

**Transcript from Epic of Evolution: Life, the Earth and the Cosmos (BEP 210A)**  
**February 7, 2000 - Lecture by Ursula Goodenough**

Hi! I am going to talk about life, so I have to do life on the planet that Mike is in the middle of creating. We'd like to hear from you at the end of the course whether this three-part version of things is going to be more confusing than stimulating, but anyway it's the only way we could think of to do it this first time around.

The handout gives the reading assignment for this week -- it's also on the Web site. The two books that I've assigned are books that cover topics that I'm not going to cover in lecture but that I want you to access. The Sand County Almanac is about ecology and the environment; it's a classic book, beautifully written, and even antedates Rachel Carson in giving a warning cry for what's happening to the Earth. The Moral Animal has to do with applying evolutionary thinking to psychology. I'll keep assigning readings in these books during the semester and toward the end of the semester we'll devote the last 2 weeks of group meetings to talking about them, so don't lose track. Questions on these reading assignments may also appear on the midterm. So keep up-to-date, but for each discussion section, I'm going to try to find each week an essay for you to read. It will be posted on the Web site and you can download it and read it, or read it on your computer, as you wish, and it will be that essay, a short essay, that will actually be the focus of the discussion group for that week.

So, if we think about the universe and the complexity of the universe, then as Claude said, in some ways the universe was most complex during the first 3 minutes when everything was changing and everything was reorganizing and particles were annihilating antiparticles and so on. Once that whole chaos was over then everything began to mellow out. Similarly, the Earth in its first let's say 500 million years was at its max in terms of everything changing and rearranging and iron flopping into the middle of it and so on, and then again it began to cool off and settle down. For sure the Earth is still doing extremely interesting things from our perspective, but not necessarily get more complicated.

I make this point only to say that in terms of life, it is very much the other way around: life had to start out very simple, and during evolution it has gotten increasingly more complicated. On your handout is a list of "life terms," and the first one there is complexification.

During the lectures this week I will be giving you the basics of how life works. This means that alas I have to start with chemistry. Even after things get very, very complicated in life, it's still always chemistry. Life is about doing chemistry in an organized fashion to bring about a result, namely, a creature. The chemistry itself, what kind of chemistry is going on and all the ways that it's regulated, keeps getting more complicated, but it's all going to boil down to the concepts that we'll be learning about this week.

Okay, so chemistry. Mike, Claude and I debated about who was going to first tell you about chemistry, with none of us really wanting to do it, and I guess I drew the short straw. So I will

give my version of chemistry. They will probably give you other versions of chemistry in the context where they observe it in the universe and the Earth.

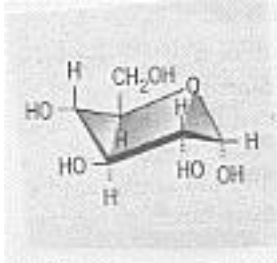
For our purposes, chemistry has to do with associations of atoms. Claude was in the midst of making atoms for you. Eventually atoms spew out of stellar explosions and come to make the Earth, where it's atoms all the way down. I'll draw an atom the way a chemist thinks about an atom (it has nothing to do with the way a physicist thinks about an atom): it has a nucleus that has positive charges in it and electrons around the nucleus that have negative charges, where a stable atom has the same number of plus and minus charges. Most kinds of atoms, not all of them but most of them under the right conditions, can become an ion, which means it carries a net charge. So if you are a particular atom and you lose an electron, then this means that you have a net positive charge. An example of that is the ion of sodium. And if you gain an electron then you're net negative. An example of that is chloride. Since plus and minus attract, sodium and chloride will get together and form salt if you get rid of the solvent. In biology we're going to see a lot of ionic interactions, attractions by charge.

The other kind of chemical interaction that we're going to be interested entail what are called covalent bonds. In this situation, two or more atoms actually come together and form a molecule, and they become a molecule because in the end (at least in the baby-chemist version of what goes on) they share electrons. So if we take hydrogen atom with a plus charge in the nucleus and an electron orbiting around it, and introduce a second hydrogen atom, what happens is they get close enough together that they actually have a cloud of 2 electrons going their two nuclei at the same time to form a molecule called H<sub>2</sub>, the shared electrons forming the covalent bond that holds the two nuclei together. A second example would be the molecule called water, wherein the electrons from 2 hydrogen atoms and from one oxygen atom interact to hold the 3 nuclei together to form H<sub>2</sub>O.

Whether atoms will form ionic interactions or covalent bonds is dependent on two variables. One variable is the nature of the atom itself. How many electrons it carries, how big its nucleus is, how stable it is, how interested it is in giving up its electrons or adding electrons to it -- all of these influence how the chemistry is going to go. The second variable is the nature of the environment that the atoms are in. The environmental parameter that we've heard a lot about already is temperature, which influences just how fast the atoms are moving. That has a lot to do with whether they'll combine with one another. There's another parameter, abbreviated pH, which describes how acidic versus basic the environment is. That has a lot to do with whether the atoms are going to give off/or take up electrons. These and many other factors influence how the chemistry is going to go.

So once you form a molecule, and particularly as you make a molecule with more and more atoms in it, the molecule will adopt what we're going to call a configuration in space. For example, let's look at a more complicated molecule, one that's very important in life, the molecule glucose. A complete glucose molecule contains six carbons and 12 hydrogens and six oxygens. We could write out glucose with that atomic numerology -- C<sub>6</sub>H<sub>12</sub>O<sub>6</sub> -- but that doesn't tell us much of

anything about glucose that's interesting. What's interesting about glucose is how those six carbons, 12 hydrogens and six oxygens go together to make up their bonds. When they do that, they adopt a configuration that looks like this.



It's kind of a flat kind of a molecule that looks a bit like a lounge chair, with particular groups -- like a particular OH -- sticking out in particular positions. It has a configuration. All of the molecules that we'll be talking about, the small molecules, have configurations. The configuration that a molecule adopts is the one that's thermodynamically the most stable. To make a glucose molecule you have to put energy into the system, and we'll talk about how that happens in time, but once the glucose molecule forms, the whole thing sort of goes "Ah!" and it settles down into its stable configuration of being glucose, and to get it to not be glucose and be something else you have to put energy back in to disrupt these stable bonds that hold it together.

To give you an example of a configuration, I have various show-and-tells. Here's a molecule (hold up a cut-out paper doll) that has a particular configuration. Now, it turns out that molecules, particularly the ones that we're interested in in life, come in families. Since we've been thinking about sugars, there's glucose, and then there's also something called fructose and also something called galactose. They are all six-carbon sugars with the same kinds of bonds and the same general shape, but they're all different. Each has an additional oxygen here or hydrogen there and so on; collectively they form the so-called hexose family. To give you a feel for this, here (second paper doll with a different-shaped head) we have, let's say, glucose and fructose. They're clearly in the same family, same kinds of molecules, but this one has a little hole up here and this one has a little thing sticking out. So they're chemically different from one another.

Our next point for the chemistry of life is that molecules in a family often have the capacity to form polymers. In a polymer the molecules make covalent bonds between them and form long chains. So here (long paper-doll chain) is a polymer of glucose, let's say, or glucose with fructose because that could happen too. Notice the important thing, which is that the arms and the legs are doing the bonding. The arms and the legs are interested in forming covalent bonds -- that's their "job.". Whereas the various head shapes are independent of making the polymer. They're free and hanging out there, able to endow the polymer with particular properties. So -- the covalent bonds hold the polymer together, and these form without any interest in what the head shape is; their formation is indifferent to head shape.

That's all the chemistry you're going to need to know until Michael hits you with a lot of it. But we have to make sure that we're on the same page in terms of when the chemistry can occur, because chemistry can occur only under certain conditions. First of all, the atoms have to be stable as atoms. If an atom goes, say, into the middle of a star, it isn't even an atom anymore. It breaks down into its component sub-atomic particles, and these can't do any chemistry. So you have to at least be at the kind of temperatures and pressures that allow atoms to be stable. That is, it can't be too hot or chemistry can't happen. And similarly, if it's really, really cold, then the atoms are not moving around and the chemistry is very, very slow. So we have the Goldilocks constraint: to get chemistry to go, it has to be not-too-hot and not-too-cold.

Secondly, particularly for forming covalent bonds, you need to have a flow of energy, the same kind of concept that Mike and Claude have been trying to give you. In order for an atom to form a covalent bond, it needs to be excited. When it's excited its electrons are more likely to be able to move into the electron cloud of another atom so that the electrons are shared. This excitement ultimately requires some sort of energy input. And then, once you've formed your molecular bond, you don't want the atoms to stay in an excited state or else they are likely to come apart again. This problem is solved by the fact that in forming the molecule, in adopting the shared-electron configuration, energy is released and the system becomes less excited. Some energy goes off in the form of heat and entropy and you're left with a stable molecule.

So, chemistry happens under conditions where you have energy flowing from a source to a sink, from hot to cold, from a more to a less excited form of electromagnetic radiation, any way you want to think of it. This kind of thinking ultimately extends, of course, to how the universe works.

It turns out that way before we have life on Earth, way before we have an Earth, chemistry can occur out in the universe. Out there in space, in addition to stars, there's tons of little tiny talcum powder-sized grains of matter called cosmic dust, gazillions of light-years' worth of this stuff. As it's floating around, a piece of dust might pick up a carbon atom here and an oxygen atom there, accreting atoms that derive from the Big Bang or from supernova explosions. Every once in awhile a photon may zap this speck of dust, or it might go real near a star and suddenly get very hot and then go by and cool off. Heat and cool, heat and cool. Any and all of these occasions of energy flow out there in the universe can allow chemistry to occur on these dust particles, the result being small molecules. We can take instruments and look out into the universe now and document that in fact, floating around on dust are a lot of small molecules and, particularly interesting for us, a lot of carbon-based molecules. We can find formaldehyde, find methane, the kinds of "toolkit" molecules that an organic chemist likes to start with in synthesizing more complex molecules. We can also find lots of amino acids and sugars, the same molecules that we find in living organisms on earth.

So, without doing anything except making the kind of universe that Claude was making, and getting the heavier atoms to be forged inside the bowels of stars (the carbon, oxygen and so on),

and then just letting them float around adsorbed to cosmic dust, you get the chemical synthesis of complex molecules.

The idea, then, is that when the Earth was forming and comets were hitting it, the comets first passed through clouds of cosmic dust and picked up a lot of molecule-laden dust, which they then “delivered” to the Earth. (At this point I said that water was also brought in by comets, but Mike tells me that this idea is now discredited). That is, the first molecules came in as “comet freight.” Whether or not this is true, it is certainly plausible, but it can be said that by invoking comets to bring in the first molecules, people who speculate about the origin of life are in fact cheating. They cheat in the sense that because there really isn’t very much time to get life going from the time the Earth formed to the time we had the first fossils, it’s a lot easier not to have to think about how you get the first molecules forming, so the first molecules are conveniently brought in from the outside, forming what is called the primal soup.

Lets look at some primal soup in a little tiny puddle, and imagine how life could have originated there. Actually, life is more likely to have arisen in an ocean vent, but a puddle is easier to think about. We don’t know anything about the origin of life, and we don’t know anything about this puddle, so all the things I’m going to say to you next are really kinds of extrapolations. By which I mean that since we know how life works now, and we know a lot about its chemistry, we can basically work backwards. We can ask, “How could you get creatures with the kind of chemistry that we see now?” And then we make up a story, and then we try to test out that story in the lab and see if it makes any sense. Let me quickly say here, though, that even if somebody manages to create life in the lab from simple molecules, even then, of course, that’s not going to say that that’s how life *did* originate. That’s only going to tell you that that’s one of the ways that it *could* have originated. We’ll probably never know how it *did* happen. So the story I’m going to tell is really an exercise in thinking about what might have happened, or what needed to happen. In the process, though, we will consider a lot of the essentials of what life is about.

All right, so we’ve got a puddle. The small molecules in the puddle’s primal soup, which derive from comet freight, are generically called building blocks. We’ve got to make life in the puddle out of the building blocks, so what do we have to do? Well, since I’m operating ad hoc anyway, I’m going to put into my puddle the kind of building blocks that I know I’m going to need (which is convenient), and the building blocks I’m going to need are small molecules called ribonucleotides. (Ribonucleotides are sometimes called bases, which is a terrible term because a base can mean all sorts of things. But they’re very often called bases when you’re doing biology so I may lapse into that.)

Ribonucleotides are small molecules so we’re back to paper-doll kind of thinking. A ribonucleotide is a bunch of atoms associated with each other by covalent bonds, generating a configuration (paper doll #1). Ribonucleotides are members of a family of ribonucleotides, so our same thinking goes (paper doll #2). It turns out that there are only four ribonucleotides in the family that are important to our life story. They have names of adenine, uradine, cytosine and guanine but we’re going to abbreviate them -- A for adenine, U for uradine, C for cytosine, and G

for guanine. The ribonucleotides can form polymers (paper-doll chain), and now I will confess that this polymer is in fact a polymer of ribonucleotides because, if you look, you will notice that there are four kinds of heads here. There's a head with a square indentation, a head with a square sticking out, and a circle sticking out, and an indentation for a circle. So, it's a polymer of four different kinds of ribonucleotides (A, U, G and C).

So how do you get this polymer? We brought in our ribonucleotides as comet freight, but now I say that they formed this polymer in our puddle. Forming a polymer like this could happen in solution if you wait long enough, but the common origins-of-life thinking here is that the process was aided by minerals that were also present in this puddle. The favorite kinds of minerals have until recently been various kinds of clays (and Mike will certainly tell you more about clays); more recently, iron pyrite has come into favor. The surfaces of clays and pyrites carry exposed electrical charges in regular patterns, and molecules tend to like to sit on them, become adsorbed to them. In so doing, the molecules come close together, meaning that bonds can form between them far more readily than if they were just floating around in solution. Whenever you have a situation where the probability that a chemical reaction will occur is enhanced, that event is called catalysis. So if we have ribonucleotides adsorbed to clays and this enhances the chance that they will form arm-leg covalent bonds and form a chain, the clays are said to catalyze the polymerization reaction. This first chain, the one that Claude is holding up, this polymer of ribonucleotides, is called ribonucleic acid and that's abbreviated RNA.

If you had to say anything about defining life, you'd probably want to say that it makes more of itself, right? It makes more of its particular *kind* of self. If we look at my timeline of what's going to happen in our puddle, at Time 1 we have a number of RNA molecules, each one drawn in a different color, each having been catalyzed via an interaction with clay. Each RNA molecule doubtless has a completely different lineup of the little dolls (ribonucleotides). And now what we want to do, to get one of these molecules to have something to do with life, is we want it to replicate, where replication is simply to make some sort of a copy of what you have.

The replication we're going to do now is again going to be catalyzed by clay in the sense that the clay, being a good surface, will speed up the molecular interactions, but what's going to happen has to do with the properties of the ribonucleotides themselves. We can now focus on the fact that I didn't cut the head-shapes of the dolls randomly. I made my heads these shapes because it turns out that there's a domain of a ribonucleotide that is particularly interested in associating, via ionic interactions, with its partner. That is, anytime you have an adenine (A), it's very interested in forming ionic-types of interactions with a uridine (U). It has just the right shape (configuration) to associate with U. And anytime you have a guanine (G), its configuration is such that it really likes to associate with cytosine (C). So if this doll is a C, with a round indentation, it's really interested in associating with a G, the doll with the round protrusion. And similarly if I'm an A I'm very interested in associating with a U. These A-U and G-C associations are called base pairs.

So this polymer is lying in the clay and these free ribonucleotides are coming along and, catalyzed by the clay, you get A-U and G-C base pairs until you get a complete copy. This second paper-doll chain can now come off and be another polymer. Now, I wish I could say that it were a direct copy because that would be easier for you to think about -- this part is kind of a drag but sorry, this is the way the chemistry works. It's not really a *copy* because every time there's a G here there's a C here, and every time there's an A here there's a U here. It's called a complementary copy. It's a copy in the sense that a mold is a copy. It's not the same thing, it's the reciprocal of it. But once I have this complementary copy, then we can make another copy of it and get back to our original. The same information is present in both strands but the way RNA is replicated is by such a template/cast alternation: the cast serves as the template and the template serves as the cast. This may be one of the parts that you got stuck on in high school biology, but it's really pretty simple.

Okay, so at Time 2, my blue RNA has undergone this kind of replication. As you can imagine, if you're sitting there on clay and waiting for all of these ribonucleotides to come and form base pairs, it's going to take a long time. It will be catalyzed by the clay, but it's still going to be slow. Moreover, any RNA molecule in the puddle is equally likely undergo this kind of replication. They're all sitting there adsorbed to clay, and they're therefore all candidates for replication. It happened to our blue RNA, but that was just the luck of the draw for the blue.

What now happens is dependent on a completely different property of our RNA molecule. We started out being interested in the fact that it can form an arm-leg polymer. We then replicated it by base-pairing, and that was good. But now we can focus on a third fact, which is that because we have these ribonucleotides that are interested in forming base pairs, what's also going to happen is they're going to start forming base pairs within themselves. It's not just the free nucleotides that they can make base pairs with; they can also start to form what are called *internal* base pairs. The paper doll chain can fold up on itself and form bonds with itself, and the minute you start doing this what's basically happened is that you've created a new shape. Now I'm going to be sort of arbitrary here. Shape and configuration are obviously (I'm sure according to Mr. Webster) synonyms, but I'm going to try to stick to using the word configuration for the disposition of atoms *within* one of these small building-block molecules, and I'm going to talk about shape when the small molecules interact with one another to form a second conformation in space, something that's independent of, although dependent on, the component molecules. So configuration, we will say, is something that we talk about when we're talking about a molecule, and shape is something that we talk about when we're talking about a macromolecule and the way it folds in space.

All of these RNA molecules in our Time 1 or Time 2 puddle presumably start folding and forming various shapes. But now we can focus on a fourth fact, the fact that each one of these chains, having been formed by tacking one ribonucleotide on to the next, is going to have a different sequence of bases. One RNA might go G-C-A-U-A-G..., and because of that sequence it's going to be able to fold this way. Another sequence has different folding possibilities: it may

fold that way, okay? The different shapes are ultimately determined by the different sequences; the sequence of bases determines what shape is adopted.

So here's the crux of it. These RNA molecules are all forming these shapes randomly, dictated by their random base sequences, but one of these guys -- the blue template strand -- happens to form a shape that's just the right size for a ribonucleotide to fit in. It's got this lovely little pocket in here for putting a ribonucleotide in, and because it's blue, it also has a lot of interest forming base pairs with the complementary blue strand -- that is, it recognizes its "own kind". Therefore, this blue template strand has the capacity to bring ribonucleotides over to the blue complementary strand and facilitate its replication. That is to say, this shape gives this RNA molecule the ability to catalyze replication. The blue RNA no longer has to sit there on the clay and wait for free ribonucleotides to diffuse by and form base pairs. Instead, its partner brings them over and offers them up. As we said when we were talking about clays, anytime we get chemistry to go faster than it would just by waiting around is an event that we call catalysis. In the case of biological molecules, molecules that catalyze chemical reactions are called enzymes. Enzymes are given names, and this guy that's able to bring nucleotides in and speed up RNA replication is called a replicase: an "ase" is usually put at the end of the name of an enzyme, so an enzyme involved in replication is called a replicase.

What has happened is what we see in Time 3. We've waited maybe 1,000 years. When we come back 1,000 years later, because the blue RNAs are able to serve this replicase function with their complementary partners, when we come back we're going to find a lot of blue guys. Everybody still has the chance of being replicated on the clay, but the blue ones now have this additional ability to be replicated by themselves, if you will. So we arrive at a key concept in understanding life. The shape that this RNA polymer can assume generates the catalytic function we call replicase, and this new property is called an emergent function. Another fun way of expressing an emergent function is to say that "you get something more from nothing but." The "nothing but" is this polymer and this polymer's ability to fold on itself. We're still just doing chemistry as we form internal base-pairs and generate the shape, but because of this chemistry we are getting a new function. We are getting replicase activity from a string of ribonucleotides.

Emergence is what biological evolution is really all about, as we'll see throughout this course. What keeps happening during biological evolution is that you make various macromolecules, and because of their shape they do something new, like we have here with our first replicase enzyme. If you just sit back now and think about life in general, whatever it is that you know about the evolution of life, you'll realize that that's what keeps happening over and over again (fins and flippers, and wings, and skin). What is of course the most interesting to us is a most recent emergent function, one that is to our mind the most important (not necessarily to an eagle's mind), which is this whole human ability to be aware of our awareness. There are lots of creatures that are aware -- indeed, I will argue that all creatures are aware -- but we have this other thing where we're aware of ourselves, an emergent function that happened during the course of evolving our enormous brains. Okay, I'll stop there.

[end of lecture]