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NOTES:	

[MARTIN?]: Biology and paleobiology has got to come right mainstream back into this whole question of mass extinction.

This is the parable I tell and it's a little story of a happy couple called Albert and Emily who are in their 40s or whatever and they live in a little block of flats. And Albert's taken to smoking cigars and Emily gets tired of him smoking cigars in bed and asking him to go out on the balcony to smoke his cigar. And eventually she gets tired even of this because it stinks the flat out and she gives him a little push. A very slight push. He's on the edge of the balcony. Over he goes and he falls down into the flowerbed. It stubs his cigar out but Albert gets up and climbs back up because they're on the first floor.

But she repeats exactly the same operation after she's had them relocated to the 12th floor. She pushes with exactly the same force, but because of the energy built up in the system of course his fall is fatal not only to the cigar but to him.

So you have to ask the question there what caused the push? And my point there is it's not the meteorite, it's the nature of the system that the meteorite or anything perturbed. And what we're showing with this [foram?] work is often systems which experience mass extinctions seem to have tuned themselves right

to the edge of efficiency so they've got enormously large, very complicated structures, protozoans and other things. And they are of course set up for the kill in some kind of a way.

The answer to that then is that mass extinctions are caused by what happened in the 5 or 10 million years beforehand. And it's a little bit like the economic situation we find ourselves in now. We're in a fix now because we've had 10 golden years. That's the worst possible thing that could really happen to an economy because its fitness must be constantly tested in order to prepare it for big and small ups and downs. Lots and lots of little shakes and re-tunings. A really good thing for an ecosystem is stability tends to push it more and more towards one particular kind of case strategy or whatever you like to call it at the very age of its peak and then of course the thing will collapse.

The answer to that is that mass extinctions then require use to look at the connections within a system and understand those connections and the degree, the way in which they feed through the system. And if that matters, if connections are important to extinction, and presumably connections are important to speciation and specialization too because you could argue that

mass extinctions and speciation are part of the process, part of a systems process, which we ought to see in this bigger way.

DAWKINS?: Well I suppose mass extinctions are very likely selective, but a very different kind of selection from the ordinary selection that goes on between mass extinctions.

So when you, a mass extinction is sort of more like a one-off event. And the permanent extinction most of the breaker parts weren't extinct and mollusks didn't for some reason. So that was a kind of selective event. But it's a totally different kind of selective event from the one that produces individual level adaptations within [breakier ponds?] or within mollusks.

MARTIN: Well, there is an argument slightly against that which is the [parallel?] patent of distribution of extinctions, which suggests that mass extinctions are part of a parallel spread so that there is a sort of continuum from small extinctions through medium to very large. Which to me suggests that the nature of the causes as with the explanations for avalanches, big ones and small ones are not caused by different things. [OVERLAPPING VOICES]

They're part of a continuum. So it does raise the possibility then that we don't have to look outside the system. What I'm arguing is we need to look inside the system and start to analyze system structure and to extrapolate that back through time.

MAN: I guess one thing is there are something like and if you look at the 20 largest craters on earth, only one of them, the [UNINTELLIGIBLE] crater, comes within a million years of an extinction event. So you're left with the question as to why all these other big impacts didn't really seem to --

MAN: Did not do it.

MAN: Yes. Didn't do it. Even if you found an impact with every mass extinction you know, you're still left with the question as to why did the other impacts not cause a problem? And I guess that's of a philosophical question you have to deal with.

MAN: It must be something to do with the system.

MARTIN: I'll just tag on that. I often ask geologists what would have happened if a 10 or even 15 kilometer meteorite had appeared 2 to 5 million years after the [crustaceous?]

[UNINTELLIGIBLE PHRASE], would there have been a mass extinction? Most will say probably not. And that sort of emphasizes the fact that the size of the meteorite may not be that relevant.

And what we're arguing with our little data set that I showed before is the size of the [UNINTELLIGIBLE PHRASE] is telling you something about the way the systems are connected at that time. It's really rather vulnerable. And you could have hit it with something quite small. It happened to be a meteorite. But it could have been a volcanic eruption or an [Antarctic?] event or those various other things.

So it's actually bringing the whole thing back into biology to some extent. So we've got to understand the nature of connections and model them and try to find how we get that out of the record in deep time.

MAN: I just want to come in on this particular issue before we, yes?

MAN: Mass extinctions do raise the problem of how you define success in evolution. These organisms obviously have been fantastically successful, but only for a period in some cases 2

and 3 million years or 20 million years. And then they've been completely wiped out. Is that success or failure?

MAN: Yes. I mean it obviously shows that success is not a word that a biologist would normally use, I think. It's successful for that particular series of ecological situations, but it carries risks. That carries a message for us too. It has relevance to the origin of the eukaryote cell because I've been trying to convince Lynn that actually getting towards true symbiogenesis in which organelles come together is quite a difficult thing and that symbioses clearly gets smashed apart within the scales of tens of millions of years and it might take a lot more than that actually to drive a whole series of organisms together to create new [cones?] of organisms. That may not be an easy thing to do.

WOMAN: It might not be a slow thing, I mean a fast thing.

MAN: It might not be a fast thing. It might take a 100 million years or more. Sorts of periods we worry about in geology but you biologists don't have to think about too much.

MAN: Raise this particular issue --

MAN: Yes, the mass extinction.

MAN: Yes, OK.

MAN: I just remember a simulation. I'm in the multi-agent area or was, and one of the simulations that was quite impressive was assembly language programs that had this cycle of mass extinctions simply because of the social inter-connections of the program.

And then another thing that was interesting is just because a program didn't survive doesn't mean it wouldn't survive later again. So say if we resurrect some of these things, it might be very successful later again. So I mean you do have this cyclic social behavior because one little element changes, it then gains a tremendous advantage and kills off all the other ones. But that's not what you mean. You say there's some external event --

MAN: No.

MAN: That this thing is so well adapted that therefore it's no longer adapted to the --

MAN: Well, to some extent, but I think that I agree with you that it is like those social connections. It's very much like the argument that all great civilizations have collapsed. All of them have and always will presumably by definition. And that they collapsed because they're complex structures, which tend to become top heavy or whatever.

MAN: Maybe [UNINTELLIGIBLE PHRASE] isn't necessarily connected with the structure, but the social environment in which they are, so that was the point of these programs. The one that survived had not much to do with their individual properties because they could survive later just as well. It's just that it happened to be that the constellation in which they were in then caused their at their moment [destruction?].

MAN: What this raises in my mind as this discussion develops is should we as it were throw our hands up and say that the evolutionary process is so historical that we cannot do a scientific analysis of it?

You were saying at one point, Martin, you disagreed with Gould on how [Chauncy?] [UNINTELLIGIBLE] was.

MARTIN: Yes. Yes.

MAN: But that would imply that you think you could do more than just say this is the history of life on earth.

MARTIN: Yes, I think you can point to short term winner and losers, I think, in these various stories. I would agree with Gould in the sense that I think that initial conditions are rather important in setting what happens later. And that if you reran the tape of the Cambrian explosion etc. etc. the outcome could have been different. I would sort of follow him in that way. Are you asking me the question as to whether there's progress or not in evolution?

MAN: No, no.

MARTIN: OK.

MAN: That's another issue, which I think raises very, very different questions.

MAN: But you could rerun the tape. I mean the tape was rerun in Australia, in South America, in the Old World, with really remarkably similar results. So there does seem to be a set of law [UNINTELLIGIBLE].

WOMAN: Convergent results, not [UNINTELLIGIBLE].

MAN: Convergent results.

MAN: Yes, yes. It does come down to that convergence, I suppose. I would suspect that the further back you go, the more difference those possible outcomes can be. I'm not absolutely convinced that there are just a few stranger [tractors?] in [morpha?] space like Simon Conway-Morris or other believe. I think it's much more varied and interesting that's beyond our imaging. Some of the possible outcomes could have happened if there was a massive meteorite bombardment in the middle of Earth history, which there wasn't. What we have here now might look very different, say.

MAN: But if there was a massive meteorite extinction now, I think I would predict that you'd get something pretty similar within 10 million years.

MAN: I think that's right, yes. Because we've reached a certain stage in the laws of development, I suppose that's right.

MAN: What's interesting about convergence is it never actually converges things that are particularly that far apart. I mean in terms of the tree of life. It can [UNINTELLIGIBLE] dolphins and [fit on that?] that diverse.

MAN: Well, you have the squid. A squid's [eye?], for example, I suppose, [UNINTELLIGIBLE] but it's still fairly [UNINTELLIGIBLE].

MAN: But I mean there's no giant purpose bacteria that do the same thing. And I think that's more interesting. The actually convergence only happens when you've got things that are already relatively closed related. I don't think it's a huge scale process. I don't think that you could say given bacteria, then humans, as some would.

MARTIN: I mean the little diagram I showed which shows these [forams?] keep coming back to this pattern. It shows how iterative and how there's a stranger [UNINTELLIGIBLE] that keeps drawing them to these particular shapes. The spindles and this and so on.

MAN: I don't know about [UNINTELLIGIBLE] because that comes from dynamic systems theory which I assume is [UNINTELLIGIBLE

PHRASE] point of mathematics and actually these systems aren't, they have their internal control. That's one of the things I think where Richard is strong on because you really do have some kind of internal information that in part is responsible for the ontogeny of the organism. So this notion of a tractor has a tendency to externalize that concept perhaps unnecessarily.

MAN: It's just a metaphor.

MAN: Yeah, I know it's a metaphor but it can be misleading. In the sense that if we're looking at an explanation, we have to also combine ontogeny with phylogeny and these external tractors may confuse that issue.

MAN: Perhaps you'd like to suggest another name?

MAN: Well, one thing would be that you look at punctuated at equilibrium, let's say. You can look at how particular homeotic mutations can lead to rapid morphorological changes. You can look at that kind of thing. That would be a way of looking at a tractor as given some ancestor, right? That you're within a constrained ontogenological space, right? Within the developmental space.

MAN: Let's use [UNINTELLIGIBLE] in inverted commas. Yeah, OK.

MAN: If you have a developmentally constrained space, that'd kind of like an attractor, but it's much more --

MAN: [UNINTELLIGIBLE]

MAN: Adaptable to understanding why you have a particular kind of evolution.

MAN: On this issue can I switch to a challenge to Lynn? OK?

LYNN: No.

MAN: Yes, [Steve?].

MAN: Quick question. I guess what I was reading about was often recognized your, at least in popular literature, is one of the most, one of the greatest mass vertebrate extinctions in recorded history is of [caplachroma encyclids?] in Lake Victoria after the introduction of [now perch?]. And actually I wonder if that's actually an example and particularly what you were just commenting on where the actual, it's also an example of one of the most rapid [monophilatic?] speciation events that we've

seen. Where over 500 species developed from a common ancestor. I think in less than 14,000 years, based on the time frame of what we now know is the age of Lake Victoria.

So I wonder if there's something there that suggests the actual speed of speciation at which this ecosystem reached equilibrium? It's also somehow involved with the speed of which, how the extinction of that actually took place. And kind of your analogy about an economic boom kind of setting up a crisis.

MAN: I know about the radiation of cichlids in Lake Victoria in that short time. I didn't about the extinction. What's the extinction story?

MAN: Well, now perch were introduced to Lake Victoria in the 1950's.

MAN: Oh, I see, OK.

MAN: And then since, I think eradicated nearly all indigenous species.

WOMAN: And when you say you know about the original radiation, what is considered the basis for the extraordinary rapid speciation in those fish?

MAN: Well, we know that Lake Victoria is only just over 10,000 years old. 14, 15,000 years old. And it looks as though all the cichlids in Lake Victoria have radiated from a single introduction.

MAN: You know, it was actually I think established through mitochondrial DNA.

WOMAN: Well, what is considered the reason? I mean, it's clear that you've got the new species and it's clear that you have very rapid speciation. Then what is considered, what is the difference among these that's considered to be, well, what is the cause of that, what is touted to be, at least, the reason that you have that rapid speciation in those fish?

MAN: Just ordinary evolution by natural selection.

WOMAN: Well, I mean yes, but that's not ordinary, if you've got to ask what the environment is that's correlated.

MAN: I suppose it was a virgin environment with nothing there.

WOMAN: And so you have different feeding habits on different --

MAN: Yes.

WOMAN: I mean, the idea is that niches were just vacant, is that the best --

MAN: Yeah, and it's convergent with Lake Tanganyika and Lake Malawi as well.

MAN: It seems like that's an example where morphological evolution outpaces molecular evolution. You know, at least on the timeframe that we would suggest the accumulation of random mutations. Go out, you know, 14,000 years to see that speciation.

WOMAN: That's very short.

MAN: Very short, indeed.

MAN: Yes.

MAN: It might well be the Cambrian explosion's quite like that. But the genetic diversity early on in the Cambrian is quite a lot lower than you might expect given the great disparity of the frogs. And there's quite a lot of rising feeling amongst practicing paleontologists that things that look very dissimilar like, you know, agnostics and paradoxides just to pick two trilobites that look tremendously different might be on to genetic states of the same thing. And then they're in fact so disparate I think they're in separate orders, that they may actually be juvenile and adult. And so you have --

MAN: Or another way to look at it is just that you have a different ethnogenetic control system that you have the same genes, I mean, basically genes don't evolve, really, in a sense. But the control system can evolve very rapidly in comparison to the genetic evolution, in sense of these protein-coating sequences. So in that sense, you could have rapid evolutionary development in the terms of morphologically with still keeping this, relatively the same set of genes.

MAN: Interesting. I mean, it certainly looks as if the Cambrian explosion was very fast, and they had been operating at something like the Lake Victoria rate, whatever that was.

MAN: But the Cambrian explosion, 10, 20 million years is a hell of a long time.

WOMAN: Relative to 10,000.

MAN: Whereas Lake Victoria is 10,000 years.

MAN: Yes, yes, but the disparities are pretty huge, too, so we've got to scale it up. But it's, geological scales, that's considered a pretty short period of time. And that 20-30 is probably an outside estimate. It might be less than that.

MAN: OK, I'm going to switch tack if the meeting agrees, to show a challenge over to Lynn. The question, I think, is how frequent, or how rare is symbiotic change. Let me try to put the question in terms of two what seem to me to be pretty remarkable discoveries of genetics in the last, what, 10, 15 years or so. One is the extent of genetic buffering, that you can actually play around with the genome to a considerable degree with not too much effect on the phenotype. The system seems to be able to, as it were, buffer out an enormous number of genetic changes. The second observation is that cross-species clones, by and large, don't work. I mean, you can make stem cells, you can get the embryo to, what is it, the eight-cell stage and a big

beyond, but you usually can't go much further. The only examples I know are ones that are not open to open science investigation because they're the wild ox that was cloned by one of the companies in a cow, the banteng. And as far as I know, it's the only example.

WOMAN: In mammals --

MAN: Bos javanicus.

WOMAN: In mammals, in mammals.

MAN: Yeah, in mammals, now --

WOMAN: Or if you're talking about mammals.

MAN: Now, you're already beginning to answer my question, but you see the direction in which I'm going which is this. That it seems to me to be quite, I don't want to sort of get an anthropological view into this, but it seems to me to be, we get caught up in language all the time, don't we? But it seems to me to be quite reasonable that cells should go on evolving just as genomes go on evolving. And therefore it's not too difficult to see why you might end up with this species having an egg cell

that can't accept the genome of that species, and form an organism. But if that is general, then symbiosis, at least in certain parts of the kingdoms, will be really very rare indeed, won't it? Now, let me just throw the challenge to you, then, because clearly you've got to respond to this, haven't you?

WOMAN: Well, I'm an mammalian idiot, so I can't, I mean I don't, but there's a couple of mammal cases that are really fabulous, though. And we don't see symbiogenesis when there's a disparateness in size. We see it always with lychins. 100% of the people who study lychins are Schwendenerists. There are no, lychins are not plants in any way, because the partners are very equal in size and you cannot study the fungus without the fico bond. But let's take the cow. All right? That's one of my favorite examples. The bovidé in general. Cow, oxen, I think sheep and goats, sheep and goats might be in there, too. I told you, I don't do mammals. But the point is that these animals are 40 gallon fermentation tanks on four legs. And when you look at the speciation that's gone on, in fact higher taxol levels, [isotricocilliats?] and [todiumorphidcilliates?], yeast, bacteria, and of course, they're studied because of milk, so we really know. We have fistulated cows we can study. They are dependent upon Miocene grasses to eat, and cellulose is a hell of a thing to eat, as you know. We just can't make it. If you

don't have a cellulolytic hypertrophied, what is it? It's the esophagus. It's a hypertrophied esophagus. And this is the basis of the taxonomy of all of these animals. And the placenta is sucked, licked and all that, why? Because the ciliates all insist. And if you don't get the ciliates, you're dead in two weeks with starvation. Now, we don't talk about that as symbiogenesis. That's [OVERLAPPING VOICES].

MAN: No, we do. I mean, there's no question that the bovidé are incredibly reliant upon their symbions. But you've suggested that speciation within mammals were the invertebrates.

WOMAN: No, not mammals. I never say anything about mammals --

MAN: Vertebrates, let's just take animals. You suggested that speciation in animals is nothing to do with mutation and selection and ordinary [OVERLAPPING VOICES].

WOMAN: No, not nothing to do. Not nothing to do. I'm saying, there's two things, let me say it very clearly. I have no cases where just simply the gradual accumulation of mutation has led to a new species. And the touted case was [UNINTELLIGIBLE] with a wonderful experiment. But we now have great insight into that experiment. That was the cold and hot [UNINTELLIGIBLE] cages,

that after two years they couldn't mate again, you know, this is the famous case. In fact, I was just written by somebody, written to by somebody who's worked on that again. You know that case? Yeah. Well, let me just, of course mutation occurs. And of course mutations are cumulated. They are not sufficient in any case to make speciation, in my opinion. And let me give you what's the most beautiful case of all. It's a dyed in the wool guy who's a neo-Darwinist from way back, population geneticist and so on, named Werren who has studied --

MAN: It's a wasp.

WOMAN: I think it is, parasitoid wasp. Something like that. Anyway, Wolbachia variance, these are, which are they, they're [U?] bacteria for sure, but I mean, which one, are they gram negative U bacteria of some kind. The story of the inordinate fondness of beetles is missing the last line, the inordinate fondness of beetles and their Wolbachia symbiots. What do I mean? They've found spectacular cases where differences in Wolbachia, which you don't see, they all look like beetles. I mean, they don't, you don't see them because you don't see those bacteria. They, nitrogen metabolism varies in the Wolbachia. Hormone production that changes gender differs in these Wolbachia. But the coup d'état was when the entire Wolbachia

sequence was, the genome was sequenced, and it's not even the size of typical bacteria, it's smaller. The genome was labeled with [UNINTELLIGIBLE] DNA. And the whole damn genome of the whole Wolbachia is on one of the odd assemble chromosomes as a little clump of chromatin. The entire genome is segregates. Now, I would say that the fact that the entire genome of that bacteria has been incorporated, how much more intimate can you get into the chromosomes of the nucleus, that that is a much more important event. And so it's genome acquisition. It's not gene mutation.

MAN: You're not serious suggesting that, I mean, that's a lovely example, it's one off example --

WOMAN: No, it's multiple.

MAN: You don't really think that if you look at the entire family tree of animals --

WOMAN: No, beetles. Let's just stick with beetles. Well, I don't know animals, I don't know mammals.

MAN: I mean but no, you've suggested in your book that speciation events are matters of symbiotic --

WOMAN: Symbiogenesis. I have, and I stand up for it.

MAN: I don't believe you can. I mean, you cannot be serious --

WOMAN: Yeah, well, you give me, please, this is wonderful, you give me any example. I mean, I asked Niles Eldridge, I asked everybody, I ask everybody, just give me the poster child for simply documentation, even in the fossil record, in laboratory cages, or in the field, any case where it's documented from the beginning to the end, this is one species, these are the events that are accumulation of random mutation, and that has transformed to the other species.

MAN: You don't have the documentation for symbiogenesis, either.

WOMAN: Oh, no, that's not true. I can show it to you right now.

MAN: You have it for Werren's wasps, I mean.

WOMAN: No, no, no, Werren's wasps solved the beetle aspect. My cases are really clear. They're much clearer because they're green. Once they're green you can follow anything. And the cases

are, for example, on the coast it's actually Jersey and Guernsey, it's right around here, I mean, relative to Massachusetts it's around here, and it's also West, it's also Atlantic Spain, where it's a flatworm. It's call convoluta roscoffensis, you've seen it huh? Robert, you've seen it? More than in the movies? You've really seen it? Recently?

MAN: Well, when I went to Roscoff, yeah.

WOMAN: Oh, Roscoff, yeah. But not this week, in southern --

MAN: No, not this week.

WOMAN: Yeah, OK. Well this is, you, I've never seen them live, but I've seen all the literature and the movies and I have the movies. What you have is convoluta roscoffensis was described be Keeble in his little book called, Plant Animals, because he'd see them every summer, 1920 book or something. Anyway Roscoff is a marine station in France and so it's very well known that people go there in the summer. Well, convoluta roscoffensis is, covers the entire beach in these channel islands and Spain, and you think it's green algae. It looks just like green algae. But when the tide comes in and it thumps, the green disappears. It's because convoluta itself is a flatworm. And convoluta convoluta

lives right around there, so they know, and that eats algae and it's got totally wormlike behavior. Convoluta roscoffensis has eaten platimonas, and we know that that's three different genomes there, because it's nucleocytoplasmic chloroplastin [angelopodium?]. And the eggs hatch and they just are regular convoluted eggs. But the animal eats the seawater and it keeps, of all the things that come in with the seawater, it keeps one, it's a parafertilization event. It keeps this green algae, and every member of the population is 100% green, and they all photosynthesize, and so David Smith has shown that the carbon dioxide is incorporated into photosynthate, and their mouths are no longer doing anything as far as feeding. Now, and they grow in huge patches, whereas the other ones are not lying in the sunlight, they're not phototropic, in other words, the ones that don't have the algae. So we have convoluta convoluta, no algae, standard flatworm. And I don't make the names up, convoluta roscoffensis, which is the green one that we're just talking about, and then there's convoluta paradoxa, again, I don't make the names up, the naturalists make up the names. Convoluta paradoxa does not grow in large groups, it's solitary and it doesn't have any green algae symbionts, it has diatom symbionts, and therefore it's brownish color. So the naturalists have gone in there and said, here we have one genus and three different species, and it's very clear that that's a, speciation is

totally correlated with the presence of no symbionts. Green algal platimonas symbionts and the diatom symbionts.

MAN: But you know, I think though you're missing the point, though, because, yeah, sorry.

MAN: Yeah, OK, Eric first and then --

MAN: Because I mean --

MAN: I'm looking out to see, and you want to come in.

MAN: And my goodness, [UNINTELLIGIBLE].

WOMAN: Your witnesses?

MAN: Where did we get? There's Eric first, please.

MAN: So I mean, what Richard was talking about is really the, any, you know, in a particular instance where something gobbles up something, OK, then incorporates its genome, that doesn't mean it, that's the way evolution works in general.

WOMAN: No, I'm saying that's the way evolution works in general.

MAN: No, yeah, exactly that's what you're claiming.

WOMAN: Yes.

MAN: So you're claiming from a particular --

WOMAN: I've just given you one example.

MAN: Yeah, exactly but if anything [OVERLAPPING VOICES].

WOMAN: Let me say something very clearly, too, first --

MAN: And what we also have to explain with evolution is not just the gobbling up and utilizing the genome for catching whatever light rays, we have to explain the morphological evolution. What you have to do, in order to make a case, is actually have some kind of symbiotic effect that then effects the ultimate structure of a multi-cellular organism that gives Dennis two heads instead of one head, for example.

WOMAN: Not Dennis.

MAN: And your theory doesn't explain that. I mean, I agree with you in a sense that you can have rapid evolution with genome incorporation, right? Where you have the bacteria incorporate --

MAN: Happens once in a blue moon, and very important when it does.

MAN: That's the point I was going to make as well, is that there's a fundamental problem with that as well on the biochemical level, which is that the machinery that the bacteria used to express their genes is different from the host organism. The host's replication and transcription machinery will not recognize the appropriate signals in the bacterial genome, so that genetic material becomes junk DNA, becomes simply a passive component of the host genome, it's not actually going to contribute because it can't be expressed.

WOMAN: Well my answer to you is that you don't know this until the detailed examples are studied, and I would maintain that in all the good cases, now you see the symbiosis that you can study are the ones that are very recent and new and one is green and one is, one is green and it's an algae and the other ones a worm. The ones that are really well known and best are in the

insects and [biosis?] literature because in all these cases that are really studied you have an insect, which is a eukaryote with all of its features, and you have a bacterium, and when each partner is very similar, that set of partners, like all beetles, are very similar to each other, and each of the other symbiont are very similar to each other, like all the Wolbachia. Then the changes are subtle and they're very hard to see as dramatic changes. But I will say something that I haven't said at all, and that is, in my opinion, prokaryotes are very distinguishable. They are differentiatable. But I do not believe that speciation as a word is appropriate for prokaryotes. That's my opinion.

MAN: Well that's probably right, but if you take the standard story for ordinary animals, and what's wrong with it, you've got a distribution of animals. You've got a promontory or an island or something and so you end up with two distributions there.

WOMAN: This is a geographical diagram?

MAN: Just geographical. And then on either side of this promontory, you get different selection pressures and so this one starts to evolve that way, this one starts to evolve that way, and what's wrong with that? It's highly plausible, it's

economical, it's parsimonious, why on earth would you want to drag in symbiogenesis --

WOMAN: Because it's there.

MAN: -- when it's such an unparsimonious, uneconomical --

WOMAN: No, let me say something about this. I don't want to get into a big fight about this, but in addition to the standard symbiosis events that I'm talking about, there's also, in mammals, a wonderful history and literature on karyotypic fissioning, which is not directly symbiogenesis. It is indirectly, I can show you also, it's ultimately symbiogenesis. And that's a chromosomal level phenomenon comparable to polyploidy in plants, I would never argue that polyploidy is not involved in speciation in plants. So when you get to eukaryotes, there are chromosomal phenomena that are unique and so on. But you. I want you to answer my question, which is give me any case in the fossil record, in the laboratory, in the field or anywhere else where simply the accumulation of random mutations has led to a step from one species to another where it's the naturalists that are changing the names of the species. And, you know, and not like in Daphne Island where they have wonderful

stuff, but no one has changed the name of any of those species because they [OVERLAPPING VOICES] species.

MAN: Well, while people are thinking about that, there are two other people who wanted to come in, and then we'll see whether somebody's come up with --

MAN: Might I actually comment directly on that question, actually?

WOMAN: Do you have an answer.

MAN: Oh, OK.

MAN: Well, I mean, the allopatric speciation mechanism you've just drawn up is not necessarily about the accumulation of mutations, it's about the movement and selecting of variety that always [OVERLAPPING VOICES].

MAN: Even within the same genome.

MAN: That's already there. And so you don't actually have to have the mutation to do that. So that's [UNINTELLIGIBLE] just to throw that back. The second thing is that I remember vaguely

reading something in Natural Science Research, potentially dangerous, and but there was some report of the snail in Hawaii that had, you know, had its gonads on the left side of the body. And there was one gene the coded for the [corality?] of the shell. And because the shell came out so far that if you changed the direction of the corality they couldn't get the gonads together between a left and right [UNINTELLIGIBLE] snail. So if you've got this mutation, which was sort of one in five from right to left, then the left-coiled child had to go and join a different species to its parents because it couldn't actually interbreed with the right.

WOMAN: And the changed the name of the species?

MAN: And, well they gave them subspecies names. And I don't know, I mean, I guess the question here is whether there was a backward mutation that allowed the lefts to go back to rights, and maybe there was, which over potentially, you know, multiple generations would mean that there wasn't actually speciation, but you know. But I do think it was interesting that this case exists. I mean, it's quite close to being the sort of hopeful monster situation, but it's, it's all sort of interesting.

MAN: Can I bring in the, before we come back to you then, and maybe to Richard, can I bring in --

MAN: Yeah, I actually have a string of arguments, so be free to jump on all of them, but the first thing is that you criticized that they haven't seen speciation event, and you haven't either, you've just seen three different species that have three different properties, and humans have a different group of symbiotic flora in their gut --

WOMAN: Flora, they're microbiota, please --

MAN: -- as do, [OVERLAPPING VOICES] see this is, you can't actually have an argument until you actually hear what somebody has to say.

WOMAN: That's right, thank you.

MAN: That's a problem, actually.

WOMAN: Yeah, it is a problem.

MAN: So if you were to look at humans and gorillas and orangutans, you would find that they had different symbionts, so

I could conclude based on your logic that the symbionts are the reason that there's a difference between orangutans and humans. And that is just completely illogical. The second things that's illogical is, you can't argue a generality from an example because both things might be true. So nobody's arguing that symbionts aren't important in terms of the biological environment that creatures live in that cause their evolution. That's just, nobody's actually saying that. If you want to look for a speciation event that involves DNA, all you have to look for is poliploidia plants. That's an example where something actually speciates and it's all based on DNA, it has nothing to do with symbionts. It's, but it doesn't actually address this other question which is that when the environment changes that there is material. And if you want to say that there's no examples of that, then you actually haven't looked at the fossil record because what we don't, we don't see any record of symbionts changing, we see gradual change over time in different structures and organisms, I mean that's what the entire fossil record, and if you say, well you don't have the DNA evidence, that's because yes, we don't have the DNA evidence because we can't get DNA from fossils but we don't have any --

WOMAN: Yes you can.

MAN: What?

MAN: Well, not very far back.

MAN: OK, not very far back. And as far as the question about speciation is concerned, yes the definition of species is problematic if you actually look at the data from the grants. The grants actually believe that a true speciation event in birds takes about 30 million years which according to, if just interbreeding, that there are no species on, in the Galapagos and finches, that they're actually all capable of interbreeding. So, but it doesn't mean that you don't have distinct groups of birds that do distinct things that have different species names to them.

MAN: Did you want to come in on this?

MAN: Yeah --

MAN: I'll bring, I'll give you an opportunity later on. We'll accumulate the --

WOMAN: That's all right. [UNINTELLIGIBLE]

MAN: On your shoulders, you can accumulate the weight, yes?

MAN: I do think it's in danger of becoming slightly unfair on women, the sense that since we're now accusing her of arguing from a particular to the general when she made a perfectly general statement about what the role she things symbiogenesis has in evolution and then was asked to provide examples of that. And then --

WOMAN: You don't have to have defend me, it's all right.

MAN: Everyone sort of saying that because she's provided examples, she's arguing from the particular to the general. It may be that she believes that there are many, many examples, but we can't sit here and talk to all of them.

WOMAN: Symbiogenesis --

MAN: It's terribly important in evolution --

MAN: Yeah, and --

MAN: But not in every speciation event.

MAN: I'm not arguing [OVERLAPPING VOICES] at all. All I'm saying is that we can argue over the particulars of any example that she's given, I think that's perfectly reasonable, but I don't think it's fair to attack just because an example was given, and that she's arguing from a particular general question that you lobbied.

MAN: Well, you can argue that she gave an example of speciation that wasn't an example of speciation. We didn't see something go from one species to another after accumulating a symbiont. All we saw is that there's a correlation between the presence of a symbiont and the difference in a species. That's not a speciation event.

MAN: I think, I mean, I think it does come also down to, you know we often talk about the level of our definitions but when we, it depends on what we define as an organism. I mean, and the difference between an organism and an ecosystem is not really an arbitrary distinction when we're talking about something like speciation. Because the suggestion is that by incorporating a symbiont, this relationship actually forms a new organism, and then it's actually the composite, I mean, I've read it in one of your papers where you say that individuality is relative. And it seems like that suggestion is that any speciation event, I don't

know. The way that we define our organism I think depends, has a lot to do with the way we would define what that species is. Is that two separate species that are working together or is that actually, or can we say that this ecosystem or this community has become a new species?

MAN: Well, the lichen is a perfectly good example, because according to the argument that you make, if one particular fungus picked up one algae, then it would be one organism, but if it went and picked up a different one it would be a different species and we should give it a different name. But that's not actually what happens. What happens is they've actually evolved so that the particular lichen actually is a combination of one particular species of algae and one particular species of fungus. So they've actually evolved together in a co-evolutionary way.

WOMAN: Well, first of all, there are lots of lichens that have the same fungus, I mean, the same fungus, and on one side of those, that lichen it's lichenized with a cyanobacterium and the other side of that lichen is lichenized with a green algae. On the side with the cyanobacterium, the carbon that flows is glucose. On the side of the green algae, it's a sugar alcohol like mannitol or ribitol, and that you could just, you could cut

it and the morphology is completely correlated with one or the other of the symbionts. You could cut it in half and just show this one, and that will have a name, its lichen name to a lichenologist, and you could show that one, and it, so the same organism is changing its name as a function of its symbiont.

MAN: In fungi, many of the species that are actually, have a sexual phase that's identified, the sexual phase has one name, and the asexual phase has another name, and they look completely different, but they're not different species. Giving them a name doesn't mean a thing.

WOMAN: Oh, so we are not to trust the naturalists on the names, either?

MAN: No, because if you find they have identical DNA, then --

WOMAN: Oh, they do have identical DNA, these have, well these, they have different DNA. They have different DNA depending on the partnerships. It's, there's a very fundamental kind of investigative aspect here. If the organisms are very different from each other, it's, that is the partners are very different from each other, and they are cyclical, like lichens, that is, they can be separated, then it's very clear they're two

different organisms. But when the integration is first of all permanent, it's not temporal, it's permanent, and the integrate, and the partners are very similar to begin with, then nothing is left but the Cheshire Cat's smile. In other words, if you want, you can't have it both ways. And when we trace the good cases, then you have to have differences. I have with me a case which is an answer your question to some extent, of an organism that was put in a barium called geosiphon pyriformis in the 19th century, and it was put as an algae, they didn't know what it was. An algae. It turns out that not only is it not an algae, there's nothing about it that's an algae. In its form, the organism itself looks like a moth, and I can show it to you, you can see it forming yourself, it is formed by a fertilization, that is a fusion, a breakdown of cell walls, and the complete fusion of organisms not of different, very close relatives, not of different species, not of different genera, not of different families, not of different orders, not of different phyla, different kingdoms. And one of them's a cyanobacterium and whatever, however you, it's a prokaryote. Absolutely, 100% nostoc. And the other one is a fungus, and to make this organism, every six weeks you have to have a para-fertilization. Now, that's not allowed by biology, but there it is in nature.

MAN: Of course it's allowed, why shouldn't it be allowed? It's a perfectly interesting phenomenon.

WOMAN: Because you can only have a [fertilization?] with your own relatives of the same species.

MAN: No, rubbish. I mean --

MAN: I wanted to come in [UNINTELLIGIBLE]. And I want to try and return to the original question.

MAN: I think the generalization maybe that you're giving is that you think that evolution proceeds more the by the combination of the genomes, which may be from disparate organisms --

WOMAN: Heterogenomes.

MAN: And then, whereas Richard is saying, evolution proceeds by mutations of a given genome, and I can [OVERLAPPING VOICES].

MAN: Occasional major events, yes.

MAN: Or even, or even without mutations.

MAN: Yeah, I mean, you bring some beautiful examples of, you know, I come from a multi-agent area where you have these cooperating agents with different strategic abilities. And the kind of thing you're talking about fits beautifully with that sort of view of things. So you can no longer really define an individual because they're cooperating so much they tend to become an individual. And so those examples are quite striking. I like it, so maybe --

WOMAN: It's individuality on a more complex level of an organization.

MAN: Yeah. But maybe evolution proceeds both ways. I mean, obviously you have to have mutations to get your original genome that combines with the other genomes. So you do have mutations that actually develop a species at some level, right? Whereas you could have rapid evolution by the kinds of mechanisms you suggest. It's just very hard to see how that happens with multi-cellular organisms.

WOMAN: You mean with animals. Please, all the cellularities of, yes.

MAN: Well, big things with lots of cells and they're different.

MAN: [UNINTELLIGIBLE], you wanted to [OVERLAPPING VOICES].

MAN: We have raised this question of whether symbiogenesis is important, and I just want to give a geobiologist's view of what is important compared to what might be an evolutionary biologist's. And we tend to view a creature according to a spectrum of their impact on the planet. OK? So it's not like looking at the enormous diversity in the rainforest, but what is their impact on the carbon cycle and the biogeochemical cycles? These are the things we focus on. So I'm going to bring the discussion a little bit back to foraminifera. And back in 1856 when they were trying to lay the first transatlantic Morse code cable across the Atlantic, they had to learn out what the bottom of the Atlantic was like, because they had no idea how deep it was, if there was any life down there. And Captain Berryman of the US Navy started with a series of deep sea trolls. He took 12 across the Atlantic. And they went down, of course, to three or four thousand meters, or whatever it was, and they discovered the sea floor was absolutely covered in foraminifera. There's nothing but this enormous, great deposit of chalk, that Huxley so evocatively wrote about. Nearly all of that is foraminifera, and nearly all of those are symbiogenetic foraminifera. The vast

bulk of the calcium carbonate that ends up in the deep sea is the product of symbiogenetic evolution between particular forams, in this case, dinoflagellate symbionts. So although it may not be quantitatively important, there's only about 40 species of planktonic foraminifera, in terms of geobiological importance, it's really rather a significant thing for us to look at. And like both the coral reefs and everything that Darwin was so fascinated by, the corals themselves, where actinions cultivate dinoflagellates and most of that wonderful star sand that accumulates around them is foraminiferal symbiogenesis. So importance in a geobiological sense shouldn't be dismissed here.

MAN: I bet it's vastly important, but it's not, nothing to do with speciation. I mean, all these animals are symbiotic, we're all symbiotic. We're all, I mean, joining up of different things and all, but as we speciate, our simbionts speciate with us. I mean, they go with us. It's not that speciation causes, so it's not that symbiogenesis causes the bifurcation between at least animal, but it's, I mean nobody is saying that symbiogenesis isn't important or that they --

WOMAN: Oh yes they are. In the Oxford museum, what's the name of, the Natural History Museum?

MAN: It's the University Museum, yes.

WOMAN: What is it?

MAN: Well, it is the Natural History Museum now, yeah, that's right, yeah.

WOMAN: Yeah. And they're going to have an exhibit of Bishop Wilberforce and Thomas Henry Huxley, and I was told when somebody asked, well, what are you going to do about symbiogenesis, you know, when you have this big Darwin evolution exhibit, a zoologist professor said, well nothing, that's only relevant to protists.

MAN: Well, look, it's very important. Let's say it's fantastically important. But it's not, it's nothing to do with speciation, that's the only thing I'm going to say. I mean, you were trying to imply --

WOMAN: Well I, I see. I am, no I'm not trying, I'm saying it.

MAN: I emphasis, you know, for the microbiological standpoint, I emphasis the importance of our relationship with

microorganisms by saying the following thing. First of all, if you count the number of bacteria in the human body, it outnumbers the number of human cells ten to one. So we're much more bacteria than human. If you count the number of mitochondria in every cell, they greatly outnumber the number of human cells. So we're much more bacteria than we are, and if you count the number of genes that are devoted to retroviruses, it outnumbers the number of genes that are devoted to humans, but it doesn't mean that humans evolved because of that.

MAN: That's the point, that's the point. Exactly right.

MAN: That's all part of our, that's part of our biological endowment. We are way more microorganisms than human, but that's not what created humans. And if you look through mammalian --

MAN: That's not what split us off from chimps.

MAN: Exactly. And you can't really make that argument for any mammalian evolution or most different organisms.

MAN: Or [UNINTELLIGIBLE], animals general.

MAN: Animals, yes.

MAN: So your argument is for coevolution rather than causation [OVERLAPPING VOICES].

MAN: We have evidence by sequencing that these, you know, that the web of life thing happens at intervals. I wouldn't say it happens frequently, but I think it's very important. We find mixing and matching of kingdoms and things like that. So we know it happens. They may be critical events in evolution, but they're not the thing that goes from one species to another.

MAN: Well that was part of the reason why I originally posed the question in terms of frequency. Are we talking about events that, while rare, are nevertheless important and importance doesn't necessarily have to go with high frequency.

MAN: Very rare and very important.

MAN: Now, the question that I would like to come to is a sort of, now, I return to my roots as a physiologist for a moment, you see. What astonishes me, I'm going to be a very naïve person just for two minutes. What astonishes me about this debate amongst all the various evolutionary theorists here, is the almost certainty with which they state some of what they state.

I don't, this is an accusation against all of you, clearly. Now, that sort of clears me of any partisanship. However, isn't the problem this? Would you, just to be totally naughty, let me imagine the following. Let us imagine that Lamarckian forms of inheritance have been vastly more common than we think at the moment. How would we know?

WOMAN: We don't study it.

MAN: Just looking back through the record and looking at, you know, each and every one, how would we actually know, either from the genomic record or from the phenotypic record, to the extent that we can measure it, that that was the case or not?

WOMAN: What kind of Lamarckian --

MAN: Well, what I have in mind, you see, is the, it's obviously going back to the Waddington idea that you can by cannolization, as it were, lock a genome into a particular direction which then gets selected, so you end up with the evolutionary line going in that direction rather than that direction. But looking back on it, how would you know that that was prompted by the environment rather than by some mutations?

WOMAN: Can you answer?

MAN: No, I can't. That's the point. That's the whole point. You see, I find the degree of certainty with which people are saying, it's this, it's that, utterly astonishing given my views as a physiologist, you see? I don't know if anybody wants to take up that challenge, this is rather shaking the boat deep down. He's going to take it up.

MAN: Well, Simpson wrote about horse evolution, that all trends aren't real. And effectively, you know, when we look back through historical data, the fossil record, you know, you can always see evolutionary trends in whatever way you like, because you can always draw a straight line between two points, a start and an end. It doesn't make it real. So I guess that's what I'd say to it.

MAN: Yes, but it's the problem of mechanism, isn't it?

MAN: Sure, but the point is that the mechanism presupposes that there's something that warrants the explanation. There's actually a direction already that has a mechanism, whereas in fact, if there is no directionality, then in a sense it doesn't have to have a mechanism. That's what I mean.

MAN: Now we get on to the question as for do we --

MAN: That's [UNINTELLIGIBLE] procreation is [UNINTELLIGIBLE].

MAN: I'm just a geographer, I'm a poor farm boy from New Hampshire, but it seems to me that one of the problems is that we have lots of definitions, and the definitions are all completely arbitrary because the Earth isn't divisible. And all these systems aren't divisible. So we've invented lots of divisions which are not real. Lynn has a definition of symbiogenesis and it has to do with the contact of one organism with another for the major part of at least one of their lives. And, but if you go out into nature and you loosen up that definition of symbiogenesis a little bit, you find that everything lives in some kind of loose symbiotic relationship with other things. I mean, nothing lives in isolation from anything else. It's, the definition, is there a definition of speciation that anybody here in the room can enunciate that everyone else in the room would agree to? It's a completely artificial --

MAN: Well, the separation of a previously interbreeding population into two new populations which can't interbreed.

MAN: Well we have wood ducks in Massachusetts and we have mallards, and they are completely separate species that do not interbreed, but if you put the wood duck in captivity with the mallard, they interbreed just fine and have offspring. They're two, they're called two different species.

WOMAN: But even worse, we have, all the protoctis we work with have no sexuality at all, so interbreeding's not relevant.

MAN: No, no, no, it doesn't work for, that's absolutely true.

WOMAN: That's an animal definition.

MAN: Yeah, yeah. It doesn't work for --

MAN: I guess my other point is just, I'm curious, Professor Dawkins, this business of it, these symbiotic events being very, very rare and that's a statement that's made a lot, but, and I just wonder why, if you have an event that gave you the use of oxygen, you have an event that gave you the use of photosynthesis in higher organisms, the symbiosis events that the incorporated mitochondria and chloroplasts, where nature has had this fabulous success with taking things that are ready-

made, off the shelf, just like people did when they built an automobile, they didn't invent all these things, they took things off the shelf and stuck them together and they made an automobile, why would this huge success, would nature abandon that and go for something where the odds are so incredibly long?

MAN: It doesn't abandon it. It's been, it's extremely common in the sense that we all are symbiotic things in which, it's gone on, what's rare is the incorporation of new genomes. Whereas Lynn is suggesting that every speciation event, the separation between humans and chimps, the separation between chimps and gorillas, the separation between chimp, gorillas, and orangutans, every one of those was involved with the incorporation of a new symbiont. I mean, that's an incredibly unparsimonious idea. It could be true, but you need evidence for it, it's not the sort of thing you just --

MAN: Let's, could we just, I want to follow up on that. Can, I mean, Lynn has asked, can you give an example of a case where you have the accumulation of random mutation causing a speciation event?

WOMAN: And you have the documentation of it?

MAN: Well let's not, why concentrate on mutation? It's selection we're talking about, or simply drift. Drift in geographical separation.

WOMAN: This is back to what Lerner's saying. That selection is going on all the time, and geological, geographical separation is going on all the time, and certainly that doesn't preclude, it's, the process of evolution absolutely requires what you're drawing here. And nothing I've said has anything to do with natural selection acting, it's, whether it acts on symbiotic partnerships or individual lineages where mutational change is the [OVERLAPPING VOICES].

MAN: But do you think a new bacterium was incorporated with every speciation event, for example, the separation between chimps and humans? Did some new symbiont come --

WOMAN: No, I actually think that it's, in addition to geographical isolation, and in addition to some mutations also, I think that the big event there is karyotypic fissioning anyway. You know about karyotypic fissioning.

MAN: Yeah.

WOMAN: Yeah, well that's what I think is the best for mammals.

MAN: But that's not a new symbiont.

WOMAN: It's not a new symbiont, no. What it is is a behavior of the symbiotic residue in the chromatin relative to the rest of the chromatin. I mean, it's a function of a certain, it's really not, it takes a long time to explain, and it's not, it's a dry feature of something that ultimately started as a symbiosis, but no it wasn't a new symbiosis. The case you guys ought to know about is [Hautina?], thought, do you know about Hautina? It's a case. It's a single case.

MAN: We don't want another anecdote. I mean, this is --

WOMAN: OK. No anecdote.

WOMAN: [OVERLAPPING VOICES] comment. One is that we're thinking about evolution in terms of mutation, but technically speaking you can really measure the number of mistakes polymerase can do at copying the DNA. So you can measure that and that is very low. And as far as I know, well, what we're saying here is, evolution in organisms that have the classical sexual reproduction both symbiosis theory's more like classical

transferral, transfer, division, like bacteria and so on. And I start getting [UNINTELLIGIBLE], breathing heavily. I'm sorry [UNINTELLIGIBLE]. But my [UNINTELLIGIBLE] like, we think like, OK, chimps to humans, and but how many mammals really in the planet compare with all the bacterias are, we are really low numbers.

MAN: Oh, that's true.

WOMAN: It seems to be important because we are humans we care about humans a lot.

MAN: That's true.

WOMAN: But technically speaking, it's a very weird phenomenon where you have a mutation which really keeps [UNINTELLIGIBLE] change. It's not changing the code. Basically, the big important mutations is in transcription of [UNINTELLIGIBLE] wherein you change the way they read the code. So I think incorporating a piece of genome really give you a large amount of new information that you can interpret in new forms. So, well anyway, humans, I don't know --

MAN: That's hugely important in prokaryotes, no question. But Lynn was suggesting it's important in eukaryotes and in animals, and that's just overstating the case.

MAN: Actually, this is a really interesting example that has to do with mutations. It turns out that if you were to graph the size of the genome and the number of mistakes that the polymerase makes, you get almost a linear relationship. So that we make approximately one to ten mistakes every time we replicate, based on the accuracy of our genome. HIV and flu make about one to ten mistakes every time they replicate their genome. And you can do it through, and basically that mutation rate is actually optimized in evolution so that you have a certain rate of evolution, not too fast, not too slow, and the critical experiment --

WOMAN: The rate of mutation or evolution?

MAN: -- the critical experiment is, this is, I was working with E. coli, and there are mutations that you can make in E. coli that either increase the accuracy of the polymerase or decrease the accuracy of the polymerase, and if you let them free run, in every single case they mutate back to the optimal rate of mutation. Because that actually, it shows that there's some

advantage to mutating at a certain rate, not too high and not too slow. And it's not because that helps them incorporate symbionts, it's because it allows them to undergo a progressive change to the environment.

MAN: How would that know, I'm puzzled about the mechanism there. How would the system, whatever you define the system there to be, know what is the correct rate? Because this looks like a backwards explanation to me.

MAN: It does, the system does know because it actually mutates back to the [OVERLAPPING VOICES].

MAN: Well that's right, but I think without an explanation of how that happens --

MAN: Well, explanations are human, phenomenon are nature.

MAN: Oh dear. [LAUGHTER]

MAN: The human explanation is that if you mutate it at too high a rate, that you make so many mistakes that you can't actually function. If you make too low a rate, then you're not flexible

enough to the changing environment, so you actually don't outcompete your competitors.

MAN: Now, who are you, though?

MAN: The bacteria.

MAN: Oh, if it's bacteria that's fine. It'll work. OK.

MAN: Are you suggesting, though, that it also works for eukaryotes, right? And the fact that you have some --

MAN: Our mutation rate is on that, in that --

MAN: Optimum mutation rate in eukaryotes, I would suggest, is zero.

MAN: But we could easily make a polymerase that's [UNINTELLIGIBLE].

MAN: I think the point of having a mutation rate is to maintain some variety in the gene pool.

MAN: If that's the group selection explanation, yeah.

MAN: The mutation rate in mice, [OVERLAPPING VOICES] the mutation rate in mice, because mice basically have about the same number of, they have the same number of cancers, they have the same number of mutations approximately we do. They live for about one twentieth as long and they have about 100^{th} as many cells. And so they actually have a higher mutation rate than humans do. Why don't mice have exact, I mean, they're eukaryotic polymerases, why don't they just have the most optimal low, low mutation rate polymerase possible? But they don't.

WOMAN: Yeah, but [UNINTELLIGIBLE] they can, you can mutate all the time, but you can get cancer or illness or whatever. Their mutation must be in the [germinal?] line, which is even more weird event. So it's kind of like, very low, low, low number.

MAN: I think you're also bringing us back to the point that the human, in the earlier session, that if we look at a gene as a replicator, we also have to appreciate that it's not just the gene, but the mechanism by which the gene replicates. And that, do we call that whole system the gene or do we recognize it as just the gene? And that, I think that that does suggest, I don't know. It complicates this argument to say that the optimal rate of mutation is determined within the gene. That --

MAN: No, it's determined by the organism.

MAN: Well, then if it's determined by the organism, then that suggests that it's relationship around it --

MAN: You've shifted the concept of a gene away from the molecular biological definition.

WOMAN: This is just want he's [OVERLAPPING VOICES].

MAN: You mean you've turned the gene into something that's actually, the replicator into a relationship between those things as opposed to a code of DNA?

MAN: Yeah. Do we want to return to that debate? Because I --

MAN: Excuse me, sir.

MAN: No, no. I, this goes in, I mean, this is in evolution. It goes in whatever direction you want it to go. No, seriously, that was an issue that we left a bit in the air, actually, though we did debate it. So if people want to return to that issue, that's fine.

MAN: I mean, I'd be interested in what, you know, you and Richard have some difference of opinion about the replicator concept. You know, in your book you [OVERLAPPING VOICES].

MAN: Yes, that's right, because I sustain --

MAN: -- have the opposite interpretation of, how do you call it? You have the --

MAN: Well, I though --

MAN: I would like to have you and Richard directly address that issue.

MAN: OK. I think we're using the word replicator in slightly difference senses, you see, because I regard a cell as also a replicator, and he says no, it reproduces. Now I, what I then need to know is what's the difference replication and reproduction.

WOMAN: There is a big difference.

MAN: Let me try --

MAN: Yeah, so should we try to clarify this?

MAN: -- try an analogy. One that I used before. It's the analogy of forest fires, bush fires. So we have a great prairie with dry grass and a fire starts, and sparks fly up and they land and they start a new fire. And sparks fly up and they start a new fire. So every fire can be said to have a mother fire. So we have mother fires and daughter fires, and there are lineages of fires. So these little fires clearly are reproducers. They are, if they are, they have parents and daughters, and sparks fly up from one and start a new fire. In order for there to be heredity, it would be necessary that something passes from parent fire to daughter fire which determines or influences the form of the fire. Now, these fires are different. Some of them have a slight blue tinge because there's copper in the soil, some of them burn faster than others because there's, it's a windy place. And what I'm saying is that the characteristics of these fires are all determined by the local conditions of the grass, the wind, the soil geology, etc., the soil chemistry. Nothing passes in the spark that goes from parent fire to daughter fire. If something did pass from the parent fire to the daughter fire, if something went in the sparks such that a blue

fire here gave rise to a blue fire there, that would be true heredity. That would be true replication of something.

MAN: Well, if it was something that was carried that made that happen.

MAN: That's right.

MAN: Yes, that's right.

MAN: Yes, something that determines the difference between these different fires.

MAN: So using that as the base story, I mean, it seems to me that the early cells must have done something that's different. Because they must have transmitted their membrane systems to the daughter cells. I mean, they just divide and they transmit that. So I'm saying that in that sense, cells are inheritors that replicate.

MAN: Well, but only if there are differences between cells, and the focus is always on differences. If something non-genetic transmits differences, then you've got a point. But I'm suggesting that it probably doesn't.

MAN: Ah. Yes, that probably is where the fault line lies, then, because I think that I'm more inclined to take seriously the specificity of the cell in addition to the specificity of the genome. Which is my explanation for why cross-species cloning is so extremely rare. And I'll also repeat the point I made earlier [UNINTELLIGIBLE], I don't myself see why cells should not have evolved, just minute the genomes [UNINTELLIGIBLE], as well as genomes evolving, which again would be an explanation for why cross-species cloning is so extremely rare. So probably the real fault line between us lies on the question of how specific is the cell information?

MAN: Specific for me would have to mean individual differences.

MAN: Between individuals [OVERLAPPING VOICES].

MAN: Well, between cells at least.

MAN: -- tend to be variations --

MAN: Well, let me then, I think I'll have to do another step as a physiologist. I find my cells, when I study heart cells, none

of them are the same. It's actually remarkable. The stochasticity is [OVERLAPPING VOICES].

MAN: Within one heart?

MAN: Yes, within one heart. The stochasticity --

MAN: They're a clone. They're not, the genetics are identical.

MAN: They've got, yes, but let's try to sort of focus on what it is that is actually different here. Clearly these have all got the same genome. Their expression levels, I'm saying, are different from one cell to another. Now, we also think that it is the case that, you see, to some extent this makes sense in terms of preventing cardiac arrhythmia because some of those differences are actually functionally significant in terms of trying to prevent reentrant arrhythmia. Sorry for the technicality here. Now, a cell that's in the right region to be, say, an endocardial cell, or an epicardial cell, with different expression levels, knows that it is that. And therefore, its inheritance is actually carried through to the next generation. So I would say that within multi-cellular organisms there are processes that at least --

MAN: Yeah, thought this can be cytoplasmic inheritance within mitotic --

MAN: Would it be, would be what, it would be what the old geneticists would have called cytoplasmic inheritance, yes that's right. Though again, I find I have a difficulty here, because of course part of the way in which that is expressed is by that cytoplasmic inheritance effecting epigenetically the genome. So --

MAN: Well, if it does --

MAN: So it's, you know, it's such an inextricable mix-up, isn't it?

MAN: Yeah. But sort of, we've known about this because liver cells give rise to liver cells and kidney cells give rise to kidney cells.

MAN: Yes, indeed so, yes.

MAN: They're all having the same genetics in this case.

MAN: Yes, exactly, yes. But the variations on that which come down to saying that there's also both nice gradations, nice in the sense that they're meaningful, gradations in expression levels that seem to mean something functionally in the case of the heart. I don't know about the liver because I don't work on it. And in addition to that, there is considerable stochasticity so that if I, for example, put one of Rodger Chen's nice florescent proteins to measure the gene expression levels in neighboring cells, I find even neighboring cells light up to enormously different degrees, which is pretty astounding. So I'm not, so what I suppose I'm suggesting is that if that happens in multi-cellular organisms, I don't see why it shouldn't happen in unicellular organisms, and then we're back to the question, well, could there be differences that get transmitted? You see why I'm at least coming from a very different position to pay more attention to the inheritance of epigenetics than would be usually the case from the kind of position that you've come from?

MAN: If you study the mitotic lineages of cells within a body, liver cells beget liver cells, heart cells beget, so quite clearly there is a nongenetic inheritance mitotically within an organism --

MAN: Yeah, I'd, which is straightforward and called epigenetic inheritance because --

MAN: You could call it epigenetic inheritance.

MAN: -- it's sort of, somehow the old idea of a cytoplasm inheritance doesn't quite capture the process of epigenetics, does it? [OVERLAPPING VOICES]

MAN: And then if that then carries on to the next generation, and which it appears to do, at least for a few generations --

MAN: Yes, that's right, yeah.

MAN: That's kind of interesting. But it doesn't really infringe the patent that DNA has on eternity.

MAN: Ah, well I see.

MAN: Which is an empirical question as you've said.

MAN: That's right, we agreed on that, that's right. The question of immortality, you see, I come back to the case that my germ line goes back, you know, an immortal line.

MAN: Oh, but that's your germ line --

MAN: Yes, and goes all the way back to the cells of [UNINTELLIGIBLE].

MAN: Yes, but as far as we know, that's the DNA and --

MAN: No, that's where I'm not sure.

MAN: We don't know. We don't know. We might be surprised.

MAN: But it's very nice to get to the point, Rich, where you I now agree on what we don't agree on, which is a very, very good place to be at. We've taken 30 years, roughly speaking.

MAN: We should also point out, though, that epigenetic cues and epigenetic phenomena are restricted to, for want of a better work, higher organisms. I mean, those are really metazoan-specific phenomena, and maybe, to some degree, in yeast. Certainly there's no evidence that I'm aware of in bacteria [UNINTELLIGIBLE] of epigenetics.

MAN: Yes, and if I can just answer that, I'm not a, I'm not a geneticist. So you know, I'm talking out of the back of my head here. I happen, though, to be in a department that is now called the department of physiology, anatomy, and genetics, and so everybody somehow thinks that I'm now entitled to speak about genetics. But let me try to answer what I think you're getting at. It seems to me that the reason why it's in the higher organisms that one really should, and really quite high up in the scale, that one should be looking for possible epigenetic inheritance even across generations, let alone within a same body. It's simply this, that it's in those organisms that the genome is so completely broken up. The number of possible expressions of the same gene is so large, I quoted earlier on the dscam example. But there are many other examples now. But I think it's probably the case that raw genes in man are broken up are than are not broken up. But then you've got to have something else that tells the system, as it were, that works out what it expresses from that gene at this time, at that time, and so on. And if you look at dscam again and drosophila, what you find is that the expression levels of the different slicing that could occur, occur differently during these various stages of development. Now, what makes all that happen, what as it were, to use a word, programs all of that, is very, is very interesting. But whether that lies all in the DNA or not, it

seems to me, is an open question. And I think it's open in the case of the very highest organisms precisely because the genome is so broken up. That's the answer I would give.

MAN: But it needs --

WOMAN: I just, I just now, in talking about that, it's just about the [UNINTELLIGIBLE] genetics. You can put marks in the [histose?], like [UNINTELLIGIBLE], and stipulation, and that can tell you which gene transcribed or which gene silenced. And even in [UNINTELLIGIBLE] there is no [UNINTELLIGIBLE], there is some light protein which can [fold?] the beginning as well. And these kind of errors, which is now coded in the DNA itself is just passed through a cell to another in the division and at least in the brain, that's quite important. That's --

MAN: I mean, but that a fundamental difference --

MAN: Yes, you [OVERLAPPING VOICES] yet, so sorry, was there --

WOMAN: I mean, they're all sort of, I think I mean even this argument itself is too simplistic. Because if you look at the level of the immune cell, for example, their differentiation processes depend on cytocon environment, what kind of --

MAN: Exactly.

WOMAN: I guess what kind of microbe or organism or even antigen or peptide are effecting the differentiation processes. So to simplify epigenetics to just things like methylation or [histose?] [OVERLAPPING VOICES].

MAN: Indeed, yes.

WOMAN: -- is far too simplistic to [OVERLAPPING VOICES].

MAN: Yes, I agree, and it's no surprise, is it? That the, if I remember rightly, the dscam system is actually used a lot in the immune system as a fruit fly. Somebody needs to check that, because again --

WOMAN: Yeah, I'm not sure about that.

MAN: I think that's the case. But you need, it would make sense, because it would give you an enormous range even before all of the factors that you are referring to, is that right?

WOMAN: That's true, and also, there's also some evidence, there's this phenomenon called paramutation which occurs in plants, where there's a pandoragen effect such that the actual effect of the gene or the variant of the gene differs based on the parent that it's inherited from. And they've only just found an example of this in mice, and it was published in science, I can't remember the details of the paper. Basically what happens in the sperm is that there's a lot of accumulation of RNA. And that actually effects the expression of the gene even before the organism develops. So I mean, it's even changes like that that need to be considered.

MAN: Yeah, the case, the few cases that we know, I think, of paternal effects transmitted down the generations have been attributed to RNA in the sperm.

WOMAN: Yeah. Maternal effects exist as well, but I think the statistics that are needed to prove that maternal effects exist haven't yet been developed.

MAN: There's a lot more work to be done here, I would agree, yeah.

MAN: Let me get into the, can I get into the [OVERLAPPING VOICES].

MAN: Yes, [Eric?].

MAN: -- issue of the interpretive mechanism that interprets the genome, executes its instructions, shall we say, of the [UNINTELLIGIBLE]. This is what, Steve, was that your name? Steve's example showed that even the evolution of these, what are they? These bacteria, if you have a gradual coevolution of the interpretive mechanism with the genome. Right?

MAN: Right. And that's what [UNINTELLIGIBLE] is.

MAN: So in effect, you do have this coevolution. You have this high dependence between the interpretive system and the genome. But I think, I tend to side with Richard more in the sense of that, there seems to be a programmatic aspect. I think what he's getting at or [UNINTELLIGIBLE] it's pretty obvious from the amount of information in the genome, which seems to be far, far out ways, and here we go. Far out ways --

MAN: That’s where you and I disagree.

MAN: -- what's the information in the cell. And what Richard is saying, and what I'm saying too is that the information that's transferred, right? Is primarily, that's actually involved in the morphogenesis, given an interpretive mechanism, is primarily in the genome. That's what determines whether you have three arms or four arms or ten arms. It's not the egg. And you're saying, and this is, you're on thin ice there, because --

MAN: I don't like to be on thin ice. I'm an explorer.

MAN: -- you will be effected by the Muller's ratchet. Right? Because the egg, the cell, even if it has a defect, right? This defect would be continued by template reproduction and the next thing. Any defect, by Muller's ratchet, any deleterious effect would continue.

MAN: Yeah, this is playing off Smith's argument.

MAN: Yeah, it's Muller, you know.

MAN: That's where I first heard of it, yeah.

MAN: Whereas with the genome, through sexual reproduction, they would be trying to get rid of that. So I mean, that's where the

problem is with having just cell template reproduction. And that's why the genomes are so nice, because they're digital, relatively, they can reproduce, they can remodify them, and all that.

MAN: Yeah. The difficulty, I think, is that it seems to me that most mutations are deleterious, too.

MAN: Well, more than seems to you, it's true. Yeah.

MAN: Yeah. So I'm not quite sure that that is the criteria.

MAN: Well, but the trouble is, you don't have sexual reproduction ahead of it. With, if you rely on the cells with sexual reproduction, you can get rid of the Muller ratchet problem. And, whereas if you just have the cell, which is passed on from the maternal whatever to the next generation, that would then copy the defect.

MAN: I would --

MAN: And that's one reason you need genomes.

MAN: I would suggest that those, if I can just finish this particular point first, and then we can come back to you. I would suggest that it's worth reading a book that has come out just recently, Freaks of Nature, by Mark Blumberg, which is another variation on how, from the same genome you can get extremely different, sometimes, anyway, extremely different phenotypes. But I agree with you, [Eric?] though, this is where our fault line lies. But for you and I, we've tried for about two years now to argue out, is there more information in the egg cell compared to the genome, and we don't seem to have gotten to the point where we agree.

MAN: We're getting closer.

MAN: We're getting closer maybe, yes.

MAN: Actually, I wanted to pose --

MAN: OK, two finishing comments, and then we'll go around the panel.

MAN: Yeah, well actually I'd like to pounce, I want to pose two experiments that are both doable. First experiment is taking the genome, the nucleus of, from one organism and putting it into

the egg, the cytoplasma of another organism, what are you going to get out? OK?

MAN: Nothing. We know already, it's been done many time.

MAN: No, in fact Dolly, the original experiment was put into, I mean, it wasn't a different species, but it was actually a different breed, and the progeny, Dolly reflected only the genomic information, it didn't reflect the cytoplasmic information.

MAN: No, no, excuse me, I think the, we need to go through the references clearly, because I think the biggest range of evidence in cross-species cloning is that they nearly all do not work. You can get stem cells, certainly, you can get embryonic stem cells, but you can't get an organism. I'll give you the references for that.

MAN: But also the fact that it doesn’t work, I mean, cloning didn't work for a long time until it did work. The second experiment is, we can actually eliminate all the symbionts --

MAN: If we wait a minute, evidence is evidence.

MAN: No, no, lack of, you're saying lack of evidence is proof of non-existence.

MAN: No, no, no. This is evidence. It did, you don't get organisms. Also, I mean, I have a difficult, you see, with why did we transfer the whole nucleus, because that is also already not transferring the genome.

MAN: Agreed. The second experiment is, you can actually eliminate all the symbionts in the human gut, which is the majority of cells in our body. You can replace them with symbionts from another organism. Will that cause a speciation event?

MAN: Can I just actually though address your first point, first, which was the DNA transfer experiment. I agree with how [UNINTELLIGIBLE] doesn't work, but with bacteria it's been done. Craig Venter has actually taken the genome of one organism, stuck it into the shell, if you like, of another organism, whether we can call it a species, or not, two different bacterial species, and shown unequivocally that you restore life to that chimeric organism. So it can be done, at least in the microbial field. But again and --

MAN: You wanted to [UNINTELLIGIBLE], and I'm going to ask the panel to do their sort of summing up. Yeah.

MAN: I was just going to, because this is about Darwin and natural selection, an example of symbiosis I would say, is infection. For instance, the black plague. I don't know how many, how much of Europe was exterminated by the black plague, but I would submit that that is a, as a selection event, has had a very definite effect on evolution. And it has nothing to do with genes or, well, I mean it has something to do with genes. If you were lucky enough to have the right genes, you survived.

MAN: Was [UNINTELLIGIBLE PHRASE].

MAN: You have these culling, you have these culling events. You know, HIV being another one, that certainly have huge impacts on evolution. And they're essentially a symbiotic event.

WOMAN: They're not speciation.

MAN: OK. I think we've, I think we've got the point, though. Should we do that final round up and see whether any of the panel, maybe starting with Martin.

MAN: Thank you, yes. Can I just say to my colleagues how much I've enjoyed the discussions this evening? It's been very convivial, refreshing. And I think we have found, certainly, those points of disagreement. And actually quite a measure of agreement. It's delightful to hear Richard say he though symbiosis was important, if rare. I would simply make the point that, as seen from the point of view of a geobiologist, these symbiogenetic events were actually, you know, were significant, and were important, and have had, certainly it's a thing we have to take very much account of. Have a huge impact now on the [UNINTELLIGIBLE] of the planet and obviously some of the major evolutionary stepping stones such as the origins of the eukaryotes.

MAN: OK. I'll leave Lynn to the last, because it's her show. Steve, if you want to say anything.

MAN: Sure, I just, I think a lot of what we've heard tonight has been argued from a very eukaryotic perspective. And I'm not a eukaryote.

MAN: You would say that, yes.

MAN: Yeah, and I am very prokaryotic. And I think what we have to remember is that many of these events may have occurred early in evolutionary history, and they may be restricted with the systems [UNINTELLIGIBLE] in higher organisms, if you like. That's certainly, you know, the events of the symbiogenesis, I think arguably have occurred during evolution. Certainly [before?] organisms and possibly in the birth of eukaryotes. Think of the bugs, basically.

MAN: Richard, do you want to say anything in conclusion?

MAN: Well, obviously, I mean, prokaryotes are hugely important, and you know, most organisms are prokaryotes, we're mostly prokaryotes, and so much of what I know about biology is irrelevant to the majority of biology. [LAUGHTER] But on the other hand, claims have been made about eukaryotes which seem to me to be a kind of imperialistic generalization from prokaryotes. So just to reiterate that point, within, eukaryotes are almost entirely prokaryotic in their own cells, that undoubted. The only point I was disputing after dinner was the suggestion that speciation events are themselves initiated by new symbiotic incursions. I'm pretty sure they're not. While fully admitting that eukaryotes are, themselves, massively symbiotically invaded. But it's all in the past. So I reiterate

that symbiotic invasions are relatively rare, but very important when they happen. On the pre-dinner discussion, I would reiterate the point that, what really matters, the difference between Dennis and me is that no matter how important non-genetic elements are in life, and of course they're important, as far as natural selection is concerned, and only as far as natural selection is concerned, what matters is what makes the difference between individual entities that are selected versus individuals that are not. And those differences have to be hereditary differences, and they have to go on for many, many generations. So it doesn’t matter how complicated the relationship of genes to their embryonic environment is, it doesn't matter how intricate the feedback loops are, if the differences between individuals can be dissected out by geneticists, natural selection is just like a geneticist. Natural selection simply cares about individual difference, who survives, who doesn't survive, and the consequence of who survives and who doesn't survive is ultimately only a genetic consequence, where genetic is defined generally to include anything that is potentially eternally heritable. That's my point.

MAN: Should I do my little sum up --

WOMAN: Please.

MAN: -- and then hand to you to finish off?

WOMAN: Be my guest.

MAN: Yes, OK. There's often, in these discussions, a lot of debate about bringing evo and evo together. And somehow or other bridging the difference between the gradualists and the saltationists and so on. I would like to suggest, and I hope that this discussion has partly illustrated that, that it might also now be useful to bring some physiological cum systems biological perspective into these discussions because I think that the, while I would accept what you've just said about complexity per se, I think also that two some extent at least, the devil lies in a lot of the detail. And I think that as, well I'm a physiologist, so why shouldn't I say this? As physiology resurrects itself after it's been swept aside by molecular biology for the last 40 years, roughly speaking, I think it's going to make many more contributions to these kinds of discussions than has been traditional in my subject in the past. I'm extremely rare, being a physiologist who's prepared to take part in these debates, even. That is extraordinary. Because somehow or other, with one or two exceptions, like Jerry

Diamond, also a physiologist, but interestingly enough, also a bird evolutionist, or at least a bird behavior observationist, there's been very little input from the physiological end into all of this, and I think that there should be more. But with that, Lynn, over to you. This was your show, and you can have the last word.

WOMAN: No, it's your show. I don't really want it. I'm just feeling humble, and not because lots of criticisms were made, but I would take your point about, there's never a single cause. You can never do only one thing, and to take an exclusivist attitude toward any of this as if there were a single, correct answer, is suffering from test-itis, I guess it was called. That is, that's true on a test. It's true for tests, but it's not ever true for nature. And so I just --

MAN: You don't mean testosterone-itis?

WOMAN: No, maybe that, too. [LAUGHTER] No, but it's only the tests that there's a one correct answer that's definitive. It's never true at all in nature. And I just, I think, I just think, well I quote McHarg, I mean, the Earth is not divisible. And furthermore, everything is a function of history. Everything. Which makes us underestimate the importance of a very good

fossil record in almost everything we talk about. It can't be interpreted because we don't have any protistologists who know what, who are alive any more. So I mean, and to sort of dismiss that record, which is done all the time by evolutionary biologists, makes me very sad. Because a lot of data's known. Almost everything that I've discovered in our own work was done by really fine scientists. But they didn't publish in Nature and Science, and they didn't publish in the last ten years. They published over a long period of time, and they didn't get paid for getting grants. They got paid because they were professors allowed to pursue the scientific questions that they were interested in. Kerby, Cleveland, and all the rest of it. So I think it's terribly important to realize that between, I mean, let me see if I, human history is a very tiny subfield in something called natural history, and I for one am very proud to be in the field that doesn't have any grant money, I mean, doesn't exist. But that's really the field that is of interest. That's all.

MAN: Well, I think this is where we close and say that [palial?] is extremely privileged to have the Eastman professors, and to particularly have one who's been so provocative, so active, so, well, I know the word is to stimulate the whole of a debate like this. But not just this

evening, throughout virtually the whole year that you've been here, Lynn. Thank you very much. [APPLAUSE]

[END]

Thank you.