Transcribed by
A.D.S. - Alice Darling Secretarial Services
144 Mt. Auburn St., Cambridge 617-876-8750

TRANSCRIPTION OF AUDIO FOR: UMass Amherst

SUBJECT:	Homage to Darwin, Part 1
DATE:	Transcribed 5/12/11
FILE #:	1 of 2
TIME:	41:31
FILE NAME:	Homage to Darwin Part 1

NOTES:

MARGULIS: Welcome to Balliol. So, the subject, for everybody, are issues like neo-Darwinism, and what the sources of evolutionary novelty are. Group selection, groups, populations, communities, ecosystems and units of selection. Thought styles of neo-Darwinism and other things, and I just listed there. So, all of those subjects are open. Any aspect of evolution is open for discussion, when we get started. OK, Denis is now [OVERLAPPING VOICES] yes, that's fine, thank you.

NOBLE: I'm going to stand up, most of the time, because my job is, largely, to control you all. And, as Lynn Margulis has said, we really do want this to be interactive discussion. And with no more to do, I think we ask, to get it in the order, as you said, Lynn, we ask Stephen Bell to give us his five-minute view on the origin of life.

BELL: So, I'm actually a biochemist. My lab, I'm studying biochemistry processes such as DNA replication, gene expression, cell division. And in doing so, we're studying these peculiar little organisms, the Archaea, which are simple prokaryotic organisms, which are devoid of any interesting features, really, whatsoever. You can see they're simply a bag of protein and DNA, and they certainly have nothing like the complexity of present-day eukaryotic organisms, with their multitude of

subcellular membrane-bound organelles and complex trafficking systems. But the biochemistry that we've done, I think, is beginning to help shed some light on the evolution of these vastly more complex eukaryotic organisms. That's what I'd like to talk to you about, briefly, today, and just highlight a few of the questions that interest us. So, thanks to Carl Woese, we now know that there are three principal domains of life. There's two prokaryotic domains, organisms that lack nuclei, and are devoid of subcellular structure, as I showed you. And that's the bacteria and the archaea. And then, of course, we have the eukaryotic organisms. What's been central to our studies is the observation. The archaea appear to share a period of common evolutionary history with the last ancestor of eukaryotes. And it's during this period, of shared, common evolutionary history, which has been distinct from the bacteria, that certain core machineries have evolved. We've been able to exploit these, in simplistic studies of biochemical functioning. Within the archaea, themselves, there are two principal phyla have emerged, the Crenarchaea and the Euryarchaea. I'll come to this in a second or two. So, the first, hint, really, that there's a special relationship between eukaryotes and archaea came of studies of the gene expression apparatus of transcription machinery. Recently, we've established the crystal structure of the archaeal RNA polymerase, which

highlights its complex nature and its similarity to the eukaryotic enzyme, and shows how much more complex, distantly related, it is to the bacterial enzyme. Similarly, when we look at the process of DNA replication, a process that's essential to the propagation of all life on the planet, it's a complex, multi-stage process. The bacterial proteins that carry out all these various transactions on DNA, linked to its duplication, are very well-understood. But, through an amazing feature of evolution, we have an entirely distinct machinery for DNA replication, that's found in present-day archaea and eukaryotes. Again, from my lab's point of view, this is really useful. The archaeal machinery is a simplified version of the eukaryotic's useful model system. But how did this happen? How do we have two entirely distinct mechanisms driving DNA replication, two entirely distinct sets of proteins? And finally, I mentioned, already, the eukaryotes have this incredibly complex endomembrane systems. The shuttling of vesicles backwards and forwards between these membrane-bound organelles, how did this evolve? How did this come about? Well, it turns out that one of the principal players in shuttling between these membrane-bound organelles is a eukaryotic apparatus called the ESCRT machinery. Very recently, our lab's, my lab has discovered that archaea actually possess this ESCRT machinery. Now, these things don't have subcellular organelles. What, instead, it

turns out the archaeal ESCRT machinery is doing is actually carrying out cell division. So, we have an entirely distinct process of binary fission occurring in the archaea, that is, if you like, the ancestor of the eukaryotic membrane shuttling systems present in these complex organisms. So, if you look at the archaea, we see this whole list of eukaryotic-like features. We have, just to mention some of the ones I've alluded to today, multiple origins of replication driving DNA replications. Various proteins are much more closely related to eukaryotic than bacterial. We have the ESCRT machinery. We have satellite or chromatin proteins, the way we package DNA. These are all features that are thought to be typical of eukaryotes. And what we've discovered is that these features are present in the Crenarachaea, but thus far, there is absolutely no evidence for them whatsoever for them in the euryarchaea. But they're also present in the eukarya. So, this is a slight problem, in the classic Woesian Tree of Life. Have all these features evolved independently twice? Once in the Crenarchaea lineage, once in the Eukaryal lineage? Or is the topology, or the topography, of the Tree of Life, as proposed by Woese, actually slightly wrong? And a rather interesting counterproposal came from Jim Lake, a few years ago, who, instead of having the Tree of Life, we have a Ring of Life. This, to some extent, formalizes the fusion events and the symbiosis that Lynn will talk about, later on.

So, here, we would have a situation where we have one lineage giving rise to archaea, one to bacteria, and then the eukaryotes actually arose via full fusion of, probably, a protobacterium with, and in Lake's proposal, a Crenarchaeal ancestor. My lab loves this. Well, I love it. I think my lab does. Because this means that the Crenarachaea are, in essence, a nice, living fossil of the last common ancestor of archaea and eukaryotes. And, we would argue that, after the divergence of the euryarchaea, we evolved all these complex features, that are preserved in present-day crenarchaea, and, of course, continued and elaborated upon in the eukaryotes. OK, and the last, I've still got two more minutes? OK, two more, good. Good. So, the other question, specific question, is, how did, that I'd like to address is, how did two distinct DNA replication machineries evolve? As I said, there's nothing more fundamental to the propagation of life on the planet than they ability to replicate your DNA. And here, we have two entirely distinct apparati, that have emerged, during evolution. There's a rather attractive proposal that's come from Patrick Forterre, who is based at the Institute Pasteur in Paris. He says the cataclysmic [currents?] early in the evolution of life on earth, not the planet-busting asteroid, as I've cartooned, here, but on a slightly smaller scale, the collision of a virus with a host genome. Did we invoke a situation where we have a host

organism, the single origin of replication, dependent on this single site for replicating [his?] genome, and a virus happens to integrate into that host genome, at the site? Well, then, the host is a problem, because you've taken out its origin of application. It simply can't replicate anymore. Rather, the host, now, becomes dependent on the virus, and the viruses run sequences and proteins to drive replication of the entire host chromosome. So, we invoke a time, back in evolutionary history, when the evolutionary Tree of Life was the evolutionary Stump of Life. We have a virus come flying in at the point of [UNINTELLIGIBLE]. Does its little replicon transfer, takeover. And now it effectively hardwires this entire lineage with its own DNA replication apparatus, thereby supplanting the host machinery and creating this novel lineage, this novel machinery for DNA replication. I love the idea. I think it's extremely sweet. And there is, fortunately, some evidence for it, as well. Mitochondrial DNA, and again, Lynn is one of the world's experts on this. The replication transcription machineries are actually clearly derived from a phage. They're not classic bacteria, although the mitochondria, itself, is derived from a bacterium. It's actually a phage that's going to end up supplanting the bacterial machinery with its own machinery, in order to drive mitochondrial replication. We've also discovered a bacterium, Bacillus cereus, which has an integrated phage

within its own chromosome, which actually has archaeal and eukaryotic verification proteins, showing that we can get transfer between the domains of life. And also, more recently, we've also shown that the archael genomes have integrated viruses within them. They're actually helping to drive the replication, by defining start sector verification within the chromosome. So, in conclusion, I'd like to propose something that we can discuss later, perhaps, that viruses not only shape the genomic content of host organisms, but they may also play an important role in actually sculpting the architecture of replication, and, indeed, the very machinery that's carrying out replication, itself. And I'll stop there.

NOBLE: Thank you very much. Keeping to time, too, with an exciting presentation. We move on to Martin Brasier, author of Darwin's Lost World.

BRASIER: Yes, if there's anybody who hasn't got this book, it came [LAUGHTER], which seems unlikely. It came out on Darwin's birthday. And my point, in the book, was really to emphasize a number of things. One of them was that Darwin had, to some extent, misrepresented what the fossil record can tell us, and it has some very important things to tell us, about evolution and deep time, particularly for the pre-Cambrian, which is 80%

of earth history, or thereabouts. Darwin had wracked his brain, as to how to explain the lack of fossils. And, during my lifetime, there's been enormous progress on that, and I think paleontology shows that all the really important things that have ever taken place in evolution, the irreversible transformations like the origin of oxygenic protosynthesis, actually take place in that great dark age, which is the pre-Cambrian. But I don't want to talk about that here. Lynn has taken great interest in a course I gave, at Oxford, to the third years, which really explores the uses of a particular fossil, which is the most-used fossil in all of geology. And most biologists here, rather little about them. But for geologists, they're the fruit fly of our subject. We use them for stratigraphy, for environmental change, for predicting climate change, everything like that. So, it's a huge field. That's the study of Foraminifera. Generally speaking, there are five or six thousand Foram specialists in the world. It's a big field, run mostly in oil companies and geological surveys. Now, like Darwin, I was lucky enough to spend a year as a ship's scientist, or a ship's naturalist, on HMS Fawn in the Caribbean. My job was to actually look at the Foraminifera as proxies to the study of deep time. I don't cover it in this book, but I'm hoping to get to it in the later one. That's my name, on the left. Jonathan Antcliffe is on the right, there. And Jon's

helping me to explore some ideas we've had, over the last ten years or so, just to illustrate Foraminifera. He has a slightly microscopic view of some modern-day Foram, sort of the thing you might find living in Hawaii or in the Caribbean, today. There's three Forams, well, there's four or five you can actually see, there. The one in the middle is a great big thing, about two millimeters across. It's a single protozoan, a rhizopod protozoan, called heterostegina. And it lives almost entirely dependent on its symbionts, which are diatoms of particular species, [UNINTELLIGIBLE] or something like that. That's what gives it its golden color. And down at the bottom, there, you can see one that's got red endosymbiotic algae inside it, and another one, over on the left, here, which has got brown dinoflagellates. Biologists and geologists have discovered that there's a whole host of Forminifera which have specially adapted to cultivating those symbionts in just the same way as the famous reef-building corals do today. The wonderful thing about the Forams is, they have the best fossil record of almost any group. It goes right back to the Cambrian, 540 million years ago. It's enormously diverse. And it can be read in small chips of rock, or in thin sections, so it's a story we probably know better than any other group. One of the things, of course, that geologists like to do is to go to tropical lagoons like this, and study reefs and Forams. And there's a little chart

you don't need to read the details of, but it shows the kind of symbiont that different Foraminifera have, as you go into deeper water, from the back reef into the fore reef. And as you might expect, the shallow ones have adapted to cultivate chlorophyta, that's green algae, adapted to the shallow water light levels. Then there are groups that have adapted to cultivate dinoflagellates and red algae, and they usually live at intermediate depths. And then there are Forams that are capable of living about 120 to 150 meters deep, where the photic zone is very weak and feeble, but diatoms are specially adapted to low light levels. That's why they thrive, in the high and low latitudes, today. And rather marvelously, it turns out that the [form of the?] skeleton reflects the nature of the symbionts that they cultivate. So, we can actually use this, to some extent. Foraminifera that are dependent on symbionts also change their shape, or their wall structure, according to the depth at which they live. So, shallow ones have thick, robust tests, and as they have to live deeper and deeper in the water, where the light levels are dimmer and the light is normally bluer, they get thinner and flatter. There are these, and there are a whole host of other tests we can use, to reconstruct symbiotic Foraminifera in the past. This is something I've always been trying to get at. This is some mathematical modeling I did, years ago, to show that symbiont cultivators

typically have very short lines of communication. They're very conservative about energy pathways, and energy conservation. This is what some of the fossil Forams look like. Here's one, it's a bit bigger than natural size, at the right, there. It's normally a couple of centimeters across. This particular genus, nummulites, gets to 150 millimeters across, 15 centimeters across, at the core of the Eocene, 45 million years ago. It makes up the Sphinx and the Pyramids, today, and is massively rock-forming. And then, there's another type, in the Late Permian, which, again, reaches this enormous size, called fusulina, here, also rock-forming. We know, very much in detail, the evolutionary history of these Foraminifera, as they become more and more specialized, apparently to cultivate their symbionts, creating [UNINTELLIGIBLE] compartments, which the light can get through. Some even have fiberoptic type devices of calcite, to concentrate the light at greater water depths. We've been plotting the architectural evolution of Foraminifera, which starts very simple, at the top, there. And, as you come down, you're going towards more and more of advanced architecture. So, you get multiple chambers. And then you get lots and lots of openings between the chambers, to let the symbionts in and out. And then, in the ones that are really symbiont-specialized, they create these little chamberlets, like little cubbyholes, for the particular farming and the nurturing

of the symbionts. So, we know there's a whole series of indicators we can look at. And if we look at, back through geological time, geologists use these for dating the rocks in the Permian, and then the Cretaceous, and so on. So, we know the fossil record of these remarkably well. We can see, there are cycles, major cycles. I tried plotting them out this way, first, and the parsimony index means very simple and not symbiont cultivating, and number 10, at the right, means probably symbiont cultivating. And here's geological time, at the left, here. So, you can see, in the Carboniferous and Permian, there's a great radiation of symbiont cultivators. And then, there's an episodic series, followed usually by extinctions. This, plotted out in a bit more detail, there are typically three shapes that the symbiont cultivators like. Spindle-shaped, at the top right. Chinaman's hat-shaped, at the top left. And coins-shaped, down at the bottom. And we can see the evolutionary trend towards symbiont cultivators, by the arrows. It shows the point at which symbiogenesis started to kick in. And the red lines are extinction. And they usually mean the total extinction of the lineage. So, some of these are the fairly famous extinctions, like the one at the end of the Permian, and the one at the end of the Cretaceous. In fact, all the big, mass extinctions caused enormous collapse of the symbiont cultivating Forams. And just to show you how that

really works, in terms of size, this is 140 microns, at the right, here. So, you can see that there are cycles of maximum size, taking place. Rather fascinatingly, all the big extinctions are preceded by very giant Foraminifera. Now, that is either an enormous coincidence, or it indicates, to me, that the ecosystem in which giant, gigantism develops, had something about the nature of its connectedness, and the collapse is related, to some extent, to the nature of the ecosystem and its vulnerability. So, that's what I want to end with, really. To emphasize to you that we can cross-check, to some extent, what happens to symbiosis. And that Foraminifera and their symbionts have actually got their act together, episodically. And as far as we can see, it tends to dissolve about every 20 to 30 million years or so, very few examples where it seems to have sustained longer than that. OK, thanks.

NOBLE: Thank you very much, Martin. And so, we ask Richard to give his few minutes of introductory remarks. Over to you, Richard.

DAWKINS: Well, I thought I would talk about what's called neo-Darwinism, which sometimes comes in for some stick. And, in particular, what can be called the gene's-eye view, which is one particular way of looking at neo-Darwinism. The gene's-eye view

focuses on the level of genes, not specifically that they have to be DNA, although, on this planet, they happen, they are. But, anywhere in the universe, where there is self-replicating coded information, which can exert some power, which we call phenotypic power, some power over the likelihood that it will be copied on, into the future. So, the key point about the gene, which is a somewhat abstract concept, rather than having to be, specifically, DNA, for the reason I've just said. The key point about the gene, in this model, in the gene's-eye view of evolution, is that it is potentially immortal, in the form of copies. Because the copying of genes, I call them that, is exceedingly accurate, not totally accurate but very, very accurate, there is the potential possibility that the information will last forever. That opens up the possibility of competitive struggle between rival versions of these replications of pieces of coded information. Because, although they potentially can last forever, not all of them do. And those that don't are selected away by natural selection. So, that is natural selection. Natural selection is the differential survival of coded information, which exerts power over its probability, over its likelihood, over its success in being copied, in being replicated. And the power that it exerts is phenotypic power, which means it exerts power over embryological process. The building of bodies, usually,

although I would rather generalize that and say any kind of influence that a self-replicating entity can exert over the world, which improves its probability of replicating itself and passing itself on to the potentially eternal future. And kind of influence that it can have will be favored by natural selection. The unsuccessful ones perish. The successful ones don't. The vehicle of their success or failure is phenotypes. It happens to be the case that, in the forms of life that I'm most familiar with, which is animals, these phenotypes are great, big vehicles. They're great, big, multicellular entities that move around, as a unit, on legs or wings or fins or tails. They are things that have eyes and brains and kidneys and hearts. That is a very special and, in a way, peculiar way of doing it. It didn't have to be like that. That happens to be the way it is. The more general way of looking at the gene's-eye view of natural selection is to say that any kind of phenotypic power that can be exerted, will be. Now, the gene's-eye view has been criticized as being determinist, as though we are saying that genes exert a deterministic influence on bodies, which is irreversible, and inevitable, and simplistic. And I want to really repudiate that most vigorously. I yield to no one in my admiration of the complexity of feedback loops, of the details, the immensely complicated details, whereby genes actually do influence phenotypes. There is absolutely no

suggestion that it's irrevocably deterministic. There's absolutely no suggestion that it's simple. But however complicated it is, the one thing that matters is that individual differences between genes are reflected in individual differences in phenotypes. And it is those individual differences in phenotypes that count, as far as selection is concerned. So, it doesn't matter how complicated the influence of genes on phenotypes is. It doesn't matter how complicated the feedback loops are. It doesn't matter how much involved they are with symbiotic ingestion of other types of organism. This can happen to your heart's content. All that matters is that differences between genes, differences between self-replicating coded pieces of information, are reflected, at the end of this amazingly complicated piece of embryonic, embryological development. Differences between coded pieces of information are reflected in differences in survival of those coded pieces of information. And that's the important part. That's the only thing that singles out the gene, in the hierarchy of life, as being important, in the gene's-eye view. It's not that they exert a more important causal influence on bodies. The only thing that matters is that they are potentially immortal, and differences between individuals are reflected in differences in survival, via phenotypic differences, which can be as complicated as you like. Which

can, indeed, involve symbiotic relationships with other creatures. Here, I come, obviously, to Lynn's particular interest. Lynn, of course, is the great apostle of symbiogenesis. I don't think she goes far enough [LAUGHTER]. What I want to say is that things like the incorporation of bacteria to be mitochondrial and chloroplasts, and possibly other things. They're just the tip of the iceberg. We can regard the entire gene pool, of any species, as a symbiotic collection of self-replicating coded pieces of information. The other genes in the gene pool should be regarded as part of the ecological environment of every gene in the gene pool. So, every gene in the gene pool is surviving against a background of, not only the external environment, not only the weather, the humidity, the rainfall, the predators, the parasites, the hosts. Not only all of that, but also the other genes in the gene pool. And, so, the gene pool of, say, the lion species, is one particular collection of symbiotic genes who are all cooperating with one another, with other members of the gene pool, to make lions. And, similarly, the buffalo gene pool, and the kangaroo gene pool. They're all symbiotic collections of genes, in just the same kind of way as Lynn has taught us, with respect to symbiotic organisms. So, in that sense, I think she hasn't gone far enough [LAUGHTER].

NOBLE: Thank you very much, Richard. And, yes, I am actually the moderator and chairman of this, but, of course, I can't hide the fact that I'm also a physiologist, who's interested in heartbeats and how brains work, and so on. And so, a lot of my work focuses on the question of how collections of genes, or, rather, collections of gene products, interact to produce the complicated function that we observe, as physiologists, whether it be at the heartbeat, whether it be the secretion of insulin by the pancreas. All of these functions are functions that physiologists study, by looking at the way in which the gene products interact. I would just say one thing about that interaction, which I'd like you to take into account, as we proceed in this discussion. How big a space could that interaction be? If you calculate the total number of interactions there can be, between 25,000 genes, which is the present number of genes identified in the human genome, it comes out to be 10^70,000. I'm rounding the figures. You can imagine an exclamation mark after that, and the exclamation mark, of course, would not be an indication that that is factorial [LAUGHTER]. How many, I tried, once, to see, how could one compare that number with a number which we can [UNINTELLIGIBLE] grab hold of. And I thought the best number to compare it with, remember, 10^70,000, I thought the best number to compare it with would be the total number of atoms in the universe. As

Hubbell has probed into deep space, and revealed those tens of thousands of galaxies, even in just one millionth of the space that is sky, how many do you think we end up with? 10^80. There wouldn't, therefore, be enough atoms in the whole universe, for evolution to have, as it were, serendipitously tried out all of those interactions, even over the billions of years of life on earth. And, as my contribution, as a physiologist, to this, we, therefore, have to work out how evolution has serendipitously done it. How, through the various paths it has chosen, which, I would suggest, is only one path after billions of paths, and if we do find life on some other planet, sometime, maybe it will be very, very different from us. I'd love to hear the reactions of my colleagues, on that point. To a physiologist, at least, as I said, the number of possible interactions that we're looking at is absolutely immense. Well, there's my sort of, little contribution to the debate. And I think, at this point, then, we open up for people from the floor to make comments or questions. Please stand up, say who you are.

MAN: [SOUND OFF/THEN ON] I'm a developmental biologist. I was in issue with Professor Dawkins, on the grounds that it's just not terribly helpful to take a gene's-eye view. It may not be wrong, it even might be [used?], because selection doesn't act

on genes. It acts on phenotypes too complicated. We know, one of the most distressing experiments anybody can do is to knock out a gene, and see if it has, not even a [UNINTELLIGIBLE PHRASE] would do that [LAUGHTER]. We know that the individual genes are the jigsaw puzzle pieces. But we do need some images to make sense of things, and we do need real phenotypical selection. So, I just don't think it's terribly helpful.

NOBLE?: Well, do you want me to react immediately? [LAUGHTER] I won't do this for every comment and question, but I think this one deserves --

DAWKINS: Of course, we don't disagree about that. You do need to actually look at phenotypes. However, when you do look at phenotypes, and when you ask the question, as a field biologist does, what is the adaptive advantage of a certain piece of behavior, or a certain phenotype, you do need to ask, at what level you're asking that question. And, field biologists, nowadays, almost all take it to the level of the gene. They're looking at phenotypes. They're looking at tails and wings and behavior patterns and everything else. But the question they're actually asking is, how is it that this behavior pattern, or this morphological feature, increases the survival chances that don't make it, because, obviously, as you say, a single gene

doesn't make a phenotypic feature, but make the difference between an individual that has this variety of phenotype, and one that has that variety of phenotype. And so, the rhetorical convention, what's in it for the gene that makes this thing, is the way people actually work. It's enormously fruitful. If you go out to the Serengeti, if you go to the Antarctic, wherever field biologists are now working on adaptive questions, that's the question they're asking.

NOBLE: Next point, yes, please. Say who you are.

SIEGEL: Robert Siegel, and I wanted to address this to the first speaker. As a virologist, my heart beat faster, to hear your theory of the role of the virus. But doesn't that really just push the question backwards? Because, you have to actually explain where the virus got it, and presumably, they're still, it's likely that there's only one origin for the enzyme, in history. So, you just actually pushed it back in time.

BELL: [SOUND OFF/THEN ON] So, one answer, I guess, is, the number of generations the viruses go through or scramble, the coding sequence will increase the chance of diversity occurring. What we also need to recall, though, is that we're currently looking at three domains of life. Those are the ones that are

still existing on the planet today. There are, probably, two billion years prior to the divergence at LUCA, where other lineages have emerged, that tried various combinations out. They've maybe become extinct. It's [firmly?] possible that viruses may actually reflect ancient fossils of those ancestral merged lineages. And so, they've actually, again, we're just pushing the question back further.

SIEGEL: Yeah, and so, the real question is, do you think that it evolved, independently, more than once, or have you just spread it out, in time, so that you could get more diversity?

BELL: What we can do is take it back to the point where the genome, itself, wasn't DNA, but rather, it was RNA. In which case, we then have a takeover point where, possibly, distinct lineages evolve different mechanisms for generating DNA and replicating it. Why hasn't that simply happened, in LUCA? Why hasn't LUCA [written out?] an genome. Firmly possible that it could, but we note that Bacteria, Archaea and Eukaryotes all share a common mechanism for repairing DNA. The homologous recombination machinery is the same in those three lineages, suggesting that that was present in LUCA, which, in turn, suggests that LUCA was appearing in DNA genomes. Therefore,

LUCA, itself, had the DNA genome. So, the RNA-based genome, we will see, was earlier in time.

MARGULIS: Steve, please say what LUCA is.

BELL: Sorry, the Last Universal Common Ancestor.

NOBLE: Eric, you wanted to say something.

WERNER: Eric Werner. Yeah, I have a question to Professor Dawkins, about the symbiont idea of genes. One of the problems that I see with that is, in effect, are you saying that they somehow interact to, then come up with, the organism? Because, I mean, in effect, I'm wondering whether there is sufficient complexity just in the pure interaction between genes and such, versus the networks that actually construct genomes. So, I don't know if can view her view as, I don't know if you can really take genes to be symbionts, because that would, in effect, make them cooperative entities, that, then, through their interaction, produce some complex structure. And that has inherent limitations, because of the relative simplicity of those entities. So, you need a temporal cascade of some kind, which isn't necessarily in the proteins.

NOBLE: Do you want to comment on that now, or to hold it for later?

DAWKINS: I think, let's hold it for later.

NOBLE: Hold it for later, is that OK? We'll hold a number of things like this. Yes, please. Say who you are.

IVORY?: My name is Michael [Ivory?]. My training, essentially, was in the history of [UNINTELLIGIBLE]. I'm going to ask Professor Dawkins, and everybody else. But, as I understand it, there's a huge volume, or mass, of genetic material, which hasn't been selected out. It's called non-recording, or arecording, DNA. And I'm not asking for an answer, and I wouldn't [dream of?] asking you, Professor Dawkins, whom [I might disagree on?], on the matter. And that is, why, that is, can we give an account of that?

NOBLE: OK, so, that, now we'll [call that?] --

DAWKINS?: [OVERLAPPING VOICES] I'm sure you rather me that --

NOBLE: Well, I think it would be good to put this to any of the members of the panel, particularly a [OVERLAPPING VOICES]

MAN: -- to, I found it very difficult to put it forth in such a [peculiar?] way. But I can't believe that this huge mass --

NOBLE?: -- is there doing nothing.

MAN: The [stranded?] or, I'm quite sure it isn't [OVERLAPPING VOICES]

NOBLE: I'm quite sure it is not doing nothing.

DAWKINS: I think it might well be doing nothing. [LAUGHTER]

NOBLE: Well, OK. Richard first. [LAUGHTER] You think it may well be doing nothing. [LAUGHTER]

MAN: Thank you, Professor Dawkins. [OVERLAPPING VOICES] All I can say, in particular case [from?] you. This has got to be explained.

NOBLE: [OVERLAPPING VOICES] I mean, let's let, Richard, do you want to come in first?

DAWKINS: I mean, it's very easy, on the genes I view, to explain it, because it is simply the ultimate parasite, as Crick and Orgel said. I mean, it is, it's got the perfect way of replicating itself. It doesn't affect anything, so it's not selected against.

MAN: I don't think that [OVERLAPPING VOICES]

NOBLE: Let me make another suggestion. [LAUGHTER] Please, we've got the question. We've got the comment. And we're going to, now, try and reply. I'm going to give a slightly different reply from Richard, but we'll see, also, what the other panelists want to say. Because, I think the [LAUGHTER], well, consider this. When, as a physiologist, I look at the way in which a protein functions, of course I have to focus on the active sites of the protein, the bits that really make it be the receptor for this, the channel for that, or whatever its function is. But we have a very similar problem, you know, with proteins, because there's much else which contributes, eventually, to the three dimensional structure of the protein. And the way we solve the problem, there, is that we say, the problem that you're posing, what on earth is it doing? Is, we say, well, that takes part in forming the three dimensional structure within which the sites are to be found. And that has

a very big effect on the speeds of interactions, and therefore it does have a function. Now, my suggestion would be, simply, that the genome has to be folded up. We know, of course, that it's, the DNA is wound around histones and all the protein machinery that the nucleus has. We know, also, that many genes, particularly in the higher animals, are broken up, into many introns and exons. [Lowe's?] suggestion is that, when you look at the way in which the whole thing is folded, and which exon comes close to which other exon, we may be able to start to say why it is that particular splice variants appear, rather than others, or in higher frequency than others. So, I don't think it's too difficult, using the analogy, with proteins, to give some sort of functionality, particularly in the folding mechanisms, that may determine which genes are expressed, and to what extent they're expressed. Now, this is just an idea. I don't think anybody can prove this. But over to others. Richard, do you want to come in first, on that?

DAWKINS: [OVERLAPPING VOICES] there are related species of salamander, which have orders of magnitude difference in genome size. And that doesn't, I mean, any kind of functional explanation is pretty improbable. It's far more likely that this is just rubbish, that's left lying around on the hard disk, and just hasn't been cleaned off.

MAN: So, they fossilized, in effect.

DAWKINS: Yeah. Yeah.

NOBLE: These are basically fossils. Our instincts, obviously, disagree, on this, but let's [OVERLAPPING VOICES]

DAWKINS: Well, how would you explain the salamanders, then?

NOBLE: I don't work on the salamander, Richard. [LAUGHTER] What I do work on is the fact that the, taking, for example, [DSCAN?], one of the genes in the fruit fly, that has something like 35,000 different ways in which its own spread of exons can be expressed. And what we know is that those are expressed at different times during the development of Drosophila. So, something is interacting to determine that. Whether it is the junk, as we call it, DNA, that is helping to form the structure or not, I can't say. I'm only putting an idea out. We have to explain that, though, because it's clear that something else is determining the order in which the expressions are occurring, in addition to what is in the DNA sequence in the exons, themselves. That's, I think, the essential point that I would want to make. Let me leave this, also, on the table, to take up

a little bit later, and I'll make a note of it. Stephen, do you want to say anything on this issue?

BELL: Just, yeah, to agree with you that a lot of the DNA probably plays an architectural role. But we also have to recall that, until recently, we didn't know about the existence of small, non-coding RNAs, that are actually involved in the control of a great number of genes. That was previously thought to be DNA that wasn't having any coding function. Now, we know it actually plays pivotal roles in regulation. So, a lot of DNA, I think, will have as yet undiscovered roles, the sort of micro RNA type families, and genes being one example.

NOBLE: Who else wants to come burning in, right at the back, there? Again, can you say your name, and then put the point you want to make.

ASHLAND: My name is William Ashland, and I'm a [UNINTELLIGIBLE] [geologist?]. Professor Brasier, you mentioned following the PT and KT extinctions, and gigantism, in the Foraminifera. Does anybody know of any possible explanations for that? And if so, could we use those explanations, maybe, to explain the causes of the extinctions? Is there, I [UNINTELLIGIBLE] has the KT extinction [UNINTELLIGIBLE PHRASE]

BRASIER: Yes, we've done isotope work, and it looks like they lived quite a long time. Some of these Foraminifera lived tens, to possibly as much as a hundred years. So, they were probably optimizing their moments in reproduction. That's just what I'm guessing, anyway. And probably living fairly low in, low down in the photic zone, waiting for the right moment, in a way that corals do, at least. They reproduce about once a year, or thereabouts. As you know, mass extinctions tend to hit very large things with rather slow rates with reproduction and recruitment. So, it probably explains the sorts of things that are going on. More than that, I wouldn't want to interject, at this point, I think, I'm not sure, that throws too much light on the discussion.

NOBLE: OK. We take a ten-minute break, while the film gets set up. Is that correct? And then you'll say something to introduce it, Lynn?

MARGULIS: Yes.

NOBLE: OK. A ten-minute break, to let people get some fresh air.

[END]

Thank you.