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NOTES:

NOBLE: Lynn, you're going to say a few words before the --

MARGULIS: I'm going to try to translate what was said already. I mean, because I know that --

NOBLE: I thought there might be an agenda.

MARGULIS: I have great teachers, here, and I think I have some idea of what they were saying, and I just want to summarize, go back a minute. Steve Bell has an assumption that's verified by everything they do. And that is that Darwin was completely right, that all life on Earth has common ancestry. And you can tell that by the biochemistry of replication. Is that not right? That, in spite of things that happened afterwards, there's no other form of life, in fact, in the entire solar system, or universe, that we know of. Life on earth is all through common ancestry, and today's lineage has DNA as the reproductive molecule. Then we can start arguing, and we'll start arguing next. He shows the topology, that all life comes from a common ancestry, and I think all Darwinians, we completely agree. Do we not? Everybody agrees. It's a brilliant insight of Darwin, that we can laud. But the concept, that the tree is the right topology, I think is very wrong. It's very wrong. Even Woese's tree. Because a tree assumes

that the lineages continue to branch, and branch, and branch, from a common ancestor. And Stephen Bell, himself, showed that there was movement of genetic material from one branch to another. That makes the topology a net, a web, and no longer a tree. That's the basic point I wanted to make. Let's discuss it. Then, if we go to Marlton, I would have said the man back there, the theology student? Are you still there? Is the view, [LAUGHTER] what's your name?

MAN: William.

MARGULIS: Yes, William. I would have thought you would say, [SOUND OFF/THEN ON] say about [all the fuss?], the Lord has delivered him into my hands, when he was asked, on what side of your family are you evolved from? An ape? Is it your grandfather's side, your mother's side? Why? Because William is pointing out, I think, an amazing point, that Martin really didn't express, that all of us understood. It took me a long time to understand, I'm not sure I understand it yet. But the idea is that, not just the individual or the animal is the unit of selection. Community is the unit of selection. A community are populations of organisms in the same place, in the same time. Those forams that he was talking about, although they seem like single cells, are communities, because they have, the

ones doing the agriculture inside, you know, the photosynthetic ones, the diatoms, and the green algae, and the yellow green algae that he mentioned, inside. Those are the farmers inside the bodies. These forams are body farming. They are shelled, marine organisms that are growing their own food, by growing, they're plantlike, they're not plants at all, but plantlike algae inside the tests. And therefore, what is the unit of selection? At the very minimum, the unit of selection is the foram and its algae, and if we count genomes, there, we have, usually, three for the algae and three or four for the forams. You have seven different genomes. So, clearly, the unit of selection isn't a single gene, or a single genome. Why? I love Richard's metaphor, of the selfish gene. Because it focuses attention on the science behind natural history. But of course it's just a metaphor, because a gene doesn't have a self. A gene is not a self. How can something be selfish if it has no self? The self, and I think he uses it metaphorically [UNINTELLIGIBLE PHRASE]. The self is the cell. All cells have self, and the self has been forgotten. And even in hearts and livers, the self has been forgotten. And this is my introduction to arguing, the topology that's taught is not right, in my opinion. The idea that accumulation of random mutations is the way species change, from one species to another, has very little evidence for it. And, the junk DNA is

just another way of saying, we don't know what the DNA is doing. Is that not what you said, Denis?

NOBLE: That's roughly what I would say.

MARGULIS: That's what I'm saying. You're next. [LAUGHTER] I'm saying that, what Denis is trying to point, that, as we learn more and more, first of all, there's just too, numerically, it's just too many possibilities, and the number expressed are very much smaller. And just can't play with the numbers. The idea that there's junk protein, or junk DNA, is, as Jonathan Bard just said, it's not a useful idea. It's not a useful idea. The idea that there is something, and reasons for this, for these enormous number of possibilities, leads you to seek the reasons. You don't know what they are. We don't know what they are. But Denis' point is that, let's not assume that there's no reason behind this so-called junk DNA, or these protein combinatorics, when there's so many of them. Well, I want to go back to make one point, that's expressed in this film. And that is, the unit of life on Earth is the cell, and there are two kinds of cells. And, I mean, you said prokaryotic and eukaryotic, but just think this way, bacteria-like cells, and animal, plant, fungal, and so-called nucleated cells. Those are the two kinds of life. And, yes, there's a lot of archaea,

as Stephen Bell said, archaea background, in all nucleated organisms. But there's all sorts of eubacteria, also. So, this is what I wanted to show you, in this film. First of all, that we're going to act on the self, the real self level, and that's the cell level. The cell, even a bacterial cell, shows all the properties of life, all the time. And it's bounded by a membrane that must be there, to define the self. All of those cells have the potential to reproduce, at rates beyond the environment. No environment can ever support the prodigious potential for reproduction of any life form. And the fact that the life forms do not continue into the future is natural selection. That's what natural selection is, the fact that the life forms don't continue. So, what I want to show you is a film, of 14 minutes, that shows our current model, idea, of how we got the animal type cell. Now, when I say animal type cell, I really mean, plant cell, protoctist cell, fungal cell, molds, yeasts, fungi, all of these cells that we study in biology classes, and that we don't study in microbiology classes. So, we have two kinds of cells, the bacterial type cell, that has no familiar organelles, including the nucleus, and the other kinds of cells, which are the typical biology that we all study. Now, how did we go from a bacterial type cell, that has a single continuous genome in it, to all the nucleated cells, which have more than one? And the argument is going to be, a product of

symbiosis, two kinds of symbionts at the very base, and one of them is Stephen's archaea, archaebacteria, to me, but archaea, that kind of stuff. And the other is another familiar cell, it's not familiar, it's notorious, because that kind of cell is known, to medical people, as the cause, not kind of cell, it's a phylum, of eubacteria, for those of you into that, microbiology. Phylum of eubacteria. They're called spirochetes, and you know them because they cause syphilitic cankers, and they cause Lyme disease, and so on. That's how they're familiar, because the medical profession deals with the freaks. But the claim, here, is going to be that this kind of cell was intimately involved in an archaebacterial cell, the kind of cell that Stephen Bell was talking about, in the first fusion, to form these little protists, protoctists. And that occurred before there was oxygen freely around in the atmosphere. There's always traces. But, before the big oxygen conversion. And what I, the only point, here, is that I'm not going to show you anything but live material. So, I'm going to, well, that's not true, there's a diagram. There's, Jim MacAllister is back there, over there, did the animation, there's an animation, to make the live material clearer, and put it in an order that we think is a temporal order, in [our life?]. Anyway, so, the film will start with spirochetes, which are the ancestors, if we're correct, to the sperm tails of more than half the people in the room, and

the oviduct cilia of the others. [LAUGHTER] So, between you, we all have those. So, anyway, we're going to see those organisms on their own. Then we're going to see the archaebacterium, which is a crenarchaeota. It's thermo, well, it's close to it. You say thermoplasma is not in it? [OVERLAPPING VOICES] Yeah, OK. Well --

MAN: We can discuss this --

MARGULIS: Yeah, no, that's fine. [LAUGHTER] It's a sulphur, it's a sulfidogenic acid tolerant organism, that is our best bet, right now, for the archaebacterial component. So, we have a eubacterial component, an archaebacterial, by themselves. And then we're going to have all these organisms that are swimming around together, and then we'll end up with our eukaryote at the end, and we're, there's no missing links, in the sense that we have everything represented in the live material. So, that's, you mean I have to sit over there, and [OVERLAPPING VOICES] off, off, off. [LAUGHTER] [MUSIC PLAYS IN BACKGROUND] This word means the origin of nucleated cells, the familiar cells of animals, plants, fungi, protoctis, which would mean algae and all sorts of others. Now, this is a spirochete bacterium. It's a eubacterium, with the eubacteria type of replication that Stephen mentioned. And this one, these are still photos. We

need to see what they are, live. First of all, they can't tell their faces from their ends, their other ends. Like people, some people we know, maybe. [LAUGHTER] I don't know. But, anyway, they go, this is, there are many, many spirochetes in the picture. It's the large one, that we see very clearly. It translates, as it rotates. That is, it rotates as it moves forward, and rotates as it moves back. And it has a corkscrew type or morphology, which means that it wins races to lots of bacteria, when the medium is viscous, when it's gel-like. And you'll see that there are some much smaller ones, in the background. It's a gram negative bacterium, that has bacterial flagella in its periplasm, that is, between its inner membrane, which is the classical cell membrane, and the outer membrane. And it develops huge concentrations, and these organisms interact. Now, there are some spirochetes, these are from microbial mats, this is a different one, that, when they are threatened by many things, here's a diatom, which is outside, in marine water, this is the spirochete in question, which I'll explain in a minute. Now, this is a cyanobacterium that's producing both food and oxygen. And these spirochetes have learned to chase them. Now, watch that. This is light-sensitive. The reason these spirochetes are light-sensitive is because they like to stay in sunlight, where their food is produced. They follow their food. This means that the

sensitivity to sunlight and to mechanical stimulation, and many other things, of course chemosensitivity, are already present, in this group of organisms. They are not photosynthetic at all, they just stay in the light. Now, this is a strobe light view, because, if you have the real spirochetes, it looks like this. They swim together, and we know that they're not permanently associated, because if we add water, they just swim all over the place. And if we remove the water, slowly, you'll get this kind of, not water, usually a more viscous media, but you will get this kind of group behavior. Now, it is a property of the entire group that's being studied, that, when conditions become unfavorable, they form what are known as round bodies, vesicles, there's all sorts of names for them. Cysts, in some cases. But they actively form them. Watch this one. And they produce these round bodies, that actually have spore-like structures. They're not at all boil-proof or anything, but they are desiccation resistant. And here's a round body, formed. This one is in the process of forming one. And what they do is, they swell up their outer membranes, and they bring their bodies inside. Here's, the swelling starts, first. The only reason we have this particular series of shots is because we changed the medium to a kind of food they don't like. So, watch this piece. So, you have, in these bacteria, sensitivity to light, to touch, and mechanical activity. Here's an electron micrograph of the

spirochete moving in and forming a spore-like structure. And they will wait for, we know for at least, I think, five years, before they come out again. Now, this is in the South Pacific. This is just a group of algae, brown algae. And the white stuff, here, turns out to be this spirochete, that is requiring sulfide, HS-minus ion, or H2S gas. It's the same one as this, this is the Massachusetts version. The other is the Russian version. And, to conquer the threat of atmospheric oxygen, they produce sulfur and deposit it. Now, this is a change of scene, completely. This is the archaebacterium that we think developed the association with the spirochetes in the origin of the earliest nucleated organisms. And, if you look carefully, they have little processes. They have little things sticking out. We'll see what that looks like at the electron micrograph. Now, these organisms generate sulfide. The spirochetes would like them, because they go toward the sulfide. And, in the presence of oxygen, they will, also, excuse me, they will use the sulfide. This bright stuff is elemental sulfur. They will use the sulfur, it's terminal electron acceptor. If you don't get that, that's all right. They use the sulfur, and they use these hydrogens from their food, and generate sulfide. Now, this is another scanning electron micrograph of exactly those same bacteria. And, notice that they are pleomorphic, that is, they don't have a rigid cell. We assume that the sulfur globule

dropped out, in preparation. And here, we have one, two, three, four, five, six. And the concept, here, is that this is the other partner that developed a relationship with spirochetes, to form this. Now, this is a eukaryotic structure. These are cilia, or undulipodia. These are, this is the DNA associated with the cilia that are underneath the nuclear membrane, and that's just plain nuclei. If you section the cilia, or any undulipodia, or your sperm tails, or your oviduct cilia, you find that 9+2 organization, that nine sets of microtubules. This organism is affectionately called rubberneckia, because it makes a complete circle of its nucleus. This is the nucleus, in here. And this is a typical organism, that has at least seven different bacteria making it up. And the reason we have that, here, is because the nucleus, the undulipodia, kinetosome, centrioles, and the Golgi, fall off, in an easy way. So, they have a structure that's been known, for years, to the old-timey protozoologists, that probably represents the earliest step in the origin of the nucleus. Here is the nucleus of that organism, rubberneckia. Now, this is the poster child of what we're saying. Now, what do I mean? This organism is called mixotricha paradoxa, which means mixed-up hairs, paradoxical. In 1956 or so, Cleveland went to Australia, to study this organism. Here is its nucleus and nuclear connector. Study this organism, because he was told it had flagella and cilia on

the same organism. Those are, that's both wrong. This is a symbiotic complex of about 400,000 different bacteria. And this is the nucleus, then the nuclear connector. And this particular one, well, you can see it in a live cell, [you could a minute ago?], the nucleus and the nuclear connector. Mixotricha has, is a trichomonad, like trichomonas vaginalis, but it's a hundred times larger. And these things, that look so much like cilia, turn out to be a Treponema spirochete, and another kind of basilisk-shaped bacterium. And we have 100,000 of these, and 100,000 of these, per single mixotricha. And before division, OK, so here is one bacterium, and the other bacterium, and we have something that looks very much like the cortex of a ciliate. But it isn't. It's two kinds of spirochetes and one other kind of bacterium. Furthermore, in the same habitats that this organism lives, and on the organism itself, is another bacterium, a spirochete morphologically indistinguishable from the Lyme Disease spirochete, and that's at the base, the back of mixotricha. So, here's mixotricha, it's like a garbage truck. It goes forward in this direction, and senses in this direction, and takes in wood, in the back. And if we go to the back portion, we see even another kind of symbiotic bacterium. So, here's, these are the Treponema spirochetes. These are two different other kinds of spirochetes. And this is another organism living in the same habitat, where the rear, the back

end are all spirochetes, and the front end are completely evolutionary homologous. This is the back end, those are spirochetes. The front end are the evolutionary homologues to your sperm tails or oviduct cilia, as the case may be, because they have nine tubule, arrays with nine tubules. These are, this is a different, still a different spirochete, that has tubules in the cytoplasm. We don't know the composition. But the tubules are coming out of the cytoplasmic tubule associated center, here. What we're saying is that the sensitivity to light, to mechanoreception, to chemoreception, and tubules themselves evolved in spirochetes. Now, this is a bacterial flagellum. And on the inside of that flagellum are cytoplasmic tubules, but they are not the same as those found in eukaryotes. But they show you that spirochetes have a whole range. Now, this is a single cell, mating with five other bacteria, simultaneously. These are sperm, those were sperm, and these are the naked tails. No DNA, no mitochondria, no membranes. These are the naked tails, and they move like spirochetes, because that's where they started. They will only last about 45 minutes, but they last long enough to photograph that. And if you weaken the protein bonds in the sperm tails, with a little trypsin, the sets of doublet tubules extend. They're trying to move and undulate but they can't. So, they extend the fragments nine times the size, so that you know, there are the sperm,

again. It doesn't matter whether the sperm have their DNA or mitochondria at all, their tails act. Now, this is what the sperm tails look like, nine sets of doublet microtubules with two in the center. Now, we know that the motility apparatus of the 9+2, here are 9+2's, in this particular cell, are directly involved with the origin of the mitotic spindle, and the mitosis process. Here is mitosis, in one of these protists. Doesn't have any mitochondria. The protists have the, these are the heads of them. They have the 9+2 apparatus. Here, we have, in a fungus, a microtubule organizing center. Here's another kind of protest. And, like many of them, if it's doing cell division, it has a lot of trouble swimming. Because it's using the swimming, undulipodia cilia microtubules, for mitosis. And it can't do both at the same time. This is a culture of all the same, you've seen all the same protists, in this particular picture. Now, such an organism required mitochondria, from ingestion and failure to digest respiring bacteria, and then, later, such an organism that already had undulipodia and already had mitochondria ingested, but did not digest cyanobacteria, to become an algae, basically. And all of the action is in this structure. This is tubulin, this is, these are the proteins and DNA associated with the centrioles, centrisomes and all the rest of that. Now, here is our cartoon. The spirochetes are attracted to the sulfide being generated by the archaebacterium.

Now, both the spirochetes and the archaebacterium have the entire set of genes, and the replication apparatus. The pressure, selection pressure that's maintaining them both, they're both heterotrophs and they're both fermenting, is that the motility that the spirochetes attach is about 60 times faster than the motility in the archaebacterium by itself. And the archaebacterium, on the other hand, is sticking to the sulfur and generating sulfide. So, under these conditions, we have a syntrophy, where the spirochetes are attracted to the sulfide, and the nucleus connector evolves as a way of keeping the symbionts together in a sulfide-rich environment, away from the oxygen, but oxygen leaks in. And, under those conditions, sulfide is oxidized to sulfur. This whole organism, this whole symbiotic complex, becomes a sulfur syntrophy, motile structure, in which there is a bacterial conjugation leading to, and a lot of membrance proliferation, leading to the very earliest eukaryotes. This is not LUCA, the Last Universal Common Ancestor. It's LECA, the Last Eukaryotic Common Ancestor. And they're beginning to look like what people call little amastigotes, or flagellates. And here, we have oxygen rising, oxygen rising. And this is an Alphaproteobacterium, or probably another non-Alphaproteobacterium, but one that respires oxygen, totally. We now have the origin of the mitochondrion, inside, and phagocytosis is rampant, here. And so, we have the

ingestion, and failure to digest cyanobacteria. So, we now have, really, an algae. It has two of the 9+2 structures that are used in the mitotic process. It has become oxygen-using, and, well, this is the greatest bacterium of all, because it makes all the food, and handles oxygen. Now, we have legacies of this. This is an electron micrograph, of an amitochondrium, a cell that has no mitochondria. And here, we see that the undulipodium, the 9+2, is attached directly to the mitotic apparatus. And here's another example, of a different organism. Again, we have the centriole kinetosome, and here is the cilium, one of the undulipodium, in this case. And it's attached, on the other side, to the nucleus. The credits. [APPLAUSE] So, I'm very happy to take questions.

NOBLE: It seems to me that one way of interpreting what you're saying is that inheritance is not just DNA.

MARGULIS: Certainly.

NOBLE: Right. So, do we have to redefine a gene? See, it seems to me that, what has happened, let me just explain the background to this. What has happened is that, effectively, molecular biology has redefined what a gene is. It's become a sequence of DNA. That's --

MARGULIS: It used to be a factor, and [OVERLAPPING VOICES] --

NOBLE: That's what it was, originally. Now, the question, I think, is that, to use a phrase that was used in an earlier question, is that a useful, and helpful, way of looking at it?

MARGULIS: It was. It was.

NOBLE: Or, the molecular, biological definition of a gene? Because even that has got into trouble, now, with the intron, exon story, and the epigenetics that has to go with all of that. Now, my question, really, to you, and possibly to the rest of us, as panelists, before we open the discussion up, is, do we really have to redefine what a gene is, or do we abandon the name gene to the molecular biologists, and come up with some new name, for whatever it is that is important in inheritance?

MARGULIS: Well, see, I think it's unnecessary to abandon the idea that DNA is a piece of, that genes are pieces of DNA. I think what's totally crucial is to recognize that the minimal unit of cell, of life, is always a cell, and therefore it's always a gene in a context of protein synthesis and energy transfer, and so on. And that is the unit of heredity. It's

not, the gene is [OVERLAPPING VOICES], the gene is the blueprint, it's not the building.

NOBLE: This is partly a problem of how you describe biology, isn't it?

MARGULIS: Yes.

NOBLE: You've got either to abandon, it's actually the right word, the use of the word gene, to the molecular biologists, and then say that inheritance is more than DNA, or you've got to go back to something like the original idea of a gene. That's, I think, the point I'm making.

MARGULIS: Again, I would just suggest that [OVERLAPPING VOICES] --

NOBLE: Yeah, well, maybe we'll just simply put that on the table, for the moment. Do any of the other panelists want to come in, before we start to raise, open the discussion to the floor, as it were? First of all, questions, obviously, to Lynn, on what she's shown in her film. Yes. You came in earlier, but I think, if you say your name again, it helps the recording.

SIEGEL: Robert Siegel. I have a couple of fundamental questions. One is that, you paint this view that the bigger organism is in charge, and one of the principals of microbiology is that the smaller organism is almost always in charge.

MARGULIS: No, I don't speak about in charge, or cooperation, or competition --

SIEGEL: Well, you just said it takes up, you said the cell takes up the other one.

MARGULIS: I mean it by phagocytosis, a property only found in eukaryotes. It does.

SIEGEL: It's actually not true, because what happens is, there are microorganisms that actually have the ability to go inside cells, and they actually [force?] [OVERLAPPING VOICES] --

MARGULIS: They're not phagocytosis. You're talking about the [OVERLAPPING VOICES] --

SIEGEL: That's how, no, lots and lots, [whole?] viruses have the ability to force themselves --

MARGULIS: Well, viruses are not organisms. Let's start there. We'll define --

SIEGEL: Well, that's the second point I want to make [OVERLAPPING VOICES] in terms of the unit of selection, viruses are clearly a unit of selection. In fact, they're a much more rapid unit of selection, and cells take up their genes, and pass back and forth between them all the time. So, just as, in the most basic form, you can't actually argue that cells are the basic unit of selection, because there are some --

MARGULIS: I said, I didn't say that. I said communities are.

SIEGEL: There are smaller --

MARGULIS: I said, cells are the basic unit of life.

SIEGEL: That's a definitional thing.

MARGULIS: It's all definitional. [LAUGHTER] [OVERLAPPING VOICES] but there's nothing less than a cell that shows all properties of life. Viruses are part, only show them when they get into other cells, live cells. It's, you know, a question of

calling [a bull?], from the time he's, before and after he dies. I mean, there really is a difference.

NOBLE: Yes, you wanted to come, say your name.

LEMIEUX: Yeah, my name is Jacob Lemieux. It seems like an alternate explanation for the shared organization of the, I think it was the nine --

MARGULIS: What is an alternate?

LEMIEUX: I have to finish. The shared, the nine microtubules, the two pairs of those. Is it, it evolved beforehand, and then it was passed to the spirochetes, and then, you know, the sperm and the --

MARGULIS: The evidence is the other way. That the single tubules are present, from much smaller to standard size, in spirochetes, but the 9+2 organization is only found, as far as I know, in eukaryotic cells, and that, probably, it coevolved with eukaryotes. I don't know that. If we had a 9+2 spirochete, we could argue the other way. But, right now, we can only argue that the 9+2 evolved in eukaryotes, but the important point is that they are all homologues. Nobody is going to disagree with

that. The structure, which is always a quarter of a micron wide, and it's 12 microns long. It has the 9+2. They are evolutionary homologues of each other, so they have a common ancestor. Whether they came from the microbiology to begin with, from bacteria to begin with, or whether they came in the earliest eukaryotes, we don't know. But that they came is, there's a common ancestry, there, that we can say, definitively, because there are about 600 proteins, involved in there, in common. OK?

NOBLE: Can we first see if there's any further questions directly to Lynn, and then I was going to open up to more general discussion. There's somebody over here, then here. Please, say your name.

SOLOMON: My name is [Chaz Solomon?]. I studied medical anthropology. Regarding, if we start to look at the relationships between these organisms that develop, the suggestion that you made was that DNA may not, the level of inheritance may not be at DNA. And you gave the analogy of the gene being the blueprint, and the organism being the building. Doesn't it, doesn't the notion of symbiogenesis suggest that the blueprint is within this relationship between these organisms? And the level of inheritance is actually this relationship,

that's passed down? Not so much the composite genes, themselves. Or, composite pieces of DNA. And that, maybe what we should redefine as the gene would be that relationship?

MARGULIS: That's certainly one way of solving it. The recognition that the genes, by themselves, are the, program the rest of the cell. They have, genes, by themselves, can be flushed down the toilet with no struggle. That is, they have no self. Because in order to show the properties of life, and we can talk about what those are, but there are always material and energy flow. You have to have more than the gene. You have to have the system, of a gene expresses itself. We heard a little bit about that, today. And in my view, that's a cell, minimally. It's also something much larger than a cell, often. Nothing less than that. A virus absolutely does not fit that definition, and I would turn to the Chilenos, who did this formally, and they called it autopoiesis. They called it self-maintaining. They said something, when I was a student, I was taught that evolution what, I disagree with all of it, now. That evolution was entities that replicate, that mutate, and replicate their mutations. And therefore, grandmothers, like me, and mules, who are infertile, are not alive, because they don't replicate. They don't pass their mutation. And I would say that, it's the definition, that way, that's the problem.

It's that kind of issue. And the minimal unit that shows absolutely every aspect of life is an autopoietic one, which means that it has a boundary, and that boundary is, inevitably, at least a lipoprotein membrane. Sometimes it's more. But it's always a lipoprotein membrane. And that body, that entity, can maintain itself, always, with energy flow. And the energy is almost always, it's chemical or light, usually. And that it's also, by itself, able to build up matter. And it's not programmed from the outside, at all. It's on the inside that these properties, that this autopoiesis exists. It comes from the inside. It also, of course, has to be in an environment that permits this. But anyway, I would say that the minimal autopoietic entity is a bacterial cell. That most of the diversity of life is in the bacteria to begin with, in the bacteria's [UNINTELLIGIBLE]. And that a virus is absolutely not that, at all, and never will be. It can't be, in principle. There's nothing, food or energy, that you can give a virus, to make it show the minimum properties of life. And so I would say that the unit of heredity is that, and whether we call it a gene or whether we call it a cell, that should, it has to be discussed. But we, at least, should be talking about the same thing.

NOBLE: I'm going to hold it, at that particular point, there, and also hold on, coming to the next question, because I think, Richard, you --

DAWKINS: [OVERLAPPING VOICES] quite unnecessarily confused, here. A cell is the minimal unit of living function, of course it is. But that's not the unit of heredity. Unit of heredity is DNA, or RNA, under some circumstances. We're just confusing a unit of life, which is a cell, with a unit of heredity, which is DNA [OVERLAPPING VOICES] RNA.

NOBLE: Well, that's what I'm not sure about.

DAWKINS: I know. But, why? [LAUGHTER]

NOBLE: If I were to want to send, to one of those Goldilocks planets that the astronomers think they've found, the information necessary for them to reconstruct life here on Earth, it would, obviously, make no sense for me to put on a CD the whole of a human genome.

DAWKINS: That's correct. That's correct, yes.

NOBLE: That's correct. OK. That much is obvious, right. So, I would have to send the whole of, at least, a fertilized egg cell, information, on that CD, for them to even begin. I mean, let's forget, for the moment, about the complexity, that you need a womb and all the rest of it, too. But I'd have to send the whole of that to the Goldilocks planet, too. Now, it seems to be that, what part of our difficulty is, here, is, what do we mean by inheritance? Because, to me, that means that we inherit the whole fertilized egg cell. And, indeed, we inherit more, because we inherit the maternal and paternal influences on that egg cell, as it develops. So, is this a matter of defining what we mean by inheritance? And are we, as it were, prescribing that it shall only be that DNA is inheritance? [OVERLAPPING VOICES] I think you should, Richard, yes, that's right. [LAUGHTER]

DAWKINS: When you send your, when you cede life to your Goldilocks planet, you have to send the information, the DNA, plus the water and the [OVERLAPPING VOICES] the other things that are [OVERLAPPING VOICES]. Now, the key point, that makes the difference between hereditary substance, code, and all the other stuff, is this. If you mutate the non-hereditary part, for example, if you make some kind of manipulation to the cell, not the hereditary part, but to the cell, that will not be

transmitted to the next generation. If you mutate the DNA part, it will. Now, if you mutate the non-DNA part, you may well scuttle the whole enterprise. That's possible. But what you won't get is a copy of, I mean, if you cut up a cell, or make a blemish in it, in some way, or a blemish in an organism, it will not be passed on to future generations. If you make a blemish in the DNA, it will. That is the key point, certainly from a Darwinian point of view. That is an absolutely watertight, operational definition, of the distinction between the true, hereditary part of the entire enterprise. The entire enterprise, you need to send to the planet. That's not in doubt. The entire shooting match, the entire, but if you change a bit of it, and the change is inherited, that's heredity.

NOBLE: Well, now, if I change a cell, by taking, say, an egg cell from another species, and I put a genome into that cell, I can get development up to a certain point, and then it freezes. It doesn't, you have extremely few cases of cross-species cloning, that lead to a living organism. And what that tells me is that the genetic program, if we can use that metaphor for a moment, lies as much in the cell as it lies in the genome. And I think this is a matter of language, how we choose to describe the biology that we now know about. And to the question whether cellular inheritance can occur, and whether inheritance, over

and above the transmission of DNA, can occur, I think that the development of epigenetics has thrown a cart and horses through that particular [OVERLAPPING VOICES]. Yeah.

DAWKINS: And I'm not talking, because that's coming close to being a difficult, borderline case. The reason it doesn't actually drive a, whatever you said, coach and horses through it, is that the epigenetic pseudoinheritance dies away after three or four generations.

NOBLE: Well, that's what we're not sure about. Who has proven that?

DAWKINS: That's one, OK. If it does, if it doesn't, if it goes on forever, then it's a fully [paid out, pack up?] form of genetics.

NOBLE: But then we have to redefine what we mean by a gene.

DAWKINS: Yes, we do. It's that --

NOBLE: Because it's clearly not in the sequence of DNA, is it?

DAWKINS: The key question is, does it go on from there?

NOBLE: Yes. That's --

DAWKINS: Or does it just fade away?

NOBLE: That's the question that, I think, is an empirical question, open to discovery.

DAWKINS: That's an empirical question.

NOBLE: Yeah. OK. But I don't want to dominate this discussion, or that Richard should, either. There's plenty of further things that he and I can discuss, I'm sure. But let's go back. You wanted to come in. Yeah.

GALLAGHER: Yes. My name is Alexis Gallagher. A couple of the disagreements here, I've heard the argument phrased in terms of, this or that is the unit of selection. And I was just wondering if everyone here can agree on what they mean by unit of selection, when they say that. Because it seems like that's, sometimes, wielded as a razor, to simplify the problem, but actually, it strikes me as somewhat, a phrase that has ambiguities embedded in it. I just wondered if there was an

operational definition that everyone is actually on board with, before we keep using that phrase.

NOBLE: Who wants to come in on this? [OVERLAPPING VOICES] I'm going to hold you back for a moment, Richard, OK? [LAUGHTER] Martin, you're shaking your head.

BRASIER: I don't want [OVERLAPPING VOICES] --

NOBLE: Right. Stephen, do you want to comment on this?

BELL: Frankly, no. [LAUGHTER]

NOBLE: Well, it leaves Lynn and Richard, and possibly me, but I know nothing about this. Over to you, Lynn, first, and then I'll ask Richard to say something.

MARGULIS: Well, it's a profound [OVERLAPPING VOICES] --

NOBLE: What do we mean by unit of selection?

MARGULIS: It's a pretty profound question, and it's related totally to the, where is Gallagher? Yes, hi. It's related totally to the heredity issue. It's related, one of the things

I didn't mention, but with this autopoietic entity idea, where the cell is minimal, and I think we have agreement on that, is that it's got identity. Now, cells have identity, and when Denis said that he doesn't know of many cases, and it's certainly true, in animals, when you get cross, you get hybridization between members of different, you know, slightly different species, or something. I was going to give you a case where you have hybridization, that is, you have a new organism, formed, routinely, by a fertilization-like fusion, between members of different kingdoms. They're not animals. They're not animals. But my point is that you have an identity there. And the one I'm talking about has a name. It looks like a plant, it's not a plant at all, and so on. In that case, it is clear, the identity is given by the naturalists. A name, it's given by that. And we have identity. And the name of that one is Geosiphon [UNINTELLIGIBLE]. Geosiphon only is made when a member of one kingdom is fertilized by a member of another kingdom, and you end up with this little mosslike thing, that is not a plant and not a moss at all, but sort of [virtually?] looks like it. That's identity. And what is heredity? It's the inheritance of that entity, in nature. To me, it's got to be in nature, right? And so, is that an individual? It's certainly not a virus. It's certainly a lot more than a virus. It's certainly cellular. And I would say that, when you have

this identity, and you have these parents, and they produce a living organism, that you have a heredity system, a heritable system. And it's going to last as long as that identity persists. But that's group selection, and I would say that Martin's discussion of the large forams show that, in fact, everybody, they don't even, they're not even aware, usually, that those are symbionts. They're just aware that they're forams with their own specific names. And he's showing that it's a group, in the sense that there are cells from different origins, and all of that. And the unit that its persisting, has an identity, persists, has offspring, it's a heritable unit. It's a minimal heritable unit, and it's a lot more than a piece of DNA. That's my point.

NOBLE: Before I bring you back, on whether you're satisfied with that, Richard, do you want to come in, on unit of selection? You must be, in 30 years of talking about units of selection. [LAUGHTER]

DAWKINS: There are two different meanings of the phrase, unit of selection. Replicator and vehicle. A replicator is that which persists through time, and that is DNA or RNA or something like it. That is to say, a coded information, which is copied, exactly, subject to occasional mutation, just like computer data

is copied, just like Xeroxing is copied. The vehicle is quite different. The vehicle might be a cell. It might be an individual. It's the unit which we observe, in nature, to survive or not survive. To reproduce or not reproduce. We observe wildebeests, some of them die, some of them don't. With lions, some of them die, some of them don't. This is vehicle selection. That's what we actually see, out there, in nature. But the long-term, evolutionary consequence is the differential survival of replicators, DNA, mostly, which exist inside those vehicles. And you can talk about natural selection, at either of those two levels. You can even talk about group selection, if you must. [LAUGHTER] In which case, the group you're talking about will be a vehicle, but it will be some kind of joint unity of vehicles, of bodies, or something like that, which has a certain coherence to it. I don't think it's helpful to talk about group selection, but I do think it's helpful to make a distinction between replicator selection, which is something very, very precise. It's the differential survival of alternative pieces of coded information. And vehicle selection, which means different things to botanists, and zoologists, and it's a mess. But there are times when you do need to talk about it.

NOBLE: Do you want to come back on, you triggered this particular debate. Do you want to come back on any of that?

GALLAGHER: I don't think I do, actually. I was very curious if people agreed on what they meant by the term, when they were using it. I'm aware that it's trickier than it sounds.

DAWKINS: The answer is a straight no. They don't agree. [LAUGHTER] [OVERLAPPING VOICES]

BELL: -- Richard's point, of the replicator. It brings up the interesting point that [E?] given gene [on a?] chromosome, we tend to view it as a sequence, in isolation. There is a gene, then that becomes a heritable unit. But, of course, that gene, in isolation, there's nothing, without the ability, or that DNA, to be replicated. And in many cases, the [sort of?] sequences, that define the replication and duplication DNA can be really, can be a considerable distance away from that particular gene. So, then, we have this sort of duality, or a sort of bifurcation of the definition, because we have to have those sequences that govern the replication of that gene. So, is that the actual unit, would you say, or what?

DAWKINS: From a field point of view, it would be that which makes the difference between individuals.

NOBLE: Let me put a question to you, then, Stephen, and perhaps also to Lynn. If I've understood part of what you were saying, then forms of cells must have emerged quite early on. Right. So, early on, there had to be cellular inheritance. Right? So far, so good. Now, why should that have disappeared? Or, to put the point in the terms that uses Richard's terminology, aren't cells also very good replicators, right from the very beginning? I'll ask Stephen to say whether he wants to respond, there, and then I'll bring Richard in, if he would like to come back on this.

BELL: I'm not sure I fully understand the question. Could you --

NOBLE: Well, my point is, very simply, this. Through my germ line, if I can sort of use myself as the example, through my germ line, I am connected to, right the way back, cell after cell after cell, to the original cells. So, in one sense, you can say that cells, also, are immortal replicators. What I'm really beginning to point out, here, is the difficulties of

language, and the way in which we describe the biological information that we have.

BELL: I think we would have to view, because, without doubt, a cellular organism, and we are the descendants of that cellular organism, although the continuity, if you like, as the DNA sequence, all of our components have been changed and [UNINTELLIGIBLE]. Where I take issue with some of Lynn's suggestions are in the nature of the fusion event that gave rise to the eukaryotes, we have, for example, they have thermoplasma, I think you used. That, I think, is probably the wrong archaeon to pick. I mentioned, in my talk, about crenarchaea, and the euryarchaea, the two lineages. Thermoplasma is a euryarchaeon, that lacks all these features that the crenarchaea have, that are clearly eukaryotic-like in nature. So, I would suggest that, although the fusion idea, I agree with, totally, your choice of [OVERLAPPING VOICES] --

MARGULIS: And the sulfur, too. The sulfur, temperature.

BELL: Right.

MARGULIS: So, you would say, we don't have it yet, what?

BELL: Well, there are plenty of hyperthermo-like crenarchaea that are self-utilizing. So, we could use one of those, instead. And then you would have [OVERLAPPING VOICES] multiple origins. You would have ESCRT machinery. You would have replication [license?] and all the various components that are eukaryotic-like.

NOBLE: Eric, would you like to give the last remark, from the floor?

MAN: There is evidence, first of all, that you can do modifications to cells. There are certain papers, I think, where, if you modify a cell, it will actually inherit that, independent of the genome. The other thing is, so, in effect, the cell, in that sense, is also a replicator. And then, the key thing is about the interactions. And so, the cell, in effect, is an interpreter of the genome. That means, in effect, that if you modify it in a particular way, then you get a radically different interpretation of the genome, which then, again, results in totally different phenotypes. So, in other words, you could have inheritance by a slow modification of the interpreting mechanism, in other words, a cell, as well, right? So, you can have evolution by way of interpretation, right?

DAWKINS: I will incorporate my answer in the [OVERLAPPING VOICES] --

NOBLE: OK, in the round-up. That's very kind, Richard. I think we'll go around the round-up, and, Martin, do you want to say anything, by way of [OVERLAPPING VOICES] concluding remarks?

BRASIER: I just, geologists look fondly on biology as one of its small, successful products, through Darwin. [LAUGHTER] And we're learning, in geology, after decades of reductionist thinking, that, where we've got to look for things like mass extinctions with a big [bow light?] or some single driving mechanism. We have to think in a systems way. Everything is a matter of connections, of various sorts. And this connectedness is what I've tried to just hint at, in this work we're doing. And it also shows that the fossil record is a test bed for ideas of how symbiosis and symbiogenesis could work. It's not just a theoretical concept. There is something that you can turn to. But then, I would pass the baton, on.

NOBLE: I'm being random, here, but I wonder, Stephen, would you like to go next? And then we'll ask Richard, and since this is Lynn's show, we'll finish off with Lynn. Is that a good way of going? Over to you.

BELL: I think we've certainly seen the thing, with symbiosis, and the way in which the fusion of cellular organisms has, undoubtedly, developed, led to the development of more complex lineages. But what I also think we should think more about, though, is the issue of viruses. That, maybe, we should view as not living, but conditionally living, with, conditionally within the host. But not just as parasites, but also as forces which are shaping content mechanism, and the overall complexity of genomes.

NOBLE: Thank you very much. Richard, over to you [OVERLAPPING VOICES] round up.

DAWKINS: I want to say that a cell is not a replicator. A cell is a reproducer, just as an organism is a reproducer. An asexual organism, such as an aphid, or a female stick insect, appears to be a replicator, because it appears to give rise, by parthenogenesis, to an identical daughter. And, indeed, it does. It is not, however, a replicator, for the very reason that I was mentioning to Denis, before. If you cut off the leg of an aphid, and the aphid then reproduces, as you know, the daughter will not have a missing leg. If you cut off the equivalent of the leg, of the germ line DNA of the aphid, then

it will have a change. That is absolutely a straightforward, operational definition. Now, the gentleman that, I'm sorry, I didn't catch your name. [OVERLAPPING VOICES] Eric, yes, was saying that there are examples where you can alter a cell, in a non-DNA kind of way, and that will be inherited. I don't know what you're thinking of, there. I mean, one example you might have meant is Sonneborn's paramecium, where you cut a bit of the pellicle, I think it's called, the wall, twist it round. Well, if that's true, and if that is, indeed, a non-DNA form of heredity, that's absolutely fine. I would embrace that, gladly, as a new honorary gene. That's fine. [LAUGHTER] Why not? Why not?

MARGULIS: No, I have to answer that, because we know what that is.

DAWKINS: Well, good. I'm delighted to hear that. [LAUGHTER] But, even if we didn't know, if you could find a piece of genuine heredity, which is non-DNA based, and by genuine heredity, I mean that, once the mutations happened, it potentially goes on forever. Now, of course, it may not go on forever, because it may be disadvantageous. But nevertheless, if it has this quality, that it doesn't fade away over generations, that's the key point. That's the key point, that

DNA has, cells do not have, DNA does have, organisms don't have. There may be other things that do, and on Mars, and on [beta betel?] [UNINTELLIGIBLE], there will be other kinds of things that do that. I'm not wedded to DNA. I am wedded to this operational criterion that alterations in it go on forever, potentially. The reason that matters is, the ones that don't go on forever are the ones that are selected against. But, in order for that to be evolutionarily interesting, there's got to be a difference between the ones that do go on forever and the ones that don't. And so, that's got to be heredity, in a broad sense. DNA may very well not be the only kind of heredity, but it's got to be something truly inherited, in that sense.

NOBLE: And that would be an empirical question, wouldn't it?

DAWKINS: That would be an empirical question.

NOBLE: Yes, that's right.

DAWKINS: And if somebody discovers a new kind of heredity, I'd be delighted.

NOBLE: Yes. So, one obvious conclusion, here, is that the field of epigenetics has to look, very carefully --

DAWKINS: See if it fades away.

NOBLE: -- at these possibilities, that's right. Exactly. Yeah. Can I suggest that we take this issue, of what, exactly, we mean by genes, honorary genes, and related questions, and epigenetics, to be part of the later evening discussion? But, Richard, you may not have finished your --

DAWKINS: No, no, no.

NOBLE: You have, OK. Lynn, the floor is yours, to finish up.

MARGULIS: Let me just answer one thing, about the paramecium experiment, which was what got me into this to begin with. you saw the mixotricha, and you saw how there were organisms making up the cortex, and that's what they call the ciliate cortex. And that's, basically, what he did. He picked, that, not he, it was Janine Beisson, as a matter of fact, who did the experiment. But it's based on Sonneborn. What they did is, they took a piece of cortex that really was grafted in the opposite direction. It lasted for two years, at a replication, a reproductive rate of one cell per day, so, I mean, it was indefinite, and they never got a different result. And the way

to think about that is that the bacteria that they turned around had their DNA in it. I mean, the, ultimately, that's what it is. And they, it's systems thinking. You had to have the whole system, of the bacteria, their protein synthetic system, their interactions with each other. And that perpetrated, in that direction. So, it's back to systems thinking, group thinking.

NOBLE: OK. I think, with that thought, we'll bring the formal session to a close. One or two words of thanks. Thanks to the panelists, for being willing to come to what has been a very exciting discussion. And, obviously, to Martin Brasier, Stephen Bell, Richard Dawkins, Lynn Margulis, and if I've left anybody, oh, myself. [LAUGHTER] [APPLAUSE]

[END]

Thank you.