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## How Did Life Begin?

An Interview with Andy Knoll

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What are the origins of life? How did things go from non-living to living? From something that could not reproduce to something that could? One person who has exhaustively investigated this subject is paleontologist Andrew Knoll, a professor of biology at Harvard and author of *Life on a Young Planet: The First Three Billion Years of Life*. In this wide-ranging interview, Knoll explains, among other compelling ideas, why higher organisms like us are icing on the cake of life, how deeply living things and our planet are intertwined, and why it's so devilishly difficult to figure out how life got started.

### A bacterial world

**NOVA:** When people think of life here on Earth, they think of animals and plants, but as you say in your book, that's really not the history of life on our planet, is it?

**Knoll:** It's fair to say when you go out and walk in the woods or on a beach, the most conspicuous forms of life you will see are plants and animals, and certainly there's a huge diversity of those types of organisms, perhaps 10 million animal species and several hundred thousand plant species. But these are evolutionary latecomers. The history of animals that we've recorded from fossils is really only the last 15 percent or so of the recorded history of life on this planet. The deeper history of life and the greater diversity of life on this planet is microorganisms—bacteria, protozoans, algae. One way to put it is that animals might be evolution's icing, but bacteria are really the cake.

**NOVA:** So we live in their world rather than the other way around?

**Knoll:** We definitely live in a bacterial world, and not just in the trivial sense that there's lots of bacteria. If you look at the ecological circuitry of this planet, the ways in which materials like carbon or sulfur or phosphorous or nitrogen get cycled in ways that makes them available for our biology, the organisms that do the heavy lifting are bacteria. For every cycle of a biologically important element, bacteria are necessary; organisms like ourselves are optional.

**NOVA:** What is your definition of life?

**Knoll:** I think you can say that life is a system in which proteins and nucleic acids interact in ways that allow the structure to grow and reproduce. It's that growth and reproduction, the ability to make more of yourself, that's important. Now, you might argue that that's a local definition of life, that if we find life on Europa at some time in the future, it might have a different set of interacting chemicals.

“The short answer is we don't really know how life originated on this planet.”

People have tried to find more general, more universal definitions of life. They're speculative, because we don't know about any life other than ourselves. But one definition that I kind of like says life is a system that's capable of Darwinian evolution. What does it require to have a system that evolves in a Darwinian fashion? First, you have to be able to reproduce and make more of yourself, so that fits with our local definition. You also need a source of variation so that all of the new generation is not identical either to the previous generation or to all its brothers and sisters. And once you have that variation, then natural selection can actually select, by either differential birth or death, some of the variants that function best. That may turn out to be a fairly general definition of life wherever we might find it.

### Launching life

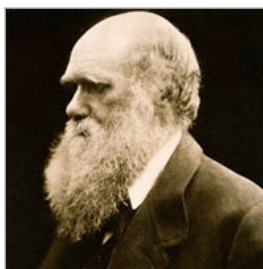
**NOVA:** What do you think was the first form of life?

**Knoll:** It's pretty clear that all the organisms living today, even the simplest ones, are removed from some initial life form by four billion years or so, so one has to imagine that the first forms of life would have been much, much simpler than anything that we see around us. But they must have had that fundamental property of being able to grow and reproduce



The particulars of the jump from nonliving to living that occurred sometime in our planet's early history is a profound enigma and will likely remain that way for some time to come, says Harvard's Andy Knoll.

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One way to define life, Knoll says, is something that adheres to the tenets of evolution by natural selection, as espoused by Charles Darwin.

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and be subject to Darwinian evolution.

So it might be that the earliest things that actually fit that definition were little strands of nucleic acids. Not DNA yet—that's a more sophisticated molecule—but something that could catalyze some chemical reactions, something that had the blueprint for its own reproduction.

**NOVA:** Would it be something we would recognize under a microscope as living, or would it be totally different?

**Knoll:** That's a good question. I can imagine that there was a time before there was life on Earth, and then clearly there was a time X-hundred thousand years or a million years later when there were things that we would all recognize as biological. But there's no question that we must have gone through some intermediate stage where, had you been there watching them, you might have placed your bets either way.

So I can imagine that on a primordial Earth you would have replicating molecules—not particularly lifelike in our definition, but they're really getting the machinery going. Then some of them start interacting together and pretty soon you have something a little more lifelike, and then it incorporates maybe another piece of nucleic acid from somewhere else, and by the accumulation of these disparate strands of information and activity, something that you and I would look at and agree "that's biological" would have emerged.

**NOVA:** In a nutshell, what is the process? How does life form?

**Knoll:** The short answer is we don't really know how life originated on this planet. There have been a variety of experiments that tell us some possible roads, but we remain in substantial ignorance. That said, I think what we're looking for is some kind of molecule that is simple enough that it can be made by physical processes on the young Earth, yet complicated enough that it can take charge of making more of itself. That, I think, is the moment when we cross that great divide and start moving toward something that most people would recognize as living.

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## Recipe for life

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**NOVA:** Is this an inevitable consequence of the conditions and chemicals and stuff that existed on early Earth?

**Knoll:** We don't know whether life is an inevitable consequence of planetary formation. Certainly in our solar system there is no shortage of planets that probably never had life on them. So it's a hard question to answer. I think the way I'd be most comfortable thinking about it is that you probably have to get the recipe right. That is, you need a planet that has a certain range of environments, certain types of gases in the atmosphere, certain types of geological processes at work, that when you have the right conditions, life will emerge fairly rapidly. I don't think we need to think about inherently improbable events that eventually happen just because there are huge intervals of time. My guess is that it either happens or it doesn't.

**NOVA:** Has there been a change in thinking about this over the years?

**Knoll:** People's ideas on the circumstances under which life might emerge have really changed and developed over the last 30 or 40 years. I think it's fair to say that when I was a boy those few people who thought about the origin of life thought that it probably was a set of improbable reactions that just happened to get going over the fullness of time. And I think it's fair to say that most of those people probably thought that we would find out what those reactions were, that somehow we would nail it in a test tube at some point.

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“To a first approximation you're just a bag of carbon, oxygen, and hydrogen.”

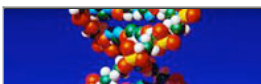
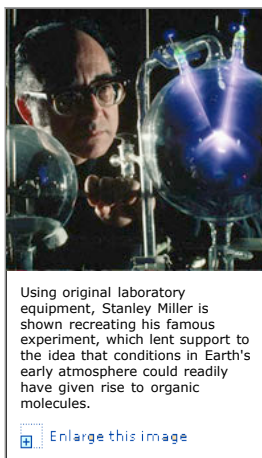
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Now I think, curiously enough, both of those attitudes have changed. I think that there's less confidence that we're really going to be able to identify a specific historical route by which life emerged, but at the same time there's increasing confidence that when life did arise on this planet, it was not a protracted process using a chemistry that is pretty unlikely but rather is a chemistry that, when you get the recipe right, it goes, and it goes fairly quickly.

**NOVA:** What *is* the recipe for life?

**Knoll:** The recipe for life is not that complicated. There are a limited number of elements inside your body. Most of your mass is carbon, oxygen, hydrogen, sulfur, plus some nitrogen and phosphorous. There are a couple dozen other elements that are in there in trace amounts, but to a first approximation you're just a bag of carbon, oxygen, and hydrogen.

Now, it turns out that the atmosphere is a bag of carbon, oxygen, and hydrogen as well, and it's not living. So the real issue here is, how do you take that carbon dioxide in the atmosphere (or methane in an early atmosphere) and water vapor and other sources of hydrogen—how do you take those simple, inorganic precursors and make them into the building blocks of life?

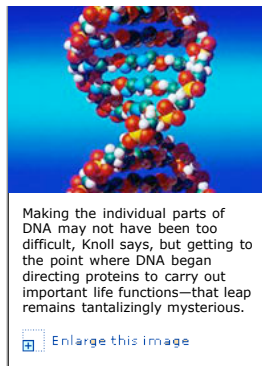


There was a famous experiment done by Stanley Miller when he was a graduate student at the University of Chicago in the early 1950s. Miller essentially put methane, or natural gas, ammonia, hydrogen gas, and water vapor into a beaker. That wasn't a random mixture; at the time he did the experiment, that was at least one view of what the primordial atmosphere would have looked like.

Then he did a brilliant thing. He simply put an electric charge through that mixture to simulate lightning going through an early atmosphere. After sitting around for a couple of days, all of a sudden there was this brown goo all over the reaction vessel. When he analyzed what was in the vessel, rather than only having methane and ammonia, he actually had amino acids, which are the building blocks of proteins. In fact, he had them in just about the same proportions you would find if you looked at organic matter in a meteorite. So the chemistry that Miller was discovering in this wonderful experiment was not some improbable chemistry, but a chemistry that is widely distributed throughout our solar system.

**NOVA:** So life is really chemistry.

**Knoll:** Life really is a form of chemistry, a particular form in which the chemicals can lead to their own reproduction. But the important thing, I think, is that when we think about the origin of life this way, it isn't that life is somehow different from the rest of the planet. Life is something that emerges on a developing planetary surface as part and parcel of the chemistry of that surface.



Making the individual parts of DNA may not have been too difficult, Knoll says, but getting to the point where DNA began directing proteins to carry out important life functions—that leap remains tantalizingly mysterious.

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“Life is really part of the fabric of a planet like Earth.”

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Life is also sustained by the planet itself. That is, all of the nutrients that go into the oceans and end up getting incorporated into biology, at first they're locked up in rocks and then they are eroded from rocks, enter the oceans, and take part in a complex recycling that ensures that there's always carbon and nitrogen and phosphorous available for each new generation of organisms.

The most interesting thought of all is that not only does life arise as a product of planetary processes, but in the fullness of time, on this planet at least, life emerged as a suite of planetary processes that are important in their own right. We're sitting here today breathing an oxygen-rich mixture of air. We couldn't be here without that oxygen, but that oxygen wasn't present on the early Earth, and it only became present because of the activity of photosynthetic organisms. So in a nutshell, life is really part of the fabric of a planet like Earth.

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### Building a being

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**NOVA:** To get back to these basic chemistry building blocks, is everything from a mouse to a bacterium to you and me made from this simple set of ingredients?

**Knoll:** All life that we know of is fundamentally pretty similar. That's why we think that you and I and bacteria and toadstools all had a single common ancestor early on the Earth. If you look at the cell of a bacterium, it has about the same proportions of carbon and oxygen and hydrogen as a human body does. The basic biochemical machinery of a bacterium is, in a broad way at least, similar to the chemistry of our cells.

The big difference between you and a bacterium in some ways is that your body consists of trillions of cells that function in a coordinated manner. Bacteria are single cells, although they're not free agents. In fact, bacteria working in a sediment or in the sea actually live in consortia as well. They're not really lone operators. They work in these very, very highly coordinated communities of organisms that help each other to grow and prosper.

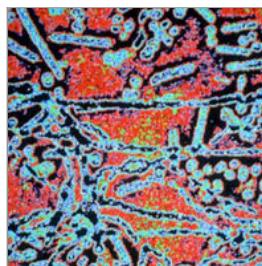
**NOVA:** Is it hard to go from these little building blocks to a full-fledged organism?

**Knoll:** Well, we don't know how hard it is to go from the simplest bricks, if you will, in the wall of life to something that is complicated, like a living bacterium. We know that it happened, so it's possible. We don't really know whether it was unlikely and just happened to work out on Earth, or whether it's something that will happen again and again in the universe.

My guess is it's not too hard. That is, it's fairly easy to make simple sugars, molecules called bases which are at the heart of DNA, molecules called amino acids which are at the heart of proteins. It's fairly easy to make some of the fatty substances that make the coverings of cells. Making all of those building blocks individually seems to be pretty reasonable, pretty plausible.

The hard part, and the part that I think nobody has quite figured out yet, is how you get them working together. How do you go from some warm, little pond on a primordial Earth that has amino acids, sugars, fatty acids just sort of floating around in the environment to something in which nucleic acids are actually directing proteins to make the membranes of the cell?

Somehow you have to get all of the different constituents working together



When it comes to understanding how our world gave rise to advanced creatures, “I think we have to admit that we're looking through a glass darkly,” Knoll admits.

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and have basically the information to make that system work in one set of molecules, which then directs the formation of a second set of molecules, which synthesizes a third set of molecules, all in a way that feeds back to making more of the first set of molecules. So you end up getting this cycle. I'm not sure we've gotten very far down the road to understanding how that really happens.

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### Through a glass darkly

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**NOVA:** In your book, you liken the study of the origin of life to a maze.

**Knoll:** Yes. There are multiple doors that enter the maze, but there's really only one historical path that life took. I think that while we've had some very clever entryways into several of these doors, at this point we still don't know which of these pathways ultimately will thread us through the maze and which end up in a blind alley.

**NOVA:** So at this point we're seeing the origins of life through a glass darkly?

**Knoll:** If we try to summarize by just saying what, at the end of the day, do we know about the deep history of life on Earth, about its origin, about its formative stages that gave rise to the biology we see around us today, I think we have to admit that we're looking through a glass darkly here. We have some hints, we have a geologic record that tells us that life formed early on the planet, although our ability to interpret that in terms of specific types of microorganisms is still frustratingly limited.

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“I imagine my grandchildren will still be sitting around saying that it's a great mystery.”

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There are still some great mysteries. People sometimes think that science really takes away mystery, but I think there are great scientific mysteries and causes for wonder and, most importantly, things that will, I hope, stimulate biologists for years to come. We don't know how life started on this planet. We don't know exactly when it started, we don't know under what circumstances.

It's a mystery that we're going to chip at from several different directions. Geologists like myself will chip at it by trying to get ever clearer records of Earth's early history and ever better ways of interrogating those rocks through their chemistry and paleontology. Biologists will chip at it by understanding at an ever deeper level how the various molecular constituents of the cell work together, how living organisms are related to one other genealogically. And chemists will get at it by doing new experiments that will tell us what is plausible in how those chemical correspondences came to be.

**NOVA:** Will we ever solve the problem?

**Knoll:** I don't know. I imagine my grandchildren will still be sitting around saying that it's a great mystery, but that they will understand that mystery at a level that would be incomprehensible to us today. ■

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Interview conducted on May 3, 2004, by Joe McMaster, producer of "Origins: How Life Began," and edited by Peter Tyson, editor in chief of NOVA online

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