Big Biology Podcast Episode 93: Assembling life in the university (with Sara Walker)

Art Woods 00:00

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Marty Martin 00:09

We'd encourage you right now, to make a donation, you can make a one time contribution at bigbiology.org. Or set up a recurring donation at our Patreon page patreon.com/big.biology thanks.

Marty Martin

So Art, suppose you wanted to find life elsewhere in the universe, what would you look for?

Cameron Ghalambor 00:33

Hmm, well, I guess I'd use the only example of life I'm familiar with, that's life on Earth, As a basis for my search. I'd probably focus on planets or moons orbiting sun-like stars, and I expect to find life forms there based on carbon and water.

Marty Martin 00:48

Great ideas...probably because you're not Art. But who are you? And what have you done with him?

Cameron Ghalambor 00:55

Well, Marty, I'm Cameron Ghalambor, new co-host of big biology, and I'm a professor at the Norwegian University of Science and Technology and Colorado State. I'm also your longtime friend and colleague so this question is a bit weird. But anyway, and don't worry, Art is fine, he was just preoccupied with research in South Africa when we interviewed today's guest.

Marty Martin 01:18

Ah, okay, good. And now that we have that straight back to my question, how to find life off Earth. So why those three conditions?

Cameron Ghalambor 01:25

Well, the carbon part is partly due to its uber-abundance in the universe. The fourth most common element, but also has a very special molecular binding ability, carbon and less so silicon can make stable or reactive bonds with other elements with very little energy. Water too has very important properties. But one of the most important is its ability to dissolve many types of things, especially carbon based molecules. Carbon based reactions are much easier to achieve with water than without it.

Marty Martin 01:54

Okay, all well and good, but that just can't be it. For instance, we've known there's water on Mars for a while. And we've learned recently of water on the moon. My favorite example, in 2011, scientists found a water cloud inside of a quasar that's 140 trillion times bigger and volume than the total water on Earth. Surely, even with all that water, there's no life inside that quasar.

Cameron Ghalambor 02:16

Definitely not. And don't call me Shirley, that's where the sunlight star part comes in. Life won't just be anywhere, at least not life like on Earth. There are between 40 and 80 billion sun-like stars in the Milky Way. And conservatively, only about 1% will have planets of Earth size in the not too hot, not too cold or Goldilocks zone from the star.

Marty Martin 02:40

Okay, great. Now we're getting somewhere. But that does leave us about a billion planets to consider just in our own galaxy. And I don't see anyone funding a systematic search of all of them anytime soon.

Cameron Ghalambor 02:51

No way and more problematically, we know we need water and carbon, but those are crappy things to look for, because they're going to be in many different places where life is not.

Marty Martin 02:59

Yeah, just what is it about a physical object that we could detect and be pretty sure it came from something alive?

Cameron Ghalambor 03:05

Enter Sara Walker, our guest today. Sara is an astrophysicist. She's a professor at Arizona State University, deputy director of the Beyond center for fundamental concepts and science and Associate Director of the ASU SFI center for bio social complex systems.

Marty Martin 03:21

Sara, collaborator Lee Cronin, and others have recently proposed assembly theory as a way to think about the kinds of things we can detect as sure signs of life. In a lot of ways their idea resembles others: look for complex stuff that couldn't have been made by anything except something alive.

Cameron Ghalambor 03:36

For instance, if we find chlorophyll or hemoglobin on one of Saturn's moons, we can be pretty sure that life was there.

Marty Martin 03:43

Plenty of big multifaceted molecules like nucleic acids and some peptides can form spontaneously as the Miller Urey experiments famously showed.

Cameron Ghalambor 03:52

But some molecules are just far too unlikely to arise without being the product of living systems.

Marty Martin 03:58

What distinguishes Sara's and Lee's idea is that this assembly index is calculable for anything, we can compare with the same number, a simple peptide to a mega molecule like hemoglobin, to even a bacterium or the whole human brain.

Cameron Ghalambor 04:12

Only things with very high indices are likely to be signs of life, it's far too unlikely that such things would have arisen spontaneously without help from living systems.

Marty Martin 04:22

Sara used the example of a Lego Hogwarts Castle in the show today to flesh out the idea. As she says there's practically no way that a giant pile of colored Lego bricks could be assembled randomly into a Hogwarts Castle. That particular finished form is the one built using a set of written instructions. You could get a castle or some other kind of Castle-like building, but there are only a very few particular ways to become Hogwarts.

Cameron Ghalambor 04:47

Something with so many pieces put together without a plan would much more likely be a mess than a castle.

Marty Martin 04:54

IN a Nature Communications paper from last year on which our chat was based, Sara and Lee said that to find life elsewhere in the universe, we can search for things with high assembly indices.

Cameron Ghalambor 05:02

Overall, we had a great time talking with Sara about assembly theory and its promise as a means to detect life.

Marty Martin 05:08

But we challenged her to explain assembly theory's, utilities for the origins and especially the actions of life. Previous guests, Dan Nicholson, Nick Lane, and others have emphasized that life is a process more than a thing. We find that perspective really powerful as it integrates many factors we view as key to life: metabolism, information processing, plasticity, and complexity.

Cameron Ghalambor 05:28

Sara claims that assembly theory captures these facets of life. But we had questions about how assembly theory gets us from life indices to actually being alive. You'll hear more about this in the show.

Marty Martin 05:40

So Cam, which has the higher assembly index of beer, or a 10 year old single malt Ardbeg Scotch?

Cameron Ghalambor 05:46

Hmm, well, looking at Sara's paper, it looks like beer has an assembly index of 34. And Scotch only has an assembly score of 16.

Marty Martin 05:56

So victory for Bud Light, I guess

Cameron Ghalambor

I'm Cameron Ghalambor.

Marty Martin

And I'm Marty Martin,

Cameron Ghalambor 06:00

and this is Big Biology.

[music break]

Marty Martin 06:13

Sara, thank you so much for coming back to Big Biology to talk about your research, and especially this new work that you've been doing with Lee Cronin and others on assembly theory, we'll get to that, but I think a lot of it has to do based on our last conversation and what you work on is about the origins of life. So just in a nutshell of such a thing as possible, tell us about the sort of major ideas about origins of life, and how yours differs or where the overlap is.

Sara Walker 06:38

Yeah. So I guess you're referring to like, historically, how we thought about the problem about the origin of life. And I think there, it's really interesting to me, because there's been a long history of chemists working on the problem trying to synthesize components of life, which of course, we think life emerged in chemistry. So it seems like a natural starting point. But that's become really sort of like the focus there has been these are molecules that life on Earth uses. So if we make those molecules, we should be able to find the evolutionary pathway to life. And we might make a specific molecule. And so this is sort of the field of prebiotic chemistry, synthesizing building blocks of life on Earth, based on the conditions of Early Earth. And then there's a whole other sort of set of research that's focused on what's called the RNA world, which is in sort of a similar paradigmatic framework, which is, we know RNA is really important in modern biology and might have been, and it's speculated to be the first genetic material. So if we can show how an RNA based system alone can evolve, or how it could emerge on a prebiotic planet, we might solve most of the origin life problem. And so that's sort of a genetic first approach. And then there's like this metabolism first which is kind of thinking more about energy cycles, and how you might get self reproducing chemical systems. So a lot of this is focused on how do I take pieces of life on Earth and build them without life. And it's kind of almost like a reductionist approach to studying the origin of life. Like, if I can make the parts then I've solved a problem. And my perspective on that is like, the first thing I can say is, when I was a PhD student, I was in a cosmology group, and I was trained in theoretical physics, and it was going to the origin of life conferences. And I remember being really shocked by the culture, of origins of life, because you would go to an origin of life meeting, and almost no one would be talking about what I thought was the actual origin of life, the transition from non life to life, they would be talking about all these other problems.

Marty Martin 08:25

That seems important. Yeah, that might be something that should come up.

Sara Walker 08:28

Yeah. So and I think it's because people thought I mean, that is a really hard problem, right? So if you're a practical scientist, it's not really like the first order question you ask, because, you know, the challenge is like, how do you even make entry points to that problem. And also, it's been the case that it was discouraged to actually, like, even try to figure out how to define life, because that seems like you know, everybody has to implicitly take a definition of life to do an origin of life experiment. But the actual act of going through the process of like, rigorously vetting your definition, and really like saying, Is this really what I mean, when I say this thing is alive, or it's life was sort of skipped? Because maybe that's not tractable on a PhD lifecycle, or whatever the you know, the social dynamics of science are really quite challenging for hard problems. And so my perspective on it was, I care about working on the transition of non life to life. I think this problem is pretty fundamental. I got into theoretical physics because I was romanticized by these, like major revolutions in the way we thought about how reality worked. And I was doing cosmology, but I didn't see the next revolution in how we think about things happening in particle physics and cosmology, or even in most of the problems that physics departments were studying. Also a little bit controversial. But you know, most new physics has happened in areas we didn't expect. And so I saw origin of life as being like a fertile area for thinking about what other kinds of physics might operate in our universe. And maybe we didn't we didn't recognize that yet, because we hadn't invented that. And if you look at the history, science is, you know, kind of clear that like, probably at any point in history, we haven't discovered everything, so why should we think that we've discovered all the fundamental laws now, so I'm very open to the possibility of new principles. And so then that became, for me, what's different about life versus non life. And the key concept there became this one of information being a fundamental category of nature. And so most of the rest of my career has been built on this idea that the origin of life has something to do with when physics associated information being a causal category, or actually doing things in the universe becomes a prominent feature. And I still think that's what the origin of life transition is. But I think like the way that that physics might look might be very different than the way we originally posed that kind of problem. And so most of my career, I've gone through these what people think are pretty radical conceptual shifts, like someone told me once, like, I've seen you give a talk two years ago, and this talk is totally different. And I'm like, but it's the same idea.

Marty Martin 10:46

That's good. I mean, it's showing your ability to adjust as the data tell you otherwise, and the new ideas come, Yeah, that's, that's what we should aspire for.

Sara Walker 10:54

Yeah. And also, you know, hard problems are hard for reason. Because we don't have the right concepts. So I think like being malleable to reframing it, but you have to keep sort of the core things you think are important, but reframe it in a way that becomes more and more productive.

Marty Martin 11:10

So say something more about information. I mean, I think Cam you had some pieces that you wanted to you wanted to dissect that a little bit.

Cameron Ghalambor 11:17

Yeah, I guess, you know, as a sort of like an evolutionary biologist, I think if you survey most biologists and you ask them, what do they think of when they think of information, they're going to automatically say, DNA, and the information contained within DNA, and how that is translated into amino acids and proteins, and eventually, you know, complex organisms. But I have a feeling like when you start to talk about the physics of information, that it's something much more than that. And so I'm just kind of yeah, I'd like to hear more about your thoughts on like, what is information?

Sara Walker 11:52

Yeah, it's a great question. And I ask myself this all the time. And I'm also not sure what I mean. But I mean that in both for fun, but also in a really serious sense that when you're working on sort of the boundaries of what we know, like, word choice becomes really important. And trying to map concepts to things that haven't been defined yet is really hard. So there's this whole set of words that we use in biology that we know vaguely apply, but people will, you know, have radically different interpretations of what that means. So information is one of them, emergence is one of them, complexity is one of them. And then life is, you know, sort of all of those things bundled together. So it can be really confusing. And I feel like I have a sort of precise thing in my mind when I talk about information, but mapping it to concepts that we have and we can talk about readily because they already exist in sort of common sense of knowledge is not exactly there yet. And so I don't mean it in the sense that most people mean it in terms of like, there's certain, you know, standard senses, like, you know, information is something that carries meaning. So this is one of the things with DNA, like the information in DNA has a function in the cell, therefore, DNA has information. And I also don't mean it in like a Shannon sense of information, in terms of reduction of uncertainty. So like, if I was holding an umbrella or something, you might know that it was raining in Arizona, because why else would I or maybe it's too sunny? I don't know. But you would have some information about the weather. I guess since you know I'm in Arizona and I have an umbrella, then you know, it's sunny, if I just had an umbrella you might think it was raining.

Cameron Ghalambor 13:27

Depends if it's monsoon season.

Sara Walker 13:29

Yeah, that's right. So obviously, like your uncertainty in the weather outside is reduced by this extra information. So a lot of people will talk about information in that sense. And I think those are definitely relevant. But you know, there's a lot of smart people working on trying to think about information and how it maps to life. And so far, a lot of that landscape, I don't think has really addressed this fundamental question about how life emerges, or how we address the origin of life, or, you know, even understanding "life", I'm gonna put it in quotes, the phenomena we recognize is the set of living things from, you know, like a more fundamental theory that the properties of those might be derivative from. And so for me that the properties of information that are most interesting are actually more closely tied to the concept of causation in biology and the fact that there are certain things that we think are abstract properties that actually have a causal role. And so words carry information in the sense that, you know, maybe I can tell you both to raise your hand right now. Okay, so Cam did it so okay, I had some action at a distance. I'm in Arizona, and Cam's in Norway, and you know, words, some firing of neurons in my brain formed an abstract thing that, you know, like I articulated and traveled over the computer and, you know, cause something to happen somewhere else, but describing those in terms of traditional material accounts is very hard, but they seem very natural. If you think that there's a property that's abstract like a word that can exist in a human brain can exist in sound waves can exist in a computer and then can, you know, come out your computer have roughly the same kind of causation and cause something that was intended on the other end. And that property I think, is quite strange. And DNA, you know, you think about information, or you could think about it with DNA too. So DNA, obviously, like the information is read out and has a function in the cell. And so you can copy that information, say, from a

DNA strand, maybe to an alternative nucleic acid. And as long as you have an architecture for reading out that information, it means the same thing. Or I could type up a gene on my computer nowadays. And you could actually print the function of that sequence so that information retains the same meaning, even though it's in silicon now, because we have technology that actually can now copy that information back into a protein in a different lab somewhere. So information has disembodied property. And this is one of the reasons it's hard for physics, because physics is used to dealing with material properties. And so the sort of original proposal that came up with Paul Davies years ago about the origin of life transition was it was something about when information became a causal category, and actually had this property of seeming to have a quote unquote, life of its own, as Paul would say, which is kind of a pun on the fact that we think information is describing life. But it doesn't seem that that like, if you think information is causal, now you're saying higher level things can have causes, minds can be causes. And now it's not just microscopic physics that's causal. And that enters this whole deep philosophical territory, which is problematic. So there's this whole conceptual territory here where we think this is a real phenomena. And things are really happening. But we don't have the right scientific language for describing it at the level that we would describe things in physics. And maybe it doesn't exist there. But my personal bias is it does.

Marty Martin 16:44

Well, can we get back to this to assembly theory? Because information, at least must have been an inspiration for you to start working on that, to what extent is that useful? And I mean, just generally, what is assembly theory? And I think it's exciting, but maybe you want to convey to the audience why it's so exciting about it.

Sara Walker 16:59

Yeah so I also think is exciting, which is why I work on it. And I also think, in terms of like this conceptual territory that's really quite difficult that I've been talking about, I think it's the one place where I've seen a path that resolves a lot of these like, really deep conceptual philosophical issues that most people don't even recognize are there with trying to address the origin of life transition. And to me, that's really deeply interesting. So one of them, is this this sort of property of what does it mean for information to be causal? And how do you think about material properties? Because basically, it's like, we think we have matter. And we have like, a platonic world of, you know, ideal objects, and they're completely disembodied from the physical world, like a perfect circle is a perfect circle, no matter how you represent it, but you can't actually build a perfect circle, you know, and so some people are Platanus, because they think mathematical forms do have a separate existence. And then some people are like, strict materialist. And they're like, No, it's all elementary particles. And in reality, I think it's somewhere in between where you can talk about the physicality of things that we think are these abstract objects and look abstract to us. But it's just because we can't see ourselves from the outside and actually look at ourselves as physical systems building abstractions. And I think assembly theory has some nice ways of addressing that that are kind of inspiring to me, because they give me some new conceptual territory for thinking about that. But where this comes up that I can most clearly articulate it maybe is this issue of like, top down causation and emergence, which are related concepts that people worry about quite a lot in some of the fields that I work in, as far as the intersection of physics and biology. So in biology, we assume you know, we're okay with minds having thoughts and you know, like narratives at that level, or DNA, causing something to happen in a cell. And in physics, those things seem intractable. And what you really want to say is like, it's all just the elementary particles can be described as Standard Model of particle physics. And you're just coarse graining out some of those details to describe it at these levels. And so basically, what we do is we take like the, the material particle physics narrative, and then we assume cells are sitting on top like, so you can take elementary particles and atoms to make the elements and then you make molecules. And then you make cells and cells make multicellular organisms, and they make societies and then they make technological civilization. So we're sitting up here sliding on top of reality, but all the real stuff is happening down here. And that sort of is one of the ways we talk about it. And so top down causation becomes perplexing, because it's like, well, how can you know a technological civilization do a quantum physics experiment, because now it's manipulating matter at the lowest scale of reality? And so that seems really perplexing. And what assembly theory does, or at least this is the conceptual thing I think is most useful from the theory whether the theory itself, is right or not, is to say that these things that you're building up in a hierarchy are actually it's not a spatial hierarchy. It's a temporal hierarchy. And you're really talking about how extended in time is that object and so in evolution, evolutionary biologists in this way I like biologists sometimes better the physicists because they think in terms of time and physicists have for 300 years just pretty much that time doesn't exist because Newton said, time doesn't exist. You know, it's not it's not a natural category for us, it's always an emergent property, or it's something that, you know, like equations of motion have to change with respect to something so we invent this variable called time, but we don't really treat it as a property of things. But when you look at an evolved object, there's very clear that it arose because of a lineage of historical events leading to that object. And so what assembly theory is basically doing is saying, when you're talking about the histories of formation of objects they are actually an intrinsic feature of the object. And so in elementary particles, they don't have that feature, because they don't require history to build them. Nothing had to evolve with information to produce an elementary particle, it doesn't require any memory in the universe, they just spontaneously form. But if I want to say I want to make a complex molecule, I have to learn how to do that like DNA doesn't spontaneously fluctuate out of chemical systems, it has to be evolved in the context of a system that learns how to build it. And then we have a way in assembly theory of basically taking a molecular object and fragmenting it. So like, imagine you have a molecule or if you're not a chemist, which I'm not either, so I can sympathize. I'm a physicist that likes to think about chemistry as the scale of reality life emerges in but that's about all the chemistry know. You can think about a Lego object. So imagine over here, I have the molecule Taxol. And then over here, I have a Lego Hogwarts Castle, okay, they're kind of maybe equivalent complexity objects. And I deconstruct them. So over here, you have Lego bricks, and over here you have atoms. And now the operation of building up the assembly space for the object is basically to take two things, so I'm playing with Lego, but maybe you're playing with molecule, and take two and stick them together. And then now I can take any piece I've built so far, so it could be that piece I built or when that's in the pool of elementary objects, and stick it together, and then build the next step. And you basically do this recursive process of trying to build up to the original object by using pieces that you've built in the past. And so for molecules, it ends up being the case that we build it up by making bonds. So you can't build it in an assembly space in an arbitrary way, it has to be physically meaningful, which is where I think some people get confused with computational complexity, because I'll talk about it in a few minutes, if it becomes relevant, but our bio signature measure is based on a minimal path in assembly space. And that gets a little bit confused with the way people talk about shortest path and computer programs being related to computational complexity. But we don't make an arbitrary graph to build a molecule, we have to do it based on bonding rules and how bonds are formed in the real physical universe. So there's a very specific graph you can build. And the idea and the implication there and why it's relevant for thinking about the physics of how molecules get built in the real universe, is in order to build a molecule, you do it by making bonds. So there has to be a constraint in the environment that forces that bond to form. And that constraint could be geochemistry, it could be an autocatalytic set, it could be an evolved organism, or it could be a chemist in the lab, but something has to exist, that constrains the space for those particular bonds to form. And then the recursion part is an implication that there had to be memory in the system. So in order to reuse a piece, it means it had to be built in the past. So assemblies spaces capture the physics of the object. So in Lego, you can't, you know, if I had super glue, I could maybe stick my Legos together this way. But usually, you know, they have the little dots on top, and you have to put them together this way. So there's physical constraints on Legos about how you can build Hogwarts Castle. And that constrains the set of objects you can build. And so this is sort of the idea of assembly space. And you can do that for all possible paths for building something. And then that becomes the fundamental object in the theory is an assembly space. So Hogwarts Castle has a set of ways that you can make Hogwarts, and that is Hogwarts. And a molecule has a set of ways of making it. And that is, that is the object. So now you're not saying a Hogwarts Castle is an instantaneous object, you're saying a Hogwarts Castle is a physical representation of all the ways the universe can build it. And this becomes an informational concept, because now you're not saying the thing is the material. The thing is the actual set of operations to build it, which is meaning that there has to be information in the environment, something has to have knowledge of this particular step or constraints for this particular step.

Marty Martin 24:14

Right. Right. So this is the structure, the result is in a way, kind of all the aggregated information through that, you know, that long time series of things. Yeah.

Sara Walker 24:22

Yeah. And the thing that's interesting to me about this is like the huge inversion in logic, because most people want to talk about information in terms of context, like a strand of DNA gets read out and has some meaning in the cell. And what assembly is doing by saying, a DNA molecule, is all the ways of making it is making that information intrinsic and treating DNA, any strand of DNA as a product of evolution, because there's a lot of steps involved in making it which requires some historical contingency and some acquisition of information to get to DNA. And so you've completely removed this question of this DNA has meaning in the cell and this one doesn't. What do I do with it? And how do I understand that? You just say all DNA is a product of evolution. And so it's like, it's just a totally different way of saying it. And then just for the audience, I guess this becomes relevant to the life question and origin of life question, because we have -

Marty Martin 25:13

Good I was gonna ask you about that part.

Sara Walker 25:14

Yeah sorry it was a really long winded explanation of the assembly space stuff. But I really want to have this conceptualization and think about objects in time before we like relate it back to life, because I think it's a major innovation. And it's like it's fertile ground to play with. But the reason we think this is related to life is if that minimal steps is too long. It requires a system that evolved or learned or has some information in memory about how to make that object. So with Hogwarts Castle, for example, imagine I just put the Legos on the table. And I didn't give you an instruction. And maybe you're a child that never read Harry Potter, and I said, make Hogwarts. Like, what is the likelihood of you even being able to build that object, right? So the fact that you can even imagine the experiment probably means that you have some cultural association with my cultural background, right, but like, there was a goal in mind. And you can imagine building toward that goal, and probably you were assuming you had the you know, the Lego instructions in front of you to build it. So Hogwarts has a very high assembly index, the minimal path to make Hogwarts by randomly constructing it just by joining operations is quite large. You know, if I had said, let's just stick three blocks together, red, blue, red, you know, that would be pretty easy for you to randomly assemble. And so the idea is that everything can be tiered by this minimal path, which we call the assembly index. And the things that have a larger depth in time, require more minimal steps, more memory to produce them are more evolved objects, they require more evolution to get to them more knowledge, more learning. So technological things are probably quite deep in that space. Some molecules are quite deep in that space, and might be deeper than humans even because they're so complicated. But it's interesting to me, because it's like, you can now take all objects that are combinatorially built, and stack them by the likelihood of them being products of evolution, and then have some kind of ordering there. And that that becomes the coarse graining in the theory is now one in terms of ordering in time, not a spatial hierarchy.

Cameron Ghalambor 27:12

When I was in graduate school, there was this kind of very influential paper that came out by Szathmáry and John Maynard Smith in Nature, on the major evolutionary transitions in life, kind of one of the points of that paper that I felt was a bit abstract was this kind of conclusion that these major transitions in life involve changes in how information is stored and transmitted. And whenever something happens like that you get one of these kind of major shifts, is that concept captured at all in assembly theory, is the is the way information, the nature of information and how it's stored and transmitted as you go from the building blocks of a molecule or Hogwarts Castle, is there also something changing as you're moving up that chain?

Sara Walker 28:06

Yeah, I think there's kind of a two tiered question there. There's one about like, how would concepts from information map to assembly spaces? And the other one is, would assembly be able to explain features of evolution like major evolutionary transitions? And so the first thing I can say is like, super early days of the theory, and you know, it may not explain everything in biology, it's, you know, it's like, we're designing it specifically for the origin of life problem. And really, the theory is developed, we think it's an exact theory in molecules. And actually, you can measure assembly index for molecules. So you can go in the lab and measure this depth and time for molecules. So we wanted to be able to do it to say, if we had an experiment, could we measure when life emerged in that experiment, and we actually had something that's a product of evolution. But my goal, and this is something that Lee and I have been working on together with several people in our lab is to develop it into a general theory of physics that might apply to other living systems, and we expect should apply. And so when it places I'm really interested in applying it as collective behavior, which is a project going on in my lab, but So those caveats are just to say, right now, it's very origin of life focused, but presumably, there are concepts, we're trying them out from these different spaces, and some of them are better developed than others. But for me, the concept of information is interesting. And I don't know how directly this is going to address your question. But I think it's relevant because I think we have these ways of talking about information storage and processing. And I would say that's more related to sort of the Shannon-esque information concept, and not so much this idea that I was saying earlier, which is where I think about information is copyable causation in some sense. So if you can copy causation between physical systems, and that seems to suggest something really interesting is going on to me. And so the way we build these assembly spaces, we actually think of them sometimes we'll talk about assembly pathways, a causal chain, it's all the causal sequence of events necessarily to build that object. And so now you're thinking about that object now as this layered structure the way of building it. So that object is now this thing that exists across time and has the structure associated to it. And so there's the physical thing you see. And in Assembly theory, things are only actually objects if they have multiple copies. And this is also another subtlety because the implication there is, first you can't ever measure it unless it exists in multiple copies. And the more copies you have, the more credence it gives to this idea that there was something there that could build it. So I don't believe this is true, but some people believe that the universe can spontaneously produce any object at any time, right, like it can just fluctuate into existence. And I think that's tantamount to saying that the universe has design for every object and every point in space and time, at every moment, it's the same thing, like people don't realize that it's making intelligent design every point of spacetime, if you say like brains can spontaneously fluctuate and like they are products of evolution, that's, that's what evolution does. Evolution is the universe's physical mechanism of making complex stuff. So if you completely remove that, and you're just saying, you know, spontaneous universe can make it for free, then there's no reason for evolution to exist. But that's a whole separate can of worms, and not exactly where I was intending to go. So, the thing about these objects is these things in time becomes irrelevant for talking about information because there's a physical object. And if you have many copies of the physical object, then you identify the physicality of the object like the molecule. But when we say it's a thing that exists across time, there's all these features of it that you're not directly interacting with, but nonetheless have existence to them. And so the way that I play around with that idea right now, in sort of our assembly theory working group is to talk about virtual objects and physical objects. So there's things that exist in the assembly space, like every DNA molecule shares, certain structural motifs, right. And sometimes you can't hold those in your hand, because they might be a bonding pattern that never exists as an isolated molecule. But it's actually a physical feature. And it's a feature of the assembly space. And those are propagating in the biosphere just as much as a DNA molecule is because a DNA molecule that you can physically hold is propagating in the biosphere. And so I think assembly theory actually allows you to talk about objects that we observe, but also this larger space that they exist in, in terms of the ways of assembling them this object across time, in a way that's unified as the same object. So information is actually just depth in time. I gave this example last weekend in Santa Fe, about like, you know, three classes of objects you might imagine. So there's like, elementary particles, they always exist, universe generates them anytime. And then there's, these are gonna be very human centric examples. I'm sorry, I'm a human. So I always do this.

Marty Martin 32:35

That's to be expected. That's okay.

Sara Walker 32:37

I mean, them to be biologically motivated. But there's things like rockets, right. So like, human humanity could imagine rockets for a long time before we built them. And now we have like a physical object that exists on this planet, that's a rocket that can be launched into space. So it's like something you can point at, it can't hold a rocket because a big or maybe a little rocket you could hold if it's like, you know, like a kid's rocket or something. And then there's things like I mentioned before, like a perfect circle, like it's something humanity can imagine, we can try to build circles, but they'll never be perfect circles. But that's still an object that exists in the space of like, what it is to be human. So these things have kind of different physicality to them in terms of like, whether they can actually become an independent object you can hold, or if they're just going to be features of the space. And I think assembly theory allows us to talk about all three of those cases in the same language, which is why I really like it. So basically, like what we're doing is reinventing the concept of matter to now be this causal chain of ways to make something that you observe. And so to get to the question of major transitions, you know, I'm talking about molecules. But once you have molecules and they become physical objects, now you can start talking about putting molecules together to make higher order structures. So there is sort of a sense that you can talk about major transitions being now you have an assembly space built out of objects that themselves are assembly spaces. That's very abstract. But this is sort of, and we haven't dealt with this. But that's sort of how I imagined it.

Marty Martin 33:56

But that's the kind of thing that I think that would be fun to talk about. Because that I mean, again, I really think that assembly theory is cool. And that doesn't mean very much because I you know, I'm not a mathematician, not a physicist really don't know what I'm talking about. But for what it's worth. The piece that I couldn't get my head around, though, is this. Back a few minutes ago, we talked about the origins of life, the different ways of thinking about that, you mentioned metabolism. So many people have argued that we've had Nick Lane on the show, we've talked about this a whole bunch. But where's metabolism in assembly theory? I mean, like some of the things that you're saying, I can hear that it might be there, especially that last little part, but the maintenance of a system, right and getting the resources to make things get more complex, like all of those different pieces, I didn't I just can't get my head around how that's in there. Presumably it is. But yeah, how does that work? How does metabolism fit into the story?

Sara Walker 34:44

Yeah, I can definitely explain that. I also want to clarify something about new theory, like so I think people think a theory like you're saying you can like assembly theory and not have any conception of mathematics. And in fact, we still are like trying to figure out what is the right mathematical representation of the theory. I think it's like, you should think of a good theory as a set of concepts and like, are those concepts rich? And do they open up new conceptual territory, and I would call that a good theory. And the fact you can formalize them as mathematical statements means you're just making that conceptual, written and more precise, so you can actually share it more widely. And people confuse this because they think theories are the mathematical statement. But I think that's just a compression of like, the set of ideas. So I think what I like about assembly theory, you know, from the physics and math standpoint, is it gives me a new conceptual playground for playing with these kinds of ideas. To answer your question more directly about the metabolism first, usually, people are thinking about, you know, in my early career, I was also very excited about the set of ideas like autocatalytic sets, which probably you're both familiar with, but maybe people in the audience aren't. So these are, it was originally proposed by Stuart Kaufman. And the idea was, instead of having a molecule that can copy itself, so it reproduces itself, you might have a molecule that catalyzes this reaction, which produces this molecule, that catalyzes this reaction, and you get a closed cycle. And so it became a model of how you could have collective reproduction in chemistry. And there's all kinds of ways of theoretically modeling this, people like to do what are called these like binary polymer models. So you have like a, you know, a string of zeros and ones, which is meant to model a biological polymer, and then they're acting on each other. And you assign some random probability of this one catalyzing these two joining together and that one catalyze that one. And then you can see this sort of phase transition, where if the rate of the likelihood of things being catalytic is high enough, you'll spontaneously always get cycles. And so Stuart had proposed this as a phase transition associated with the origin of life. And that life was like this kind of crystallization, where you would just no matter what, as long as you had enough diversity of polymers and enough catalytic rate, you should get life forming. And a lot of people have been trying to build these things in the lab. And it turns out, they're actually really pretty brittle. And what I mean by that is, it's very hard to make an autocatalytic set work. It's a beautiful idea. And I do think there's a lot of merit to this idea of these self reproducing cycles, but we haven't really been able to get one to form de novo. And even when you build them in the lab, you kind of have to sort of fine tune the parameters of your experiment to get it to be stable. And then there's all these other issues of evolvability, although some people are developing some really interesting things about selecting on motifs and molecules. And then that's the thing that propagates. And that actually gets closer to how you would think about it in assembly theory. And the way the way I think about it. So imagine again, a molecule as an assembly space, in a Kauffman-esque model, you would just deal with the objects and the objects act on other objects. But now if you're thinking about a molecule as an assembly space, any pieces of the molecule can become a part of an auto catalytic cycle. And so this feature that it has to be the molecules acting on other molecules, I think, is not actually looking at the fact that molecules themselves are hierarchically structured objects. And so in ecosystem ecology, of course, like people know, there's like all of these hierarchies of cycles of things interacting, like so we have chemical cycles in an ecosystem. And then we have like, you know, organismal cycles, maybe the microbes, and then they go through like multicellular organisms. And so we know things are hierarchically organized. But when you get to the molecular level, people just want to treat molecules as whole objects, and not actually as hierarchies themselves. And in Assembly theory, they're hierarchically assembled objects. So any piece of that can actually be part of autocatalytic cycle. And so we're doing some things in my lab trying to develop, like, what that looks like, and how autocatalytic sets emerge out of that, and how that's related to this concept of information in terms of like, the virtual spaces and stuff I was talking about before.

Cameron Ghalambor 35:23

So if I follow that argument, somewhat, rather than thinking of like, metabolism as like an alternative sort of explanation, it's actually assembly theory is robust enough that it can encompass having a hierarchical molecular structure, and having an autocatalytic sort of component to it, as opposed to those being alternatives.

Sara Walker 38:58

Yeah, so if I ignore assembly theory for a minute, and I just go back to like, sort of original motivations and origins of life, and what we talked about the beginning of discussion, there's always this kind of like, genetics first metabolism first. And if you want to think about it from an informational perspective, people talk like digital origin of life, I'm copying bits of information from molecule to molecule, or it's like more analog, because the rates matter and all this other kind of stuff. And so in some sense, it's really got to be both, but you have to think about it at a level of abstraction where those categories emerge over time as biology becomes more sophisticated. So like, what would be the unification of those two approaches? And, you know, my feeling about it is assembly theory and what we're doing exists at that intersection somewhere, but it doesn't look like those things, like at all on the surface, which is why it's so hard, conceptually hard, but also like if you look at you know, again, going back to the history of physics, because I'm trained that to think that way, indoctrinated, I always think about like the history of unifications in physics like there are all these, these places where like thinking about Einstein and like thinking about unifying the constancy of the speed of light with the fact that all observers, you know, have to observe the same thing. Like he's like basically making laws and the speed of light, like a law like property. So he unified these kinds of things and said, these are the same things, I'm gonna hold this true. And then you get like curvature of space and time out of that, like, anytime we unify things, the structures you get out of it as far as how the theory looks, and what it tells you are totally different than your starting point. And so I guess this was part of my point about, you know, the concepts need to be able to evolve, because in order to do this tunneling operation, to get to these new ideas they will, I think, in most cases look radically different than what you expect or how to map them back. But I like this process. And I like what you guys are asking about, like, how does how does this thing I know in biology fit?

Marty Martin 41:00

Can I try to pull it full circle? I mean, I think this is all great. And I feel much more comfortable. I think I understand it more than I did 10 minutes ago. But one of the one of the really nice examples that Cam picked up on, Cam I'm going to use your question here. You mentioned Taxol just a minute ago. And we've sort of touched on these molecular assembly indices. But you guys wrote in the paper that E. coli and Taxol have the same number. So this is a bacterium and Taxol have the same or about the same number. How would you think about that, I mean, for a biologist to read that, that is very surprising so help me understand that.

Sara Walker 41:35

So Taxol is obviously like a human constructed object, right? So I think there's like depths and time in terms of like the evolution of objects, and then there's depth and time about how hard is it to make that object. And so we're used to thinking in terms of historical sequence of events, and assembly theory is really dealing with how hard is it in the universe for, for this object to be generated, in terms of like minimal number of steps in the structure of the assembly space, and Taxol is a very, very complex molecule and requires a lot of features associated with it. E. coli is a composite of maybe a bunch of molecules that are lower complexity, and maybe we're not dealing with like macro molecular stuff, but maybe like metabolic stuff, it becomes a question of like this architecture of like, the minimal amount of information to produce that object. And so I think these kinds of features of it are really challenging because the concepts of time like I say, it's a theory about time, but the concept of time is not like this linear time or evolutionary time. It's this other kind of arrangement about, it's almost like molecular time, like how hard is it to build this thing.

Marty Martin 41:37

Right. But doesn't some part of that have to account for the fact that E. coli can do amazing things throughout its lifetime or lineage time that Taxol can't?

Sara Walker 42:48

Right. So that but this, this, again, goes to the point we made before like so we're not dealing with the function of the object, right? So like, I made this point, actually, with DNA, like, it's not about whether this strand of DNA is functional or not. It's like, is this a product of evolution? And how much how much had to go into like how much memory and knowledge is necessary to exist to construct this object? And so E. coli will have different properties, in terms of the dynamics of how it interacts with other objects, what features it shares, and the fact that it's alive. And Taxol is a product of life, right? But that's not what the assembly index itself is measuring, or assembly number. And so there are some features of the theory that I want, so I wrote this essay with Michael Lachman, also a couple years ago on this concept of life versus alive. And Michael's always, like, assembly theory's about life, it's not about alive. But I think it's actually about both. And I think we agree, it's about both. It's just a matter of the stage of development of the theory. But the distinction there was that life is the set of all objects that require evolution to produce them. So things like water bottles, or Taxol are life, but there are objects that are active in that process and construct new possibility spaces in E. coli certainly does that whereas Taxol well, Taxol does in the sense that, you know, it's an anti cancer drug, and it does certain things, but we don't deal with the diversity of functions of the object, we deal with the diversity of ways things could functionally operate on the object to make it.

Marty Martin 44:15

Yeah, yeah. I mean, that's what I have. I mean, I'm a biologist, right. Everything that I see is through that lens. It's hard for me, not just as a biologist, but as a physiologist to think about anything biological, that doesn't have function. I mean, just in the same way that you're talking about information, it doesn't make a lot of sense. This is maybe the life alive distinction, too. It really doesn't make a lot of sense to talk about life, if it doesn't have an alive element.

Sara Walker 44:41

Right. But it's also not absent of the concept of function. It's just inverted it. So you we're used to thinking about function as something an object does to other things, and assembly treats function as what do things have to do to make that object and that is actually really important at least for the problems of origin of life and life detection, in particular, because you have to, I think a lot of the conceptually hard things about biology, are lot of the concepts are not intrinsic features of the objects that we're talking about. They're extrinsic features, they're relational features. And when you talk about relational features, that means if I have this DNA molecule in this cell, it means this thing, and if I put it over here, it's read out is something else, right? So, you know, like, just as an example, or like, if I put my E. Coli in this environment, it functions this way. And if I put it in this environment, it functions this way. But if you look at the assembly-ness of an E. coli, and you look at it in either environment, presuming that the molecular composition is the same, because it might be ingesting different food and have subtleties associated with that, it's supposed to be an invariant feature that's independent of environment, because now you've made function and intrinsic property, there had to be these sets of functions in order for this thing to come to exist. And molecule you think about that these bonds have to be makeable.

Marty Martin 45:57

Right. I mean, I, again, in the context of molecules, I can be completely on board. But it's some it's something about this other piece of it. I don't know if you know, Scott Turner, but Cam and I have been talking about this paper that he wrote recently, he's a past guest, too. He's really big into agency, and he wrote a paper with a super controversial title that I don't want to go down that road, Do Species Want To Evolve? So in the context of a conversation, yeah, I mean, it's kind of fun. But there's a reason that I don't really, I don't really find it really compelling. But then the first part of the paper, what's really neat about it is that he's pushing biologists to stop focusing on objects. I mean, biology is a discipline, evolutionary biology has been a thing of objects in the simple sense, not in the way that I think you're using in the context of assembly theory. He's advocating for a process. And so for, you know, many different people are talking about biology, it's better understood as a process. And I think, you know, reading him and hearing you in many ways, you're talking about the same thing. But it's back to the point that you were making about words being slightly different. I mean, but meaningfully very importantly, different in how they're being used.

Sara Walker 46:59

Yeah, I can translate that. I mean, I would say in assembly theory, processes are the objects. And so that that's why it's conceptually confusing, because we're merging categories that people have traditionally considered separate.

Marty Martin 47:11

Yep. Yeah. I mean, I get that now, I'm still not quite sure what to do with it. And the fun and the difficult thing with conversations like this is we're excited, we're all interested in the same kinds of things. But we just we don't know what we're talking about. And we speak a different language when we say it. So why does anybody listen to us talk about it?

Sara Walker 47:30

I know, I don't know. I mean, I keep doing this, because I'm trying to figure out the right way to talk about it. So like, I like, you know, and part of its like, you guys know this very well, like when you're developing new ideas, like you don't even understand them as you're talking about them sometimes. So I think this is like an incredibly rich way of thinking about it. But I don't know if it's going to help biologists answer their questions on a day to day basis, although I think there are certain places where I can see it really, maybe adding new conceptual dimensions and new kinds of insights.

Marty Martin 48:04

Totally so let's, let's talk about agency, because to me, it feels like that might be a place, but Cam, do you want to say your piece about agency?

Cameron Ghalambor 48:13

Maybe not quite yet.

Marty Martin 48:16

I put you on the spot. I'm sorry.

Cameron Ghalambor 48:17

I mean, maybe before we get into agency, I, you know, I read recently, the paper you had in Nature Communications, where you and your colleagues kind of build this computational model. And you describe the formation of these molecules, by this assembly process, and you come up with this MA number that Marty was talking about the molecular assembly index number, and then you test this empirically, like so, you know, at that point, now, as a biologist, I saw things in this paper, like, you know, using the same compounds that were used in the Miller Urey experiment, I'm like, oh, yeah, I remember that for my introductory biology class. And so that became much more sort of like, like real, like, more tangible, like I could see where the theory and the model and the empirical test were all starting to put flesh on the bones, so to speak. But then, you know, this is maybe a difficult question to ask, but like, in the end, I saw that like, the MA index number, and the number of peaks on the mass spec that sort of describe kind of how complex you know, this molecule was, for example, you know, they line up really nicely. So then, you know, I was I was trying to think about like, if you had written a different paper, like for a biochemistry journal, and you instead of having this very broad theory instead you, you simply, in the introduction, made some comment like, you know, more complex molecules will have more peaks on the mass spec. Let's go ahead and empirically test that and then and find it. And then hey, that might make a good way of testing for potential life on other planets. I guess from a biology perspective, you know, can you kind of fill in a little bit more about, like the importance of the theory behind those tests? Because I think that would help fill in some of the gaps I think for people and myself.

Sara Walker 50:22

Yeah. So I think the first is like the motivation. So the, the motivation is life detection. So it's not like an ancillary feature, right. So you want to be able to motivate that you have some explanatory framework that maps to some concepts we associate to life or has some resolve some of the ambiguity around that discussion, you want it to be quantitative, and you need it to be empirically observable, because you need to go out and measure it. So that was sort of the starting point for us. And of course, part of that has to be some sort of conceptual foundation about what it is you're trying to measure and how it maps to concepts of living things. And people say complexity all the time as being a feature of life. But it's such a vague concept. And there are actually a lot of molecular complexity measures that are out there that you might be able to measure from like the graph of a molecule, but you can't measure with an instrument, or you might be able to measure them with an instrument, but they don't have a natural interpretation in terms of like, what do you do for on the theory construction side. So I think what gets hard in this kind of area is when you're trying to bridge theory to experiment, the level of convergence and the discussions that you have to have, like, for me, personally, explanations almost matter more than data. So there's always this kind of thing that like, you know, Extraordinary claims require extraordinary evidence. And I think it's like the opposite. It's like, you could have extraordinary explanations for Really Simple evidence. But like, the explanation has to be like rock solid, and like explanatory and predictive, and it has to stand up to a whole variety of different tests. So the way I think about it, and why I got really excited about working in this space was there was a measure that captured some of the features that I had, for a long time been thinking were perplexing about life. And most of the things I think are really interesting are, are related to the complexity that life generates, like, I think this is when I say information, what I really mean is life seems to do interesting things in a way that, you know, it's producing things that the laws of physics alone would have no idea how to produce. And there's this huge possibility space of things the universe can create, but it can't create all of them. And biology seems to be the thing that's exploring that space. And for me, that's the most important feature. And Assembly captured, for me some really interesting features of that. But it was very clear what it wasn't molecules, and it was measurable. And so that's at the level that I got excited because being a physicist, I wanted to reason from objects, you can actually measure in the lab and properties you can measure in the lab to build theories that explain these features. And before getting involved in this particular theory, I had been talking about concepts of information and causation for a long time, without a way of actually mapping it to a measurement you could do in the lab. I mean, people could take measurements, I can apply information theory to them. But a lot of that is very subjective, because it depends on how you're like labeling the data, as far as like what kind of information you observe in the system, like what data you collect. So I think, I think the idea of having the assembly index give a scale, and that that was theoretically motivated by this idea of the search space getting exponentially larger, and the volume of hitting that target getting exponentially smaller, giving credence to the fact that this was capturing features that indicate there had to be enough something to build this object. Otherwise, like, you could just do a complexity measure. And life is different than non life. But it doesn't give you anything to go on. It doesn't actually give you I mean, people do this all the time. They want to machine learning classify data, and then there's a black box, and they have no idea why the data is classified that way. And I don't think that's a way to make progress in science. I think I think you really need theory working closely with experiment personally, to solve hard problems.

Cameron Ghalambor 53:58

Yeah, no, I think that, that that's super helpful. I mean, I think for especially for like graduate students and people who are earlier in their career, especially I think, for biologists, because I think with the advent of all the new technological advances, and the bioinformatics advances that are changing, like, almost on a weekly basis, that you mentioned that in physics, you're very concerned about the history of ideas, and I, I worry in biology that, you know, I've heard students say, like, oh, that paper was published in like, 1977. So it's, it's probably, like, not that relevant anymore. I'm like, What are you talking about? That's a classic paper, you know? No, but I think it's because of the, you know, everybody's what's the latest, greatest new technology for measuring things and it's become divorced from the theory that's why I actually really appreciated seeing that whole build up and you know, and so that that question I asked, maybe was sort of a trick question to kind of get you to kind of justify why, why it's so important to do that?

Sara Walker 55:06

No, I definitely appreciate the question. And I think also, it's hard to understand the space that we're trying to build with this collaboration that we have in this origin of life stuff, because it's trying to bridge theory and experiment and developing new concepts. And like having like, it's just covering so many dimensions of things that I think, you know, for people to really get a handle on what it is that we're trying to do from the outside is like super hard. So I really appreciate the like the care you guys are having to try to understand. I also am you know, like, people are like scared of criticism. But I'm always like, I just want to embrace as much of it as possible, because you get the feedback faster, you can improve the ideas faster. And I think one thing I really like, is like in our whole collaboration, and people working on this set of stuff, is we all are like super open to criticism among each other and also from other people and like really open talking about it, because the whole goal is to advance the science faster. So we have to bridge as many things as possible. But that goes back to the efficiency thing. It's like, I want to solve the origin of life before I die. I really do.

Marty Martin 56:10

Good luck on that. I'm right behind you. Good luck.

Sara Walker 56:13

But there's a lot of things you have to pull together to answer a question of that magnitude. So it's really challenging.

Marty Martin 56:19

But the approach I mean, what you're saying taking criticism being open, just I have this thing that a lot of my collaborators have an issue with, when we're working on manuscripts together. I'm like, Look, if you have a better way to say it, just write it, I don't need to track changes. I don't need any of that. Let's just continue to work on it until we all agree it's better. And then it's better. Right? Yeah, a lot of people are weirded out by that sort of thing. So Sara, let's go off planet, but we're gonna keep agency with us because I don't want to get away from that piece. So in a kind of lightning round, but feel free to skip questions to expound, do whatever you want to do, I just want to run through a bunch of different things about what assembly theory might say about life elsewhere. But let's start with agency, if you can briefly define it, as you think about it, and maybe in the context of assembly theory, but I want to try to push you as far as you're willing to go to be a biologist. And first tell us will there be are there biological systems that are not agential? And what kind of role do you think that agency has played in the evolution of life on Earth? I told you that was lightning round, that's like its own two hour podcast.

Sara Walker 57:27

No, I like this, actually, I was gonna make a joke where you were like, Let's go off planet, but we won't leave the agency behind. And I was like, gonna be like, it's kind of hard to leave agency behind anywhere, because it's how you get everywhere. I like the concept a lot, obviously. It's like, it's a concept that means different things to different people. But I think this idea that organisms are biological things can be their own causes and like and have goal directed behavior, and that some of these things that seem teleological are actually real properties in biology, I think, is a real thing. And so, for me, the future I think, is interesting about agency goes back to sort of all of it comes always comes back for me, like what do I think the core things that life are doing are different, and one of them is, life is the thing that builds stuff in the universe that's like, you know, non trivial stuff, better than elementary particles. And it's not just that it builds it and imagines it, and then creates it. And you know, you can wax philosophical about how much imagination E. coli has or something. But E. coli is innovative to a degree, but maybe not as innovative as a human. And so, I do think about that quite a bit in terms of what we're doing with assembly theory. And actually, Lee and I have a grant right now that's studying goal directed behavior and complex chemical systems is the title of it, which is trying to use assembly theory to try to explicate goal directed behavior. And the whole premise of it there for me is so there's kind of trivial statements that like so I'm going to tie agency to goal directed behavior because I think goal directed behaviors a little bit, and maybe you guys agree or don't agree, that's a property of agents.

Marty Martin 59:01

No I'm with you so far.

Cameron Ghalambor 59:05

I'm uncomfortable with the concept of goal directed anything.

Sara Walker 59:08

Okay. Now, why is that though, actually?

Cameron Ghalambor 59:12

Well, I think there are alternative explanations, aside from the sort of anthropomorphic consciousness associated with goal direction, because that there's certainly potential for a lot of that kind of heavy baggage to those words can be very loaded. And so I think for a lot of people, including myself, it instantly, kind of, like puts me on guard.

Sara Walker 59:38

Good, you should be on guard, we don't want any magic in the room now!

Cameron Ghalambor 59:42

It's for the reasons you said, because it starts to get into the old teleological arguments that have been debated for a long time and refuted and, you know, kind of is this now, the latest version of that? You know, that's what I'm struggling with.

Sara Walker 59:57

Yeah, so I think I actually agree with you on a lot of those points. And for me, it's always like people are talking about this and it's consistently reappearing. So that suggests to me there's something there, but we don't know how to talk about it in a way that is convincing, right? So. So when I say I believe in goal directed behavior, I think the class of things that people talk about where they say, systems have goals are probably hinting at something interesting happening, but like, what is that thing and we haven't identified it. The other thing that and this actually came out of this is gonna sound even more, it might ruffle your feathers even more Cam but this actually came out of my thinking about like consciousness originally, because people are so introspective and so focused on the problem of experience. And I, you know, that problem is really intractable for a lot of reasons. But I thought, like, if experience is a real physical thing, there must be like, ways of measuring it, but like not the subjective part, but maybe an objective part. And the objective part would be does experience have causal consequences? Or does it do anything in the universe? And Dan Dennett actually had like some rephrasing of the hard problem of consciousness as the hard question of consciousness. Like, what does consciousness Do? Not what is it? And actually, it's interesting, because when we're talking about life with assembly theory, it's a theory of what life does not what life is. And so it's kind of interesting, when you reframe the questions that way, they become, like more tractable to the methods of science and physics in particular, so that came for me like thinking about this concept of imagination. Like, it's interesting to me that we build representations of our mind of things like rockets, and then we can build them. So this is also the property of goals that seem interesting to me is they seem very abstract. And like we're saying, This object has a representation in it's mind, that of something that wants to go toward, but we can't measure the representation, because we're just measuring the physical behavior of the object. So I came up with this test with Lee, that was part of our proposal. And actually, I just want to write a paper just on the test. Because I think if I can just nail down this kind of idea be really interesting about like a actual physical, experimental test for goal directed behavior. But like, if you can imagine, like you want to say, this, it's not like it's not a ball rolling down a hill, like a goal is not an optimization problem. It's like somehow we have some sense it's a choice, right? And then, and then there might be like, equivalent outcomes, or there's some modeling of the future, to say that there's a goal in the future, but you're talking about it in the instantaneous object. And so the way that can maybe be formalized, and I don't know, like, haven't worked out, all the details it's a thought in progress. But you have experimental system like an oil droplet that you've evolved in a maze, and it has presented with the equivalent choice. So there's like a symmetry breaking that you would expect 50% of the time, it's going to go down this tube, and 50% of the time, it's going to go down this tube, because there's no physical difference. But it consistently goes down one tube, which suggests that has like, and maybe there's actually like a benefit to going down that to like, there's some other you know, like, like how we see organisms moving up gradients, there's food that they learned is there, right, that's a goal. So if you can imagine presenting a physical system with equivalent opportunities, but there's something in the future that will happen in one and not the other. And so it really requires some representation or modeling of the future in order to observe that behavior, then I think you can isolate the fact that that's a goal directed system and has representation.

Cameron Ghalambor 1:03:11

Yeah, so I'm not sure about the oil droplet. For any kind of biological system that's a product of evolution and history, then, you know, if there is a benefit to going to one side, you know, that's because there is information that is stored that's a product of that evolutionary history that helps in making that decision. And that's what I struggle with is how to separate the concept of agency from the process of natural selection.

Sara Walker 1:03:48

Oh, you can't they're the same thing.

Cameron Ghalambor 1:03:50

Okay, well, then we're in total agreement.

Sara Walker 1:03:54

No, but I but I mean, that are really serious, like, so with this oil droplet experiment, of course, you would have to, like, you can't just stick an oil droplet expected to behave that I had to learn that behavior, which again, is like it, like you have to build up an assembly space where that behavior is a feature of that space. So this is why then assembly theory becomes related to the goal directed behavior, because now you're treating objects as historical objects. And presumably some of the feature of that goal space should already be in the assembly space. So it allows you to map out the set of future possibilities based on what that system could be in the future. Then it gets into like, how big is that horizon? So Michael Levin has this concept of a cognitive horizon. And I had like a sort of similar concept about this causal horizon in assembly spaces, like what are the future set of things you can construct based on the space you have now, and for more complex objects, because they're deeper in time, and they have a larger assembly space, they have a larger future horizon of things that can be assembled from them in the past, which, you know, that feature is not in the assembly index. We were talking about E. coli versus Taxol before Marty but that feature might be embedded in something about E. coli's interaction with other objects. So there's just this is why I say there's like a huge richness here, because there's all these things we could do. And there's a lot of people feverishly working on some of these things. But it's a lot of new ways of trying to conceptualize some of these concepts. So we're behind where I'd like to be, but it's exciting.

Marty Martin 1:05:17

Okay. Well, it was really it was really great to hear that goal directed behavior and/or agency are similar to natural selection, you guys immediately came to an agreement on that done. Very simple. I didn't expect it. Let me just ask one maybe I'll throw a wrench into this potentially, this could be a wrench and I'll be a little bit as a physiologist who throw a wrench in is, is homeostasis like a kind of at least a facet of this too? Because, you know, Claude Bernard famously said that, that that is life. That's the main thing for life. So would that count too? I mean, if gold directedness is about maintaining homeostasis, it seems to fit into that mindset.

Sara Walker 1:05:57

Yeah, I don't I don't agree that homeostasis is life. But I think it's definitely a derivative property of life. But it's sort of like people focus on self reproduction as like the hallmark feature of life. And I think it's an ancillary feature. And I've had, I've had a lot of debates actually, like, during the pandemic, I had these like Friday conversations with Chris Kempes, Mike Lachman, and Lee Cronin, like every week, and we were always debating this kind of stuff. And, and one of them was like, Michael and Lee really think persistence is super important. And I was like, it's not it's not persistence, its existence. Because I have this whole philosophy that life is trying to construct objects. But in order to make something again, you have to retain information about making it. So I always think the self reproduction, the fact that things have to persist in time is actually a feature selected out of the creative process of making new things that if you want to continue to make as many things as possible, you have to retain information, what was made in the past, which means things have to copy themselves. And I think homeostasis is a little like that. I think like in general, the biosphere is a collection of things that have goals, so to speak, or agential behavior, and some of them maintain themselves. And some of them build a lot of new things. And it's a manifestation, maybe of the same physics, but different sides of it.

Marty Martin 1:07:07

Yeah. Okay, that makes sense. So I, I started this section by saying we were going to do lightning round. So that was the longest bolt of lightning ever.

Sara Walker 1:07:15

That was ever a very long lightning question in my defense.

Marty Martin 1:07:18

No, no, it's not on you. I thought that that might go a lot longer. But let, I know, you've only got a couple of minutes left. So let's truly try to do a lightning. And I want to do the first one off of what you just said. Again, this might not be lightning, and this could be the last one and that's fine. Will life anywhere in the Universe not have reproduction? Will we find life that will be there'll be sort of some thing that lasts forever, or will always be death and birth?

Sara Walker 1:07:43

I think there will always be death and birth, but there will also always be propagation of information.

Marty Martin 1:07:47

Yeah, well, the second part I'm fine with, but well, how do you get to the first part? Why must there be birth and death in life in general?

Sara Walker 1:07:54

Oh because life is sort of it's propagating information, but also trying to build more information to propagate. So unless you're actually recycling structures, you're not building new things that actually can help sustain the things that exist in the past and also things in the future. So I know it's really sad. Actually, at I one point, I realized that like selection is just literally a fight for existence. I mean, like, this is really existential. But it but it is like you don't think you'd like it, just think things are die and things, you know, like live, but actually, it's like things a certain amount of stuff can exist and all the rest of it, which is an exponentially larger space can't.

Marty Martin 1:08:30

Yeah, that's fine. But why does it have to be birth to death? I mean, if you use those things in really broad ways, it's fine. But go back to your Hogwarts Castle. What if we just embellish that castle, and yet the castle still is the castle? I mean, that's not reproduction in the biological sense, but it is doing the novel things. It is innovative.

Sara Walker 1:08:49

But how would you even get to the castle to begin with? So actually, no, but I think there's some nuance to your question, which is, I think some information on this planet is very old and has been here for 3.8 billion years, right. But physical structures in biology have not persisted that long. And my favorite example is just the ribosomes, right? Like they're rebuilt, you know, on, you know, hours. I don't know what the half life of a ribosome is. But they're rebuilt all the time. But the information persists in the biosphere. And, you know, like the interior structure of the ribosome hasn't changed in billions of years. It's just made over and over again. So I think it depends on what are you talking about as dying? What are you talking about as persisting? So I think individual physical structures will always die. And some of the information that's a part of them will always persist, if it's life. So you'll have some information on a planet that's billions of years old, and some of it that's just generated, but that's also one of the reasons that biospheres have a tendency to complexify over time. And the death process is necessary for that generation of complexity is my perspective.

Marty Martin 1:09:52

Yeah. Okay. Cam do you have another one in this lightning round that we can wrap?

Cameron Ghalambor 1:09:56

Well, I have one question that I'm sort of, you know, like, probably The question I wanted to ask you more than any other question.

Sara Walker 1:10:03

I don't know if I'm excited or scared, but I think I'm more excited.

Cameron Ghalambor 1:10:08

It's, it's more out of just my personal curiosity, I guess. But so again, you know, coming from this evolutionary perspective, I've really been thinking a lot recently about the levels of selection and the conflict between sort of selfishness and conflict at the individual level and cooperation. And in, in evolutionary biology this is sort of like a big, you know, it started off, like, why is there cooperation, it doesn't make sense in a Darwinian world, thinking about like social organisms. But, you know, now we recognize that sort of the same sort of theory applies for understanding how genes cooperate, at the level of the genome, for example, to suppress the effects of like selfish genetic elements. And so you have to work well together. So what selection is constantly playing with is this tension and conflict between the sort of the fitness of the individual versus the fitness of the group and the collective. And so as we talk about this progression of, you know, complexity and assembly theory, you know, I'm thinking as an evolutionary biologist, well, I can, I can understand how mechanisms have evolved, so that there's cooperation at the level of the genome, at the cooperation at the level of the cell for organelles to work together. And for cells to work with other cells to make like tissues and for tissues, to work with other tissues at the whole organism level, and for individuals to be cooperative with other individuals in a population. And it's, it's all the same back and forth all the way, you know, and then, you know, the, the product of that is like, you know, human civilization that makes all these great things that you're, you're sort of talking about as sort of the products of life. And I, and I'm trying, I've been trying to kind of put that in, insert that into the assembly theory that you've been talking about, but um, I'm not sure if that's, you know, for using the word emergent property? Or if that's another what you would might term agency?

Sara Walker 1:12:21

It's like air quotes on the whole conversation.

Cameron Ghalambor 1:12:23

Yes. Or is that just agency? Where does this, because you know, the struggle for life, as you pointed out is, is sort of that selfishness. So individuals that are good at replicating and making more copies of themselves and propagating information will have greater success than those that do a not so good job of doing that. And so does that question makes sense?

Sara Walker 1:12:53

Yeah it totally makes sense. And I have thought about quite a lot. And I have a postdoc that's actually trying to work on some concepts in evolutionary theory related to this, but in an assembly theoretical standpoint. So I have been thinking about this quite a bit. But I think I'll answer in kind of a non assembly theory way, but it is an assembly theory way, but like, individuals are temporary things. And I think this is like, we're always like thinking the individual is the unit of selection, which is why this raises all of the paradoxes, but individuals are aggregates of different propagating information packets, if you want to think about it that way. So if you think about the information, each little bit of information is competing for existence, sometimes they're together in this object. And sometimes, you know, that same part of information is over here with another object, but that information is still trying to propagate. So, you know, a good strategy is to have the same piece of information in a lot of objects. And maybe that gives you something like kin selection or something. And then, you know, that minimizes conflict. Or you can just try to, like, have one object that has a very high abundance is like a very selfish thing, because and then that information gets very abundant. But I think I think actually, if you look at it the information level, like the bits that are actually propagating through things we call objects, they're just competing to be selected. But sometimes it looks like cooperation, because they're distributed across many objects that are very similar So it's basically multi level selection all the way down.

Marty Martin 1:14:17

Yeah, and it's, and it's cool to see evolutionary biologists a lot of them starting to come around to that way of thinking because I think that's going to help move us in the direction of unification. Well Sara I know you're out of time. And we really appreciate you know, the conversation. I think it was fantastic. I really enjoyed it. I do want to give you the chance. Is there anything we didn't ask you that you want to you want to make sure to say?

Sara Walker 1:14:36

That's hard. I don't think so. It was just really fun. I like I'm so curious more on your perspectives, but I guess there's only so much time in a day.

Marty Martin 1:14:45

Yeah, well, we probably need to let Cam get some sleep too. I mean, you've really, really powered through the late hours, man. We appreciate it.

[music break]

Marty Martin

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Cameron Ghalambor 1:15:11

Thanks to Steve Lane who manages the website, and Ruth Demree and Brad van Paridon for producing the episode.

Marty Martin 1:15:17

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Cameron Ghalambor 1:15:26

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Marty Martin 1:15:35

Music on the episode is from Podington Bear and Tieren Costello.