming region, the Sharpless 2-106 Nebula, captured by the Hubble Space Telescope. (Image from **Wikipedia**.)

The sun is born in a stellar nursery called a **nebula**. Its thought that many stars formed in the nebula that birthed the sun, and that the sun eventually migrated away from its hometown, so to speak, away from the other stars that were born there. Because the sun is so massive—we already know that most of the mass in the solar system is contained within the sun—its gravity strongly influences the surrounding matter. This is important because as material starts to spin around the sun in orbit, due to its mass, this material may eventually form planetary bodies.

Figure 1.15: The sun is so massive that it essentially causes a dip in the fabric of spacetime that other objects can orbit. I imagine this like these coin donation games where the coins spin around the center.

The formation of planets

Not all galaxies are capable of supporting complex biological life. The formation of a terrestrial planet of a suitable size in a suitable location—away from gamma ray bursts, globular clusters, frequent supernovae, and Oort cloud comets, among other things—appears to depend primarily on the location and composition of the sun around which the planet forms. Which is to say that the pocket of interstellar dust that formed our solar system determined—long before our sun ever existed—whether or not a terrestrial planet could form at all. We need metallic elements for that.

Figure 1.16: We are still trying to figure out what a planet is, so sometimes Pluto is included and sometimes Pluto is excluded.

Let's try and first figure out what a planet even is—you may have heard a lot of debates about Pluto in the last decade or so. *It's a planet; it's not a planet; wait, it is a planet!* Nothing has changed about Pluto. The reason for the debates is that we have not actually settled on a definition of the word "planet." So really we are having debates about language. Part of the problem is that if we use a definition that includes Pluto, then there are actually *way* more than nine planets in the solar system. There are hundreds. It's just that when we first defined the word we didn't know that.

We will use the definition of **planet** as defined by the International Astronomical Union (IAU):

> a planet is a non-stellar body that is massive enough to be rounded by its own gravity, that directly orbits a star, and that has cleared its orbital zone of competing objects.

Planets typically form through a process known as **accretion**. When the protostar is born all the particles of gas that spin around it start smashing up against each other and sticking. This forms larger and larger objects over time. The planet that is produced depends on what sticks together during this process—meaning, the kinds of elements that are contained within it. A **terrestrial planet**, which is what Earth is, is made of silicate rocks and metals. Jupiter is a gas giant that contains only a liquid hydrogen core and hydrogen gas.

The terrestrial planets of the inner solar system—Mercury, Venus, Earth, and Mars—formed there because it was too hot for gas giants or ice planets to form. Only metal could withstand the blazing heat of the sun. (It is no coincidence that Mercury is made of solid iron.) Metallic elements are actually rare in the universe which is why these planets do not get very large. Beyond the **frost line**, the solar system becomes cool enough that giant planets like jupiter, saturn, uranus, and neptune can form. These planets grew large because they captured most of the hydrogen and helium not taken up by the planets of the inner solar system.

Earth is formed

At some point, the inner solar system contains 50-100 protoplanets that are the size of Mars or smaller. These continue to smash into each other and coalesce to form larger bodies. From the chaos of all this smashing comes our home planet of Earth, the only known astronomical object that contains life.

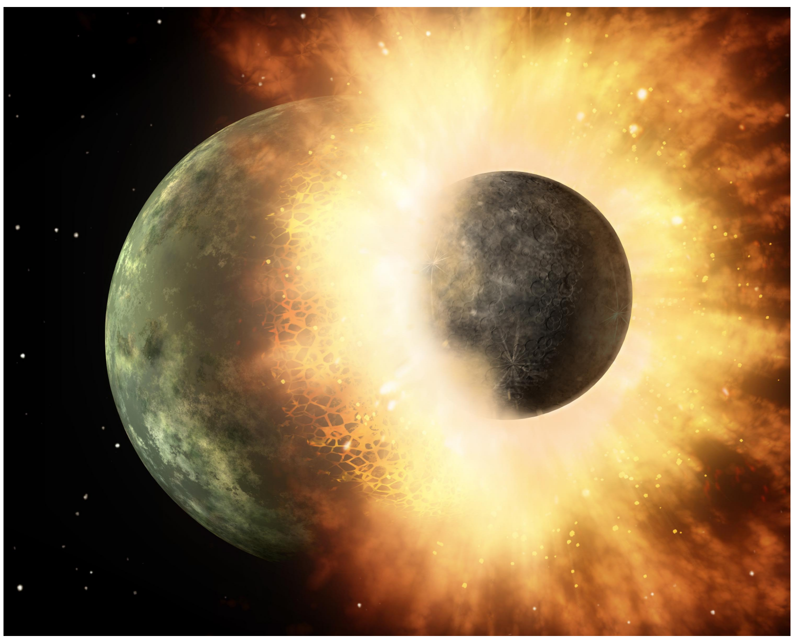


Figure 1.17: The Giant-Impact Hypothesis suggests that the moon was formed when proto-Earth collided with a planetary object the size of Mars. Analysis of lunar rocks suggests that both bodies were thoroughly mixed upon impact. (Image from **Wikipedia**.)

But first. Early in its life, Earth is not stable: fluctuations in its rotation would eventually cause severe seasonal extremes problematic for imminent life. While some organisms may adapt to extreme variations in temperature, many could not. Around when the rocks that comprise the Earth were mostly accumulated and molten, as they traveled in orbit around the sun, a collision occurred by chance with a planetary body that was roughly the size of Mars. The remnants of this collision stabilize the Earth's rotation and can still be seen today with the naked eye. We call it the moon.

The Earth is composed primarily of four layers. Once Earth was mostly formed, melting caused denser substances to sink toward the center while materials with less density migrate to the top. This process is called **planetary differentiation**.

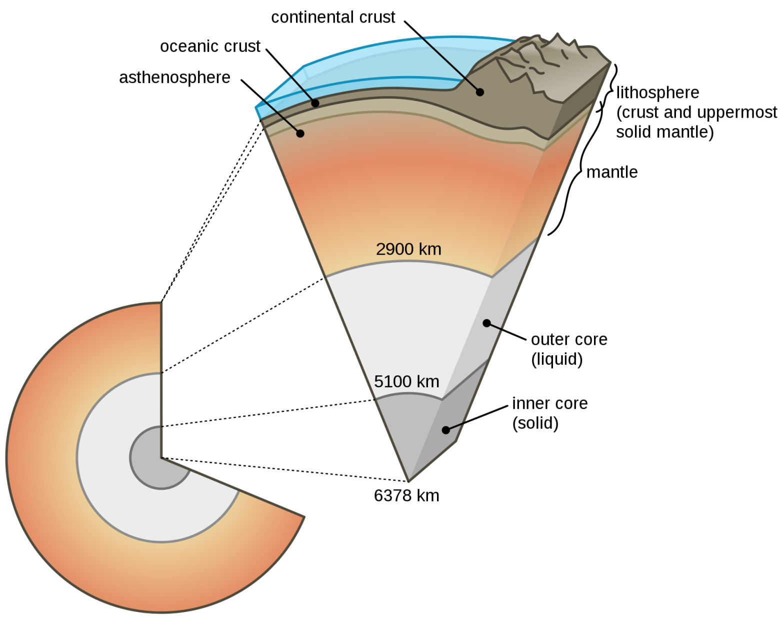


Figure 1.18: The layers of Earth. (Image from **Wikipedia**.)

1. Let's start at the **inner core**: we think it's composed of an iron-nickel alloy, based on analysis of the Earth's magnetic field. Essentially, without this, we could not have a magnetic field at all. The magnetic field is important for life, because it diverts high-energy particles from the sun and dramatically reduces the radiation impact on Earth. The core is also very hot, about 10,000 degrees F. (This is approximately the temperature on the surface of the sun.) We have never directly measured the Earth's core, which is four thousand miles below the surface.
2. Next is the **outer core**, which is also iron-nickel, but instead of being solid it is liquid. The outer core is about 1,800 miles below the surface.
3. The **mantle** is the thickest layer, and movement in the mantle is responsible for things like earthquakes and volcanoes. It is also responsible for the motion of tectonic plates in the earth's crust, causing the formation of mountain ranges, among other things.
4. The **crust** is the outermost layer of the Earth and the one we live on.

Right now, on early Earth, right after the giant impact, the scene is very, very bad for biological life. The entire planet is thought to be molten lava to a depth of hundreds of kilometers or more. There is no stable atmosphere, no liquid water, no solid crust, and no magnetic field. These components are all necessary for prebiotic chemistry to occur that is needed for the emergence of biological life.

4: The Scene on Early Earth

Water is so important to every aspect of life on Earth that many hypothesize that life without water—on any planet—is not possible. Cells, the basic building block of life, are mostly made of water. Many chemical reactions carried out by living organisms depend on the presence of water. Earth is about two-thirds water and so are we. But more than these examples, the very construction of water—and all the special properties that emerge from that construction—mean that water shapes and influences almost every aspect of the business of life. It's important enough that we'll focus our exploration of early Earth on the origin and maintenance of water on the planet.

But I'm getting ahead of myself. How do we actually know the age of the Earth? We use a special property of atoms that relates to the weak nuclear force. Remember that an atom is made up of positively charged protons and neutral neutrons, surrounded by a negative electron cloud. The mass of a particular atom is primarily composed of the neutrons and protons, because the electrons are very, very, very, very light. Now, we can't change the number of protons of an atom without changing what element it is—but we *can* change the number of neutrons and the element stays the same.

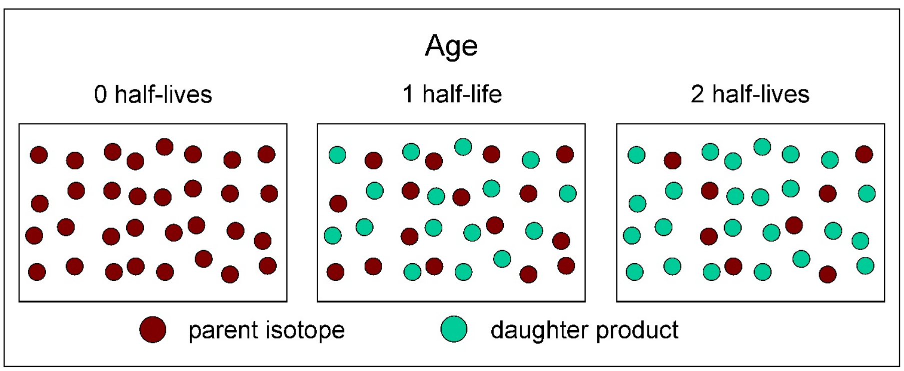


Figure 1.19: When no time has passed (zero half-lives) the atoms are all that of the parent isotope. As it decays over time, the parent isotope decays to the daughter product. There are different kinds of decay that we will not cover in class: you just need to know that the rate of decay is constant and can be measured. (**Image source**.)

You may have heard of something called **carbon dating**. On the periodic table, you'll see that carbon has an atomic number of 6; it has six protons and also six electrons (in its neutral form). Its **atomic weight** is 12, which is the number of protons plus the number of neutrons. This means that typically carbon has six neutrons. But there's another form of carbon, an isotope called ^{14}C that has two additional neutrons. Carbon-14 is actually radioactive, and it isn't stable. Thus over time it decays. The rate that it decays can be measured, and scientists use a constant called its **half-life**—the time required for the quantity to reduce by half—to date an object. The half-life of ^{14}C is 5730 years.

It's not just carbon; this can be done with other kinds of isotopes, too. We call this **radiometric dating**. Different isotopes will have a different half-life—^{3}H is ten years, and ^{147}Sm is 100 billion years. Depending on the timescale of interest and the isotopes available to measure, scientists can use this radioactive decay to learn the age of rocks, fossils, and even our home planet.

Getting back to the point: using radiometric dating, we can infer the age of the Earth. We can't actually use the rocks themselves, because conditions on early Earth were so chaotic that these early rocks have been recycled and destroyed over time. The oldest actual rock-rocks on Earth are roughly four billion years old, and several have been found across the planet ranging from 3.3-3.8 billion years old. Scientists have used several different isotopes to measure the ages of these rocks with consistent results. Radiometric dating from moon rocks provides ages of the oldest rocks at 4.4-4.5 billion years old. Since the moon was formed by a blast to very early Earth, this also helps us narrow down our planet's age. The oldest recorded material found on Earth are grains of zircon (crystals) found in Western Australia, roughly 4.1 billion years old.

Plate tectonics

You may be wondering what I mean when I say the rocks on Earth have been recycled. The surface of the Earth, the crust, is not static, which is to say that it's moving all the time. Not a lot, but a little bit (about 1-3 cm per year). Why does the crust move? Because right under the crust of Earth is magma, which is essentially liquid rock. But below that is the core, which is basically as hot as the surface of the sun. That's a lot of pent up heat—you can think about when you boil a pot with the lid on top, and the lid starts shaking as the water gets hot. The other important thing to know is that the crust of the Earth is not just one solid piece, but it's made up of many pieces—**plates**—kind of like the fabric around a baseball. Essentially what happens is that the heat from the core rises up, as it rises it cools, and then it sinks down again—this process is what fuels the shifting of the Earth's crust, known as **plate tectonics**.

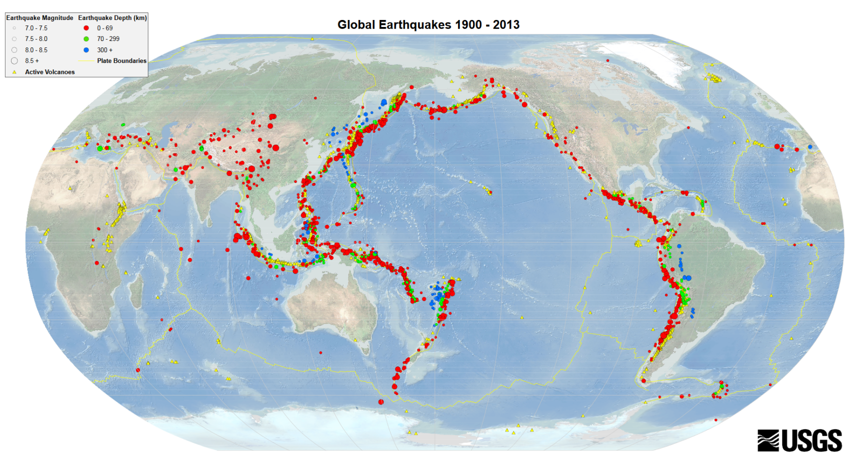


Figure 1.20: The red dots are earthquakes of a magntiude greater than seven; the yellow triangles are active volcanoes. This is the Ring of Fire, a continuous series of subduction zones where rock is constantly recycled. Volcanoes are created and earthquakes are common. (Image from **Wikipedia**.)

The plates that make up the Earth's crust have different kinds of boundaries—convergent ones, where the plates are being pushed together, and divergent ones, where the plates are being pulled apart. This results in all kinds of things, like earthquakes, volcanoes, mountain ranges, and deep ocean trenches. (California is located within the **ring of fire**, an enormous area where rock is continuously being recycled.)

We do know that after the formation of the atmosphere, liquid water ultimately condenses on the surface of Earth, creating the oceans. The Earth was really hot, probably close to 500 degrees F, but water was still liquid because the atmospheric pressure was so high due to the heavy CO_2 in the atmosphere. The Earth continues to cool, the oceanic crust also cools. This is important because atmospheric carbon slowly gets removed through a process called **subduction**. This is where the oceanic crust is essentially recycled as a heavier plate is pushed below a lighter one down into the mantle. Not only does this process ultimately create land, but as carbon is taken up rocks as insoluble calcium carbonate it is slowly removed from the atmosphere.

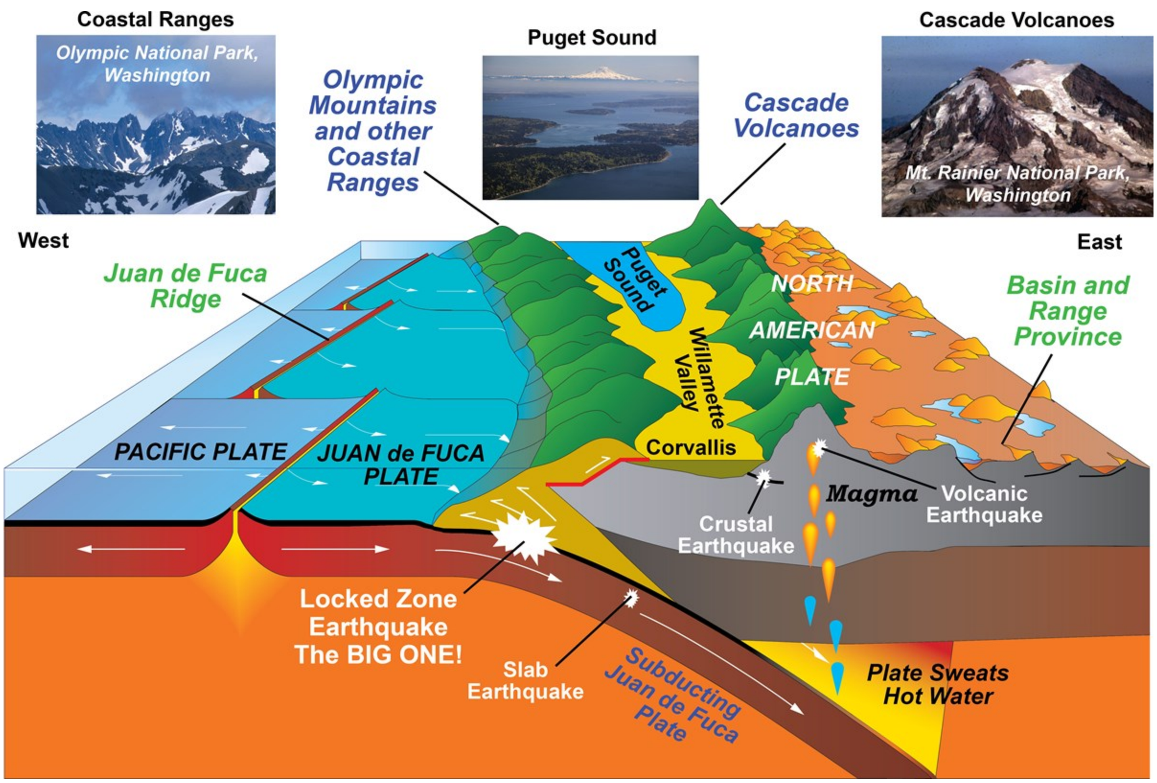


Figure 1.21: Subduction results in the formation of mountains, and also volcanoes and earthquakes. This diagram displays plate tectonics and the results of subduction in the Pacific Northwest (**Image source**.)

How did water get here?

Okay, where were we? The moon has been formed by a violent blast. Volcanic activity is very high. We call this epoch the **Hadean** epoch, for Hades, or in other words, hell. I said previously that there was no liquid water during this time. However, there is still ongoing research to understand exactly when the atmosphere and oceans formed. For a long time, it was thought that there was no life or liquid water during the Hadean, but recent work is challenging that assumption.[6] As of this writing, the origin of Earth's water is not definitively known.

Figure 1.22: An artist's rendering of early Earth in the Hadean epoch. (Image from **Wikipedia**.)

But here is a rough hypothesis. When the planetary body that created the moon hit Earth, a large portion of Earth's material was likely vaporized, possibly creating a "rock vapor" atmosphere. For the next few thousand years, this rock vapor atmosphere would have condensed, leaving behind an atmosphere heavy with CO_2. It's also likely that this atmosphere contained hydrogen and water vapor. But how did the water vapor get there? It may be that icy planetary bodies orbiting around the sun smashed together to eventually become Earth, and the water was always here. Maybe it came from the giant impact that created the moon. Maybe an asteroid (or many, as Earth was hit often in early days) brought it. The point is, we're not entirely sure.

But as the Earth cools, the oceans condense, CO_2 is pulled from the atmosphere by subduction, the magnetic field forms protecting us from heavy solar radiation—things become much more stable and favorable for biological life. The thing is, it might be possible to have very simple organisms in extreme conditions—which we will learn about soon. There are small bacteria that live in hot vents at the bottom of the ocean. But something like us multicellular mammals, we need *a lot* of time and relatively stable conditions to emerge.

The specialness of water

Last week we discussed a property called electronegativity. We said that when elements share electrons, some elements pull those electrons closer to them giving them a slightly more negative charge. We called this a polar covalent bond. NH_3 is one example, but the GOAT of polar covalent bonds has got to be water. Oxygen has much higher electronegativity compared to hydrogen, so it gives water a V shape. But because of the positive and negative charges on either end, it also makes water molecules attracted to *each other* in weaker bonds called **hydrogen bonds**.

[6] https://www.science.org/doi/10.1126/science.aba1948

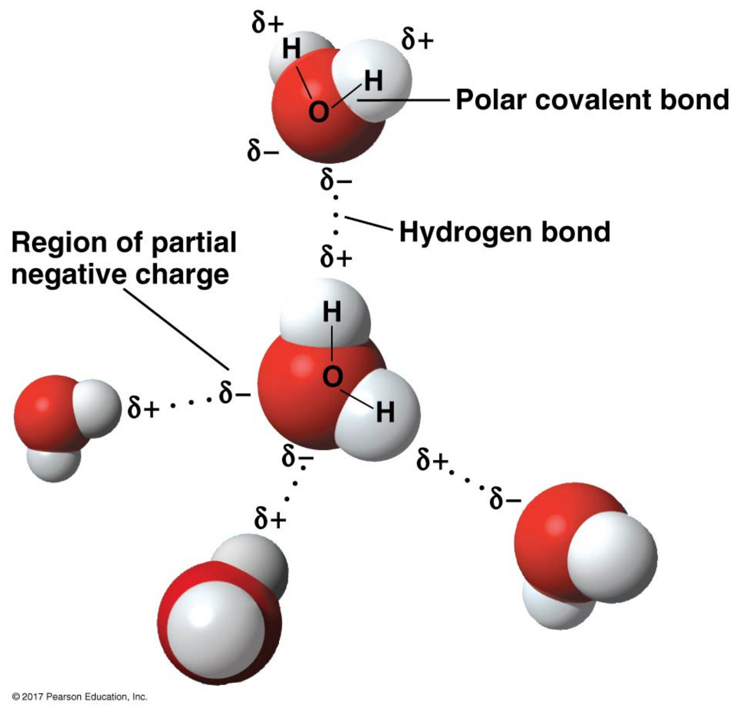


Figure 1.23: Oxygen has a slightly negative charge while hydrogen has a slightly positive charge, due to electrons being pulled closer to oxygen. The positively charged hydrogen is attracted to the negatively charged oxygen.

Because of the atomic and molecular properties of water, there are six important and emergent features that make it especially perfect for supporting biological life. Water is also a wonderful place for chemical reactions to occur, and many reactions require the presence of water. This matters for the development of biological life on Earth.

1. **The states of water.** The weaker nature of hydrogen bonding gives water special properties as it changes from liquid to gas to solid ice. In liquid water, hydrogen bonds constantly form and break as the water molecules slide past each other. If we heat up the water, the increased motion of the water molecules (higher kinetic energy) causes the hydrogen bonds to break completely and allows water molecules to escape into the air as gas. If we cool the water instead to freezing temperatures, the water molecules form a crystalline structure that makes ice less dense than liquid water. Which leads us to…

2. **Ice is less dense than liquid water.** Have you ever noticed that when you add ice to your glass of water, it floats? That if a lake freezes over, the ice stays on top of the lake and doesn't sink to the bottom? This is a unique feature of water—many molecules are more dense as solids than as liquids, but water is the opposite! This is *very* important for life, especially for the organisms that live in the lakes that freeze over. Imagine if ice sank: each winter, as the temperatures dropped below freezing, ice would sink to the bottom and the lake would eventually become a solid block of ice. Nothing could survive there. Instead, ice stays at the top, insulating the liquid water from the colder temperatures and protecting the creatures that live below.

3. **Water has a high specific heat.** Water has the highest specific heat capacity of *any* liquid. What that means is that water can absorb A LOT of heat before it changes temperature. (Specific heat capacity is defined as the amount of heat that one gram of a substance must absorb to change its temperature by one degree Celsius.) It takes water a long time to heat up and a long time to cool down. This makes it the perfect substance to evenly disperse heat throughout our bodies and help us maintain our even temperature. This also means that it takes a lot of energy to turn water from a liquid into a gas…

4. **Water has a high heat of vaporization.** Heat of vaporization is the amount of energy that it would take to turn one gram of a liquid substance into a gas. It takes a lot of energy to disrupt water's hydrogen bonds and separate liquid water from itself, so water can act heat sink, absorbing lots of heat before turning into water vapor. As water heats up, hydrogen bonds are broken and water on the surface evaporates. This process absorbs energy (i.e., heat) meaning that evaporation can also facilitate cooling. Many animals use evaporative cooling mechanisms to regulate body temperature—or in other words, sweating!

5. **Water is a solvent.** Polar molecules are ones that have slightly positive and negative charges, just like water does. You may have heard the phrase "like dissolves like": this means that polar substances dissolve in other polar solutes (liquids), and nonpolar substances dissolve in nonpolar solutes. This is why when you add oil (nonpolar) to water (polar) one sits right on top of the other (unless you shake it up!).

6. **Cohesion and adhesion help transport water.** If you fill your glass of water a little too much, before it spills over the water will form a little dome at the top of the glass. This is because water molecules are attracted to each other via hydrogen bonding and this helps water "stick" to itself, a property called **cohesion**. Whereas cohesion refers to the tendency of the *same* molecules to "stick" together, **adhesion** refers to the tendency of of *dissimilar* particles or surfaces to "stick" together.

We will continually see throughout this course how important water is for life on this planet. Now, just because us Earthlings evolved to need water does not necessarily mean that *any* organism in the universe likewise needs water. But there are just no other substances that we know of that are as special as water in exactly the same way needed for the chemistry behind the business of life to occur. (We will learn a few more as we continue to discuss the emergence of life.) But first… what even *is* this life thing?

5: Defining Life

We've so far spent all of our time discussing non-living (**abiotic**) entities. Atoms, elements, galaxies, planets. It is relatively easy for us, based on our intuition of living organisms, to say these things are not alive. But what does it mean to be "alive"? How do we actually define "life"? Why is a rock "not alive" and a coral "is alive"? I would encourage you to put down whatever device you are reading this from and think for a moment about how you would define **life**. Remember that this definition needs to encompass bacteria, plants, algae, all those weird sea creatures.

Let's start with a tricky case: a virus. A virus has impacted all of our lives dramatically for the last two years, but what even is a virus? A virus is simply genetic material stored inside some kind of case (an envelope or capsid), usually with a minimal number of proteins.

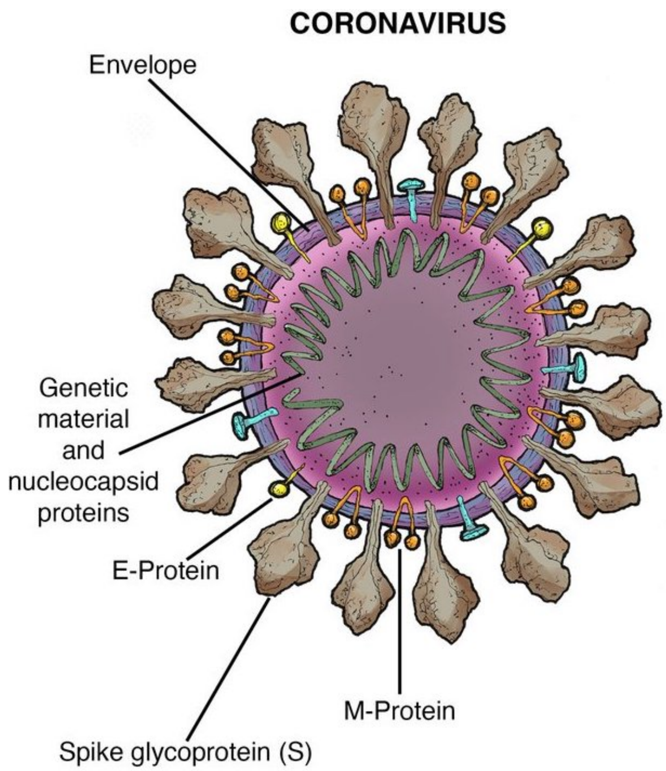


Figure 1.24: Anatomy of the Coronavirus, consisting of an outer envelope, proteins, and genetic material. (**Image source**.)

Is a virus alive? It can't do much without a host—it doesn't have any of the molecular machinery that the rest of us do, to read genetic material or make proteins. It can't capture energy or reproduce on its own. It is not made of cells. *But*. Once a virus gets inside its host, it can hijack the host's molecular machinery and use the host's energy to make copies of itself (reproduce) and spread to other hosts. A virus is even capable of evolving! Viruses that are not effective at infecting hosts and making copies of themselves will eventually disappear ("go extinct"). It's not exactly right to say that a virus is dead… but it's not exactly alive either.

One of the craziest things to me is that **there currently exists no consensus on the definition of life**. One of the first challenges is whether or not we care about defining life *generally*, or defining life only within the context of Earth. Is all life mostly carbon based? Made of cells? Mostly made of water? Or is that just us freaks on this particular planet? One paper even put together 123 different definitions of the word "life."[7] We can approach this from a philosophical standpoint, from a legal standpoint, from a biological standpoint, from a physics standpoint, from a systems standpoint. We can worry only about Earth or about life in the universe. We can include viruses or viroids or not include them.

Emergence

Life is trickier to define than say, a table:

> A piece of furniture usually supported by one or more legs and having a flat top surface on which objects can be placed.

See, a table is an object. While a table is a table, it does not fundamentally change. It is always a piece of furniture supported by legs with a flat top surface upon which we can put our crap. But life is not an object, life is *a process*. Organisms are born, grow, reproduce, and die. Organisms are constantly outside equilibrium with their surrounding environment, because as soon as you are at equilibrium with your environment you are dead. And it isn't just one thing, either. If something only grows but doesn't reproduce, that could be a mountain. If it captures energy but doesn't grow, that could be a car engine. So our definition needs to take into account not just one process, but many processes that go into sustaining living organisms through time.

Figure 1.25: Ripples in sand or snow may be thought of as an emergent structure. On their own, sand grains or snow flakes cannot have this structure. But the interaction of individual grains and wind can cause this structure to emerge, taking on a property the individual components could not have on their own.

[7] https://www.tandfonline.com/doi/abs/10.1080/073911011010524992

We say that life is an **emergent property**. What does that mean—emergence? We mean that life is a property that *emerges* only through the interaction of components—like replication, or growth, or energy capture—which alone do not have this property. Life is sometimes described as an emergent property of chemistry, because all life is really just a bunch of atoms reacting in different ways, staying outside of chemical equilibrium. It is from these interactions that the property of life emerges.

Why evolution matters

Since we will start getting into the nitty-gritty of life for the rest of the course, it's important that we all understand some basics about how the evolution of living organisms actually works. First, we need to know that organisms are born with all the instructions for their parts—which is to say that an individual organism cannot change its own instructions (or DNA) during its lifetime. As much as I may think an extra finger would be really useful, I cannot grow myself an extra finger. I am stuck with the five I was born with, based on the instructions coded in my DNA that I am unable to change.

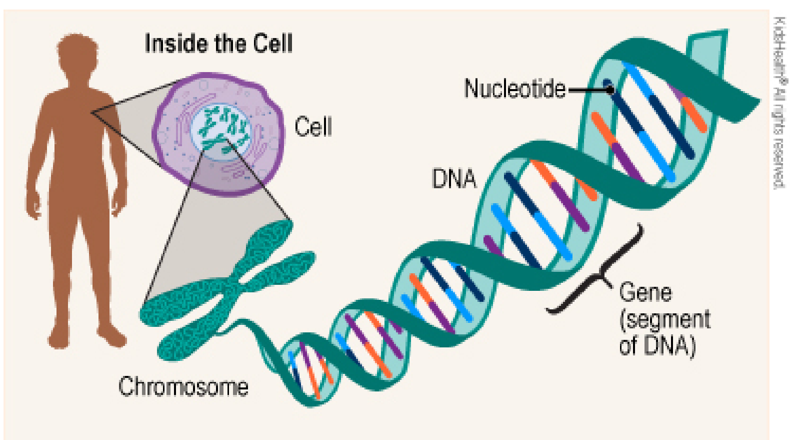


Figure 1.26: An organism is born with a specific set of instructions that they cannot change.

The second is that only those features—or traits—coded for in our DNA instructions can be passed on to our offspring. If I lost a finger in a terrible accident, my offspring would not then be born without a finger. If I dye my hair purple, my children cannot be born with purple hair. I can't transmit a suntan, or a scar, or any characteristics that I acquired over my lifetime to my offspring. Only what's in my DNA, and losing a finger does not change my DNA.

We have an intuition that organisms *can* pass on features that were acquired over their lifetime. Take the giraffe: it's easy to think that one giraffe stretched his neck a bit, passed on that stretched neck to its offspring, and so on, until the neck was very long. But we know that *cannot* be the case, because organisms can only transit to their offspring what's in their DNA! And stretching your neck does not change your DNA. So then, how does this actually work?

We observe that organisms in populations are varied in their traits. Think about human height: there are some folks that are pretty short, then medium, and then very, very tall. We are not all the same height but we vary. And

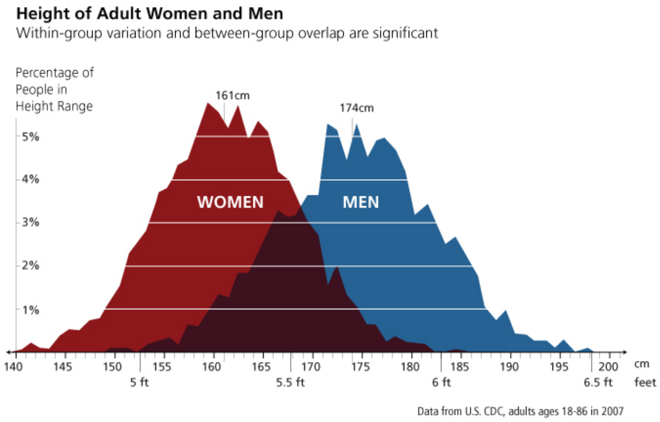


Figure 1.27: The distribution of human height, an example of variation within a species.

not only that, height is partially determined by the instructions in our DNA, so height *is* something that can be inherited. This is true about a lot of traits, in organisms across the tree of life—the traits are not the same in groups of organisms that belong to the same species.

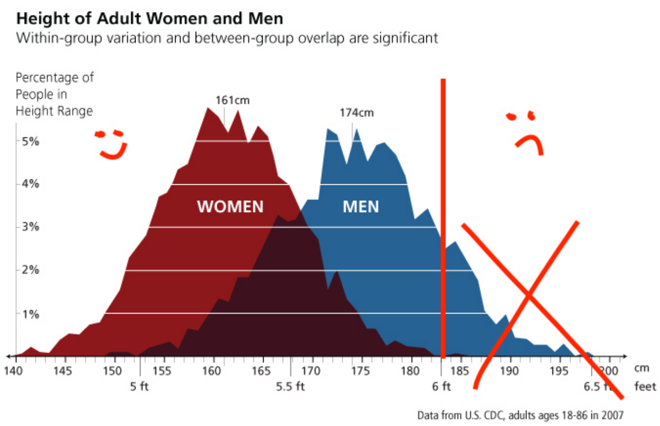


Figure 1.28: If everyone over six feet tall dies, then they cannot reproduce or they reproduce less than those that are shorter. Over time, this changes the characteristics of the population. The change in heritable characteristics of a population over time is evolution.

But let's imagine an extreme scenario. Let's say that anyone who is more than six feet tall gets their head chopped off by a vicious alien predator that now inhabits Earth. First, we lose everyone over six feet tall. But there are still the children of these people that will grow up to be six feet tall. But those children are unlikely to have children of their own, because maybe they reach six feet tall before they reach sexual maturity and they are unable to produce offspring before getting their heads chopped off. So very soon, maybe in a few generations, you will see a change in the population: no one is more than six feet tall. The folks that are more than six feet tall do not survive, and very few of them reproduce.

Now the folks that are less than six feet tall are fine. They have no issue surviving or reproducing, so they will leave behind more offspring than those that are six feet tall or more. Over generations, the characteristics *of the* *population* change because folks with certain traits—they are shorter—leave behind more offspring relative to the folks that are taller. This change in the **heritable** (coded in our DNA) traits of a population over time is called **evolution**. (Technically, I have described **evolution by natural selection**, which leads to adaptations. In this case, being shorter than six feet is an adaptation because it provides an advantage in surviving and reproducing in this environment with alien predators. But not all evolution is adaptive! More on that later.)

Why am I describing all this? Because the change in heritable characteristics of a population over time is a defining feature of life. But it *only* works if traits are heritable; that is, if the traits are coded in instructions that are passed to offspring. If there were no method of passing on instructions, how could there be life at all? Hopefully, by the end of this course, you'll fully appreciate how necessary heritability is for life, and how once you have heritability there will *always* be evolution. Heritability binds us to our ancestors and constrains the possibilities available to future generations, leading to the dynamics described by evolutionary theory.

From a biological perspective

As biologists, we take a descriptive stance when defining life. Basically, we sort of describe what life is and use that as our definition. And that's going to work well enough for us in this course. For our purposes, all life is composed of **cells**. That is the building block upon which life is formed. Beyond that, here are the seven characteristics that most biologists agree are necessary components for life (from these together, life emerges):

- **Homeostasis**: internal environment is regulated to maintain a constant state
- **Organization**: made up of one or more cells
- **Metabolism**: transform energy through chemical reactions
- **Growth**: create more cellular components than are broken down
- **Adaptation**: populations change over time in response to the environment, as some individuals leave more offspring than others
- **Response to stimuli**: typically involve senses
- **Reproduction**: the ability to produce new organisms

6: Biological Molecules

We learned, at least descriptively, what we think it means to be "alive" on this here planet Earth. But all that "alive" business—regulating the internal environment, organization, transforming energy, adapting, and so on—all living organisms use very specific molecules to carry out that business. Of course, I couldn't tell you what hypothetical alien life is made of or how it goes about capturing energy. But I can tell you that *every living creature on Earth* is made of essentially the same stuff. Everything from the single-celled bacteria living on a root in a marsh to phytoplankton in the seas to the squirrels in our yards to you and me—we all are primarily composed of the same four kinds of molecules. (Even the same elements: just four elements—oxygen, carbon, hydrogen, and nitrogen—make up 96 percent of the human body's mass, and this is remarkably consistent across the tree of life.)

Figure 1.29: The energy from the sun is harnessed by photosynthetic organisms like plants. These organisms store the energy from the sun in glucose (sugar) molecules, which other organisms consume.

I told you that the energy to power all life on Earth comes from the sun. But it's not like we lie out in the sun and recharge every day—so how do we actually get that energy from the sun inside of our bodies so that we can use it? We get it from the organisms that *do* lie out in the sun and recharge all day; namely, plants. Through the process of photosynthesis (covered in Unit 3), plants capture the energy from the sun and store it in sugar molecules called glucose. This is the most basic, fundamental currency of energy used amongst living organisms. But what actually is it?

Carbohydrates

Carbon is special because of the configuration of its electrons. It has four free electrons—**valence electrons**—that are able to form covalent bonds. It can form double and triple bonds (share two or three electrons). Or, it can bond with four different elements. The point is that carbon is extremely flexible in its ability to form bonds and it forms the backbone of many important molecules.

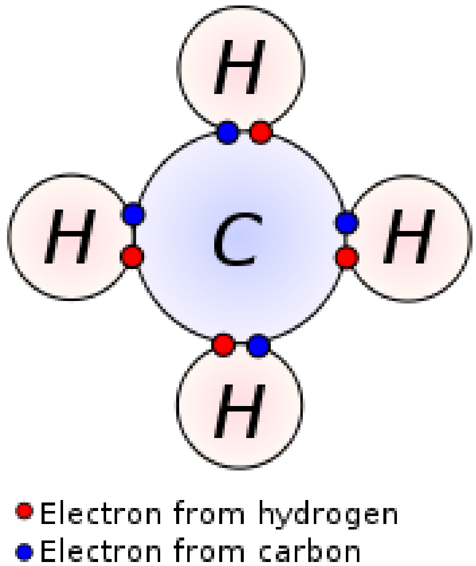


Figure 1.30: Carbon has four valence electrons, meaning it can form four covalent bonds. Four free electrons is the maximum number that an element can have, which means carbon is special. Here carbon is sharing its valence electrons with four atoms of hydrogen, making methane (CH_4).

At their very core, carbohydrates are really just sugar, plain and simple. But what is sugar? A collection of carbon atoms, hydrogen atoms, and oxygen atoms in various configurations. That's pretty much it, although it turns out that there are a *lot* of different configurations that can be made with only these elements. What's important about sugar? Simple sugars, or **monossaccharide**, can be broken down by our cells to extract energy—pretty much every cell breaks down glucose for energy in a process called cellular respiration (which we will learn about in Unit 3). Monosacharrides are known as **monomers**, which are building blocks. Monomers are put together to form **polymers**, which include multiple building blocks. Two monosacharride monomers put together make a **disaccharide**.

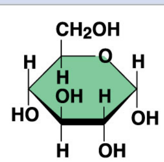
Components	Examples	Functions
 Monosaccharide monomer	Monosaccharides: glucose, fructose Disaccharides: lactose, sucrose	Fuel; carbon sources that can be converted to other molecules or combined into polymers
	Polysaccharides: ▪ Cellulose (plants) ▪ Starch (plants) ▪ Glycogen (animals) ▪ Chitin (animals and fungi)	▪ Strengthens plant cell walls ▪ Stores glucose for energy ▪ Stores glucose for energy ▪ Strengthens exoskeletons and fungal cell walls

Figure 1.31: A review of carbohydrates, or sugars, and their function as biological molecules.

Monosaccharides and disaccharides have a lot of stored energy in the carbon-hydrogen bonds, and these molecules are primarily used for energy in living organisms. But carbohydrates are also used for energy storage, usually in the form of **polysaccharides**, which are very long strings of monosaccharide building blocks (monomers). **Cellulose** is a good example, which forms the primary component of cell walls in plants. This carbohydrate is complex enough that us humans cannot digest it, although cows can (they have four stomachs!), which is why they eat grass and we do not.

Lipids

Next up on our tour, **lipids**, which include fats, phospholipids, and steroids. (We will focus on the first two.) Lipids are actually a pretty diverse set of molecules, but we group them together based on one important property: they are **nonpolar**. We talked about what **polar** means previously, which are molecules that share electrons unequally leading to slight positive and negative charges of the molecule itself. A polar molecule can easily dissolve another polar molecule based on the way their charged atoms interact. (For example, sugar is polar and dissolves easily in water.) You know what isn't polar? Oil. When you add oil to water, it just sits right on top.

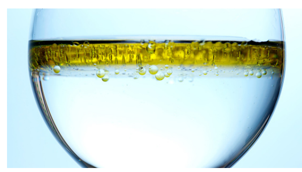


Figure 1.32: Oil and water don't mix. These two are polar opposites. Literally. Like oil and water. Okay, I'm done.

That's because oil is a fat. A molecule of fat is constructed from **glycerol** and **fatty acids**. Three fatty acid molecules are each joined to glycerol, an type of alcohol. The resulting fat, also called a **triacylglycerol**, thus consists of three fatty acids linked to one glycerol molecule. The major function of fats is energy storage, as hydrocarbon chains are rich in energy. In **saturated** fats, every carbon is bound to hydrogen atoms, as many as it can be. But in **unsaturated** fats, there are one or more double bonds between carbon atoms—meaning that they are bound to fewer hydrogens. This also creates a "kink" in the chain meaning that these molecules cannot be packed very closely together. This is the reason why saturated fats—like butter—are solid at room temperature, while unsaturated fats—like olive oil—are liquid at room temperature.

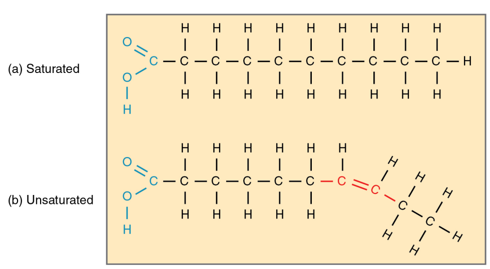


Figure 1.33: Saturated fats are "saturated" with hydrogen. Unsaturated fats have one or more double bonds meaning they are bound to fewer hydrogens. This creates a "kink" in unsaturated fats meaning they cannot be packed as closely together as saturated fats.

One of the most important kinds of fats, **phospholipids** are the major component of cellular membranes. This means that every single cell in your body is contained by these special molecules! Phospholipids have two fatty acid molecules attached to a polar head. Oooh, interesting, polar *and* nonpolar! The hydrophilic head interfaces with the aqueous (water-based) solution inside and outside of cells, while the hydrophobic non-polar tails face inward toward each other. This allows the formation of the **phospholipid bilayer**, consisting of two layers of phospholipids. The "head" portion consists of a phosphate group, along with a small charged or polar molecule like choline shown below. (There can be others, allowing for the formation of many different kinds of phospholipids.)

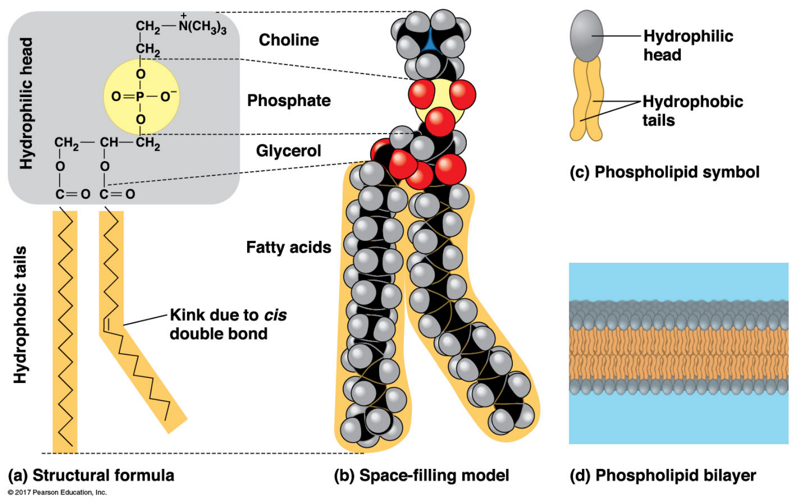


Figure 1.34: Phospholipids are made of two fatty acid tails and a polar head that includes a phosphate group. When placed in water, these molecules spontaneously form structures like bilayers and vesicles.

The last flavor of lipids are steroids, which includes cholesterol, another important component in membranes. We won't focus on these in class, but steroids also include a lot of biologically important molecules.

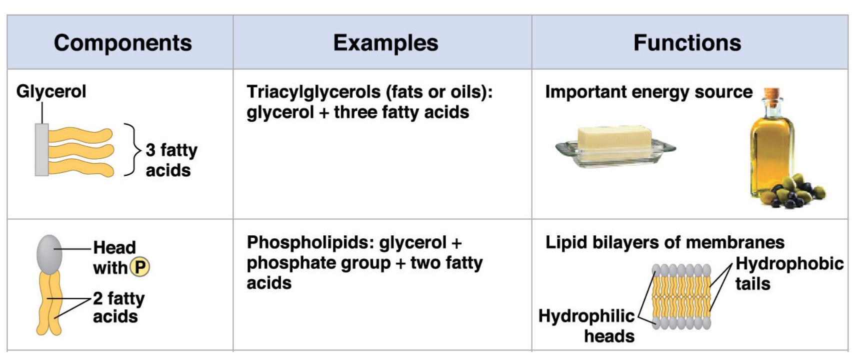


Figure 1.35: A review of some lipid molecules.

Nucleic acids

A lot of these molecules come from our diet. But our bodies also synthesize a lot of stuff too. How do our cells know how to make all the different "stuff" inside of us? Us organisms are primarily made from biological molecules called proteins, dicussed below. But how does a cell know how to make a protein in the first place? How does it know how to make just the *right* protein? The instructions to build proteins are coded inside of **genes**, which are a discrete unit of inheritance. Genes are composed of **nucleic acids** (otherwise known as DNA), build from monomers called **nucleotides**. Nucleotides consist of (1) a five-carbon pentose sugar, (2) a nitrogenous (nitrogen-containing) base that gives the molecule a unique property, and (3) one to three phosphate groups.

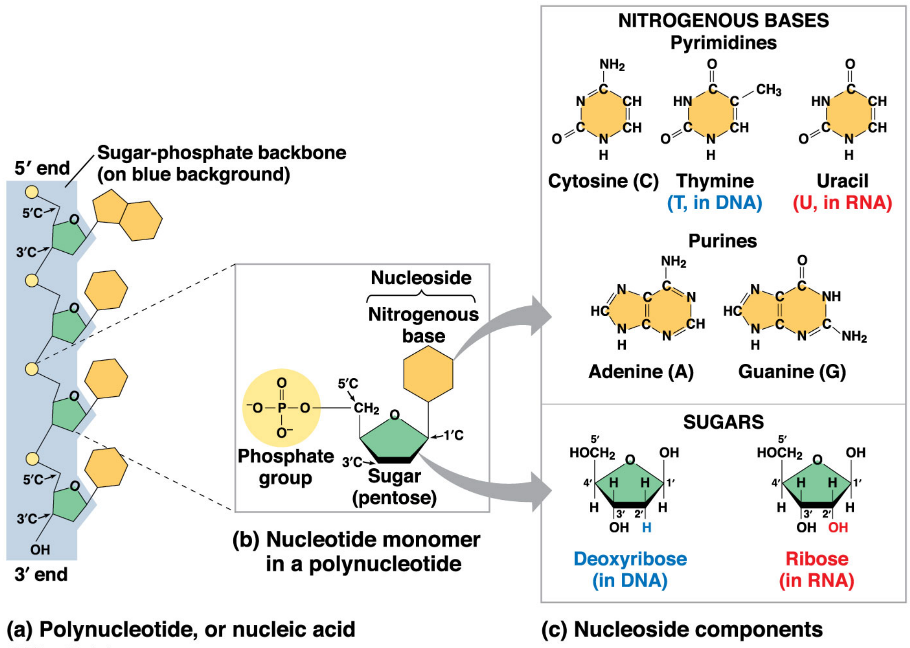


Figure 1.36: DNA and RNA are made from a sugar-phosphate backbone and nitrogenous bases.

But DNA (**deoxyribonucleic acid**) is not directly involved in the production of proteins. There is another molecule called RNA (**ribonucleic acid**) that performs much of the work of transcribing and translating the information in DNA to an actual protein. You'll learn much more about these processes later. For now, we will focus on the structural components of DNA and RNA that allow these molecules to participate in processes necessary for life to function.

- **Pentose sugar**. Nucleotides all have one pentose sugar, but the sugar in DNA lacks an oxygen atom on the second carbon ring, so we call it _deoxy_ribose. In RNA, the oxygen is there which is why it is simply ribose.
- **Nitrogenous base**. There are two different kinds of nitrogenous bases. **Pyrimidines** have one carbon ring and there are three kinds: cytosine (C), thyamine (T), and uracil (U). **Purines** have two carbon rings and there are two kinds: adenine (A) and guanosine (G). (I usually remember the difference by the fact that the longer name, pyrimidine, has fewer rings.) T is only found in DNA while U is only found in RNA. The rest are found in both.

- **Phosphate group**. Three phosphate groups are attached to the 5′ carbon of the sugar, completing the nucleotide molecule. (If you look at the diagram of the ribose and deoxyribose sugars, you'll notice that the carbons of the pentose sugar are labeled. The 5′ carbon at the top binds with the phosphate groups, while the 3′ carbon at the bottom with the OH molecule is where the phosphate group of the next nucleotide will attach to join the nucleotides together. These numbers give the DNA or RNA molecule a certain directionality.)

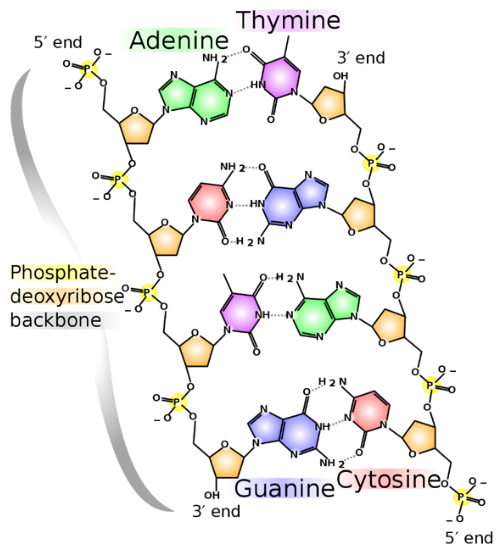


Figure 1.37: DNA is typically two complementary strands that run antiparallel to each other.

DNA is typically consists of two strands of **polynucleotides** that wind around each other to form a **double-helix**. The two strands are bound to each other in the center by complementary base-pairing. Adenine always binds with thyamine in DNA or uracil in RNA. Guanine and cytosine always bind together. The strands run **antiparallel**, meaning that the sugar-phosphate backbones run in opposite directions. What do we mean by opposite direction? Well, the 5′ carbon holds the phosphate group, and the 5′ end can only be added to the 3′ of another nucleotide. That's the only place these molecules can be joined! Because of that, DNA and RNA have a 5′ carbon at the very top, and a 3′ carbon at the "butt" of the molecule. One strand runs 5′–3′ in one direction, and the other in the opposite, like the image above.

Proteins

Proteins do everything. I'm not kidding, proteins do nearly every job in a cell that you can imagine. They provide structure, storage, they transport substances within and between cells, they serve as receptors, accelerate chemical reactions, protect against disease, aid in movement, and respond to chemical stimuli. When we say that DNA is the "blueprint" for creating an organism, protein is *the thing* for which DNA is laying out the plans (with some exceptions: it's biology!). You will learn more about the process by which DNA is read and proteins are constructed in Unit 4. For now, we will take a deep dive into the pieces of protein and how these pieces allow protein to do so many different jobs within an organism.

Proteins are made up of long chains of **amino acids**. There are twenty different amino acids that make up the proteins used by every living creature on Earth. Let that sink in. *Every living organism on the planet uses the same twenty amino acids, coded for by the same four nucleotides in our DNA*. All amino acids have the same basic structure, with an **amino group**, a **carboxyl group**, and the **R** group, which gives the molecule a special property. Below, highlighted in purple are the amino and carboxyl groups, and highlighted in yellow, green, pink, and blue are different R groups. Some side chains (or R groups) are hydrophobic, some are hydrophilic. Some are acidic, while others are basic. These varied properties mean that different combinations of amino acids can be used to build thousands and thousands of varied proteins, all with slightly different properties themselves.

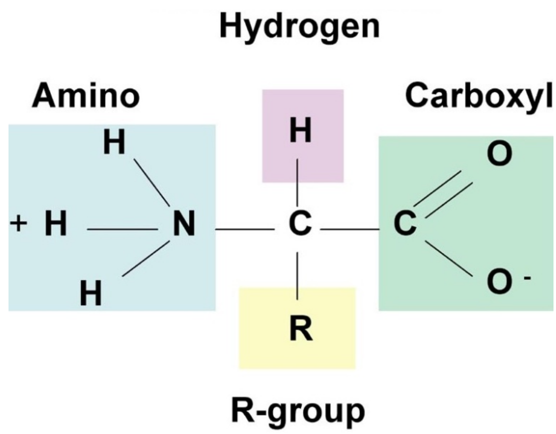


Figure 1.38: All twenty amino acids have the same basic structure. The R group or side chain differs between the different molecules, giving each a unique property.

So how do we make a protein? At first it's pretty simple: we just add amino acids together in a long chain called a **polypeptide**. Making a polypeptide chain means linking amino acids together with a covalent bond called a **peptide bond**. Based on the way that amino acids link to each other, there will always be an amino end on one side (called the N-terminus) and a carboxyl group at the tail (called the C-terminus). In between the N- and C-termini are however many amino acids coded for in the gene for the protein.

The linear sequence of amino acids that form a protein is called its **primary structure**. But because amino acids each have special chemical properties, the polypeptide chain usually folds naturally into a conformation that gives the protein the ability to perform its function. Even tiny changes—substituting one amino acid for another in a polypeptide chain of hundreds of amino acids—can disrupt the protein's overall conformation and ability to function.

The next layer of protein structure, **secondary structure**, results from repeated coils and folds into which long polypeptide chains can be organized. Because oxygen and nitrogen atoms in the amino acid backbone have a slight negative charge, these atoms can form hydrogen bonds with the weakly positive hydrogen atom attached to nitrogen.

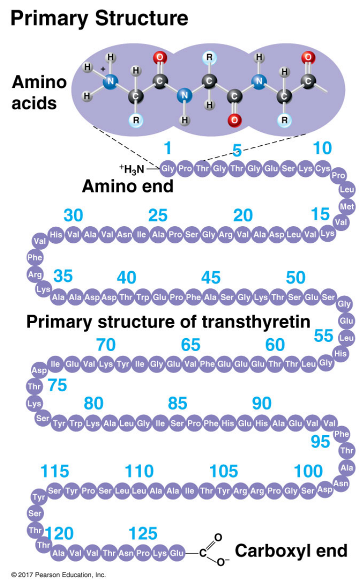


Figure 1.39: The primary structure of a protein is the linear sequence of its amino acids.

There are two common forms of secondary structure: the **alpha** (α) **helix**, and the **beta** (β) **pleated sheet**. (Coils and folds!)

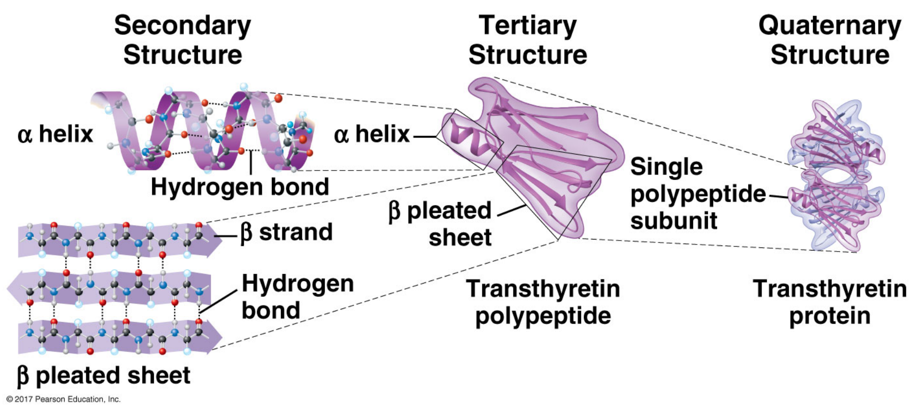


Figure 1.40: From the linear sequence of amino acids, higher order structures emerge.

Tertiary structure consists of more irregular contortions that result from bonds between different R groups. As a polypeptide chain begins to fold, hydrophobic side chains usually congregate together in clusters at the center of the protein, called **hydrophobic interactions**. Hydrogen bonds between polar side chains and ionic bonds between positively and negatively charged side chains can also stabilize this structure. Finally, proteins can have one final layer of structure called **quaternary** structure. This occurs when two or more polypeptide chains aggregate together to form one large molecule with multiple subunits.

Miller-Urey experiment

This experiment is famous. Very famous. The idea behind it is simple: what happens if we emulate the conditions of early Earth? Would it be possible to observe the formation of any biological molecules? Miller and Urey used the same gases thought to exist in Earth's early atmosphere (methane, hydrogen, water vapor, and ammonia). Electrodes simulated possible lightning. Water, from the "ocean" was heated and directed toward the "atmosphere," cooled in a condenser, and what remained was collected.

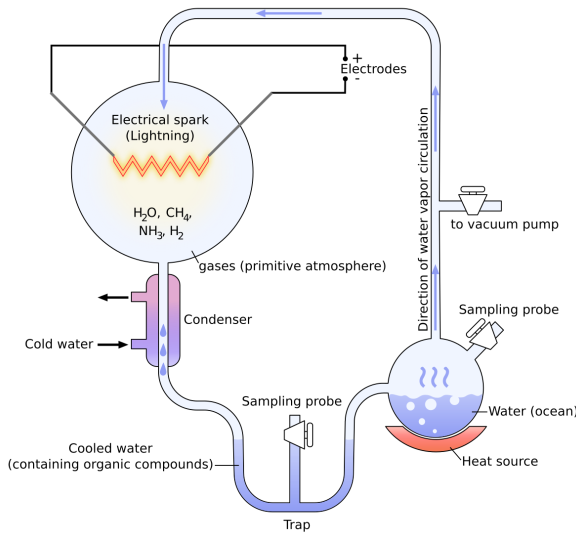


Figure 1.41: The set-up of the Miller-Urey experiment.

From just this, several amino acids were recovered, the building blocks of proteins. This experiment demonstrated that biological molecules may emerge from purely chemical reactions in early Earth. But the truth is, we don't yet know how life emerged from non-living entities. We will spend the rest of the course examining the various hypotheses while we explore the important features common to all living organisms.

Unit 2

Encapsulation

> Architecture is basically a container of something. I hope they will enjoy not so much the teacup, but the tea.
> *Yoshio Taniguchi*

[**ACCESS UNIT 2 LECTURE MATERIALS**]

7: The Lipid World and Protocells

For the next few units, we will explore the various theories of how living organisms emerged from non-living entities: how the chemistry of early Earth became the biochemistry of life. The idea that living organisms could originate from non-living entities is not new; Aristotle wrote about spontaneous generation in the 4th century BCE. But Alexander Oparin and JBS Haldane formalized this idea in modern terms in a theory known as the **Heterotrophic theory**, based on the following points:

1. The atmosphere of early Earth was low in oxygen, meaning oxygen could not steal electrons from other compounds. (We'll learn more about this later, but it's important for ~cHemIsTry~ reasons!)
2. When the atmosphere of early Earth was exposed to energy (like lightning), simple organic compounds were likely produced (remember monomers?).
3. These compounds (monomers!) collected in what we now call a **prebiotic soup** that may have concentrated in places like oceanic vents.
4. More complex polymers and life could have potentially developed as the monomers in the soup were transformed through chemical reactions.

We know from the previous unit that all organisms are essentially composed of the same stuff, and we know that experiments have recovered some of this "stuff" by simulating the conditions of early Earth. This demonstrates that there is a possible path from chemistry to biochemistry. But, while there are many hypotheses, we don't know precisely how this transition occurred or in what order. This is an area of active research with passionate debates among scientists.

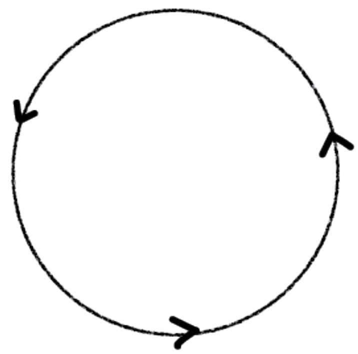


Figure 2.1: Once the loop has closed, it becomes impossible to tell where it originated.

I once heard the emergence of life described as "closing a loop." Before the loop is closed, there are two clear ends. But once the loop closes it becomes impossible to tell where it began. After the next three units, we all may have different opinions on the emergence of biological life. In fact, I hope we do! That's the fun stuff.

So we begin first with lipids. We learned in the previous unit that there is a kind of lipid molecule called a "phospholipid." These molecules are special because they are constructed of a polar head and a nonpolar tail. We call this kind of molecule **amphiphilic**, which means that it has both polar and nonpolar parts. This feature becomes really important when we consider that life originated in early oceans, otherwise known as water. (When a "solution" is water-based, we say that it is **aqueous**.)

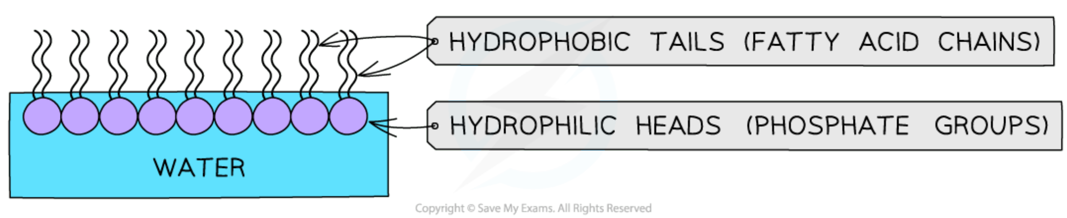


Figure 2.2: Because the heads are polar (also known as "hydrophilic" or "water-loving"), they turn toward water. Nonpolar (also known as "hydrophobic" or "water-fearing") tails are insoluble in water and turn away. (**Image source**.)

Why membranes matter

First of all, what do I mean when I talk about a "membrane" in the first place? Put simply, a membrane is a barrier between two things. These are typically selective, meaning that some things are able to pass while other things aren't able to pass. (The **Gandolf** of biological entities. Nah, just playing.) Anyway, we'll focus on **biological membranes**, which are the the objects that separate a cell from the outside world. Now, this alone is pretty essential. How could we be living organisms if we couldn't organize ourselves separately from our external environment? I mean, really, what would that even look like? How can you drink a glass of water without the cup?

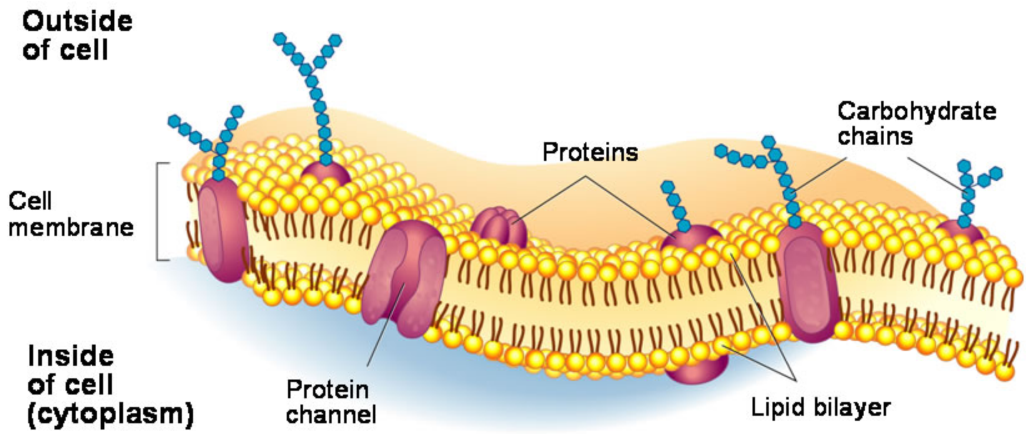


Figure 2.3: The cell membrane separates the inside of the cell (cytoplasm) from the outside of the cell (extracellular space). (**Image source**.)

So the most obvious job that cell membranes have is they provide a compartment for the business of life to occur without the external environment interfering too much. These barriers allow some things to enter the cell—important things, like molecules for energy or building blocks for protein—and some things to leave the cell as waste. We refer to this as **selective permeability**: not everything can enter or exit. We will learn more about this feature in the next lecture. Not only that, but there are also cellular components with special functions found *inside* many cells, and these too are enclosed in membranes of their own! This allows different chemical reactions to occur in tandem without disrupting one another.

Figure 2.4: A classsic color gradient from black to yellow.

The other reason membranes matter is that they allow for the creation of **gradients**. The clearest example of a gradient that we all know is a color gradient. But, there are also other kinds of gradients. In chemistry, we can have a **concentration gradient**, in which the concentration of something is higher in one area than in another area. The presence of membranes allows for a special type of gradient called an **electrochemical gradient**, which occurs when there is a difference in charged particles on either side of a barrier. Remember ions? Ions are charged atoms that have more electrons than they do protons. If we have more ions on one side of a membrane than on the other—we can actually store energy that way!

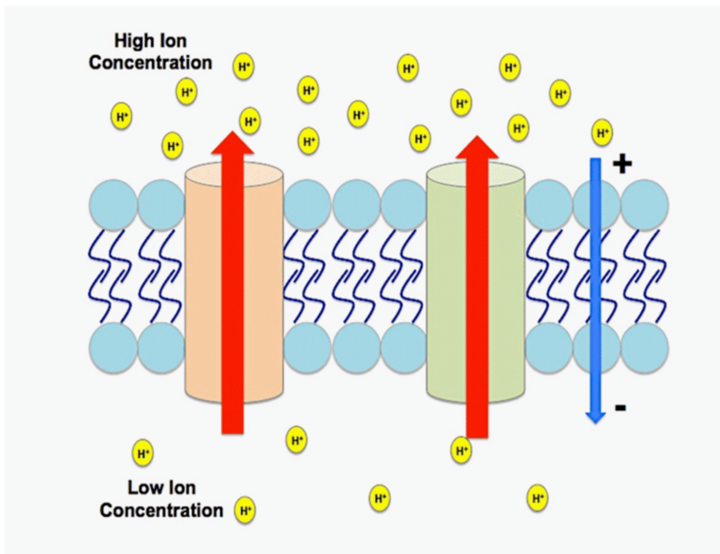


Figure 2.5: An electrochemical gradient occurs when there are more charged particles on one side of a membrane than on the other side. (**Image source**.)

The first two laws of thermodynamics

The first two laws of thermodynamics are as follows:

Energy cannot be created or destroyed. All the energy that does all the work *in the entire universe* began just over 13 billion years ago with the Big Bang. This energy can be transformed into different kinds of energy, but we cannot create energy from scratch or destroy existing energy.

Entropy in the universe is constantly increasing. When energy is used to perform work, some amount of it is lost as heat. There is an unstoppable trend toward randomization of the universe as a whole, and disorder, or **entropy**, increases as energy is transferred or transformed. Basically, stuff decays with the passage of time unless energy is used to actively prevent this.

The analogy I'm about to tell you is not exactly right, but think of the second law of thermodynamics like keeping your house clean. It requires energy to actively maintain a house in a clean state. (Actually, it requires energy to

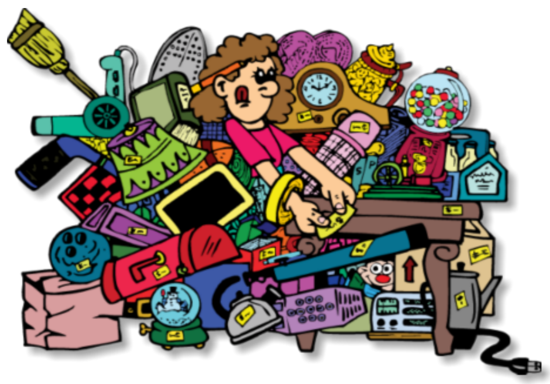


Figure 2.6: What would happen if you just…stopped cleaning? What would happen if our bodies just… stopped maintaining our chemical processes?

actively maintain a house, full stop.) If one day you no longer pick up after yourself or do the dishes, the house gets messy pretty quickly.

Now that we're thinking about my (bad) analogy, living organisms are kind of like this too. It requires *a lot* of energy to actively maintain our organization. We must exist far outside equilibrium with our surrounding environment, and it costs energy to keep that up. All of us animals have to eat food, and if we don't eat food, we die. What are we getting from food? In large part, the chemical energy we need to maintain our ordered structure in a universe that tends toward entropy. As we take in chemical energy, produce waste, and give off heat, the entropy *of the universe* is increasing. But while we are alive we exist as ordered and complex structures. One of the main features of our construction that allows for this is our biological membranes.

The broad arguments for the Lipid World

Okay, so what about lipids lends themselves to the origins of biological life? The first thing is that almost any time you drop phospholipids into water, you get the formation of simple membranes. These membranes take on various shapes. The lipids do not require anything to assemble into these shapes, they just do. The spontaneous formation of **micelles** and **lipid bilayers** seems like a wonderful starting point for life. Why? Because phospholipids do this naturally, and in the primordial soup of early Earth, these structures could have formed, encapsulating other molecules. Molecules have a tendency to spread out over available space, but the aggregation of lipids may have trapped molecules together in close proximity. Small molecules trapped inside lipid membranes could eventually form **protocells**, a hypothetical precursor to what we know today as a cell.

Another feature of lipids is that they are a very diverse group of molecules. Remember that we discussed phospholipids we talked about the phosphate group head and two fatty acid tails. But there are other kinds of lipid molecules with different groups as the polar head instead of phosphate. Moreover, the **hydrocarbon chains** (a carbon backbone bound to hydrogen) that make up the fatty acid tails can have different lengths and different arrangements

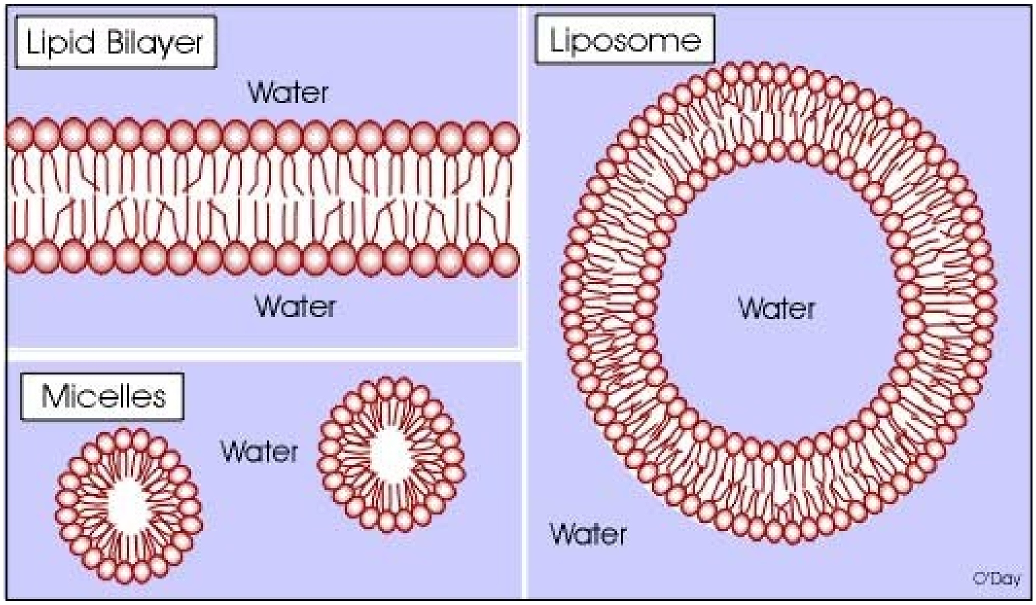


Figure 2.7: These structures all form spontaneously when phosopholipids are in aqueous solutions (e.g., water). (**Image source**.)

of double bonds. Thus it is possible to have a large diversity of structures from a variety of different lipid building blocks.

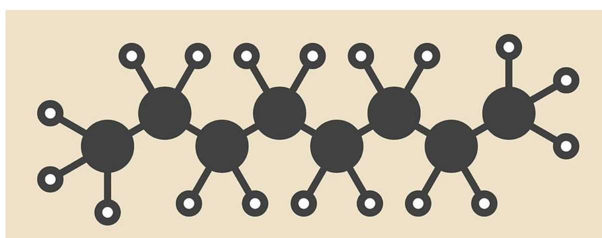


Figure 2.8: The black circles represent atoms of carbon while the white dots represent atoms of hydrogen. Hydrocarbon chains include a carbon backbone of carbon bound to carbon, along with hydrogen atoms covalently bound to the other electrons in carbon atoms.

An important question to ask is how the lipids assembled in the first place. Scientists that study prebiotic Earth have done a variety of synthesis experiments simulating these conditions, and have found the formation of lipid-like amphiphilic molecules including long-chain hydrocarbons. Another possibility is that long-chain hydrocarbons arrived on Earth from a comet or meteor. But what's essential is that lipids are much easier to assemble in prebiotic conditions—that is, without special proteins to aid in the reaction or the normal metabolic processes that occur in life now—than other biological molecules like DNA. This makes them an attractive candidate for the origins of early life.

8: Cell Membranes and Transport

It seems pretty obvious to us that living organisms are composed of cells. But of course, a mad long time ago, we had no way of knowing this. You really can't see a cell with just your eyeballs. What that means is that humans needed to develop a substantial amount of technology in order to see a cell in the first place.

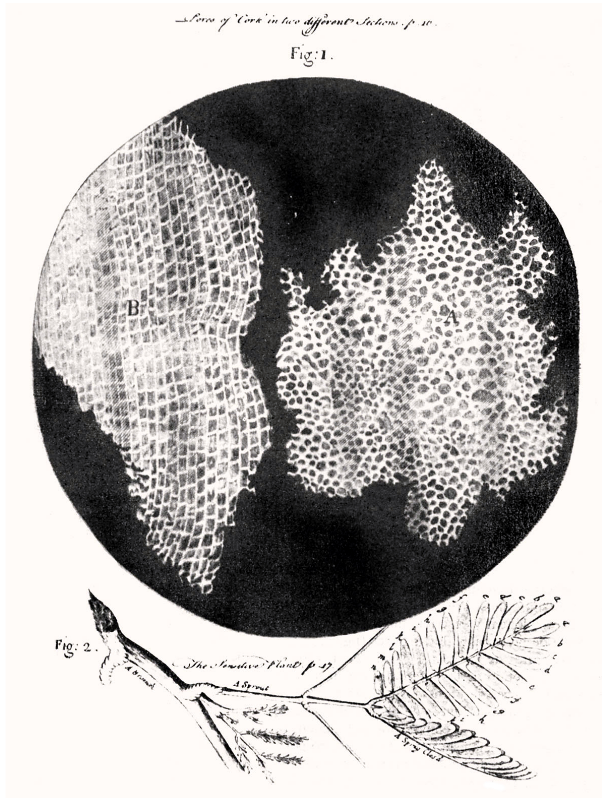


Figure 2.9: Robert Hooke's drawing of thinly-sliced cork under a microscope. He first named the plant cells "cells" because they reminded him of monk's chambers.

First, you need to invent glass. While human civilizations have been making glass for at least 3600 years, it wasn't until the 13th century that we start to see glass purified to the extent that it can be used for magnification. Around this time we start to see the first eyeglasses, which are essentially a luxury item that only few can afford. But in 1665, Robert Hooke used a microscope to write his opus *Micrographia*, drawing intricate illustrations of a lot of things, including the edges of razor blades, the eyes of insects, and also, cells. (He called them cells because they looked like the chambers that monks live in.)

Around the same time, Anton van Leeuwenhook invented his own microscope. Hooke's microscope magnified about fifty times. But this new microscope was substantially better, allowing Anton to observe objects at 300x magnification. And boy, did he observe. Pond water (he found bacteria!), spit (he also found bacteria!), and… other bodily fluids. He documented his findings in a series of letters to the Royal Society in London and these letters revolutionized the study of disease.

Now we know that every living organism on this Earth is composed of one or more cells. We say that cells are the basic unit of life. Smaller than a cell (hello, virus!), and we start to have debates. But everyone agrees that once you have a cell you have a living organism. Historically, **cell theory** has three components:

1. All living organisms are composed of one or more cells
2. The cell is the most basic unit of life
3. All cells arise only from pre-existing cells

Of course, one starts to wonder, *Then where did the first cell come from?* but that's what this class is all about! For the next few lectures, we will focus on what we know for sure about existing cells. And we know for sure that all existing cells come from pre-existing cells.

Composition of membranes

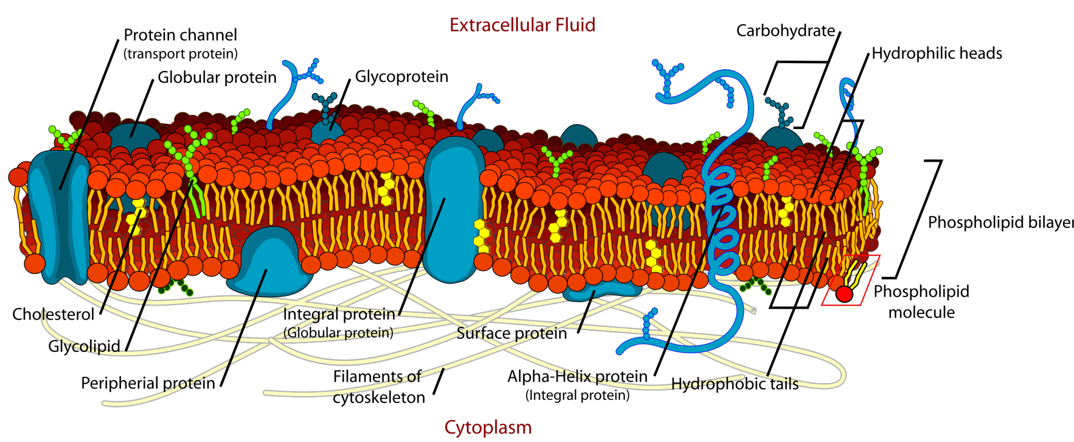


Figure 2.10: Cellular membranes are composed of phospholipids, proteins, and carbohydrates that drift around to perform different jobs.

Membranes are not static. That means that they aren't just a sheet of molecules locked in place. Rather, the lipids and proteins that make up a membrane are largely held together by hydrophobic interactions which are much weaker than covalent bonds. Because of this, lipids and proteins drift around in a sideways motion. This is important for two reasons: (1) membranes need selective permeability, meaning that specific substances need to be let in and out of the cell in a controlled way, and (2) proteins must have the ability to move where they are needed to perform work in the cell. And, because different organisms live in different environments, the membrane itself must be adapted to varying environmental conditions.

Fluidity. The fluidity of membranes is affected largely by temperature. As temperature decreases, membranes become tightly packed until the membrane solidifies (think: bacon grease as it cools). How quickly a membrane solidifies and at what temperature depends on the composition of the phospholipids—unsaturated tails cannot pack together as closely as saturated tails. Other molecules in the intermembrane space like cholesterol can affect fluidity.

Membrane proteins. Phospholipids form the main structure of the membrane, but it's proteins that do all the work (of course). There are so many proteins in so many different kinds of cellular membranes that we don't even know all the ones that exist and their jobs. The two major kinds of membrane proteins are **integral proteins**, which span the entire membrane, and **peripheral proteins**, which are not embedded within the membrane at all. Proteins are important for passage in and out of the cell, among other things.

Membrane carbohydrates. In multicellular organisms, it's important that cells can recognize other cells (cell-cell recognition). Cells recognize other cells by binding to molecules, often containing carbohydrates, on the extracellular surface of the plasma membrane.

Permeability, transport, and the fluid mosaic model

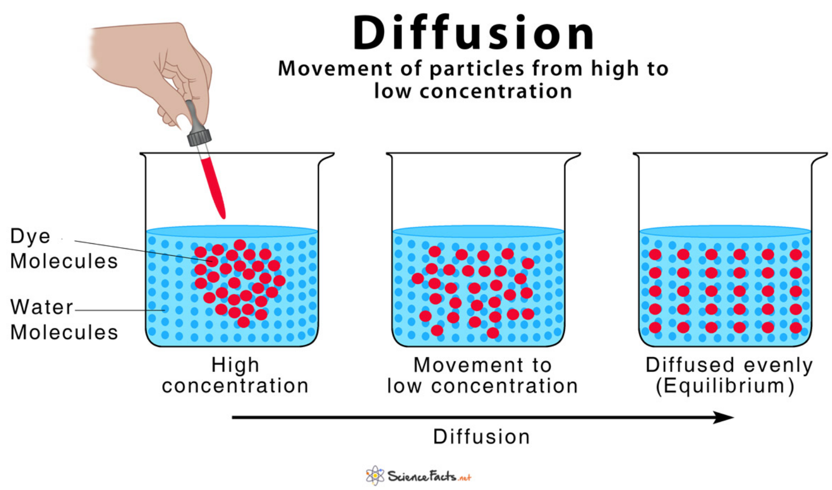


Figure 2.11: Over time, substances diffuse from areas of high concentration to areas of low concentration. This process occurs due to the random motion of particles and requires no energy expenditure.

Let's first unpack the concept of **diffusion**, which is yet another example of an emergent feature. Imagine a clear glass full of water. You put a few droplets of food dye into the water. At first, the food dye is concentrated in certain areas of the water while other areas remain clear. But if you wait a few minutes, eventually the food dye will be distributed evenly throughout the water. What causes that? The behavior of each individual food dye molecule is completely random, but as a *population* of molecules something interesting occurs. In the absence of any other force, a substance (in this case, food dye) will **diffuse** from an area of high concentration to an area of low concentration—in other words, along a concentration gradient. No energy is needed for this process. This occurs because all atoms tend to "bounce around" randomly in space, but when many of them are tightly packed the atoms hit each other until spacing out evenly (**you can check out an animation here**).

Movement without energy expenditure is called **passive transport**, and diffusion is one example. The diffusion of water across a selectively permeable membrane is called **osmosis**, which is just a specific and special case of regular diffusion. But osmosis is important because the balance of water inside and outside of the cell matters. If we put a cell in a solution that has a high concentration of solutes that are not able to pass through the membrane (called "nonpenetrating solutes") then water will exit the cell in an attempt to create an even concentration of solutes within and without of the cell. This is an example of what happens when you place a cell in a **hypertonic** solution. ("Hyper" means more, and the "more" in this case is nonpenetrating solutes.) If we place a cell in a **hypotonic** solution ("hypo" means less), then water diffuses into the cell through osmosis. An **isotonic** solution has the same concentration of nonpenetrating solutes within and without of the cell.

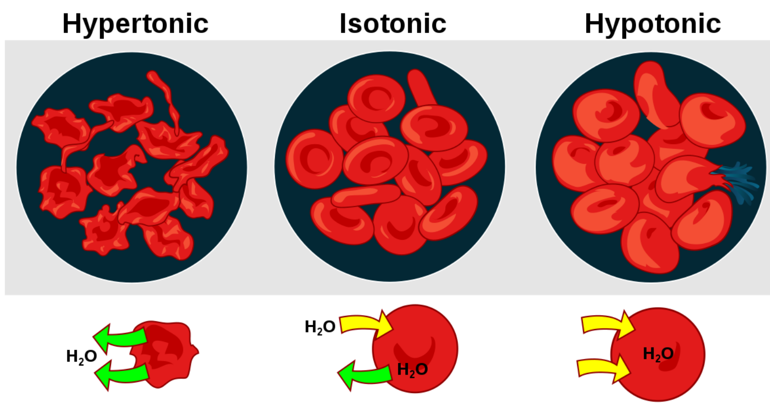


Figure 2.12: In hypertonic environments, water exits the cell to create an even concentration of solutes on either side of the membrane. In hypotonic environments, water enters the cell.

All cells have voltage—you can think of this as the storage of electrical energy. This comes from the distribution of positive and negative charges (you can also think of this as the distribution of ions) on either side of the membrane. In most cells, the cytoplasm (inside of the cell) is more negatively charged compared to the extracellular side (outside of the cell) because anions (-) and cations (+) are not distributed evenly on either side of the membrane. **Membrane potential** is the difference in charge between the inside and the outside of the cell. Maintaining a certain membrane potential in the cell is important, because certain cells like neurons or muscle cells only function when there is a change in membrane potential. Well, if substances like to spread out over available space, or move from areas of high concentration to low concentration, how do we push substances *against* their concentration gradient? (Or in this case, against their electrochemical gradient.) We use energy for this kind of movement, and we call it **active transport**.

What's crazy is that we discovered cells in the 1600s, but it wasn't until the the early twentieth century that we actually discovered cell membranes. The first roadblock is that scientists wrongly assumed that all cells have cell walls. In fact, all *plant* cells have cell walls but animal cells do not. Because of this, animal cells are more fragile and easy to tear, so for a long time it was thought only plants actually had cells. In the 1800s, scientists were actively investigating this

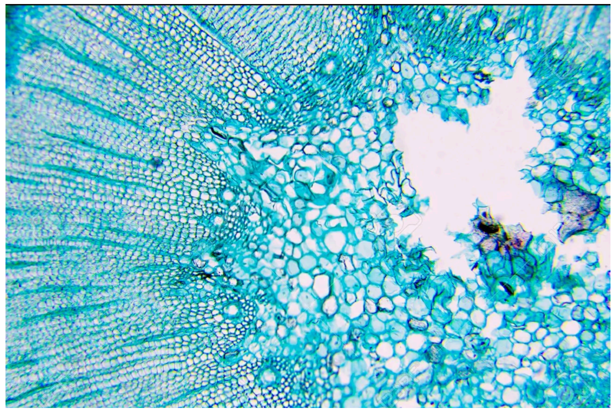


Figure 2.13: A cross section of a plant cell under a light miroscope. So cute! But these cell walls are sturdy, and animal cells don't have one.

question and hypothesized that there was a barrier and that it was potentially made from fats. Cells were observed to form spheres in water, similarly to how oil does.

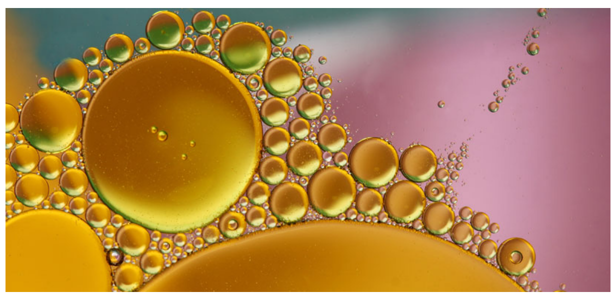


Figure 2.14: Oil forms droplets in water, similar to cells. Remember that phospholipids form micelles when in water!

Another piece of the puzzle came from anesthetics, where it was known that chemicals that were both water soluble and fat soluble could be used for general anesthesia. But the main problem is that scientists knew there *must* be a mechanism for energy-dependent selective transport. In other words, cells must be able to move objects against concentration gradients—everything can't be diffusion. It took until the 1970s until we developed the **fluid mosaic model** of cellular membranes—this model demonstrates how active transport can take place through the presence of integral membrane proteins.

9: Prokaryotic Cells

It is not clear how the first cell arose—steps in the emergence of life are lost to time, and we can only be certain of what currently exists now. We call currently living organisms **extant**, as opposed to those that have gone **extinct** and no longer inhabit Earth. What we know right now is that there are two basic types of cells, prokaryotic cells and eukaryotic cells.

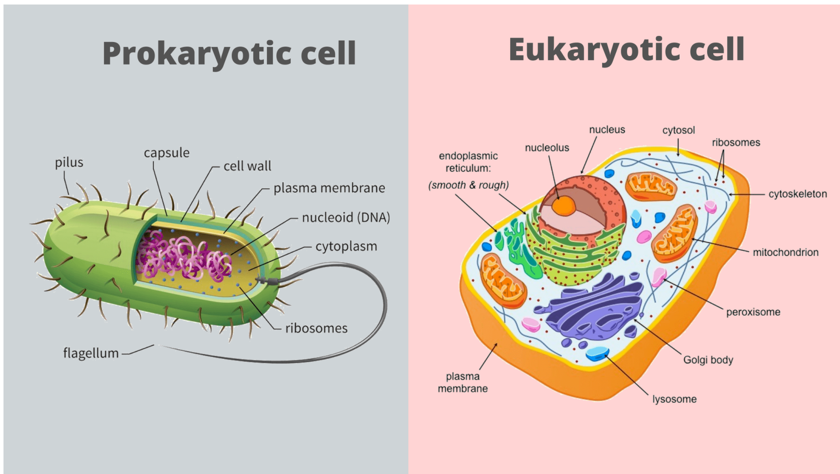


Figure 2.15: There are two main types of cells that exist, prokaryotic cells and eukaryotic cells. If all cells come from preexisting cells, then what is the relationship between these cell types?

What is the relationship between these cells? We know that all cells come from pre-existing cells. But how does one kind of cell "become" another kind of cell? In truth, that's not exactly how it works. Remember that all cells contain DNA, and DNA provides the instructions for for the cell's building blocks (in general, proteins). An organism cannot change its own DNA, and it cannot force specific mutations to happen. But, when a cell replicates (more on this in Unit 5!), sometimes little mistakes are made in copying the genetic code. Many times, these mistakes are not great and maybe the cell isn't viable. Sometimes, the mistakes are neutral and nothing happens. But every once and awhile a mistake is good, and it sticks around.

If a good mistake comes up, the cells that have that "good mistake" will make more copies of themselves. (That's essentially the definition of "good mistake"—leaving more offspring relative to others without the mistake.) Over time, that "mistake" increases in frequency in the population. Of course, one mistake does not typically change one cell into a completely different cell. But many mistakes, over thousands or millions of years, can definitely accomplish this. Think about the Grand Canyon: water flowing over rock is not going to carve out anything substantial in ten or even twenty years. But over millions of years, small things can add up to big things! (Another good example is the movement of the continents. A few centimeters a year seems like nothing, but look at the difference between Earth today and Pangaea.)

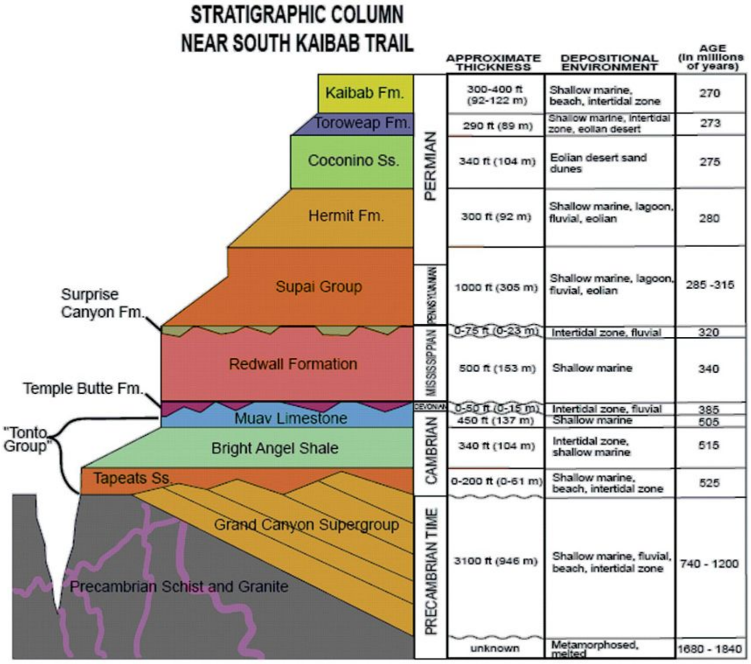


Figure 2.16: Rock layers of the Grand Canyon and their approximate ages in millions of years.

Okay, so let's get back to the two main types of cells. How do we go about figuring out the relationship between these cells even though they likely originated billions of years ago? This part is kind of fun. Essentially, we take advantage of the fact that within certain genes, mistakes can almost *never* be made. For example, there are specialized proteins that are responsible for making other proteins, called **ribosomes**. (More on this next lecture.) But ribosomes need to have a *very* specific structure otherwise they won't work—and if a ribosome doesn't work, the organism is dead! So there are very limited mutations that can occur in which the organism can still survive; we call this kind of gene **highly conserved**. So some scientists thought, *Hmmm, that's very interesting, what if we look at the differences in the DNA sequence of different ribosomes?*

Once you do that, you can organize these sequences so that the ones that are most similar are closer together and the ones that have more differences are farther apart—essentially, in evolutionary time. This method was the first to demonstrate that there are actually three domains of life: bacteria, archaea, and eukaroytes. While there is still uncertainty, current models indicate that bacteria and archaea (both prokaryotes) evolved first from a common ancestor, while eukaryotes evolved later, likely from archaen ancestors. We will discuss in the next lecture the evidence for this theory. But a major part of it is that prokaryotic organisms appear similar to the fossil microorganisms that represent evidence of the earliest life on Earth.

Moreover, some prokaryotic organisms live in similar conditions to those thought to have existed on early Earth—we call them **extremophiles**, and they survive in places like hydrothermal vents in the bottom of the ocean. Prokaroytes are also simpler cells than their eukaryotic counterparts. They are also a lot smaller. (A lot smaller. You have more

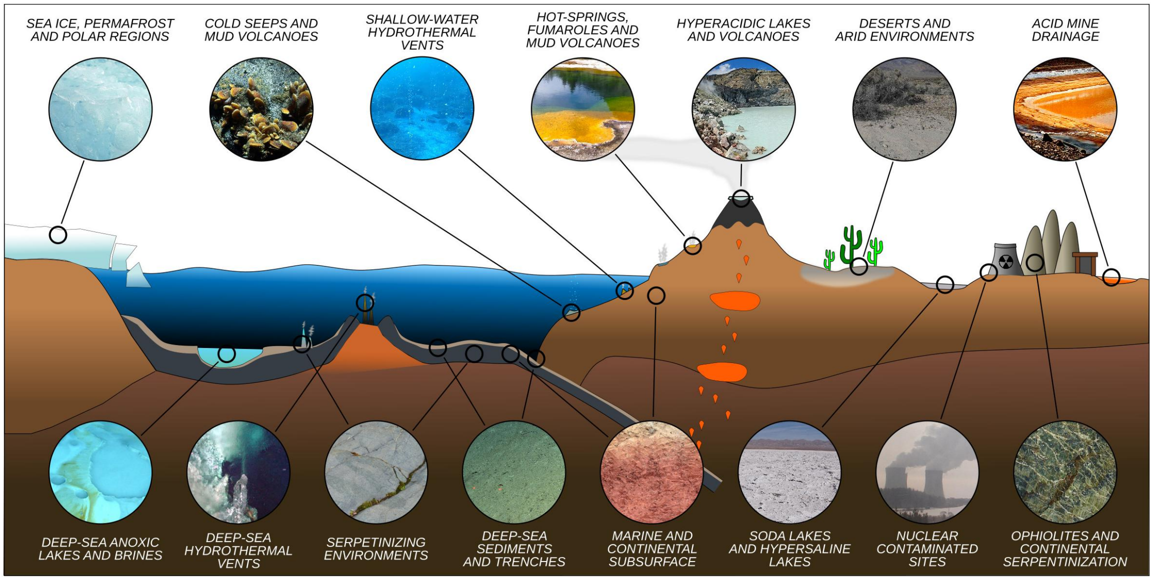


Figure 2.17: Some examples of extremophiles and their habitats. (**Image source**.)

bacterial cells living in your body than your *own* eukaryotic cells!) All prokaryotes are single-celled organisms. If you are a multicellular organism, you are a eukaryote. So let's take a look at the prokaryotic cell.

The structure of prokaryotes

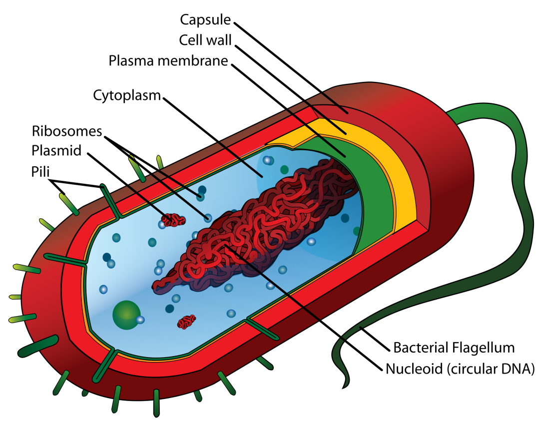


Figure 2.18: A schematic of a prokaryotic cell. Not all prokaryotic cells look like this, but this is a general example.

Prokaryotic cells lack membrane-bound organelles. What that means is there are no internal compartments in a prokaryotic cell and there is no nucleus that houses DNA. There is a region where DNA is concentrated called the **nucleoid**, but everything that allows for replication and energy capture are either floating in the **cytosol** (the liquid matrix that makes up the cytoplasm) or in the cell membrane instead of in discrete compartments. In eukaryotes, there are organelles that carry out different functions and that are bound by membranes.

In addition to a plasma membrane (remember, all cells have them!), prokaryotic cells also have a **capsule** that prevents the cell from drying out and also allows it to "stick" to its surroundings. Under that, you find a **cell wall**, that maintains the cells shape and protects the interior. Underneath those two layers, our friend, the plasma membrane.

The earliest prokaryotes in the fossil record

It's really hard to interpret old fossils. And when I say old fossils, I'm talking 3.5-4 billion years old. Which is to say that there are still debates about how exactly we know a fossil was "alive" or not. What if it was just a collection of organic materials but otherwise abiotic, or nonliving? How can you tell the difference from a rock that's billions of years old? Here it is in fancy science language from a fancy science journal (*Nature*, 416, pages 73–76 [2002]):

> Because such microorganisms are minute, are preserved incompletely in geological materials, and have simple morphologies that can be mimicked by nonbiological mineral microstructures, discriminating between true microbial fossils and microscopic pseudofossil 'lookalikes' can be difficult.

So what's a scientist to do? Basically, we're still doing the same thing that Hooke and Leeuwenhook did in the 1600s. We're building better and better ways to see things that our human eyes just can't see. I won't get into all the technology behind the methods,[1] but the earliest evidence of life appears in fossils of microorganisms that were mineralized in 3.5 billion-year-old Australian rocks. But are these prokaryotes? Not… really. It's not actually clear when a cell that looks like a modern-day prokaryote emerges. Early life is messy, and it's also hypothesized that there were cells sharing genes *not* by descent, called **horizontal gene transfer**. We'll discuss this later on, but for now, it means that the very early tree of life looks something tangled, like you see in the figure below.

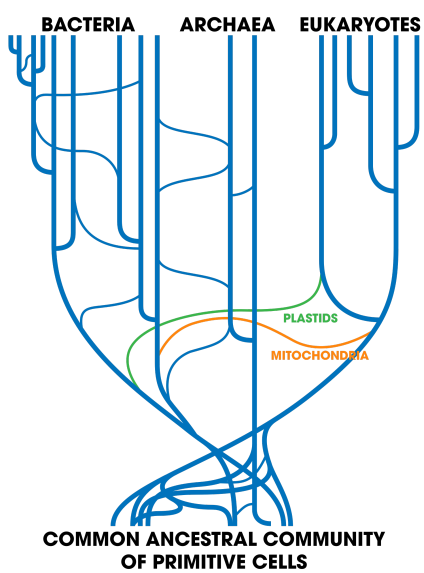


Figure 2.19: It is not exactly clear when the two distinct cell-types emerged in the history of life. (**Image source**.)

[1] laser-Raman spectroscopic imagery, if you're curious

10: Eukaryotic Cells

Prokaryotes belong to the domains Archea and Bacteria. These domains include a wealth of single-celled organisms. All multicellular organisms (and a few single-celled ones too!) belong to the domain Eukarya—this is all fungi, plants, animals. But the thing is, the prokaryotes of Archaea and Bacteria are no more related to each other than they are to the Eukaryotes. We simply distinguish the two different *cell types*, those with membrane-bound organelles and those without. But that doesn't mean those cells are more related to each other. We suspect that the eukaryotic cell type was derived from a prokaryotic cell type, in part because eukaryotic cells are larger and more complex, and for a few other reasons that we'll get into shortly. But did eukaryotes share a common ancestor with bacteria or archea? This is still an open question.

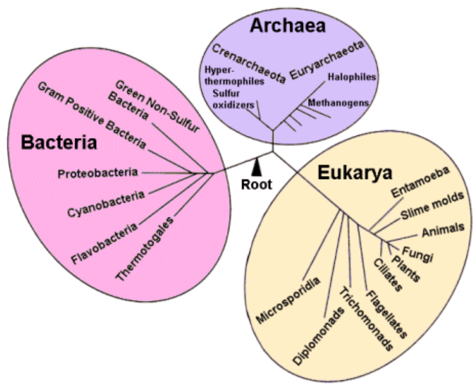


Figure 2.20: This is a common depiction of the evolutionary relationships between the three domains. However, it's not completely clear how and when these three domains emerged or their evolutionary relationships. We are, however, confident that there are three domains.

But before we get into the complicated family dynamics of cells, let's first take a tour of a classic eukaryote. We'll take a tour of both an animal and a plant cell, but keep in mind that these are broad generalizations and there are *many* types of eukaroytic cells with different structures and numbers of organelles. (Although, cells only have one nucleus. But they can have different numbers of mitochondria, of ribosomes, etc.)

The structure of eukaryotes

You probably all know that the **mitochondria** is the powerhouse of the cell. I think that's just about the only fact that everyone remembers from high school biology. We won't focus on that organelle here, except to confirm that yes, it is the powerhouse of the cell. We will discuss it in more detail in the next unit when we learn about metabolism. Plant cells also have mitochondria, but they have something else called a **chloroplast**. These organelles are the site of photosynthesis (the process that allows plants to capture energy from the sun and turn it into chemical energy), so we will also discuss that in Unit 3.

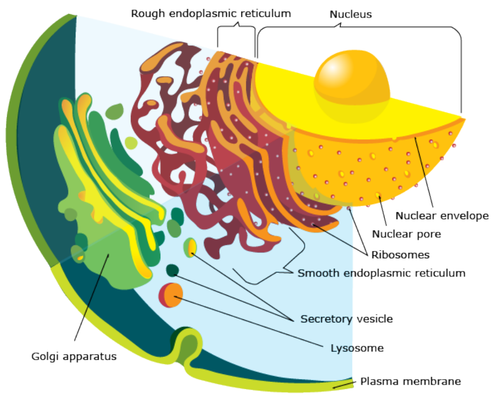


Figure 2.21: The nucleus, the ER, the Golgi apparatus, various vesicles, lysosomes, and the plasma membrane are all part of the network of membranes that make up the endomembrane system in eukaryotes. (**Image source**.)

For now, we will focus primarily on the **endomembrane system**, which is essentially all the different membranes of the eukaryotic cell that serve to divide it into functional and structural compartments. In high school, we usually learn about each organelle as a discrete entity that has a particular job. But the cell is much more unified than that, and highly coordinated. I often think about the eukaroytic cell as a series of connected membranes that work cooperatively to perform essential tasks. The network of membranes are either directly connected, or connected through the action of **vesicles**. Remember how we learned that phospholipids in water can spontaneously form vesicles? These are basically like little ships that can transport materials.

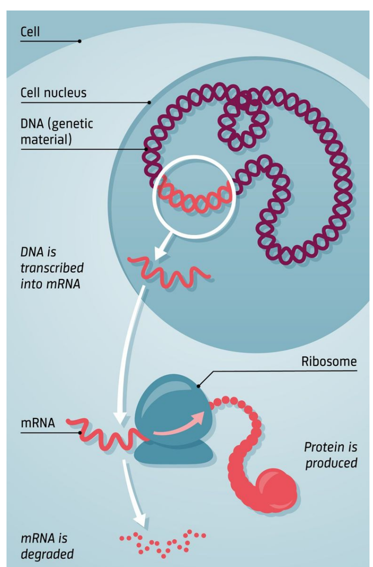


Figure 2.22: DNA lives in the nucleus. Special proteins make an mRNA copy of genes, which are transported out of the nucleus and translated into proteins by ribosomes.

So let's start first with the **nucleus**. If there are any Star Trek fans out there (LLAP!), I usually like to think of the cell as a space station (think: Deep Space 9), and the nucleus is like the computer. Meaning the nucleus, just like the computer, holds all the instructions. Now, without *executing* the instructions, the computer is kind of meaningless. When your laptop is just sitting on your desk it doesn't do anything—you need to tell it what to do. The truth is that DNA doesn't really go anywhere and it doesn't do much in the cell. It sits in the nucleus. Typically many other molecules do the job of opening DNA strands up to the right gene, copying the right gene, and taking the right gene to the place where proteins are made. So instead of dragging you through—yet again!—the basic tour of the eukaroytic cell, let's talk through what happens when we want to make a protein from a particular gene house inside the nucleus. Let's say this is a *secretory* protein, meaning that we are going to make this protein and then it will be secreted outside of the cell through the plasma membrane.

First, all the DNA that makes up your entire genome exists within every single cell in your entire body. That means there is A LOT of DNA in your body; I've read enough to stretch from here to the sun (93 million miles), *and then to Pluto and back*. Think about it for a second: how do we actually fit all that DNA inside of our bodies? Of course, DNA is small, so that helps. You can't see DNA with the naked eye. But even something very small, in large quantities, can be hard to store. So it's packed *very* tightly around special proteins called **histones** into **chromatin**, which is then organized into separate **chromosomes**. Very, very tightly packed. So tightly packed that in most of your cells, the majority of your genome is tucked away and not accessible for making proteins. And that's okay! Because a heart cell really doesn't need the instructions for making a toe cell. Different cells only need access to the genes that are relevant to their function, not every gene in the entire body.

If we want to make a protein, we first need that area of the genome to be unwound so that special proteins can access it and make a copy of it. Those special proteins enter the nucleus, attach to the gene of interest, and make a molecule called **messenger RNA** or mRNA. Because our DNA never leaves the nucleus, it's the mRNA copy that heads out into the cytoplasm. From there, the mRNA finds a **ribosome**, special machinery that makes proteins using mRNA and **transfer RNA** (tRNA), which brings the right amino acids needed to build the protein.

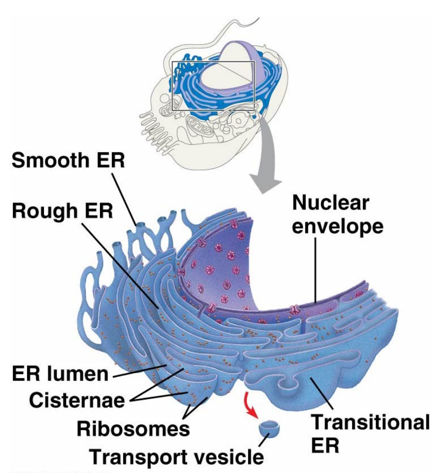


Figure 2.23: The rough and smooth ER are essentially continuous with the nuclear membrane.

The **endoplasmic reticulum** (ER for short) is basically the actual transportation system of the cell (network of turbolifts, if you're still with me on the space station), although it does a few other jobs like protein folding. It forms an interconnected network of flattened, membrane-enclosed sacs known as **cisternae**. The ER is made up of two subunits: **rough ER**, with an outer surface studded with ribosomes, and **smooth ER**, which lack ribosomes on the outer surface. (The smooth ER is responsible for synthesis of lipids, metabolism of carbohydrates, detoxification of drugs and poisons, and storage of calcium ions.) The rough ER is responsible for the production of many proteins, particularly in cells whose job it is to secrete proteins into the bloodstream. After secretory proteins are produced, they are kept separate from other proteins and transported out of the ER wrapped in the membranes of vesicles that bud off from a special area of the ER.

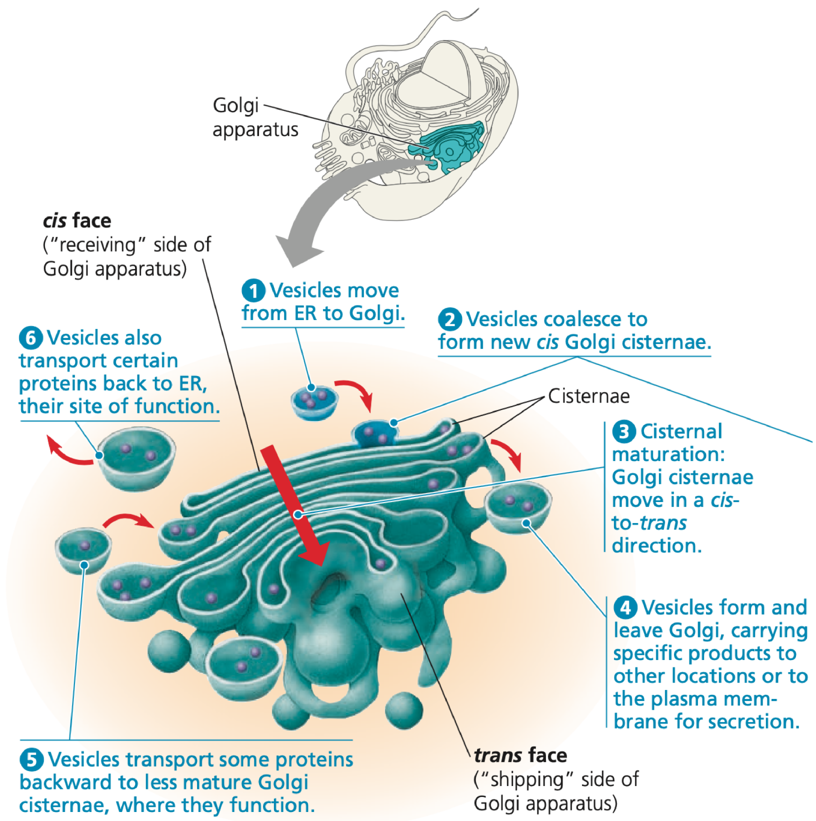


Figure 2.24: The inner-workings of the Golgi apparatus as it ships and packages proteins.

After leaving the ER, the next stop is the **Golgi apparatus**, which is largely responsible for packaging and transport. I think of this like the docking ring of the space station: essentially, it modified proteins received from ER vesicles and packages them for shipment outside of the cell. The Golgi is also responsible for lipid transport and **lyososome** formation, which degrades and recycles unnecessary cellular components.

Plant cells and animal cells

Plant cells and animal cells are more similar than they are different. You share a lot more in common with a rose bush than you do with bacteria. The common ancestor of eukaryotes that gave rise to groups of plants and animals likely had some shared features that were maintained in these two groups; also, over time, the two groups evolved separately. The main differences between plant and animal cells are:

1. Plant cells have a cell wall with plasmodesmata for communicating with adjacent cells
2. Plant cells contain chloroplasts along with chlorophyll, specialized pigments for capturing sunlights
3. Plant cells have a large central vacuole (usually a large compartment filled with water)

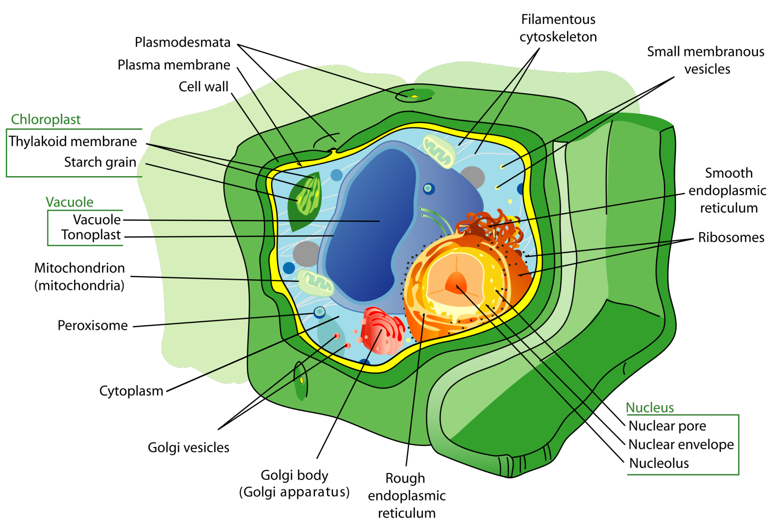


Figure 2.25: Diagram of a typical plant cell. Not all plant cells look like this, but these are the common features.

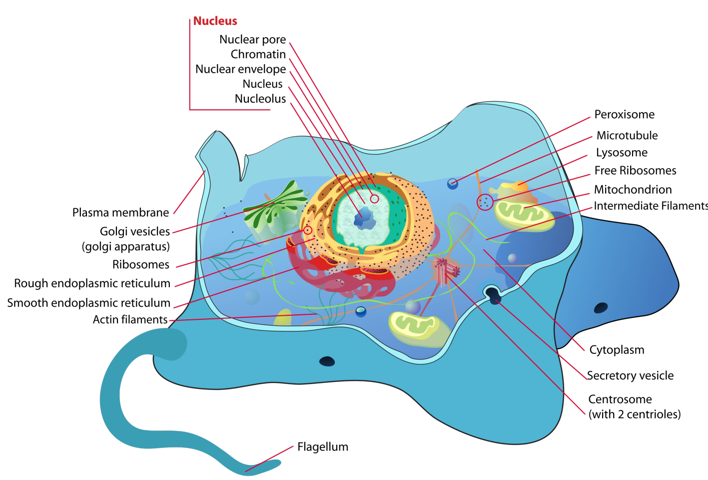


Figure 2.26: Diagram of a typical animal cell. Again! Not all animal cells look like this.

The relationship between prokaryotes and eukrayotes

There are a lot of arguments here, if I'm being honest. And by arguments, I mean hypotheses. This is what science is all about! We propose ideas based on our observations, and then we design tests to examine these hypotheses more closely, and then people argue about the hypotheses and about the data a lot until we settle on a consensus. Sometimes we never settle on a consensus. (Remember: what even is life?) Sometimes a consensus becomes obvious after some key information becomes discovered. For instance, many folks argued about how heredity worked, but the arguments started to stop soon after Gregor Mendel's work in pea plants was re-discovered. But the time when we are actively working on stuff—like the origins of life—usually involves a lot of difficult or complicated data, or worse, no data at all, and varying interpretations about what that data could mean.

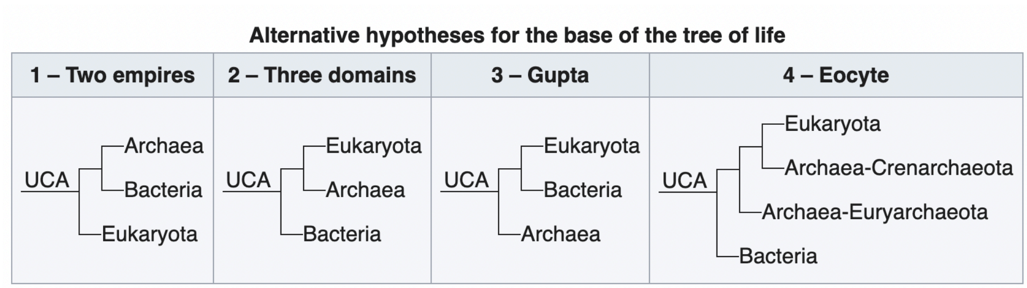


Figure 2.27: UCA stands for "universal common ancestor," the ancestor of the three kingdoms. These are four different scenarios of the evolutionary relationships among these groups.

A common hypothesis of the origin of modern eukaryotes is that some kind of "protoeukaryotic" cell engulfed a prokaryotic cell. Instead of digesting it, these two cells began to work together in a mutualistic relationship. What was this prokaryotic cell that got engulfed? You would know it today as the mitochondria, the powerhouse of the cell. Mitochondria have membranes that are more similar to bacteria than to eukaryotes; mitochondria have their own circular DNA; mitochondria have their own ribosomes; mitochondria make copies of themselves similar to how bacteria reproduce. For all these reasons, the **endsymbiont theory** is one of the most strongly supported hypotheses. We also think that at some later point, this cell engulfed another prokaryote that was capable of harnessing energy from the sun, which would eventually become the chloroplast. (See the diagram on the following page.)

Another hypothesis is that Bacteria, Archaea, and Eukaryotes all represent different lines of descent from a very early colony of ancestral organisms. Maybe even before cells existed, we're talking primordial soup days, when there could have been a lot of horizontal gene transfer and mixing of various molecules. Eventually certain genes were "fixed" in certain populations, which over time ultimately gave rise to the three modern-day kingdoms. Below is a summary of the various evolutionary relationships (from **Wikipedia**). There is currently no consensus, but numbers two and four are the most favored by current researchers in the field.

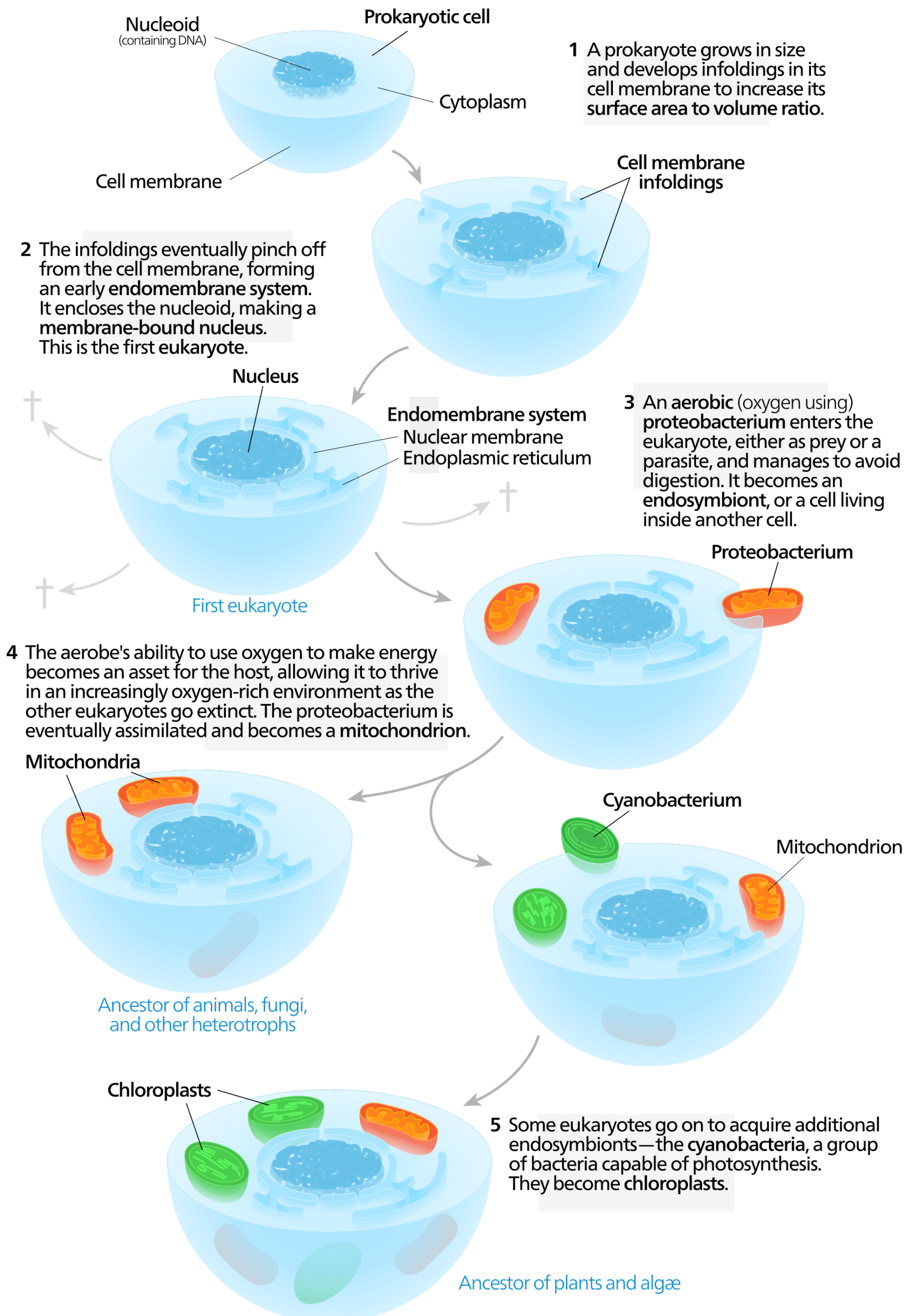


Figure 2.28: One of the most well-supported hypotheses for the evolution of modern-day eukaryotic organisms, developed by Lynn Margulis.

11: Why Membranes First?

What are the features that all of us living organisms on Earth share? Forget for a moment the difficult task of defining "life" in general terms, let's just think about the commonalities we can point to in extant organisms. The first is that all living organisms are composed of cells—which is to say, we all are composed of compartments of various complexity. Another way to say this is that we all have cell membranes. All living organisms contain DNA, and all living organisms essentially use the same twenty amino acids to construct proteins. That's kind of wild if you think about it. From four base pairs and twenty amino acids we get all the billions of creatures that have lived on Earth. All living organisms have ribosomes. All living organisms use something called **ATP**, which we say is the "currency" of energy. Not only do all organisms have a metabolism in which they harvest energy from their surroundings, but they also *all* make ATP to use that energy meaningfully in their cell(s).

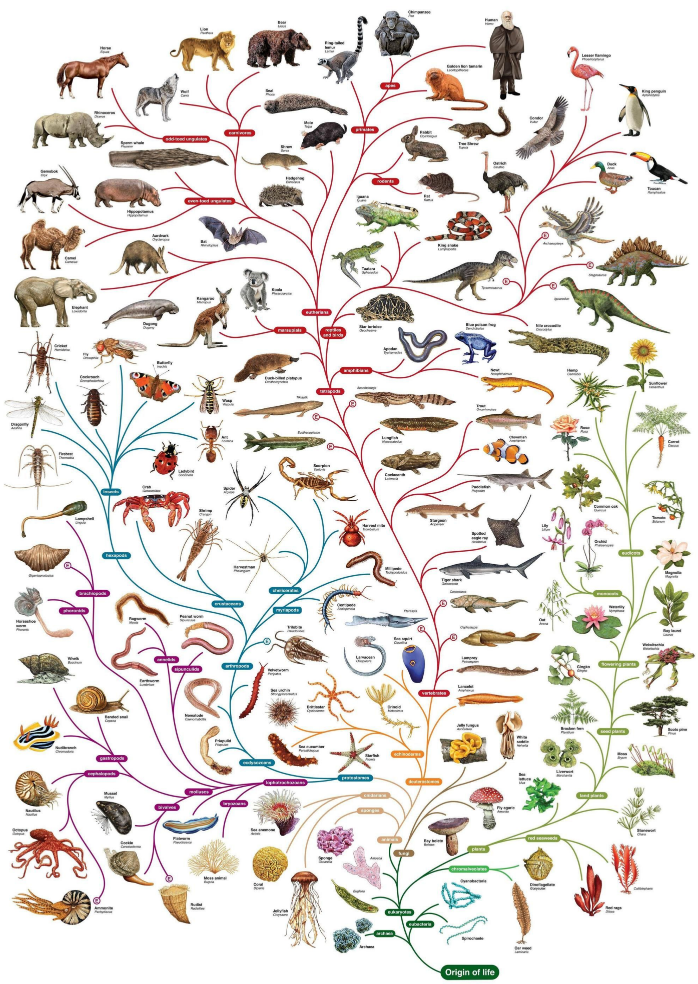


Figure 2.29: Every organism stores their genetic information as DNA, makes proteins from the same 20 amino acids, has cellular membranes, and uses ATP.

There is a lot of evidence that demonstrates that all living organisms descended from one common ancestor. Of course, we can trace fossils through time. We can observe the differences in organisms as continents split apart and such organisms evolved separately—while still observing the features they continue to share. We can sequence the DNA of organisms and compare that DNA to other organisms, using that information to determine how close or distantly related those organisms are to each other. While there is still a lot to learn about the processes that shaped the diversity of organisms on Earth, data from hundreds of disciplines and millions of studies all corroborates this basic fact: *we are all related*. (We can also observe the process of evolution occurring in real-time in populations of bacteria or fruit flies, but that's a story for another day.)

It becomes trickier when we search for the answers to more ancient, deeper questions like how life first emerged. We don't know exactly what the conditions on early Earth were like. We don't know exactly what molecules or atoms were here, or exactly how they got here. There could have been thousands or millions of different iterations of early life forms or cells that all went extinct, before the one that survived and gave rise to all of us. Another thing to keep in mind is that just because a lineage is "older," like bacteria in comparison to eukaryotes, does not mean it has "stopped evolving." The collection of genes among bacteria are still changing, and bacteria are still adapting to their environment! Some genes are highly conserved and change very little. But plenty of genes are not highly conserved. Mutations occur all the time, and there are likely many genes that have been lost or changed substantially over time. Not to mention, horizontal gene transfer makes it challenging to tease apart which groups are related to whom and how. (It is hypothesized that this is why eukaryotic organisms share genes with both Bacteria and Archaea, despite Archaea being sister to us.)

What lipids bring to life

Let's review the processes that we discussed as essential to the definition of "life": homeostasis, organization, metabolism, growth, adaptation, response to stimuli, and reproduction. Of course, some of these processes also occur in non-living entities, but taken together, you generally get a real living organism. I would argue that compartmentalization is necessary for five of these.

1. Homeostasis—where the internal environment is regulated—is not possible if there is no "internal environment."
2. Organization is not possible without compartmentalization.
3. While metabolic reactions can occur without cells or compartmentalization in general, the way that most living organisms capture energy through cellular respiration or photosynthesis is dependent on the presence of membranes. (We learn more about this in the next unit.) Moreover, performing multiple chemical reactions at the same time without interference definitely requires compartmentalization.
4. An organism cannot grow without having an ordered structure from which to grow.
5. Replication is possible without compartmentalization, but reproduction—the production of new organisms from existing ones—requires compartmentalization.

I didn't include response to stimuli, and I'm torn on it. In one sense, chemical reactions must be responsive to the environment within which they occur, regardless of whether or not there is a compartment. But one of the important features of a membrane is that there are special proteins and carbohydrates on its surface that allow the cell to gather *information* about the environment and adjust its internal processes based on that information. So in another sense, compartments may also be necessary for response to stimuli. Like many things, it comes down to exactly how you define each of these components, and there is room for varying interpretations.

But why did I leave out adaptation? As we'll learn in Unit 4, all you need for adaptation to occur is stored information (e.g., DNA) that is replicated with some error rate. Basically, all you need is coded information that is imperfectly replicated. (If this sounds confusing, bear with me until Unit 4!)

Now, just because we need membranes for five (or six?) of the seven characteristics necessary for life does not say anything about whether or not membranes came first in life's origins. We are using evidence based on what we currently observe to form conclusions about past events. That is not good science! All this tells us is the membranes are an important aspect of living organisms as we know them on Earth. I think this is likely why the encapsulation hypothesis has persisted in the literature for some time: compartments seem fairly critical to what we know of as "life." Imagine that you took all the cells of the world and dumped their contents into our lakes and oceans. We'd have a lot of cellular building blocks in there, but no life. Put another way:

> The discrimination between inside and outside, applicable to compartments, is the first structural pre-requisite for the living cell and the living in general.
> *Luisi, 2006, pg. 185*

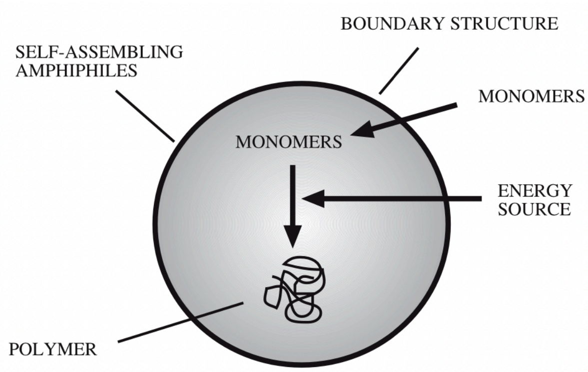


Fig. 3 A protocell would have had a minimal set of functional properties, including self-assembly of boundary membranes, transport of monomers, and capture of energy to drive polymerization reactions, and encapsulation of polymer systems capable of growth

Figure 2.30: Figure from "Chemistry and Physics of Primitive Membranes", Top Curr Chem (2005) 259: 1–27, DOI 10.1007/b136806.

Prebiotic compartments that contain molecules undergoing chemical reactions are generally referred to as **protocells**. Many have hypothesized different variations on what a protocell actually is and whether or not it constitutes "life." But in general, the story goes something like this: in the prebiotic soup, there are organic molecules. Whether these organic molecules came from space (e.g., comets or asteroids) or were assembled through chemical reactions is not known. Amphiphilic molecules assemble into various structures, and occasionally capture other organic materials. Some of these compartments will ultimately contain chemically reactive molecules. Over time, compartmentalization would allow for organic molecules to exist in close proximity, potentially leading to some kind of metabolism. Perhaps the complexity of these protocells is able to increase over time, leading to an ability to replicate components.

Okay… but how do they replicate? How can they possibly replicate, without instructions for their components? And moreover, how do they replicate without a sustained energy source?

What is missing in a lipid world

One of the first things we need to wonder about is how the heck we got the lipids in the first place. I'm no chemist, but from what I understand, branched carbon chains[2] are more likely to emerge from the prebiotic soup rather than long chains. And remember, phospholipids are made from long fatty acid tails, which are just long hydrocarbon chains.[3] We already know that lipids as they exist today were not in the prebiotic soup—but other amphiphilic molecules consisting of long chains will also do the trick. But where exactly these early amphiphiles came from is not known. One hypothesis is, surprise, that they came from space: molecules consisting of only hydrogen and carbon (alkyl groups) have been found on meteorites. Although these molecules could not spontaneously form amphiphiles on their own, it's a starting place for possible prebiotic chemistry on Earth. But the fact remains that we do not know how the lipid-like molecules required for encapsulation originated.

Figure 2.31: The production of bilayers with amphiphilic molecules extracted from the Murchison carbonaceous meteorite. From "The Lipid World," Origins of Life and Evolution of the Biosphere 31: 119–145, 2001.

Another thing we should wonder about is how we go from a spontaneously formed compartment to a cell that is capable of reproducing. In order to reproduce, there must be instructions. How could we build the same kind of structure with any consistency if we didn't have instructions? Some have argued that it may be possible for the lipids themselves to provide the instructions. The first important point is that there is a diversity of lipids in general. As in, there are lots of different kinds of lipids. The second has to do with the way that membranes grow. Essentially,

[2] Instead of a chain of carbon like C–C–C–C–C–C, a branched chain can have a shape like a "T" (or other shapes), where carbon is bound to other carbons in the center of the chain.

[3] You need at least ten carbons in a chain to get the spontaneous generation of things like lipid bilayers and vesicles.

this occurs through an addition process where the original membrane is used as a template. Once more lipid-like molecules are added, eventually the membrane becomes large and undergoes "division."

And the last thing we will wonder about is how we go from compartments to organized energy capture in the form of cellular metabolism. Remember that entropy in the universe is increasing. When a chemical reaction occurs—if it occurs spontaneously—it results in a release of energy and less-ordered products. But remember that life takes a constant input of energy. When we are at equilibrium with our surroundings we are dead. So encapsulation alone is certainly not enough for the maintenance of life—it requires a sustained series of metabolic reactions. Capturing some stuff inside some lipids is not the same as sustained metabolism, because it doesn't allow for consistent capture of energy. And you cannot have life without that.

Unit 3

Metabolism

> I merely took the energy it takes to pout and wrote some blues.
>
> *Duke Ellington*

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12: The Catabolic World and Metabolism

We've been getting at this for a long time throughout the course: living ain't free. We know about how atoms are constructed, and how their construction gives rise to properties that influence the way they interact and form molecules. We know that from this arises special molecules—biological molecules—that build the substances that make life possible. We have toured the two types of cells and discussed some of the jobs those cells carry out, the jobs of life. Where do we get the energy from life? We get it from the sun. Seriously. The sun powers all life on Earth. But we are not solar panels. So how do we actually harness that energy from the sun so we can use it? That's a big part of being alive: taking the energy from this thing, and using it for that thing.

We also know how much living organisms have in common. And all living organisms need energy to live. We know this intuitively, because if we don't eat food, we die. What are we getting from food? We are getting energy and supplies to perform the work necessary for us to continue surviving. This was a major component missing in our exploration of the lipid world: it's great that lipids spontaneously form boundaries, and boundaries are definitely necessary for most of life's processes. But where do we get the *energy*? To look at a cell today, it's hard to imagine how such a complex ballet of chemical reactions originated. And I'm not even talking about multicellular organisms,

Figure 3.1: The energy for all life comes first from the sun. Living organisms harness that energy through photosynthesis and cellular respiration, the main processes of metabolism.

that have billions of cells, all performing their own complicated dances. The fact is that we don't know a lot about the origin of cellular metabolism.

While we know how essential boundaries are to life, some scientists argue that perhaps it was metabolism that originated before true living organisms. Metabolism is essential for the maintenance of life—in particular, the ability to generate the building blocks necessary for growth and reproduction—because this allows the organism to exist somewhat independently from a changing environment. If you rely solely on the immediate surroundings for all the pieces necessary to grow and reproduce you'll eventually run into problems. First, you'll burn through whatever is in the immediate surroundings at some point. (It's not like there are an infinite amount of amphiphiles in prebiotic soup.) Second, you can never colonize a new area. So for life to transcend the realm of random chemical reactions constrained to a specific area, we need metabolism.

In every organism we know of, the core structure of the metabolic network is extremely similar. You will even notice some similarities between cellular respiration and photosynthesis later in this unit. Because the metabolic network thus appears highly conserved, its suggested that it arose very early in the origin of life. But, remember that this can be misleading: there is a difference between the first living organism, and the organism that gave rise to every extant organism (our common ancestor)—these need not be the same! Perhaps the first living organisms are long extinct, and we are remnants of a derived population. But anyway, let's consider these two hypotheses[1]:

1. modern biochemical reaction sequences are the result of evolutionary selection, and thus are likely very different than the first metabolic systems, or
2. the initial metabolic reaction network was pre-established on the prebiotic earth and was consequence of the chemical and physical environment when life first emerged

Evidence in favor of the second hypothesis would then suggest that the basic reaction sequences present in modern metabolism may still be similar to those of the first living organism. So now let's take a look at metabolism and learn about some of the important kinds of chemical reactions that power all life.

[1] From *Archean catalysts for metabolism-like reactions*, Markus A Keller et al

What is metabolism?

Metabolism is the sum total of all chemical reactions carried out by living organisms. There are three main jobs carried out by various metabolic pathways:

1. converting energy from food into energy that can power cellular processes,
2. converting food into biological molecules that can be used as building blocks for the cell, and
3. eliminating waste from metabolic processes.

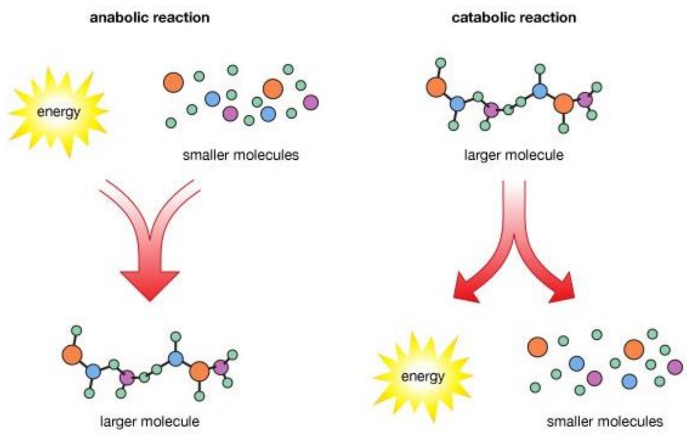


Figure 3.2: Metabolism is essentially just breaking stuff down and building stuff up.

So then, how does metabolism actually function? Enzymes, which are special proteins, catalyze reactions in intersecting **metabolic pathways**, where a molecule is altered in a series of defined steps, resulting in a product. These can be **catabolic** (breaking down molecules, releasing energy) or **anabolic** (building molecules, consuming energy). Entropy is constantly increasing in the universe. But living systems are composed of highly ordered structures. This increase in order is ultimately balanced by living creatures taking in organized forms of matter from their surroundings and replacing them with less ordered forms. We eat proteins, and produce waste like feces, CO_2 and H_2O. During metabolism, the depletion of chemical energy is accounted for by the generation of heat. If you've ever been in a packed room with lots of humans, you'll know how much heat we can generate just by standing there.

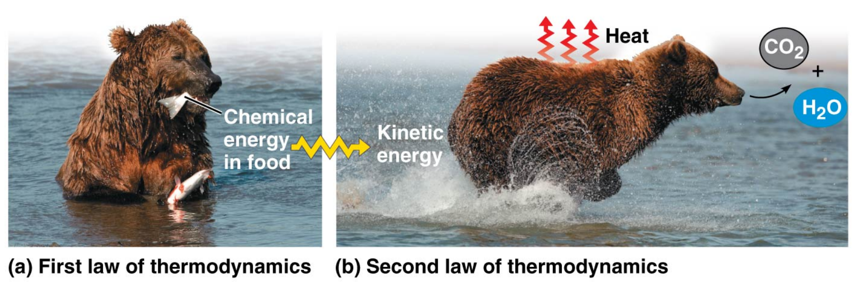


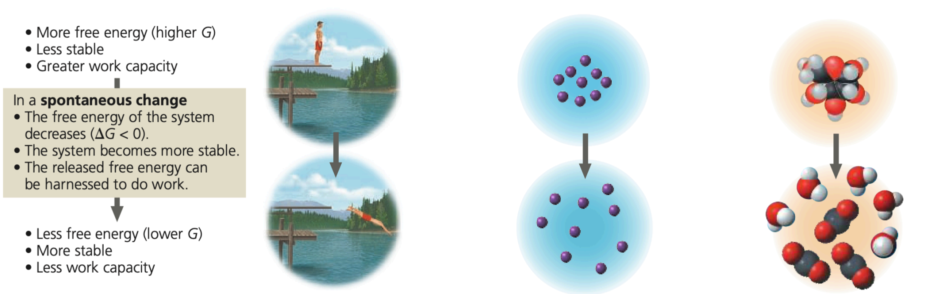
Figure 3.3: Metabolism allows organisms to capture energy and use that energy to perform work. We eat food, break down that food into the pieces we need, and then let off heat and carbon dioxide as waste.

Special kinds of reactions

There are a lot of different kinds of chemical reactions. But for now, we're going to focus on one kind, called a redox reaction. In a **redox reaction**, electrons are transferred from one reactant to another reactant. Basically, you can think of these reactions as the transfer of electrons. Rememeber that electrons have a negative charge, so when something gains an electron, its charge is *reduced*. So we say that the addition of electrons is called **reduction**. When something loses electrons, it becomes more positively charged. I wish I could say that we call this something intuitive or smart, but we call it **oxidation**. The reactant that donates the electron is called the **reducing agent** and the substance that accepts the electron is called the **oxidixing agent**. Redox reactions must always occur together, because one substance must transfer the electron and one substance must accept it.

Okay, who cares? Well, these reactions are important because they are the main source of energy for biological organisms on the planet. Also, they are the main source of energy for a bunch of other stuff too, like fire, and also how your car runs on gasoline. Photosynthesis, cellular respiration, combustion, corrosion… all of these processes are actually redox reactions. Rust is basically just the oxidation of metal—we call this oxidation, iron gives its electrons to oxygen, which is a very powerful oxidizer (ha ha). So ultimately we care about these kinds of reactions because they essentially power everything. There is a lot of energy to be made in transferring electrons around.

Now, in an isolated system, all reactions will eventually reach an equilibrium. Once an equilibrium is met there is no more energy left to perform work. Chemical reactions that occur in a test tube will eventually stop as they reach this equilibrium. But if you were to reach equilibrium with your surroundings you would be dead. As I've said, in metabolic terms, equilibrium is the same as death. But of course, we are not dead, so how does that work? All living organisms require a continual input of energy to maintain the multitude of metabolic reactions in a state far from equilibrium. The key to maintaining this lack of equilibrium is that the product of a reaction does not accumulate but instead becomes a reactant in the next step until waste products are expelled from the cell.



(a) Gravitational motion. Objects move spontaneously from a higher altitude to a lower one.

(b) Diffusion. Molecules in a drop of dye diffuse until they are randomly dispersed.

(c) Chemical reaction. In a cell, a glucose molecule is broken down into simpler molecules.

Figure 3.4: Let's say that a system has more free energy, it's less stable, and it has a greater work capacity. When a reaction like this occurs spontaneously, G is reduced (the change in G is negative) and the system releases energy, becoming more stable.

We know that some reactions build things up, and some reactions break things down. We use a mathematical equation to describe ΔG, which is called the change in **free energy**. ΔG can be measured for a reaction, and once we know its value for a particular chemical process, we can use it to predict if the reaction will be spontaneous—occur on its own—or not. A **spontaneous reaction** is energetically favorable and will occur without any input of energy. Essentially, ΔG must be negative, meaning energy is released from the reaction. All spontaneous processes decrease the system's free energy. Processes that have a positive or zero ΔG are never spontaneous because they require a positive input of energy.

Now that we understand ΔG, we can understand more about the kinds of metabolic reactions that can occur. Either they require energy, meaning energy must be added, or they release energy. An **exergonic** (prefix *ex* means "out") reaction occurs spontaneously and releases energy, meaning ΔG is negative and the chemical mixture loses free energy. An **endergonic** (prefix *en* meaning "in") reaction requires energy, does not occur spontaneously, and ΔG is positive. This kind of reaction will absorb free energy from the surroundings. The size of ΔG represents the amount of energy that would be required for the reaction to occur.

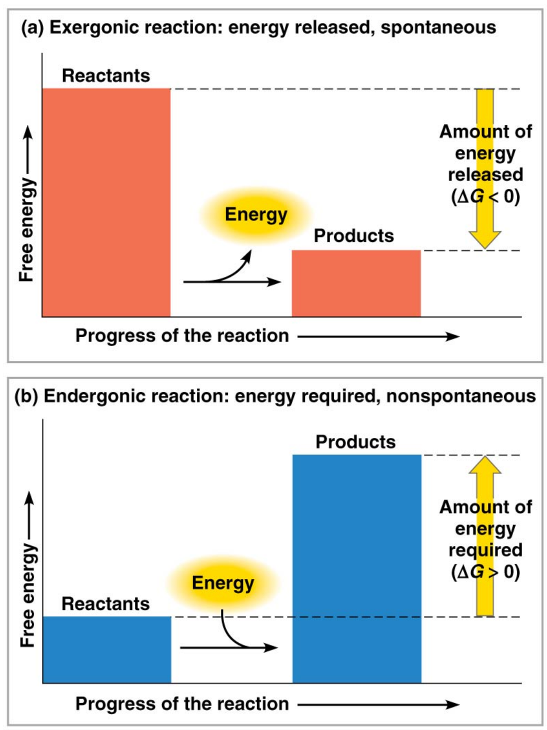


Figure 3.5: Exergonic reactions start with more free energy and proceed spontaneously, releasing energy. Endergonic reactions require energy and never occur spontaneously.

So let's quick put a few concepts together. Catabolism, the breaking down of molecules, usually releases energy and is thus exergonic. Anabolism, the building of molecules, usually requires energy and is endergonic. Metabolism is just a series of catabolic and anabolic reactions, producing energy, consuming energy.

The currency of metabolism

We will talk a lot more about ATP when we discuss cellular respiration. For now, we will simply introduce the structure of ATP and explain in broad terms how ATP is **hydrolyzed** (broken down) to release energy. **ATP**, otherwise known as adenosine triphosphate, contains the sugar ribose, with the nitrogenous base adenine, and a chain of three phosphate groups. ATP is built from carbohydrates, nucleic acids, and phosphate groups! Fun fact: organic phosphate can react with water and release energy. What I mean is that bonds between the phosphate groups of ATP can be broken by hydrolysis. When this happens, a molecule of inorganic phosphate ($HOPO_3^{2-}$, usually abbreviated as P_i) leaves the ATP, which becomes adenosine diphosphate, or ADP. The reaction is exergonic and releases 7.3 kcal of energy per mole of ATP hydrolyzed. Why does this reaction release so much energy? It's not because the phosphate bonds are especially strong. Rather, it's because the phosphate groups are negatively charged. Because the same charges repel each other, when they are crowded together it causes instability in that region of the molecule. I've seen this described as a compressed spring, ready to pop.

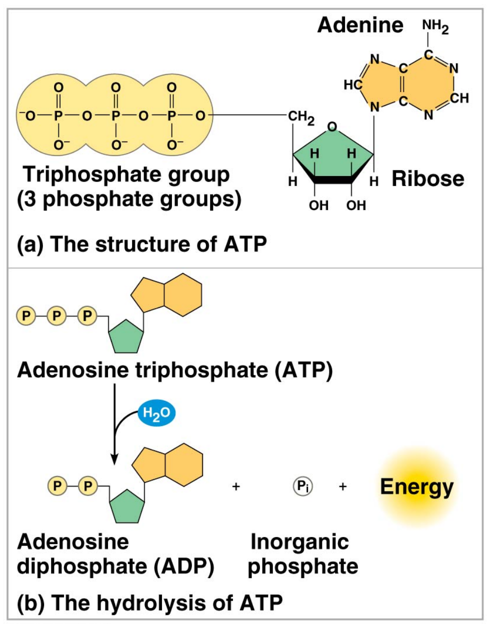


Figure 3.6: ATP is the currency of energy for all living organisms. When it is hydrolyzed and a phosphate group is released, energy is also released.

ATP is a renewable resource that can be regenerated by the addition of phosphate to ADP. The free energy required to phosphorylate ADP comes from exergonic breakdown reactions (catabolism) in the cell. This shuttling of inorganic phosphate and energy is called the ATP cycle. It is common in living organisms to couple an energy-yielding (exergonic) process with an energy-consuming (endergonic) process.

13: Enzymes

There is a lot of energy in gasoline. We know this, because we pay a lot of money for it so that we can drive our cars around. But we also know that if we just lit gasoline on fire, it would explode and we couldn't harness the energy inside of it to do anything meaningful. This is the idea behind metabolism—instead of gathering energy explosively, we want to gather it in steps so that we can actually use it to perform work in the cell. The thing is, if we examine life from the perspective of *thermodynamics* as opposed to simply *chemically*, we may wish to form a different argument about life's origins than what we have so far in our prebiotic soup.

Figure 3.7: We can blow up a gasoline tank, but that's not going to get us to work.

The argument goes that there is nothing "life specific" about the building blocks of life, in and of themselves. We have hydrocarbons, along with nucleic acids and amino acids. Maybe the fact that we find hydrocarbons in space, on comets, simply attests to the fact that these molecules are… ordinary. Because it's not the molecules that make us alive, it's the fact that we are highly ordered structures existing far from equilibrium with our surrounding environment. Here it is in fancy language:

> As pointed out by Erwin Schrödinger already in 1944, and even earlier by Ludwig Boltzmann as well as numerous further physicists and physical chemists ever since, all living entities share the same characteristics. They generate order, that is, highly structured and regulated networks of processes, from disorder, i.e., relatively randomly distributed chemical elements. Therefore, they are entropy-decreasing phenomena.
>
> *Minerals and the Emergence of Life, Duval et al., 2021*

We know that living organisms are able to do this because they are **open systems**, which is to say that they are constantly taking in energy from the surrounding environment and producing waste. The way us life forms get around the second law of thermodynamics is that we maintain our own order by increasing the overall entropy of the universe itself. Our limited *decrease* of entropy is lower than the *increase* in entropy of the larger system of which we are a part.

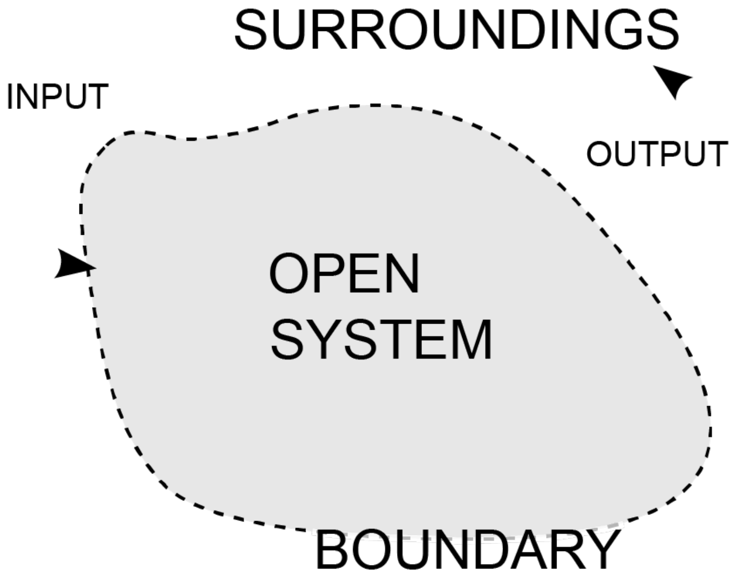


Figure 3.8: Living organisms are open systems that exchange matter and energy with the surrounding environment.

Okay, so all us living organisms need a constant influx of energy, and we use this energy to create order from disorder. As long as we maintain our own order relative to the larger system, we will need this energy, because we ourselves exist far outside equilibrium with our environment. So how do we achieve that? At the core of all living organisms is our cellular metabolism. How nutrients get absorbed and what particular nutrients are consumed depend on the organism, but all cells essentially carry out the same process once we get to the cellular level. It's called cellular respiration, and we'll learn all about this week. But we already know the currency of energy—the output of cellular respiration—a molecule called ATP. How organisms make that molecule and how it gives us energy relies heavily on the exploitation of electrochemical gradients, or electrical "tension." But what makes this possible? How are we powering highly specific reactions, many at the same time, at exactly the right time and place? Enzymes.

What enzymes do

Put simply, enzymes are proteins (some enzymes are RNA, but we'll talk about that in Unit 4). And what do they do? Basically everything. I'm a little bit kidding, but also every single life-sustaining metabolic process requires enzymes, because such processes would not occur at rates fast enough to do the "life-sustaining" part. But anyway, enzymes are **catalysts** that accelerate the rate of chemical reactions. They do this by lowering the **activation energy** required to start the resultant chemical reaction.

Let's think back to our chemistry classes in high school (please, bear with me!!). We did all kinds of reactions with beakers and flasks and titrators and all that. But what else did we do? Well, we heated stuff up. Sometimes we cooled stuff down. Sometimes we added an acid or a base. All you really need to remember about high school chemistry is that in order to really “get stuff going,” so to speak, we needed to change things like temperature or pH. Many reactions simply will not occur without this kind of input. But the problem is that the body maintains a pretty constant temperature, and it *has* to maintain a constant pH, or we will die. So then, what’s a body to do? The body can’t increase the pH over here, or crank up the bunsen burner to boiling. That’s where enzymes come in.

Enzymes are pretty amazing, because they make reactions trillions of times more likely to occur than they would without their presence. There is one example on **Wikipedia** where an enzyme catalyzes a reaction such that it occurs in seconds, whereas it would otherwise take millions of years to occur. This is why one of the main arguments against the prebiotic soup hypothesis is that spontaneous generation of some of these building blocks is so mind-bogglingly unlikely (statistically speaking) that it may well be straight up impossible. The fact is that enzymes are the workhorses that make the processes of life happen. They also regulate when and how reactions occur through their particular shapes and whether or not they are present or absent.

How enzymes work

Enzymes are highly specific to the reactions they catalyze—in other words, enzymes are specific to the “reactant” it acts on. In science terms, this is called **substrate specificity**, the reactant being the **substrate**. This is important, because many pathways have one particular enzyme that catalyzes one particular step. We need this kind of specificity if we are going to actually harness energy to perform meaningful work in the cell. Remember the gasoline analogy: we can’t just set the glucose molecule on fire. We need to break its bonds in a controlled way, so that we can, metaphorically, power the car. In our case, “powering the car” means making ATP. ATP is the currency of energy, and the *particular* currency is the electrical tension created when three negatively charged phosphate molecules exist in close proximity. All organisms exploit this tension to power life.

Enzymes bind to the **active site** of their substrate. This typically induces a conformational shift and the entire complex changes shape. Here are some of the methods that enzymes use to speed up (or catalyze) reactions:

- if the reaction involves two or more reactants, the active site can help the substrates coming together in the proper orientation for the reaction to occur
- when the substrate is bound to the active site, it can stretch and bend the substrate itself, because distorting chemical bonds allows them to be broken more easily
- enzymes can create “microenvironments”—like a pocket of low pH—because of the R groups attached to the amino acids in the enzyme
- speaking of amino acids, sometimes the side chains of amino acids in the enzyme directly participate in the reaction by binding to the substrate

Regulation of enzymes

In large part, enzymes can be regulated through inhibition. This essentially means preventing the enzyme from functioning in some manner. We will cover the two main kinds of enzyme inhibition, although there are others.

Competitive inhibition. A competitive inhibitor is a molecule that greatly resembles the substrate. If the competitive inhibitor is present, it will bind to the active site of the enzyme and prevent the substrate from binding. If the substrate concentration is high enough (much higher than the concentration of the inhibitor) then this kind of competition can be overcome.

Non-competitive inhibition. A non-competitive inhibitor binds to the enzyme in a location other than the active site. In doing so, it reduces the catalytic efficiency of the enzyme. The substrate can still bind, but this no longer has the same effect on the resulting chemical reaction. This kind of inhibition cannot be overcome with high concentrations of substrate.

14: Photosynthesis

15: Cellular Respiration

16: Why Metabolism First?