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An interview with Eörs Szathmáry

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Professor Eörs Szathmáry is a theoretical evolutionary biologist and director general of the Centre for Ecological Research in Tihany (Hungary), and director of the Parmenides Center for the Conceptual Foundations of Science in Pullach (Germany). He is also a member of the Hungarian Academy of Sciences (MTA). He has made important contributions to the major evolutionary transitions, systems chemistry, replicator dynamics, origins of the genetic code and eukaryotic cells, multicellularity, emergence of natural language, learning and evolution, and open-endedness in evolution. His books with the late John Maynard Smith (The Major Transitions in Evolution, Freeman, 1995; and The Origins of Life, Oxford University Press, 1999) have been translated into a dozen languages. I have had the privilege of working with Prof. Szathmáry since 2000, and he is actually (March-June 2020) hosting me within the MTA Distinguished Guest Fellowship Programme in Hungary. Here I took the opportunity to interview Prof. Szathmáry for eVOLUCIÓN as an outstanding example of a deep thinker of evolution.
Q - One of your beloved mentors was the late Tibor Gánti, who was a chemical engineer and a theoretical biologist interested in the origin of life. What has been the influence of Gánti in your career?

R - His influence was very strong and I could even say it was decisive. Very luckily for me, at that time in Hungary there was something, which I do not think it exists any more, called the Free or the Open University. We are talking about the period between 1974 and 1978. They organized popular lectures and series of popular lectures, and they were looking for the best lecturers. Actually, in a sense it was better than the University. Of course talks were at a lower level but were given by top people, and Gánti was one of them. He was lecturing about the basic phenomena, the basic organization and the molecular biology of life. This was very captivating. I was at the secondary school at that time. Mind that Gánti was also the first person who wrote a book in Hungarian about molecular biology, published in 1966. Although it was meant to be a popular book, it was also used as a textbook at the medical University. In 1971, Gánti wrote his famous book The Principles of Life, where he asked the question of what kind of chemical systems do we need in order to have a minimum living system. His theory has been developed for decades. His vision was extremely novel, extremely insightful and very clever. This basically broke the symmetry for me because I was doubting whether to become a cosmologist or a biologist. Although Nick Barton told me that within evolutionary biology, my work is closest to cosmologists. Yes, Gánti was decisive and extremely important for me.

Q - You have been working actively in the problem of the origin of life, considered as one of the most difficult problems of science. However, in 1972 the famous philosopher of science Karl Popper (A realist view of logic, physics, and history. In: Objective Knowledge. An Evolutionary Approach, p. 309. Clarendon Press, Oxford) wrote: “I believe that ‘What is?’ or ‘What are?’ questions or, in other words, all verbal or definitional questions, should be eliminated … Questions such as, ‘What is life?’ or ‘What is matter?’ or ‘What is mind?’ or What is logic?’ I think should not be asked.” All of a sudden, Popper wants to eliminate the title of the highly influential book written
by Erwin Schrödinger in 1944. As a scientist, what is your defence against Popper’s claims? As a scientist interested in philosophy, what would be your criticism of Popper’s remarks?

R - Popper’s point of view is of course an important one because it is a claim made by a very distinguished philosopher of science. Mind that not many philosophers have had any influence on science and most scientists do not care about philosophy, they would even consider harmful many philosophical papers. Popper made a philosophical career that is respected among scientists, but he was not as original as people think. The logical root of what he was doing can be found in scholasticism, where some clever people said that you do not have to defend religion by positive arguments, but you have to negate negations. This is the right methodology for defending a faith, a falsifiable argument. There were also the American pragmatists, who used the term fallibility. In essence, Popper’s ideas, although highly influential, were not very novel. However, he was very sharp in exposing these ideas. I think he is wrong when he wrote that we should not inquire about ‘What is matter?’ or ‘What is life?’ because logically, these questions do not have the same status. Matter is a primary ontological thing; life is not, life is a derived property. This is Popper’s mistake. Matter is matter; it can have many structures but is not the structure that often matters. For life it is the organization what is important, and you can inquire what is the organization of living systems. Going back to Gánti, his point was that what constitutes a living system is not a philosophical question. It is a biological question. But what is life in a general sense is a philosophical question. In this sense, Popper is right and wrong at the same time. I agree with Gánti. When Popper was attacking the title of Schrödinger’s book, he was attacking it for the wrong reason because in that book there are questions that are legitimate, and we are working on these questions. As Gánti also said you have to be careful about these statements, because you have to consider evolution. But if you go for the overlap between science and philosophy, you have to focus on a minimal system. Multicellular organisms have a double life so to speak, they are already composed of units that are living. Cells are alive, and multicellular organisms are alive at a second level. There is a lot of mess to be cleared away, but I do not think Popper knew anything about many of these problems.

Q - You worked with John Maynard Smith as a postdoc in the University of Sussex. What impressed you the most of John?

R - This is again an exciting question. I was educated during communism; I finished my university studies in 1984 and obtained my PhD in 1987. The political
change happened in 1990. Around the middle of 1980s the political system was dying, and allowed certain things to happen. An example is the very famous (some people would say infamous) Hungarian George Soros, who created a scholarship in Hungary for people to study and work abroad. I spent half a year with Maynard Smith, from October 1st, 1987 to the 3rd of April 1988. This was a unique opportunity and the scholarships were very competitive, not all Hungarians could get it. For the record, Viktor Orbán (the actual Prime Minister of Hungary) also got one. I thought it might be a one-life opportunity, and had to think soundly where I should go. It was absolutely clear from his writings that John Maynard Smith was my target. He was a theoretical biologist and I am a theoretical biologist, and the clarity of how he was writing about biological questions was overwhelming. Mind you, John was also an engineer, Gánti was an engineer by training, Lewis Wolper is also an engineer, and my father was an engineer. I think this background makes these people to be clearer than other sort of theoreticians.

Q - Your book with John Maynard Smith The Major Transitions in Evolution has become a classic in evolutionary biology, which has been cited 4,965 times (Google Scholar) to date. To put this into perspective, some of the founding books of the Modern Synthesis such as Dobzhansky’s Genetics and the Origin of Species (cited around 8,000 times), Mayr’s Systematics and the Origin of Species (cited 8,429 times) or Simpson’s Tempo and Mode in Evolution (cited 3,137 times) have received less citations considering that they were published around fifty years before. How would you summarize the main take home messages of the book?

R - When we wrote the book, John said that we could not know whether it could have an influence on a very small number of very clever people or if it would have a much broader effect. We did not know. We were more positive or hopeful when we saw the first reviews. With the Nature review, John said that it could have been written by ourselves. Some other colleagues were also positive. When I said to Paulien Hogeweg that this is the first book about these transitions, she said no, this is the first book about evolution. Why can somebody say this? I think a very important effect of the book is that it does not have the usual if, then. This is the structure of the standard book on population genetics, where if you assume this and that, then you can work out the consequences. But, what about the ifs? This book is more about the ifs; under what conditions these ifs arise. An additional thing is that the book does not deliberately get stuck at a certain level; organisms, genes or whatever. It also has the global view, from the origin of life to
the origin of language, and the take home message is that there are two things that go side by side and both are extremely important. One is the evolution of inheritance as such, it is not only DNA because there were and there are another inheritance systems before and after, for example epigenetic inheritance. Let alone language; we could not be sitting here because we could not talk. The other is that there are several times in evolution where things that were reproducing independently came together to form a higher level; to such an extent that now they cannot reproduce independently. Mitochondria, plastids and the cell nucleus cannot reproduce alone at all. Some things are now irreversible. We have now DNA, RNA and proteins linked by the genetic code. Nobody has ever seen a creature that would have lost the genetic code, although logically it is possible but practically it is impossible. These are two important things in the book, the evolution of individuality and the evolution of inheritance. As David Queller wrote in his review in 1997, it is almost like two books in one.

Q - Are you preparing a new edition of The Major Transitions in Evolution?

R - The short answer is no. I have a contract with Harvard University Press, but there are a number of issues here. I have to fight for academic freedom in Hungary because there has been an important interference by the government with the Academy of Sciences, and I was in the delegation of the Academy. As the Romans said *inter arma silent Musae* (in times of war, creativity suffers). Furthermore, from January last year, I took the present position of director general of the Centre for Ecological Research in Hungary, and therein I established the fourth Institute, which is the Institute for Evolution. As you know I did not stop science or writing papers, but the book is really out of question for the time being. To write it, I would need more tranquillity.

Q - Let us consider some of the topics included in The Major Transitions such as the origin of life and the origin of language. What substantive advances have occurred since its publication in 1995?

R - There are. First, I want to make the statement that one of the most important advances that happened in the last decades is that we know much better what we do not know. This means that we can ask sharper questions. If you know information theory that is already knowledge. If I ask you, how did life originate? And you answer, I do not have a clue, this is a different thing than saying well, there are certain important unsolved problems in the origin of RNA replication. In general, and this also applies to the origin of language, we can make sharper questions, and partly there
is some experimental tractability of these problems. We can now make beautiful experiments on the possibility of non-enzymatic RNA replication on the ice, and one can realize that might be it is better to use trinucleotides as building blocks rather than mononucleotides. There are many unknowns, but people are asking cleverer questions and doing much better experiments than a few decades ago. This is also true for language although experimentation here has obvious limits; for example, we cannot take away kids from their parents and set up an experiment. There are serious ethical considerations. But if you look at how language processing can happen in various artificial systems, for example with Luc Steels’ fluid construction grammar, and witness how robots can acquire language in a given environment, we can slowly know more and more how the brain is processing language. We know more about the genetic background of language capacity. There are also ideas on how the brain works when it is solving complex problems, and it might be the case that some Darwinian mechanism is taking place, as we discuss later. Let me put a concrete example of some advances. Jack Szostak showed that the presence of citrate, which is an intermediate of the Krebs cycle, is actually good in RNA replication in a compartmentalized system. These are the type of things that a few year ago, nobody could have imagined. Let alone do targeted experiments. Or the work that we have done with Andrew Griffiths using microfluidics, where you can run experiments with thousands of droplets in real time to investigate things as molecular cooperation. Albert Eschenmoser, the famous organic chemist, said that probably we would never know how the origin of life happened. However, if we have a scenario about which everybody agrees upon then the hard job is basically done.

Q - One of your recent interests is the relationship between learning and evolution. In 2016 you published a paper in TREE with the title: How can evolution learn? What is exactly the connection between Bayesian learning and Darwinian evolution?

R - In general, both of them, learning and evolution are producing adaptive solutions, solutions that can be complex. In this general sense, the relationship has been observed and there were particular realizations. For example in the case of Skinner’s operant conditioning where there is spontaneous variation, and there is a reward for performing a particular task and the frequency of the behaviour is increasing. People already said that there is an analogy, and that is Darwinian selection. This is one line of thought; the other line comes even before with the famous psychologist William James. The brain comes up with complex functional solutions, we do not know
how it does it but we know that evolution works. James proposed that maybe something like an evolution process is happening when we perform complex thinking. Later, some neurobiologists like Jean-Pierre Changeux and Gerald Edelman suggested that there is pruning and selection over the production of different variants, different connections, and different cells in the brain; and that there is functional elimination of the wrong ones. This is sort of a Darwinian view of the brain. However, after a second thought we can realize that it is incomplete, because this is a one shot game. A Darwinian process happens when there is ongoing variation and selection, not with the variation that is generated once early in development, but with a continuous input of new variation. Evolution by natural selection is an algorithmic process, or it has a very strong algorithmic element, and it is important to look for solutions in parallel. It is also a stochastic process, there is always some noise; and there is redistribution of resources. This is important. The non-functional or hopeless solutions are literally thrown away. This happens with natural and artificial selection, and it should also be the case with the brain if we claim that a Darwinian process takes place inside the brain. For this, you have to generate the new variants out of the ones that were already present in the previous round of selection. This iteration process is a key element, but it is unknown whether it is working in the brain or not. This would be an ultimate goal to claim that evolution is important during learning. Now we can ask the reverse question, how important is learning in evolution? People like Richard Watson in UK and Uri Alon in Israel initiated an analogy between evolutionary and learning systems. For example, if you have a genetic regulatory network, which obviously every organism has, this regulatory network is of course subjected to selection because it was the evolution of this network that led to the evolution of the organization. An interesting question is whether this genetic regulatory network can have a memory, as it happens with artificial neural networks. That is, put the genetic network in a certain environment and select for functionality in that environment. Then switch the genetic network to a different environment where it will likely evolve new connections. The question is whether this genetic network keeps a memory of the previous environment. If this is the case, when the network is again turned back to the first environment it readapts much faster than if it has to adapt de novo. Then you can look at the evolution of the coupling strengths between the genes in the genetic regulatory network. For example, two genes can be co-selected in the sense that both have to be simultaneously active in a particular environment. How does evolution influence
the genetic regulatory network? A simple answer would be that it is like Hebb’s rule, which states that neurons that fire together wire together; that is, one could argue that genes that have to be active together are going to have a strong co-expression. Obviously, it is not as simple as this because Hebb’s rule is already an evolved phenomenon, it is a dedicated learning process. In the case of genetic regulatory networks, the two genes can also influence each other indirectly, so it is not necessarily a direct influence. However, we have found in some recent experiments that if you look at how individuals react in different environments and the connectivity between their genes, you find that at the population level what happens is actually Hebbian learning. This is one link between learning and evolution. Another link, pointed out by other people not a long time ago, is that if you look at the Bayesian update as a process, where the probability for a hypothesis is updated as more evidence or information becomes available, it is formally analogous of what they call a discrete time replicator equation. In retrospect, this seems obvious because every new organism is a hypothesis of how to make a living in a particular environment. Those hypotheses that are bad are thrown away. We call this natural selection.

Q - In 2005 the editors of Science highlighted 125 unsolved scientific questions that they thought could be answered in the coming decades. Second on the list was “What is the biological basis of consciousness?”, and sixteenth was “How did cooperative behavior evolve?” Do you share the optimism of Science editors?

R - With cooperation, I do agree. We have now so many mechanisms that can work in favour of cooperation that we may not need more. It is more an empirical work now to find what particular mechanism dominates in a particular situation and under what conditions. This is important because some cooperation models, like the
Prisoner’s Dilemma, were over-researched and, in many cases, they are not relevant. With the case of consciousness, we are far from that. We can do nice research now in neurobiology to look for neuronal correlates of consciousness, but what this means is far from obvious. We face a hard problem here. For example the qualia problem. You see the colour red but you also “feel” it; that is, the colour red gives you a subjective feeling. Where does this come from? This is not only an interesting question; it is also a serious question. There have been cases where, apparently, people that had an accident lost part of the qualia, the instances of subjective conscious experience. For example, a person did not have the usual, subjective sensation of the red colour although remembered that it should be there, but did not have the sensation. I personally know someone that also had an accident. For months, he was living in what he could describe, with no better words, that he lost qualia. This is a terrible feeling. No one knows what is going on when you realize what is around you but you might not have the “feeling”. You lost the association. It must be an extremely dramatic and frustrating experience.

Q - People working in artificial intelligence believe that the sheer complexity of modern computers, or of their interconnectedness through the internet, will trigger a singularity, a term popularized by Vernor Vinge in his 1993 essay The Coming Technological Singularity. Machines will become conscious. This sounds quite farfetched, especially if we take into account that there is no agreement among neurobiologists how the brain produces consciousness. What is your opinion?

R - First, we have to remark that consciousness arises under conditions of individual selection. I do not believe in panpsychism, the view that all things have a mind or a mind-like quality. What I do believe is that if you have the right constraints on artificial systems, then consciousness might arise. Why not? Although, suppose that conscious artificial systems will have qualia. That would be very different from our qualia. It is as the old question of what is it like to be a bat? I think that there will be some advances where interfaces between the brain and artificial systems will improve. I think that we could actually login into the brain of a bat. Some people might become mad if this is the case, I do not think that this is without risks. However, I think we have a better handle on these questions, and I do not exclude the possibility that machines can become conscious but it is quite far still. The stunning performances of those systems that can play go is important, but we also know that humans work very differently. For example, people are forming hypotheses even after seen one example, but the artificial systems need millions of
examples. Also, as someone remarked very nicely, compare the energy consumption of artificial systems that were fighting against the human brain. The human can be sitting and eating two sandwiches, but those systems were consuming a huge amount of energy to fulfil that kind of performance. Also from the point of view of an algorithmic approach, and from the energetic approach, what the human brain is doing is still very different from what machines are doing. Moreover, it is possible that some of the things that we are doing have to be done in exactly the way that we are doing them; otherwise we might not have consciousness. Brain algorithms might have components that are not yet in the artificial algorithms, and it is possible that unless you have plugins that you borrow from biology, you will not get conscious machines.

Q - A few years ago, you suggested the neuronal replicator hypothesis, the idea that Darwinian selection can happen within the brain. How does it work? Is there any empirical evidence?

Nobody knows how it works; there are proposals of how it might work. Going back to a previous question, the crucial problem is how you can do something like replication in the nervous system. I mean, neurons do not reproduce; what has to be produced are variations, candidate solutions to a problem. Even in this case, you have to be able to store alternative solutions in parallel, and you have to be able to execute a process where you have to send a variant of the same information to another place. An interesting question is how is it possible that the meaning of an activity pattern will be the same as the meaning of this activity pattern in another part or context of the brain? In a sense, it is a linguistic problem. Different parts of the brain that are involved in this hypothetical process must share the same language or be able to translate between a few languages; otherwise, it will not work. We did suggest candidate mechanisms in the past, but I was never satisfied with them. This is a very technical issue and let us skip it, but I never was satisfied. Suddenly, I stumble over a solution that is not mine, is from another Hungarian named Zoltán Nádasdy who is in Texas at Austin. He was working on questions related to how do you store information in, e.g., the workings of the hippocampus. He figured out something that is called phase coding. To cut a long story short, there are oscillators in neural activity patterns and they oscillate in different phases. He pointed out that if there are two neuronal groups where one has an activity pattern and there is a similar spatial distribution of the possible phases in both groups, then information can be transmitted and reconstituted —I would say effectively replicated. If you are sending spike trains from one group to the other, because of the phase coding the ultimate result is
that it will be understood in the same way; of course, because of stochasticity there will be some variation. Therefore, I think that the mechanism for potential Darwinian selection within the brain is there, and what happens is that there is a reconstitution. It is similar to what Eva Jablonska said about how memes can replicate, it is not digital replication, it is reconstitution of neuronal information from group A to group B. I asked Nádasdy whether this could be applied to the cortex, and he said that almost certainly yes. This is something that we are investigating. To sum up, we do not know how Darwinian selection happens within the brain, but I think that we are getting closer to a potential solution. There are also other approaches in linguistics and insight psychology. For example, if you look at Luc Steels’ fluid construction grammar, it is practically impossible to do it without some form of replication. The important point is that Luc did not want to create an evolutionary system; we just realized that his is in fact an evolutionary system.

Q - Economists are famous for being terribly bad at forecasting recessions and predicting the future. Because you are not an economist, I would like to know your view of the future of the biosphere.

R - Unfortunately, I think that the future of the biosphere is largely dependent on us, which is not encouraging. According to the data, we are undergoing a major mass extinction that is anthropogenic. This is an incredible disaster, and we are in the middle of it. As you know it takes millions of years to recover from a mass extinction, and we have already done an almost irreparable harm to the biosphere. Having said this, what is at a real risk of extinction is not the biosphere as such; it is the human race. At least in the sense of technology and culture. Bacteria will not care a damn; they will even survive an atomic war. But we do have to care. There are a number of very big negative factors. The first is that, overall, it does not seem that bankers have learned that much from the past financial crisis. Second, there is the political unrest, almost everywhere in the world including the big powers. Third, the anthropogenic climate change. Unfortunately, these three problems can link together in a vicious circle. We have examples where local civilizations were collapsing themselves; now our links are global and will affect all of us. Humans will survive as individuals, but the question is if it will be worth living. And this is not far. Talking to some experts on these problems, which I am very worried about and want to help this not to happen, it seems that we have probably a few decades. If there is no substantial change, the game will be over. To put it in a sarcastic way, the records of carbon dioxide emission scale very well with the number of meetings about climate change. Obviously, there is a problem and the attenders to those meetings
do not seem to solve that much. There is also another problem related with climate change, and it is the problem of emerging diseases. As you know one of our colleagues, Dan Brooks, together with other authors wrote a book about this problem, The Stockholm Paradigm, published last year. Take the present COVID-19 crisis. It is only one virus playing around, and look at the mess it is causing. Because of the climate change, we are expecting more and more emerging diseases. Imagine that you have two, three or four of these diseases spreading at the same time. Even if individually they are weaker than COVID, what could happen if they come together? People do not realize how fragile civilization is. Humanity is a combination or superposition of devils and angels. The angels have generated so much knowledge, science, art, and many other valuable things that I am personally very reluctant to go back to the cave. Some people might have heard of Fermi’s paradox. Enrico Fermi was discussing, I think at Princeton at lunchtime (probably Leo Szilárd was also there —there is no clear record), the question of where they are, meaning extraterrestrial intelligence. We believe in evolution, we believe that it is a natural process, we believe that it can lead with some probability to intelligent species so, where are they? One of the explanations was that perhaps civilizations have a short lifespan, and we will never detect any. As a corollary, another civiliza-

tion might never detect ours.

Q - In 2004, Craig Venter and Daniel Cohen wrote: “If the 20th Century was the century of physics, the 21st Century is the century of cybernetics, biology and ecology.” For someone who is pursuing a future career in evolutionary biology or theoretical biology, what would be your recommendation?

R - I tend to agree with what they said but only partially. I was thinking about this. Obviously, biology has become very important, and some biologists feel very “imperialistic” about this and say we will take revenge. This is stupid, because we forget that there is the more general problem of complexity. Complex systems are not restricted to biology. The first scientific approach to complexity did not come from Darwin; it came from Adam Smith. His theory on the wealth of nations is a kind of theory of complexity. There are also complex situations in non-living systems, and some of them can be translated to living systems. I would actually add complexity to their list, but this should not be taken as an arrogant statement. It is a consequence of the natural development of human knowledge and history. And let us hope that it will contribute to the chances of our survival, because it is also the society that matters. This is what we were discussing a few minutes ago. If we cannot handle the complex
issues that human societies are facing, then there will not be essentially biology or ecology; it will be the century of extinction of human civilization. There is a general problem here. As you know, I have many ties to the Parmenides Foundation in Munich, and the core of the Foundation is about the study of thinking with its implications in computer-aided thinking and strategic problem solving, medical diagnosis, etc. We discussed some years ago about that problem. People are learning many things, but not about the various instantiations of complexity. If they learn it, it is only within their subject. For example, imagine a politician that learnt physics. What was he learning? He was learning Newtonian physics, and he is completely right in saying that it did not help him to solve many of the problems he faced. To know about complex systems, nonlinear phenomena, percolation, graphs, interactions, etc., could be critical to solve multifaceted social problems. I would even say that nobody could have a physical degree at the University without knowing a small but very important segment of biology, and the other way around. How do you do this? We came with the idea of the mental survival kit, called the cognitive excellence program. It is centred around two dozen of what we call thought patterns of cross-disciplinary relevance. For example, the idea of what is called self-organized criticality, that happens in physics, in biology and in other areas, is of course cross-disciplinary. Students should know about these things, but overall they do not. I think this is a very big problem, and we generalist scientists have a cultural mission trying to change the actual state of affairs.

This interview with Prof. Eörs Szathmáry took place in Budapest on June 4th, 2020.

Notes

1 Fluid Construction Grammar is a linguistic formalism designed to explore in how far a construction grammar approach can be used for handling open-ended grounded dialogue, i.e. dialogue between or with autonomous embodied agents about the world as experienced through their sensory-motor apparatus. (L. Steels and J. de Beule. 2006. Proc. 3rd Workshop on Scalable Natural Language Understanding, pages 73–80.)