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Round Table

Werner Arber, Manfred Eigen, David Hubel, Hubert Reeves,
Günther S. Stent, Victor F. Weisskopf

Arber: In the course of the sessions I felt that there were some problems of cognitive limits. I cannot express this concern in the language of the specialists, but one simple question which I would like to ask now in order to start the discussion is the following: It is our habit to consider space as 3-dimensional, measured in metres or centimetres in a linear scale, and we are accustomed to measure time in minutes or hours, also in a linear scale. Particularly, thinking of the first talk on the universe, but also of all others, I just want to ask: is it relevant to consider other scales than the linear, both for space and for time? exponential for example?

Weisskopf: I believe that this is a very interesting question which one cannot answer suddenly in any definite way but I would like to mention one point in this connection. Evidently many of you, including myself, have asked: what about the «Big Bang» and the time zero? What came before? Is there not something wrong with our way of measuring the time? For example, the real unit could be a logarithm of the time which then goes to minus infinity at zero. This is not only a mathematical trick in order to avoid zero, because what is the essence of time? The essence of time, for example, is frequency. Let us take the frequency of the light that fills the universe, as Haydn has described so well. At times when the universe was much denser, the frequency was much higher. So if you use that frequency as your time element, then the time element at the beginning was very much shorter, and so time goes to infinity. Indeed, if you do this quantitatively you find the logarithm of time as the right measurement. One might even in that sense, avoid the question of «before» by just changing the time unit.

Eigen: But what about the direction of time?

Weisskopf: Well, it is very interesting in the spectacle of the universe, because there is this idea of the – as our colleague Sorkin has expressed it – harmonica world. For example, if the mass density in the universe is big enough, the universe expands, then comes to a stand, comes back again and starts over again. The direction of time depends upon what period you live in. But it does seem that this idea runs into serious difficulties. First into experimental difficulties: The density which we observe seems to be too low to pull the universe back again. The second difficulty is a statistical one: if there was really a harmonica, the entropy should be somewhat larger after each expansion and then, after infinite time, at the end, there would be all in disorder. So this is a very questionable idea. In some ways therefore, the direction of time is seemingly inscribed in the fundamental laws which, of course, we do not know yet.

Arber: Would you say that if everything were in equilibrium the direction of time would disappear?

Weisskopf: Yes. But of course the infinite expansion of the universe prevents that, it isn't in equilibrium.

Arber: If we compare time with 3-dimensional space or, if you like, a 2-dimensional space: we know that – and you mentioned it in your presentation – if we have a sphere, you walk on that sphere and you never come to an end and you don't see the beginning. Does something like that exist for time?

Weisskopf: I must admit that I cannot answer this question. H. Reeves, maybe you could?

Reeves: No. But I was going to ask about something you just said. This increase of

entropy would be represented ultimately by photons. And in the case that the universe contracts back, then the photons will re-equilibrate with all the particles, and then it seems to me that this increase of entropy is levelled and comes to zero. I have worried very much about what would be carried from one chapter of this harmonica to the other one and I have no answer to this. Do you have one?

Weisskopf: No, no. But I do believe it is an important question.

Stent: I ask about this logarithmic time. If that were so, then the word Big Bang would not be an appropriate metaphor. There would not have been a Big Bang, everything was just «going on».

Weisskopf: Absolutely, yes. It is the singularity which is anyway fathomless.

Stent: There is no singularity then.

Weisskopf: That singularity is in minus infinity. This means, whenever you are on a finite time measured in logarithm you will have a finite density which increases and going backwards.

Stent: The conclusion will be, as I take it, if we consider time logarithmically, things which we think happened tremendously fast during the Big Bang, actually occurred no faster than anything which is happening today.

Weisskopf: It depends what you mean by fast. If you define fast relative to the average frequency of the radiation, then it is not fast.

Reeves: I like very much this exponential scale because it reminds me of the absoluteness of the velocity of light and of the zero of temperature. In the linear scale you would say «Why is light going at that speed and why is there a zero of temperature? In the logarithmic scale you understand this in terms of the effort you have to make to reach the velocity of light or to reach zero Kelvin. In the same way, the effort you have to make to understand the universe becomes larger and larger, the more you approach its origin.

This is why, when we make a step from 10^{-35} to 10^{-31} seconds, it takes chapters of physics to understand what is going on, even for such a small period of time.

Eigen: But I think that such an extrapolation, c.e. to say that time has a logarithmic scale is worth nothing, because there is evidence for many phenomena in physics that they started by bifurcations, through an instability. A similar phenomenon might as well be behind the Big Bang.

Weisskopf: Yes, I fully agree. I think this would be a good moment to remind everybody including myself that whatever we say about things that happened in these first fractions of seconds, they are purely hypothetical. They are on a much less safe basis than what we say in any other field of physics, including high-energy physics and astrophysics.

Eigen: We are facing similar problems in the evolution of life. There is a certain continuity as to prepare the conditions for something to appear, but in between we have many discontinuous processes. In other words, the sudden appearance of a certain mutant might completely change the scene of evolution.

Reeves: However I would qualify the uncertainty: when we say that after one second or one minute there is a chapter of primordial nucleosynthesis, we are on much better ground than if we say that at 10^{-35} seconds we have the reaction which explains why we live in a universe which is made of matter and not matter and antimatter. Although the second one is much more speculative, it is more interesting than the first one which is, I would say, almost believable.

Weisskopf: I would like to make a remark concerning Gunther Stent's lecture which I found extremely fascinating, stimulating and, how shall I say, irritating. In particular, I would like to take issue with his first point. Namely, the first of these three limits where he says that, for example, quantum chromodynamics is already outside of the legitimate limits of science.

Stent: I didn't use the word «legitimate».

Weisskopf: No. You know, always in order to be short, one has to be rough. I fully agree with the fact that science begins with the natural concepts that personal evolution has brought us, as Piaget has shown. But after all, science already for a long time added still further new concepts to these concepts. For example, a child certainly does not know anything about electrical charge. And the electrical charge plays, as you know, an extremely important role just in that type of physics which G. Stent certainly agrees to be reasonable physics. Now, in many ways, those categories that G. Stent has criticized, for example, those different quark types are very much in the nature of charges. Indeed they were sometimes called hypercharges. So, in the whole development of science, always new concepts were added to those which were naturally in us from childhood. The concept of atoms, by the way, at the end of the 19th century, was criticized as non-scientific in the same way as G. Stent now has criticized chromodynamics as being non-scientific. Now we can see the atoms. And let me now make a third remark. I do not think that the reality, the truth of a scientific recognition, depends on the practical applications. As long as one can make provable predictions, as long as, for example, chromodynamics says if you make this and this observation you will find that consequence, or you find in the stars these and these phenomena because of the mechanism of chromodynamics, that, I think, is as good as any practical application.

Stent: I am afraid that apparently I did not make myself sufficiently clear. First, of course, I do not wish to suggest that chromodynamics is illegitimate or that their activity is not admitted. But the point I am trying to make is one of pictures and I am very much inspired by Bohr's argument about the necessity of picture-making in scientific theories. Now, as to your first point about the electric charge, I certainly do not wish to claim that one is not allowed to do science that cannot be understood by a child, because naturally most of the things children cannot understand. But the new concepts to which you referred and which have been

introduced as science developed, nevertheless have some nexus continuous with infantile ideas. You mention electric charge. Sure, a baby has no experience with electricity. When, finally, the child learns about electricity in elementary school, the teacher tries to explain in metaphorical terms, what electric charge is, always connecting it with something. I think that they told me it was some kind of a fluid or something like that – I can't remember – but nevertheless I did finally get some understanding of electricity in terms of metaphorical pictures: repulsion, things were being pushed away and they showed me amber and all that stuff. All I say is that – I am only repeating Bohr – scientific theories are in the end pictures which are built from everyday language, although they are altered and modified. What to me is novel, at least alleged in chromodynamics, is that no such attempt is made any more. Frankly, the words are without any metaphorical content, they are purely formal operational symbols.

The second point I want to make is about atoms: you cite the 19th century. I think you probably were referring to Mach and the criticism was not semantic or linguistic, it was positivistic. Mach said that atoms are nonsense, not because conceptually it was nonsense that they should be little balls; he criticized that they had never been seen and that no-one at the time was making any kind of empirical experiment. He was some kind of an early member of the Wienerkreis, a person who said that if you have no empirical proof or experiments or something like that, then it is nonsense. So, it was a different criticism that was made of the atoms, not a conceptual or a linguistic one, but an empirical one.

Weisskopf: The «charm» and «strangeness» will be seen too, very soon.

Stent: However, the novelty is, that at least at the time that the terms were passed there was no obvious connection between the terms and properties.

As to the last point: I do not wish to say that practical applications are a necessary condition for proof. On the contrary, I was claiming that they can be an additional methodological proof, and when some theory leads to

practical results, then you have a good feeling that your theory was not all that bad. It is the same level of abstractum. Dirac equations are here to stay, probably chromodynamics also. As an example, you could invent a way in which cars would run on water or something like that. That would then to me be a true miracle which could not be explained by the Darwinian hocus pocus. That is the point I tried to make.

Weisskopf: Quantum mechanics is also hocus pocus and has tremendous practical applications.

Reeves: There is no major difference between Dirac equations and quantum chromodynamics. It is the same level and Dirac equations here are good to state, and probably chromodynamics also.

Arber: Let's now shift to talk on the origin of life. From several of the questions received and also from private discussions it seemed to me that some people had difficulty to see where life really comes in. Not everybody is ready to admit that relatively short, replicating RNA molecules already represent life. It is my feeling, that an answer to these questions was hidden in M. Eigen's last slide.

Eigen: In this context, the question was raised: what is the criterium for an optimum template. An answer is found in the experiments of Spiegelman with the bacterial virus Q_{β} . The genome of phage Q_{β} is an RNA molecule which can be isolated from the virus particle. Spiegelman isolated the enzyme Q_{β} -replicase and he put the enzyme and the RNA template together and fed the mixture with energy-rich nucleotides. The system then started to make new copies of the genome, but after several generations all the new copies were as infectious as the original viral RNA. But then he went on and put the system under selective pressure for fast replication. Then the copies go shorter and shorter and the original, 4500 nucleotides long template got shortened down to about 500 nucleotides. In addition, the shorter templates were able to replicate faster; the speed of replication per nucleotide was increased by a factor of 3 to 4. It was estimated that this very efficient replication

reaches the upper limits possible within the limits of physics and chemistry. Hence the criterium of optimal replication was fulfilled by these short templates, but they were not infectious any more. They had lost all the information to enable them to penetrate a bacterial cell. All they could was to replicate quickly.

In the experiments I reported, we did not start with the Q_{β} genome as a template, we rather started only with the replication enzyme and energy-rich nucleotides. And the enzyme started to line up the nucleotides and to connect them to new templates. Again, the rates which we found approach the upper limits we could think of, and furthermore the process is reproducible, regardless of the environment. That is our criterium of an optimum. In this case, it is still trivial that we get reproducible results, because the estimated number of possible alternative products under the particular conditions is about 10^{12} , and having 10^{14} enzyme molecules around, we could always hope to materialise the best template. Now, of course, for the true living beings, which comprise much more information, one cannot scan through all possibilities. Here we have the constraint that larger sequences must evolve from shorter ones until they reach their optimal length. Thus, in order to define a criterion for the optimum, we have to consider that historical route becomes part of the boundary condition.

Arber: Let's assume you have these primary elements. You start to build up, at what time does the new principle «life» come in?

Eigen: We could also ask: what is the lowest molecular weight one could associate with life? There is always the question: what is life? and I don't like the question very much because such a definition doesn't tell us very much. There is no disagreement to call bacterial cells alive, and we all agree that we are living beings, but what do we have in common with the bacteria? – Just the chemistry: To give a definition of the term «life» doesn't tell us very much about the living beings. Now there is the question how far can we go down? Do we want to call a virus a living being? If you are willing to do so, you should admit that the smallest viruses now known are plant viruses with only a few hundred

nucleotides in their genome. Their size is of the same order of magnitude as the molecules we produced *de novo* in our experiments.

One could use an operational definition. Namely, that the system, in order to be alive, has to be able to reproduce itself and to adapt itself by mutation to environmental changes. Furthermore it requires a metabolism. The metabolism is even a necessary prerequisite because of the fact that all these processes can only occur far away from equilibrium. If self-reproduction for instance occurred at equilibrium, one would not expect an effect of selection because of microscopic reversibility which is effective at equilibrium. So, self-reproduction as a prerequisite of selection works only far from equilibrium. You might then say: a molecular system which fulfills these conditions, which starts to reproduce itself, mutates and can thereby adapt to any condition, might be called a living system. But that might not yet satisfy molecular biologist who request the system also to make proteins, in other words, to translate its genetic information in order to gain an unlimited functional capacity. In any case, if we talk about a living system, we have to specify what type of system we mean.

Arber: That reminds me of the problem of cognitive limits. In some way, we are unable to define life properly.

Stent: Oh, I think not, but we might perhaps better devote the discussion to the origin of a bacterium such as *E. Coli*. And we might try to trace a reasonable history starting from the atoms and ending up with *E. Coli*. We would of course like to know what is in between.

Eigen: I agree that there is a big jump to an *E. Coli*. It is quite clear to me, however, that an evolutionary process which takes that direction can only do so after self-replication was established. It is thus clear that the nucleic acid had to start this kind of process although the proteins, being chemically simpler, might have been around long before. But they had no way to optimize their functions.

Arber: Let us go back to the universe: In fact, can one expect, if the universe is infinite, that there is an infinite number of planets on which life has developed? If so, what is the chance that there is also on some of these planets actually intelligence developing?

Weisskopf: Probably we should first ask the astronomers. This question entirely depends on the probability to find planets with conditions and histories like our own.

Reeves: Yes, this you can divide into two questions. What is the probability that stars have planets and then, what is the probability that these planets are habitable.

The probability that stars have planets is, I would say, very large. In fact, when we look at the stars, we find that the stars which are alone are quite rare. At least two-thirds of the stars live in couples or triples or more complex systems. If you look at a star which is a double star and you then improve the visibility, you often find that it is triple or quadruple and so on. So there is a very large probability that planets in existence like ours are very, very common and perhaps one star out of two or three has planets. Since we have a hundred billion (10^{11}) stars in our galaxy and since in the observable universe there is in the order of a billion (10^9) galaxies, you see that this makes a lot of planets.

Then you ask the next question: what is the probability that some of these stars have planets with life? One limitation to the development of life is given by the orbit of the planet. If our earth, for instance, had a very elliptical orbit, if it was going far away from the sun, and close by again, we would have large variations in temperature which would probably be very harmful to development of life. If our system belonged not to one star but to two and was going in an eight around two stars like you can have with double stars, you would probably have a similar type of difficulty. Nevertheless, I am ready to assume that probably a good fraction of stars, certainly hundreds of billions, have habitable planets getting some ultra-violet light although not too much, and where the temperature is quite constant. The astronomers cannot go past this statement. Everybody wants to know how many of these habitable planets have developed life. We have experts

here and I am glad to pass the question to them.

Eigen: Well, the question again is difficult to answer, because of the word «life». The earlier organizations about which I have talked are almost so deterministic that whenever appropriate conditions are created, those organizations will show up; Thus, whenever there is a planet with earthlike conditions such as reducing atmosphere, it will start to synthesize all these chemicals, which then start to polymerize. If it were not so, we wouldn't have a chance to find it in the laboratory. I would therefore propose that those primitive states of life certainly must exist if habitable planets are around. Now comes the difficult question, on which no experimental results are available, namely whether a cellular organism such as *E. Coli* also could have formed just due as a consequence of environmental conditions. And what about the evolution of higher life? We know that life came to a standstill almost at the level of unicellular organisms and we guess also why: because bacteria already have a genome of a few million nucleotides. In order to keep it stable, it had to reproduce it with an accuracy of 1 in 10^7 , or so which means that a particular mutation which could have brought about progress, would have been very rare. If the mutation rate is 1 in 100, it happens every day, as we have shown by experiments. If the mutation is 1 in one million, it takes much longer time. The rate of evolution decreases. The way out of this situation was a mechanism to exchange information between two organisms, i.e. recombinative processes or sex. That immediately allowed to spread advantages through the whole population. One can estimate that it took about 3 billion ($3 \cdot 10^9$) years from the existence of unicellular life up to evolution of higher organisms. Mankind is not older than a million or a few million years.

The process of evolution from unicellular to higher life is subject to fluctuation. Suppose that fluctuation in time is only 1 percent. One percent in a billion years is 10 million years. It appears thus unlikely that the appearance of higher forms of life on neighbouring planets is synchronous. It is thus doubtful if we will ever have an overlapping

time to communicate with intelligent organisms of other planets and find them in a state in which they are able and willing to communicate with us.

And who knows, whether we are still willing to communicate with anybody outside after another hundreds of thousands of years. But that is a completely different question.

Arber: I have just one little restriction to what you said, to which I otherwise fully subscribe. We do know that viruses, which we usually do not consider as organisms with sex, are also able to transport genetic material from one cell to another, and various molecular mechanisms are known to promote this exchange. That is one point, and the second: I could imagine that bacteria which usually divide into two every half hour, lose the capacity to separate completely, which would probably lead to a very primitive multicellular organism. This might allow for a compartmental evolution by mutation, perhaps helped by viral infections, bringing segments of genetic material from foreign sources.

Stent: In his new book, Francis Crick has developed an argument which is relevant to what was just said, and whose devilish, fiendish conclusion is that it is entirely possible that life, as we know it, has no natural origin. The argument, that he makes, goes in short as follows: If all calculations come out the way that was suggested here, in a large number of stars, many of which have their planets, sometimes with the conditions for life, it is a necessary consequence that life arises, and one may perhaps assume even intelligent life. There is then also a likelihood that – maybe two billion ($2 \cdot 10^9$) years before us, this waiting period which M. Eigen has described did not take place on some planets. Some two billion years ago people like us, or little more advanced than us, could then have existed on a planet. They might have had a space committee and high technological means. They had perhaps also molecular biologists. They might have known that there was a planet here, Earth, in the solar system and so the said committee could have designed a bacterium as being a perfect organism for the conditions of this planet. As to themselves, their life could be based on

silicon and selenium, and have arisen under conditions entirely different from ours. But their acquired knowledge might have enabled them to construct a terrestrial bacterium and to send it in a rocket to the Earth. It then could have infected our ocean, and the rest is history. So, at first, this seems like science-fiction, but it shows that if you develop all the general arguments about necessity, if you really believe that there is something necessary about the origin of life and that the probability of its arising is high, then the credibility is also seriously diminished that our own life has actually a natural origin rather than being created somewhere else according to a particular design. This is the argument developed by F. Crick.

Weisskopf: If it is really true that the universe is infinite, one can say that life must be there. Intelligence must be somewhere because even if the probability is extremely small, multiplied with infinity it becomes 1. Now the problem is only this: the communication radius. We can only speak sensibly about that part of the universe with which we can communicate. This radius, of course, expands as time goes on. Therefore, the question should really not be: «Is there life in the universe?», because I think that somehow logically the answer must be «yes», but: «Is it within our communication radius».

Eigen: Well, I have no idea what the probability is to find life within that radius. That is a question you should answer. The fact is that we haven't yet received any message.

Weisskopf: The probability that two civilisations are in exactly the same state or in approximately the same state is rather improbable. Either they are ahead of us and they are not interested in us, or they are behind us, then they cannot communicate with us.

Arber: Another problem is that if they are really far away and even if they are some time ahead of us, their communication may not have reached us yet.

Reeves: There is also the problem of how long a civilisation is developing technology and whether it will survive its technology?

Weisskopf: May I just add one point: It is not only the ability of technical development. It is by no means sure that any civilisation develops technically. They might be interested in completely different things – in writing poetry for example.

Hubel: The original question was what are the chances that intelligent life could develop. However, some other species than ours are enormously successful, insects for example, although they don't have anything that we would call intelligence. It isn't entirely clear that intelligence is a very great advantage and I don't see any way of knowing how much of a chance occurrence the development of intelligence is. I don't see any way of assigning any kind of number to that. Of course, if you multiply anything by infinity you get something, so that doubtless, somewhere, there will be people with two legs, two arms and perhaps ten fingers. It could just as easily have been that life would not have any intelligence even as yet and still have many very successful animal species.

Arber: On the other hand, we have a tendency to believe that our intelligence is of the highest level that could develop. Perhaps this is a very wrong idea.

Hubel: Certainly, one cannot think about the origins of the brain without wondering how much further this can evolve and, of course, there isn't any answer to that. Our cortex, our thalamus is so much bigger than that of the highest ape. It is rather hard to think that it won't go on getting bigger. But it's even hard to know how to think about it, would we be allowed to.

Reeves: May I bring in a pessimistic view? If intelligence, I should probably say technology, should bring selfdestruction, then it may not be the best thing that happens to a civilisation.

Arber: We could then also ask, how far selfdestruction can go? We can probably destroy life. Can we also destroy the planet as such?

Reeves: No. Not really, not at the moment. Perhaps later.

Arber: Then, according to M. Eigen's view, things can start again.

Weisskopf: It's a good hope.

Reeves: Yes, with a delay of a few hundred million years.

Arber: Maybe, we should close with this hope.