

## Life is Fine-Tuned in a Fearful and Wonderful Way

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Robert Marks:

Welcome to the Mind Matters News podcast. I'm your ever more ignorant host, Robert J. Marks. They say that the more you learn and the smarter you get, the more you realize you don't know. Boy, that's true with today's topic. We're talking about fine tuning. Fine tuning is ubiquitous in the universe. Today we're going to talk about fine tuning in biology. How biology is fine tuned to allow us to exist here. It allows us to live, breathe and have our lives that we enjoy them. We have the perfect guest to do this. Both are published in the area of fine tuning and we want to tap their brains today. Dr. Daniel Díaz is a research assistant professor of biostatistics at the University of Miami and comes to us today from Columbia. Daniel welcome.

Daniel Díaz:

Thank you Bob. Pleasure to be here.

Robert Marks:

Okay. And Dr. Ola Hössjer is a professor of mathematical statistics at Stockholm University and joins us today, directly from Sweden. Ola, welcome to you too.

Ola Hössjer:

Thanks a lot, Bob. It's great to be part of this.

Robert Marks:

Okay. Let's get right into talking about fine tuning in biology. Ola, you coauthored a well-received paper entitled, using statistical methods to model the fine tuning of molecular machines and systems. We are going to put a reference to this paper, as well as some other papers in the podcast notes, for those that are interested in digging deeper. Using statistical methods to model the fine tuning of molecular machines and systems. I know little about fine tuning and biology. You guys are really going to have to help me out.

Robert Marks:

My car is not a molecular machine, but it's a machine, and it has a gas cap that unscrews to give me access to the little pipe that goes to my gas tank. It allows me to fill my car with gas and then replace it so the gas doesn't get polluted. I suppose I could talk about fine tuning of the gas cap. The threads for the screws have to be just right. The gas cap can't be too big in diameter because it won't fit in the little hole. To me that doesn't sound very compelling in so far as fine tuning. But I suspect, and I know from perusing your paper, that fine tuning and biology is much more sophisticated than that. Ola, what are some of the more sophisticated examples of fine tuning in biology.

Ola Hössjer:

Yes. Thanks Bob. In order to talk about fine tuning in biology, we have to go into the small things within the cell. During the first episode, we sort of talked about different ways of quantifying or defining fine tuning, and it's closely related to specified complexity that Daniel talked about. We can say that something is fine tuned if it's complex, if it's unlikely to occur by chance. Secondly, if there's an independent description or specification of the thing that is fine tuned. Now there are a number of features within the cells that satisfy these two requirements. The first thing are proteins. Most proteins are sort of all over the cell. In order for the cell to manufacture proteins, there is an amino acid sequence written in a 20 letter alphabet of amino acids.

Robert Marks:

Yeah. Amino acids. They're the components... I'll interrupt when I understand something, that I don't look too ignorant. Amino acids, these are the building blocks of DNA right?

Ola Hössjer:

Yes. There is a correspondence between the nucleotides of DNA and amino acids through the genetic code. We can say that from DNA, we have coding that corresponds to amino acid sequence. Yes. That's correct. Amino acids form the building blocks of the protein. In order for a protein to work, when these amino acids are manufactured in the ribosomes of the cell, this amino acid string has to be folding in a certain complicated three dimensional structure that is specific for each protein, and that is necessary for the protein to work.

Ola Hössjer:

This is a complex structure because if we look at all possible amino acid sequences of a certain length, it could be a few thousand amino acids that comprise a protein. What is the fraction of amino acids that give us a working, a functioning three-dimensional protein?

Ola Hössjer:

It turns out that it's a very small fraction of amino acid sequences that give us a functioning protein. That is the first definition of fine tuning. It's complex. It is unlikely to happen by chance, to get a functioning protein. The second part, we should have an independent specification. In this case, the specification is that the protein works. For that reason, a protein is an example of a fine tuned structure in biology. Then we could get up to the next hierarchical level and look at complexes of proteins, like molecular machines. The ribosome itself, ribosome manufacturer proteins in the cell that is itself a molecule or machine that consists of many proteins that have to be arranged in a certain structure, in order for it to do its work.

Ola Hössjer:

Another example is mitochondria in the cell plasma. These are the power stations of the cell that generate ATP. This is also an example of a molecular machine where all its parts have to be structured in a certain way, in order for it to function. One could say, we talked about this during the first episode, a specific case or a special case of fine tuning are irreducibly complex systems.

Ola Hössjer:

Something is not only complex, but it's complex due to the reason where that it consists of many small parts, and all parts must function in order for the whole system to work.

Robert Marks:

So if you remove one of the parts in the process you're talking about, the whole thing breaks down. Let me give you a guess as an example. This is on the macroscopic level. Things such as our lungs, for example, have a bunch of individual cells, and one of these cells has no idea what the other cells are doing, but for some miraculous way, they all work together to allow us to breathe and put oxygen in our blood and other things. Would that be a big example of what you're talking about?

Ola Hössjer:

Yes. And another, you could view the whole cell as a cellular city. It has a network of roads, or factories and power stations, you could view a larger part of the cell as a network. That consists of many molecular machines or protein complexes. Yes.

Robert Marks:

These are things which display irreducible complexity. You take away one piece, the whole thing falls apart.

Ola Hössjer:

Yes. Because it's one layer above, it's one hierarchical level above the protein complexes. If the parts themselves are the protein complexes, the molecular machines that we talked about are either deducible complex. Then that will be the case also on the next level, not by definition, but typically, that is the case as well.

Robert Marks:

I see. Okay. Well, thank you. That's fascinating. Daniel, do you have any other examples of fine tuning and biology that you know of?

Daniel Díaz:

Yeah. There was a paper that we published, actually Bob and I published a paper last year on population genetics.

Robert Marks:

Well, let's talk about population genetics before we talk about it, let's define it. What is population genetics?

Daniel Díaz:

Population genetics try to study how populations evolve in time, usually taking that evolution in terms of genetics. That's why it is called that name. You're looking at some sequence of genes or some gene actually, and then you're looking how it is evolving in time, trying to infer some properties out of that process. That is basically a stochastic process.

Robert Marks:

Stochastic, by the way, I tell my students, if they want to impress people, they say stochastic. If they don't want to, they say random. Stochastic is a synonym for random. Okay. So it's a random process. Go ahead.

Daniel Díaz:

Yes. It's a synonym for random. That's the formal name that is given to that process in probability theory. It sounds quite impressive, but it does mean that it's random over time, or that it has some randomness at least included over time. It's not necessarily just pure random, but it has some random added to it over time. That's the way to think about it. In population genetics, actually, something that could be a study in terms of fine tuning, for instance, is the time to fixation of some allele. Allele is just a variation of a gene.

Robert Marks:

Could you say that that was a mutation?

Daniel Díaz:

Yeah. It's possible to have a mutation. Then what you're looking at is the possibility of that mutation to become fixed throughout all the population. Once it happens, then you can say that the gene was fixed. That's a technical name again. So when it has spread throughout all the population, then you can think and you can study the time that it takes for that mutation, for that allele to get fixed in all the population again. That time can be just an example of fine tuning in biology, if the time for instance has a more probability again.

Daniel Díaz:

So we're coming back to the same concept, again. We have that now the time to fixation is going to be the specification, but that specification also has some probability of occurrence. If the probability is small again, we can talk of fine tuning in biology, and in particular in population genetics. That being said, I'm thinking here that we were talking about a specifications and we're being very informal, but just let me mention that, even though we are speaking about it here informally, there's a formal definition to it. Actually this is one of the great ideas Ola had, and it is just defining it in very simple terms as a function, a mathematical function I mean, with some interpretation, usually in reality, that is maximized.

Daniel Díaz:

Even though we are talking here in very informal terms, I just want to mention that this specification can be formally defined in mathematical terms.

Robert Marks:

Okay. I want to talk about that next. Ola, you came up with a general theory. We talk about in physics, for example, a theory of everything. It turns out the fine tuning is something ubiquitous in our universe. It occurs in biology, chemistry, and physics and cosmology, the specific area of physics. The question is, is there a general theory, a general way that we can look at fine tuning across all of these disciplines? You've done that, by something called a specificity function, I believe. Could you explain the specificity function at as a high a level as you possibly can, so that we can understand what's going on here about your general theory?

Ola Hössjer:

Yes, Bob. We introduced this idea in my joint paper, with Steinar Thorvaldsen originally, and then I have an ongoing project now with Daniel, where we elaborate on this idea more. We start with a sample

space of all the possible outcomes of a certain algorithm, and this could be in cosmology, this could be the algorithm on generating the universe.

Robert Marks:

Okay. An algorithm for generating the universe is, how would you describe that as a theory or a model of by which the universe came into creation?

Ola Hössjer:

Yes. In the previous episode, we talked about the possible values of a certain constant of nature. This algorithm, if the universe was randomly generated, the different constants of nature could have different possible values with different probabilities. The sample space is a collection of all possible outputs of the algorithm.

Ola Hössjer:

In cosmology, that would be the process of generating a universe. In biology, that could be, as Daniel talked about, population genetics, which is really describing small evolutionary changes. Then the outcome could be the outcome of an evolutionary process to generate a protein. We talked about proteins as being fine tuned. It could also be in biology, the process of generating, and that's more challenging, a whole protein complex or a molecular machine. That is the first part. We need to have a sample space of possible outcomes.

Ola Hössjer:

Then we introduce, now comes the specificity function. To each possible outcome in this sample space, we assign a value, which is how specified is this particular outcome. If we go back to cosmology, for each possible universe, we could look at a specific constant of nature. Then the value of the function will be binary, either this value of the constant of nature outcome corresponds to a universe that permits life or not. Or when we talk about a protein, we have a certain amino acid sequence that folds to protein. So each amino acid sequence is a possible outcome.

Ola Hössjer:

That outcome either corresponds to a functioning protein or not. In this case, the specificity function is binary as well. One, if something works, if the protein functions, and zero if it does not. But then we could also, if we're talking about a molecular machine, we could also say that the specificity function is whether it works or not, but we could also have a more refined, like it could be the number of parts it consists of, and so on.

Ola Hössjer:

If we talk about population genetics. If the purpose is to generate various organisms, not only a protein or a protein complex, but a whole organism or population, or to generate a species with organisms, what is the biological fitness of each organism? That quantifies that organisms reproductive ability, how many offspring it is expected to have. In this case, that's another example of a specificity function.

Ola Hössjer:

That was the second part. The first part was the sample space of all possible outcomes. The second thing was specificity function. To each possible outcome, you assign a number that tells you how specified

that particular outcome was. Then the third part is, I call it a null distribution. That is, if you think of these, an outcome being generated randomly by chance, you have a certain distribution on it.

Ola Hössjer:

We talked about in cosmology, the distribution of a certain constant of nature, we could think of a randomly generated amino acid sequence. We could talk about a random evolutionary process. The purpose of it which is, or the target is a functioning protein or a molecular machine, and so on. Now we have these three components, the list of all possible outcomes, the sample space, we have a specificity function and we have a null distribution that gives us the distribution of all these possible outcomes.

Ola Hössjer:

Now we can define what is fine tuning using these three components. The first is, we talked about this in episode one, we need to have a target. The target consists of all the outcomes in the list of outcomes that are specified, that have a sufficiently high value of this specificity function, above a certain level. In the case of the universe, it's simply all the possible generated outcomes that permit life for a certain constant of nature.

Ola Hössjer:

That gives us the target, the function, or the subset of all highly specified outcomes. Then, because we have constructed a distribution for randomly generated outcome, we can talk about the probability of ending up in that target of highly specified outcomes. If that probability is small, then the system is finely tuned. We could apply that in cosmology. What is the probability of a certain constant of nature ending up in a... And then we call the target, life permitting interval. We could apply it to evolutionary processes for generating proteins.

Ola Hössjer:

What is the probability of that process generating a protein that works or functions? Or we could also talk about an evolutionary process. This is a chance with a certain null distribution. What is the probability of that evolutionary process generating a certain molecular machine? Which is irreducibly complex. If that probability is small, then the structure is fine tuned.

Robert Marks:

Excellent. One of the things I really like about your theory is including all possible successes. I've heard for example, that if you make a bowl of alphabet soup and the letters arrange themselves and say, good morning, Ola, that that is specified. And you can talk about the probability of that happening by randomly selecting numbers. That probability is very small. A more meaningful thing to do is to ask, what is the probability of anything, which is meaningful coming up and floating in your soup. That's a more important thing. It sounds like you've done that, by looking at all of the possible solutions that are specified. You've looked at all the possible successes. Am I right in that interpretation?

Ola Hössjer:

Yeah. That's kind of a goal of this project. I think that's the beauty of mathematics. You have some general abstract objects, and you could sort of model things from different areas of applications in a similar way. I think that's an important part of the beauty of mathematics, that seemingly unrelated features in cosmology and biology and in algorithmic theory, and so on, they could be modeled in a very similar way using similar concepts.

Robert Marks:

Ola, this looks like a landmark paper, and I hope it gets the attention it deserves. Do you per chance know, off the top of your head, the title of the paper, for people that want to dig deeper?

Ola Hössjer:

Yes. It's published in the Journal of Theoretical Biology, by myself and Steinar Thorvaldsen, and the title is, Using Statistical Methods to Model The Fine Tuning Molecular Machines and Systems.

Robert Marks:

Okay, wonderful.

Ola Hössjer:

Yeah. This paper, we mostly talk about the biological application, but we also gave a historical background, because fine tuning was first mentioned in the context of physics and cosmology. So we also introduced some of these examples.

Robert Marks:

Okay. Excellent. I hope that the paper gets the attention it needs. I'm in the world of artificial intelligence, and I looked up artificial intelligence on Google with quotation marks around it and put 2020, just to see how many hits I got. It was in the millions! It turns out to be like over two papers per minute, 24/7. There's no way that people can keep up with the literature. There's lots of jewels in the mud of the literature that exists out here. I'm certainly hoping that your paper kind of floats to the surface, as people realize the importance of it. I also know that sometimes papers lay dormant for a while until somebody discovers them and begins championing it, then it becomes more popular. I hope that indeed that happens.

Ola Hössjer:

Thanks a lot, Bob.

Robert Marks:

Yeah. Really this is really a landmark result. I wanted to talk about the last topic, and this is kind of a general idea too. It's a paper that Daniel, Ola and I wrote, and it was about introducing the idea of probability to measure the degree of fine tuning. We talked about this a little in the prior podcast. If you want the background, you should go back and listen to that. It's really, really great. Daniel, could you talk about how we introduced the idea of probability to measure the degree of fine tuning? This looks also to be a universal model that can be applied to a number of different things in biology, chemistry, and cosmology.

Daniel Díaz:

Yes, Bob you're right. It is a general reading, a kind of universal setting to work in different areas. Some of the areas were mentioned actually by Ola. As we have talked, fine tuning is studied in cosmology. Now there has been some applications of it to biology as well, I was mentioning. Actually, there are a couple of papers that appear this year in the literature talking about fine tuning also in cell membranes. These are very specific things that are being done in biology. There is also fine tuning, as we mentioned in the first podcast, on search problems in computer science that is machine learning. There is also this

very interesting area that has generated a lot of response, positive, negative, among every possible different view about the simulation hypothesis. In the simulation hypothesis, there is also required that there's some fine tuning.

Daniel Díaz:

So it's very interesting. As we can see, fine tuning is kind of spreading throughout all the sciences. There was an important realization that we had in our previous paper when we were finding a way to measure fine tuning, cosmological fine tuning, actually. It was to notice that the fine tuning problem can be divided into two parts, two stages. The first stage is just finding what is the life permitting interval. That is basically a physical problem. That is a problem pertaining to the science of physics.

Daniel Díaz:

The second problem is determining the probability of that life permitting interval. That is a mathematical problem. When we realized that then we could use all the mathematical power in order to find that probability. That is the realization that I think allows to generalize the whole concept to all areas of science, because even though the first step is going to be determined by the particular area that is being looked at, so biology, physics, machine learning, whatever, the secondary stage is going to be a general mathematical theory that can be applied throughout all the sciences.

Daniel Díaz:

That is what allows the concept to be generalized. That realization that finding the probability is basically a mathematical problem. The way that we do it in our paper was then, as Ola mentioned before, by using base theory, and trying and looking for a maximization of entropy, that is something that is maximizing a level of ignorance that is using all that we know, and then making as random as possible, all that we don't know, so that we could circumvent previous criticisms that we're doing to previous attempts also to measure that probability.

Robert Marks:

Let me ask you a question Daniel, and this will probably come from some different people. I think has been one of the obstacles for developing this general probabilistic theory. We have different cosmological constant, say for example, the speed of light, but we have no idea of the distribution. We have one statistic, which is currently the speed of light as it exists. How can you take one statistic and figure out, for example, in a model, how much it's spread out, those with a background or a course in statistics. You know that it takes at least two numbers to figure out or estimate the variance, and usually that's pretty bad. So what do you do? How do you take one statistic and milk it for all this probabilistic information?

Daniel Díaz:

Yeah. So that's precisely what we did in this previous paper, cosmological fine tuning of how to measure cosmological fine-tuning, for the listeners that are interested, you can look for the paper. It is titled, *Is Cosmological Tuning Fine or Coarse*, and it is published in the *Journal of Cosmology and Astroparticle Physics*. That's the name of the journal.

Daniel Díaz:

What we did in that paper then was realizing that there were some previous problems with the way that probability was considered for those. There is a famous paper that was written almost two decades ago

by some philosophers. This paper talks about how, trying to use the uniform distribution that is trying to constrain basically the life permitting interval to a finite space, to a finite set of possible outcomes, is not permissible for finding the probability of fine tuning.

Daniel Díaz:

There was this big question that was kind of the origin of the quest for a way to measure this probability. We realized that if we wanted to do that, we should replace that basic idea that was underlying the uniform distribution for this problem, and generalize it to a more general situation. When we generalize it, or the way to generalize it was using, as Ola mentioned before, the maximum entropy principle. When we went into that direction and together considered a base theory, then we were able to actually use that life permitting interval in order to measure that probability, without having those previous problems that previous attempts had, when they were measuring the probability.

Robert Marks:

That's great. I would suggest those of you who are sufficiently nerdy to understand the math, to go to the paper and the solution, which I believe was due to Ola, is really ingenious, how you can stretch this one statistic into a more general framework by assuming maximum entropy.

Daniel Díaz:

Yeah. Let me just mention here that two things that we achieved in the paper, first, then to solve that previous criticism to the measuring of fine tuning, that is that criticism is usually called in the literature, the normalization objection. Our method overcome that criticism. Then, Ola's idea also of base theory using it as background, also overcame some criticism that is usually done to these measurements that is called a weak anthropic principle, in which this is basically said that we are biased to see a universe as we are seeing, because we are here to see it. It sounds like a puzzle, but it has some weight. Then the combination of the maximum entropy and base theory solve the two problems in tandem. We were able to solve the normalization objection, to find a way to go around the normalization objection, and to find a way to the base theory, that Ola also expert working with, for the work and topic principle.

Robert Marks:

Yeah, we recommend for those that are interested in digging deeper and getting more into the weeds of looking at these two papers, the one that Ola mentioned, and the one that Daniel mentioned also. We will post the citation and a link to the paper on the podcast notes, so that you can have quick access. We've been chatting with Dr. Ola Hössjer from Stockholm University, and Dr. Daniel Díaz from the University of Miami, about fine tuning and biology. Next time, we'll talk more specifically about fine tuning in the cosmos with physical constants that allow life in our universe, that allow you and me to live. Until then be of good cheer.

Announcer:

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