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FUTURE SIGHT PODCAST

Ep. 26: Synthetic Biology



Future Sight Podcast by Capgemini Invent

As business and technology move forward at a rapid rate, it has become increasingly important to explore new ways to adapt and grow for the future. This podcast is your guide to that future journey.

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Episode Transcript

Ollie Judge: This is Future Sight – a show from Capgemini Invent. I'm Ollie Judge. On this show, we explore new ways for you to adapt and grow for the future in business.

On this week's episode, we're exploring the exciting world of synthetic biology. For many, synthetic biology may seem like a new and emerging area of research development and technology. But its roots have been around for a long time and it is now presenting innovative solutions to some of the world's most complex problems such as food securitization, intuitive design, and pharmaceuticals, as well as some critical opportunities for businesses of all fields.

Joining me today. I have Kary.

Kary Bheemaiah: I am Kary Bheemaiah. I am Chief Technology and Innovation Officer at Capgemini Invent, and a large part of my job is in working with emerging technology and creating new and novel products and services that come out of it.

Ollie Judge: And Ellen.

Ellen Simmons: My name's Ellen Simmons. I'm a bioengineer for <u>Cambridge Consultants</u>. My main interest is in being able to figure out how to work with biology as an engineer.

Ollie Judge: Very smart people in the room today. I feel a little bit ganged up on slightly, but we'll get through it.

So, we're going to be talking about synthetic biology today. But, obviously, that's probably not a term that all of our listeners have heard of, let alone even thought about. So, it's probably worth starting off with a little bit of an explainer and kind of the history behind synthetic biology.

Ellen Simmons: Okay. So, let's go back to what is biology, just to start off and give us a good foundation. Biology is the scientific study of living things, right? And there's lots of different principles that make things common inside biology.

So, one is that we have code within living things. Every cell, every organism has a code inside it which is passed on generations when they reproduce. So, hereditary information. And that code, that we call: genes, G E N E S. And so, that's a common element to it.

One is that we evolve, living things evolve. So, that means that they can change over time. And usually that change is naturally occurring so that the organism can survive better, be bigger, be stronger, be more efficient at using energy. Energy processing and energy conversion is also a big part of living things. We convert fuel like food into outputs, energy, in different ways.

And then the other element to remember is that living organisms tend to be very good at regulating themselves inside. So, their main priority is to stay alive so that they can reproduce. And that goes from everything from the tiniest organisms that are living on the surfaces of our laptops at the moment, all the way up to we have drivers in us to make sure that we can survive, that we are superior and that we have the most food and everything, and we can work efficiently.

We're really good at making sure that we can look after ourselves, even in difficult environments. We have all sorts of hormones and things inside ourselves that allow us to survive if we have to drink less water, or if, we're in a cold environment and things like that.

So synthetic biology is us looking at how we can actually harness all the mechanisms within living organisms and then be able to adapt it, change it. And that could be anything from how can we change plants to be able to better survive in harsh weather conditions?

Because maybe those have changed, or we want to avoid droughts and famines and things like that.

All the way to saying, can we use biology to actually make things that we never would have thought of before? Can we use biology to make our clothes? Can we use biology to recycle plastics? Can we use it to drive our computers and what synthetic biology is a science of – how can we treat organisms as if they are pieces of hardware like machines? How can we apply the same principles we apply to machines, to these living organisms? So, it's all



by how do we look at biological systems, these organisms with the things I was just talking about, how do we characterize that, simplify it, and then map out that system as if we're designing any system?

I should also say there's a bit of a difference between genetic engineering and synthetic biology in terms of how people define it. So, genetic engineering is very explicitly chopping and changing those pieces of code within an organism. And that is part of how synthetic biology operates. But I think the wider goal of synthetic biology is how to create actual novel genomes. How can you build from the bottom up and create organisms, which we have designed from the beginning instead of trying to change existing organisms or just change one small part of it.

And a big part of synthetic biology is standardization, making it simpler and then using that to be able to harness the fact that biology is self-replicating and works in these really amazing ways, can be adjusted in very interesting ways.

How can we harness that to actually impact our lives, impact society, and to the main areas in which there is interest in doing that is, how can we use organisms to help create things so that we can then stop having to create those things from finite resources, for instance, but then also, how can we use biology to help us process things? How do we get rid of the waste that we accumulate in a way that's going to ultimately be carbon negative or reduce toxic substances in the environment?

So that's an explanation of biology and synthetic biology. Do you want me to go into the history of it here?

Ollie Judge: Let's pause on the history for a second. I think, so, that was a very scientific perspective and that how it works and what kind of the building blocks and the difference between genetic engineering and what synthetic bio is.

I'd be quite interested to hear from Kary. What gets him excited from a business standpoint and why this is relevant and why people should be paying attention, particularly now, to what's going on?

Kary Bheemaiah: So, the way that I look at synthetic biology and the reason I started getting really interested in that was because the way that we've been doing a lot of manufacturing processes today, they haven't really evolved in a lot of ways.

When we think about the fact of how we actually use a lot of the products on an everyday basis. The way that they're manufactured, that's being, it's had improvements of course, in different ways. But what synthetic biology allows us to do is actually do multiple changes. And these changes can be expressed in different ways.

So, in one case you could have... let's take some kind of an ingredient. And an ingredient could be a textile, or it could be palm oil, things that we use on a daily basis. And synthetic biology can either replace certain elements of those ingredients, which allow it to be able to be used for different kinds of purposes.

It can also enhance certain kinds of ingredients so that you can use them in a much more sustainable way. You could use them in a much more intelligent way; maybe you're creating less waste. It could also be able to create a completely new ingredient, which doesn't really exist naturally out there. But which we really want to use certain characteristics of that, for whatever means and purposes that you have.

And it could also probably create an entire new category of ingredients. And why is this kind of important for us is because we do have multiple challenges, which we are trying to deal with today in the market. Being able to have different kinds of optionality, to be able to address those changes, I think just gives us much more flex in terms of addressing problem space.

At the same time, I also do have to keep my business hat on and see that okay, fine, it's really cool that we can do these things. And there is a reason that we can do it today. So, there's a lot about timing. And I'd love to actually talk about that once. Ellen's doing a bit more of the history because if we don't know where we're coming from, we don't know where we're going to go.

But if I do return to the point in just in terms of market opportunity, we can start looking at the fact that, we've got all these kinds of different ingredients that I mentioned, whether it's textiles, dyes, fragrances, palm oil, vitamins, different kinds of chemicals, you could say. That by itself, by most estimates, comes up to around a \$1 trillion market.

And if synthetic biology in the way that I express can actually change some of these ingredients that we use on a daily basis. Let's say that you even capture 5% of that. That by itself was around 50 billion in market opportunity.



So, that makes a lot of sense for us to start thinking about it. We were to think about it from the perspective of a sector, whether it's in terms of food, food is definitely a big part. So, meat, dairy beverage, or anything like that, cosmetics, the beauty industry over there and right up to kind of anything which is related to nutrition. Those segments, those market segments, that's around 2.5 trillion total addressable market.

So again, if you're going to put in 5% of that, through synthetic biology, that's 125 billion market opportunity. So, when you've got those kinds of figures in front of you, it starts becoming really interesting for us to kind of take the concept of applying synthetic biology to industry or the intelligent industry or manufacturing.

Something that's very interesting for us to look at because it's really got wide-scale impact. And impact, not just in terms of financial return, but also in the way that we actually do a lot of things today. And yes, I just end on the reason that we are thinking about it with a lot of seriousness at Capgemini today is because there is a factor of, "the time is now," but I'll get back to that after Ellen explains a bit of the history.

Ollie Judge: Alright, Ellen, let's talk about history. How did we get to here? And what were the building blocks that kind of got us to this point?

Ellen Simmons: I also, can I, before I do that, just go back to some of the points that Kary said.

Ollie Judge: Yeah, of course. Go ahead.

Ellen Simmons: Yeah, I think one this might be also considered a bit controversial to say, but I, to get on my soapbox for a minute, I think that the really exciting thing for business in terms of what synthetic biology can allow us to do, is that we know that organisms, living organisms can confer all sorts of strange things into different types of other things in a way that we would really struggle to be able to do with machinery or with chemicals alone all the time.

And the point is that a lot of that time, you can create a sort of circular economy where you're able to use waste or undesirable products and feed that into the sort of biological factory to create something else. And I think that's really where the business driver, the market driver would be for me is saying that we're at a time where we need to shift from being a petroleum-based economy into a bio-based economy.

And a lot of the reasons why people will shut down conversations on things such as biofuels is because there's a misunderstanding of why fossil fuels are cheaper today.

And one thing I'm really interested in to see is how regulation could really shape how economically buyable these new things are and how we could be in a situation where we can sustain the innovation and the development that we are doing as humans nowadays. But in a way, that's not going to mean that we're constantly having these stressful conferences about our earth dying, that to me is a very important part of this. And I see biology as a means to get us there.

Anyway, I'll get off my soapbox now. So, do you want me to go to the history?

Ollie Judge: That'd be great.

Ellen Simmons: Where we got here... I was talking earlier about the fact that organisms are common for the fact that they have a code within them.

We talk about machine code or machine language with computer programming. That's like going into the finest detail of how you can talk to a computer, and that's built of ones and zeros.

But with cells, you've got more than just ones and zeros. You've got A's, you've got T's, you've got C's, you've got G's, you've got the way that they fold together. You've got epigenetics, which is some other complex things around how those all fit into DNA, double helixes, and chromosomes.

So essentially it all began from when people started to really understand that's what drives organisms. And before, I think a lot of it was just an unknown, it was a black box of, we don't really know how these things do these things and why.

And this goes way back to the 1800's even, at the first people to discover DNA. Usually, I think that was done through looking at T-cells – human white blood cells. And then that grew, and obviously... I'm in Cambridge at the moment, and this is a place which is very DNA-centric. We've got the Sanger Institute down the road who did the human genome project.



But a lot of the work with DNA, with Crick and Watson and Franklin it was talked about so often here because it's really by understanding DNA that we then understood that we could change DNA. Basically, from the 1970s, that was the time when people were starting to look at using that to do other things.

But it's still very much started with people saying do we even know that something that we build in a test tube is going to be equivalent to the thing that's living in the world today? So, a lot of the early work was done in just trying to prove that there's a bacteria phage, which is essentially a virus that could infect e-coli called Phi X 174.

And that was a model that's used quite a lot in the early days of synthetic biology. And proving that you could produce this synthetically, and that it would exhibit the same features as natural virus was where it started. There's someone called John Craig Venter who's done loads of really exciting work in the sort of building blocks of synthetic biology.

And then things like the development in the early 2000's of making DNA synthesis much faster and much cheaper has been a way that we've managed to progress this because then it's not unrealistic to say we can just create the DNA that we need to make these novel organisms that we're talking about.

A lot of that was done through people like George Church, MIT, and various other places. And it's still something that people are working on a lot today. How can we produce synthetic DNA fast? And then how can we read it back as well? So, it's still quite recently in many ways, but then, the way that it has changed from then now to 2021 and how it's looking for the next 10 years is really exciting. So, I can maybe briefly talk about now where we are with it in terms of how we can separate it and some of the main areas.

And then maybe I can hand over to Kary again to think more about that.

Ollie Judge: I think it'd be interesting if we put the context of where we are right now. And I think by listening to both of you talk about the potential of everything, it's very easy to get your head stuck in the kind of light science fiction world of "we could do anything".

So, it'd be quite good to figure out how we can actually, or what was the grounded version of what's going on right now? And where are we at? That would be super useful.

Ellen Simmons: I should say that I think half of the time my brain is in the sort of, "oh, what's realistic and what can we actually do?" But then the other half of it is like, "this is going to change everything in the world forever."

So, I'm maybe a bit biased. But yeah, it is a simple way of separating the field is looking at where synthetic biology produces chemicals from the organisms. Engineered cells produce some chemical or enzymes for instance, help produce another chemical. But then you also have the areas of field where the product is actually the organism itself.

Sometimes if the field of what we are producing by manipulating biology and using enzymes. So, we've got things like food so we can create proteins where they are derived from plants that have beneficial properties that allow us to then put that into things that we're eating. If you've ever tried an <u>Impossible Burger</u>, that's held up as a really great example of synthetic biology producing something called leg hemoglobin, but it's basically yes, it's from a plant that bleeds and then that's fed into that alternative meat.

And basically, the way that's achieved is that you take something that already exists and just put it in a production host. So, you're taking like genes from something already and producing that and, Impossible Burger, you can get it. You've been able to get it for many years now. And so, that is going into food that is affordable today.

You've got areas like drugs. One thing, for say like the pharmaceutical industry, there's quite a lot of materials that are very difficult for us to produce in factories, for instance. There may be used quite a lot of energy or they use quite toxic chemicals, like heavy metals. And so, synthetic biology can actually make the manufacture of this easier.

So, the idea of using synthetic biology in order to produce chemicals for the pharmaceutical industry is actually one of the first examples of use of synthetic biology to create a useful chemical. And so, in 2006, re-engineered yeast was used to be put in a chemical factory to produce <u>Artemisinin</u>, which is an anti-malarial drug.

Kary Bheemaiah: You get a bit more, contemporary context Ollie. Let's say that you wake up in the morning and you wake up on in your bed, which has got some bedsheets on it. You stretch your arms out, reach for your smartphone, grab a cup of coffee, and wear a pair of jeans.



This sounds like a pretty normal routine, right? Already in doing all of these things, synthetic biology or biotechnology has affected you in some way. So, for example the sheets that you, you woke up on, they're made from cotton that's genetically engineered to make sure that they don't get attacked by, all the different kinds of parasites and worms that actually come and attack the cotton plant. The plastic on your smartphone, that could probably be bioplastic.

Even though the jeans that you wear, there've been probably a wash using some kind of enzyme biological catalyst so that it can help breakdown those organic materials in cold water. So, while we don't go around, stating this on a daily basis, pretty much a lot of the stuff that we use today, and hence the reason that I was focusing so much on stating ingredients in the initial part of the conversation, has already got the use of synthetic biology going on in some way, shape or form.

And I, this is the reason why it's so important to understand that history, which Ellen was talking about, because on one side, it shows you why it's already so prevalent all over the economy.

It is new, it's new in the fact that there are different technologies that have evolved to a certain point and they can now mix because they're now at that commoditization phase of the revolution; that makes it, this is what is opening up, the application of synthetic biology into different sectors and industries, but it's been going on for quite a long time.

And I think what's interesting right now is not that we've got an understanding of how some of the history, it is to understand what are the key driving forces that are allowing this opening of the aperture.

Ollie Judge: Oh, so I'm going to take that slightly and then twist it back on you. So yes, there are driving forces moving things forward, and that there's now the potential to productize things in different ways and elevate beyond just being an ingredient and building it out and potentially bringing synthetic biology more to the fore-front, as Ellen said, with things like impossible burgers and stuff like that, we can begin to see more of it. But what are the challenges and problems that are facing the industry?

Kary Bheemaiah: I think the first one is definitely when it comes to scale, right? So, the same way that a synthetic biology process works on a small scale doesn't mean that it can work on a large scale. There are different factors that you have to think about, because one of the things that one of our colleagues, Steve, keeps telling us again and again, is that when you're working with a microorganism, they have a tendency to evolve.

So, you need to control that evolution and that pace, it's not just being able to control it, but if you want to be able to apply it to these large-scale industries, then it becomes a totally different kind of problem in which, they won't evolve in one direction, but you're trying to control it at the same time, apply it for a large mass of applications.

Secondly, a lot of these ingredients, as I mentioned before, making them change through synthetic biology means a lot of testing. There's a huge amount of experimentation that needs to go into it. This is why AI is very useful, but at the same time, it also means that you have to have a product development approach that is very iterative.

And that by itself is, it's got difficulties in terms of time, intensity, and cost. And then of course, there's also the fact that you're trying to get a lot of switching costs, right?

So, there are well-established processes, which are in different parts of industry today in manufacturing, especially. But if you're trying to tell them, okay, fine, now we want you to start using a different kind of a process, that switching cost doesn't happen very easily. It's extremely capital intensive. And then there's other things as well, like regulation and consumer acceptance. But when I look at it from a big macro perspective, these are like the main changes, that are the main hurdles that we have to get through.

Ellen Simmons: I can just maybe build a bit more on, on what you're saying Kary. The way that we often work with synthetic biology, especially in an industrial sense, is that you're trying to do something to it, to force it, to do what it doesn't normally do. You're forcing it into an uncomfortable situation to say, "oh we'd really like to squeeze out as much of this product as we can."

And we're going put you in, we call them stress states quite a lot. And by stressing out an organism that often gets something to change. But unfortunately, as I was saying, like organisms tend to really try and self-regulate



and also mutate away from anything uncomfortable. So, especially when you're trying to have these really intense growing conditions, you're providing the perfect opportunity for your organisms to just be like "sack this, I'm going away from here."

I'm going to, or find ways, to grow the organisms that are not getting stressed out by it. So, you're constantly having to work with these things, but a line that I hear all the time is, especially in pharma, pharmaceutical use of bioprocessing: "We're optimizing things that we don't understand."

And even though, yes, we get what DNA is and we get this, that, and the other, there's just so much more about what's actually going on inside that organism when we do this. And what Kary's saying about scale is it's just a whole other level of unpredictability that we're having to work with.

And especially when you're working with anything that's been genetically modified at all, it's much more susceptible then to mutations. For instance, a lot of processes are done in batch and have to be stopped at a certain day because if you don't stop it at that day, then it's going to mutate away, and they'll have to throw it out.

There's a lot of waste involved in that which can affect how cost effective it is. If you're not really sure why the organism doesn't like this thing, it's then very difficult to understand how to improve that without, as Kary was saying, a lot of experimentation.

So, we really need to understand more. We call it like Omics. And so, the study of genomics and transcriptomics and metabolomics. So, essentially what's going on in the deepest code of the cell. And then how is that manifesting in the functions of the cell and ultimately, how does that affect the product that we're either trying to create or the end state of the cell.

And actually, one thing that you haven't mentioned, Kary, it's just actually quite a lack of people with the skills needed to really ramp this up. It's quite well known, apparently that there's just a big lack of data scientists and so we're also having to really do a lot of this on a shoestring. Like a lot of the biotech companies that are coming out of universities with these cool ideas and startups, can't necessarily afford to bring on the right sorts of people in those early stages when it's really crucial for you to be optimizing everything and making it robust.

Ollie Judge: So, I want to talk a little bit about, tangible application and what synthetic biology can be good for and what it's not. I think this is useful for any kind of topic that we tend to talk about on Future Sight.

I think it's like AI, it's very easy to get excited about something without actually understanding the context and how it can be super useful. We've been talking a lot about startups but to get synthetic biology right, it sounds like you need quite a lot of capital and good data scientists, to get all your data in good order and also real scientists to be able to think about these things.

I'm going to put it like that because I'm podcast guy, but let's call it a core level. Number one, who do you need on your team to really get something done? And number two, what kind of projects should really work for this and what doesn't? And where does that divide live?

I'm going to start off with Ellen, for this question.

Ellen Simmons: Okay. So, what people and what projects, I think that the way that we look at it here... I think it's really important is to be very realistic about the benefit that the biological element is going to offer you in whatever you're trying to do.

So, I think what we always need to think about is the problem that is it just that we need more investment in this area of technology? Do we think that with that investment, we will crack it and that will be possible? Or is this all based around a limiting factor that we're not sure we're going to get through? <u>Chris Voigt wrote a really great</u> paper about this recently.

And you have to really understand the balance between, like, when are you using, like living factories versus when are you using chemicals still? Like, when are you going to involve cells and when should you not? So, I would just say generally, I think to, although I would love it to be the case, like use of synthetic biology, is not going to solve everything.

And you really have to look at the energy inputs and outputs. You have to look at, as I said which organism are you using? Is this an organism we understand, are we going to be able to really tell what's happening with it? And you can compare things like some photosynthetic organisms which are ones that, can turn light into energy, have very different inputs and outputs and, things that they tell us about how they're feeling to something like e-coli.



I would say in terms of the actual projects, it's probably ones where you think that you can make use of an input. And you're confident that input can be converted into something new organism can use. I would say anything that's going to require like a lot of energy in order to do that is then, I just doubt that it has much of a future. And making sure that you can see how it would scale that, that it's realistic, that it could scale.

And that you can see it becoming robust enough that whatever you're trying to do with it, that you could do that on a larger level. It sounds quite evasive; cause I'm not saying specifically. But say for instance with lab-grown meat, one of the problems that we have right now in really scaling that up is that to actually structure the synthetic animal cells that are being created; you have to use very complex scaffolds, a lot of new materials coming out, require very novel pieces of machinery and novel processes.

And so that's what's really restricting things like that. Whereas, if you think of how we create beer, for instance, if you can try and create something in the way we create beer and just, if you can use yeast for instance, which is something we understand loads about we've been working on for decades, then there's a good chance that's a great project.

So yes, I guess it's a mix. Like you have to be pragmatic right now anyway. And I think that the people you need, you definitely need people who understand biology quite well, molecular biologists or people who've worked in industrial biotech environments. You need people who understand sensing well, especially if you're trying to introduce anything novel; someone who understands optics; people who understand how you can convert different inputs and outputs into useful information.

And then you've got, say, people who can just help create that hardware. So, if you have to create novel bioreactors to do this, bioreactors are essentially like the oven that you put everything in, to bake your organisms. How are you going to put that all together?

How is that going to look infrastructure-wise? And then people to look at the data that's produced. All that information you're getting from those fancy sensors you've created, who's going to look at that data and actually do something constructive with it. And then from that, then looking, do you want to apply something more complex?

Do you need people who understand machine learning? Do you need people who understand how to funnel that information into a neural network of some kind, for instance? And then you need to loop it all back and keep that in a control system, right? So, you need people who understand all the different parts of it.

But then I think also, that's purely just on the technical execution of it. Then you need people who really understand in industrial production of these things that we're trying to replicate, what are their pain points? What are the things that they need? And like at some conferences I've been at this year, one of the main things that kept coming up is just, it's really hard for us to convince management, to take down the factory line for the length of time we need, to do something different with our process. And I think if you ignore like the sort of social implications of what we're trying to do, as Kary's talking about with intelligent industry and things, you're proposing quite a big change to some quite traditional industries sometimes.

And people need to really feel like they're part of that change. You need to make sure that you're really clearly explaining the benefit and not in some cases, like not measuring stuff for the sake of it. Maybe that's not worth the time. Maybe you don't need to know how the genome changes, like when you add this chemical or change the temperature.

But I think just making sure there are people involved like process engineers who know what it's like to be performing these processes in factories, people who manage the industrial scale of manufacture of different materials. And it really varies across industries too.

So, you can't underestimate the need for a good sort of commercial head with that. And people who are actually going to be able to help listen to those, the stakeholders, and be able to make sure that whatever you're build-ing is going to be inclusive of all the people using it.

Another sort of element that I've not touched on is the sort of human factors and design like human, that the user interface side of everything, I think also you have to remember that a lot of the people who are going to be operating these processes, for instance, like it needs to be, a seamless process for them to be able to integrate these complex things. If you have got things like algorithms or different inputs and outputs, like how is that actually easy for us to incorporate into the factory environment? So, yes that's maybe the basis. There are lots of things.



Kary Bheemaiah: Yeah, it's a lot. And this is kind of the reason why, when you have a company like Capgemini, where we've got a lot of industry experts, you've got people who've got deep sectorial contacts and understanding, you can really cherry pick all those people and start thinking about, okay, fine. How do I make this cross-functional team that's going to be able to build something totally new and novel? It's grounded on the fact that there are limitations and challenges that we are trying to address today.

And synthetic biology especially has got this very intimate relationship with these large, big social changes and problems.

And the big change that's happening today is the fact that climate change has become such an important topic for us. There's more and more government-led initiatives. There are carbon credits that can be gotten in terms of some way of gaining capital for it and subsidy programs.

And there's a lot of stuff happening in climate change. So, climate change, to a certain extent, it has heightened the focus again on synthetic biology, as it rightly should. And this is the reason why we are seeing a rekindling of that flame all over again.

Ollie Judge: So, before we move on to a bit of the grand potential of what we're talking about here, I'd quite like to understand who's getting it right, at scale, like a good example of how far we can go with this and what's been done in the market right now.

We've spoken a little bit about startups and how people have gotten going. But who would you say, and you don't necessarily have to give a name, but or, but just a good example would be nice to understand: who's doing this right in the market and why?

Kary Bheemaiah: So, <u>there's one company that I like</u>, and it's related to my previous life in the military. I used to wear Kevlar. And I was going to like, just, I'm trying to understand Kevlar and came across this company. But it turns out that spider silk is like one of the most amazing materials in the world.

It's stronger than steel. It's tougher than Kevlar. The problem is you can't really build it at scale because every time you put a bunch of spiders together now in a box, they have the tendency to eat each other. So, it becomes hard to get it to that scale. And what these guys did was they started using synthetic biology to create spider silk, but without the spider.

Essentially, they studied the silk proteins which are spun, and they understand what gives them these incredible properties. And then they develop proteins, which are inspired by these natural silks. And then put that into yeast and put into large quantities through which they can isolate and purify the silk protein, you could say. And then spin that into a fiber much like you would do with acrylic or rayon. So that's a company that's out there and it's building it today, at scale.

Ellen Simmons: Yeah. I've actually heard of a company that did <u>a collaboration with North Face</u> a few years ago and created this moon parka and it's this amazing jacket all made of a synthetic spider silk. And yes, the problem with these is the scale-up challenges, I think, with these types of companies.

There's a lot which are emerging where it's like, they're making real products, but it's about making that product actually affordable. And to the consumers where, the majority can then replace what they're buying. Obviously, it's really amazing to make these sustainable materials, for instance; but if they're not affordable, then it's putting a lot of onus on consumers to then buy these premium products.

I would say that a lot of the really exciting stuff that we are interested in synthetic biology is at the stage of "we can make it and it works," but it is just impossible to scale then.

That really seems to be me... I go to, I'm very involved with SynBioBeta and you can see there, like this is where all this is emerging and you can see that it's about to get to a point where we are going to be able to afford, to have a way more synthetically, biologically produced things in our lives.

But yes, it's just the manufacturing of these in a way that means that they can overtake what's already existing in the world is hard. I would say I did talk about <u>LanzaTech</u> earlier, in terms of the fuels that they produce. They seem to be doing a really great job and they're cited quite a lot as good examples of things that are going on. Impossible burger, as I said, is also doing a great job.

I think these alternative proteins that are more plant-based rather than trying to go into lab grown meat is definitely the way to scale that as well. If you imagine that you can very cheaply produce protein, and, you can make



quite a nice story about it; if you can make protein really cheap, then it's easy to feed people. But there's even a lot of thin films, for instance, being produced from like bio source monomers.

And that's really exciting area because if you think of just electronics use a lot of like polyamide films. So, if you can then choose these things going into electronics, that's like a massive market. And yeah, I would say the companies doing it are probably the ones who have invested quite a lot in the beginning, in making sure that organism that they're centering their product around is a good organism for scale.

And I think that's where people just need a lot of work in the early stages as I said to get good models going. The investment is high, but I think the investor pressure is also quite high. And so, like we can see that often, companies will need to show their outputs; they need to show it in a small space of time, which means they can't really make the best thing ever or hire as many people as they want to hire.

I'm really interested to see more of what the bigger companies are doing. And I guess a lot of those say like in the pharmaceutical space, you'll see that they'll maybe acquire smaller companies that are useful to then allow them to scale up these smaller biotechs, which is great.

And that's probably going to be the way that it will end up being more scalable is that bigger companies who want to include this as part of their business will need to take in these smaller ones.

Ollie Judge: So, to open up that, where's SynBio going a little bit.

We've I think we've sketched out what the current landscape looks like and where things are going up and down, but I'd quite like to understand, what the new developments in technology are pushing us towards and what impact that can have in different ways? Ellen, you touched on a little bit earlier about climate change and some of the bigger problems that we're facing at the moment.

So, it'd be good to understand, how far can we go with this? What's the potential now and what are the cool things that both of you are seeing at the moment that you see on the horizon that you think our listeners would be really interested in?

Ellen Simmons: The thing I am super interested in is: how making bulk chemicals sustainably at scale, I think is super interesting. And again, that's something that's going to be really shaped by regulation.

And I think policies will really drive how easily these can take off. And so, I hope that they will change. Like I know that there's regulations and for instance, with like aircraft fuel that's going to have to shift to being synthetic and bio-derived in certain proportions.

That's a really interesting area because then you think, then of course we can start producing airplane fuel with biology, and then that's amazing because then you're taking away like a massive source of fuel use.

And even in the Cambridgeshire and Peterborough area, we are an area that has quite a lot of rural space. And it means that our emissions are much higher per person, just because people have to drive to get everywhere. And there's a lot of agriculture and things like that.

These areas where you don't want to say to people "oh, you have to stop driving, or you have to get this bus" in an area where maybe there's one bus, every two hours. I like the idea that synthetic biology can really drive down a lot of emissions from people and allow us to continue living our lives, but then do it in a way that is being a bit more sustainable.

So, I'm hoping that is definitely going to be driven, especially, with conversations happening more recently.

In terms of an area on the other side, which I just find completely fascinating is the area of DNA computing. And so, that's a bit less about using cells and more about what we can just do with DNA as a material in itself.

And we worked with <u>Cataloq, we're working on large-scale DNA data storage</u>. But the area that they're now looking into more is the idea that you could use DNA in terms of memory on a computer. And I don't understand enough about computers to really be able to articulate this well, but it's the idea that with DNA, with this code, you can access all different parts of the code, all at once.

And so, if you can apply that logic to a computer, it can allow you to do things, say for instance, mining of cryptocurrency and do that, and in a potentially way more energy efficient way; and the idea of combining biology with computers and computer chips is probably the area where I'm just like, "wow!" If that's something that we can



realistically do over the next few decades, I just think that's going to be really groundbreaking. We're so privileged that we are able to conduct so much business using our laptops.

And obviously we're recording this though on our computers and the internet is a massive source of also energy use and carbon emissions. So, anything that we can do to change that area I think is really exciting.

Ollie Judge: Kary, your thoughts on the future?

Kary Bheemaiah: Yeah, it is hard. It is hard to go after that. No, I totally resonate with what Ellen saying, and it's the reason why we made the effort to launch an initiative, get some kind of funding around it and really identifying, even within a company, which has got 300,000 people who have got talent in all the respective technologies that you need to make synthetic bio a reality, it wasn't easy. That was like a handful of them in such a big company that we've got, we've got experts coming out from every nook and cranny.

So just like getting all of them together and then coming to a consensus on what we need to work on and how does it align with the strategic objectives of the group. That itself was an interesting kind of process to go through. And now that we've got it, we know that there's so many different kinds of opportunities out there that we can explore. We've identified a few that we want to go for, whether it's for financial reasons of strategic objectives or just because it's got social impact behind it.

Ollie Judge: I've got a couple of questions that I want to start to conclude on. But I know that we're trying to stay optimistic, but I think something that is really interesting is maybe the kind of fear behind synthetic biology. Are we over optimizing a little bit? And are we losing some of the stuff that maybe we haven't identified why something is useful, but we're getting rid of it through this process? How as an industry do you guys think about it and how do you tackle that kind of fear and how do you educate people in a good way that this isn't so big and scary and science fiction-y and it's more something that's here to help?

Kary Bheemaiah: So, I'll go first and then Ellen can indefinitely build on top of my poor ramblings. But I think a lot of the conversation that happens today in terms of criticism is, with regards to GMO. And I do definitely understand that the GMO narrative exists for a reason and that there've been massive issues in the past.

I do feel that the GMO narrative is due for an update. Because when you think about synthetic biology, not every process that leverages synthetic biology results in a GMO. And this is partly due to the science.

It's also because of the lack of an official definition or an interpretation of what constitutes a GMO. Everyone's got their own kind of opinion about it. And this kind of conflation that happens between synthetic biology and GMO. Maybe it doesn't even matter if there wasn't like a, long-standing stigma with GMOs in general. But I think that's something which is really important for us to just as a society and even as an industry to figure out; if synthetic biology is a means by which, you can actually benefit consumers in the environment, then does that current narrative and perspective that a lot of critics actually extol, does it actually make any sense?

And so that's like my perspective on this, it's still very broad. I think we can delve into a lot more detail with regards to that. And I'd defer to Ellen to do that because she's thought about this in a lot more detail.

Ellen Simmons: Yeah, I can pick up on that. I totally understand the fear. I think even I will not realize that what I'm talking about is such a foreign language, even to people that I work alongside at my company. So, of course, to people who aren't scientists or who aren't interested in these things, it's frightening. But it's very reasonable for people not to have trust in the governing bodies of wherever they live. I think what's really important is help-ing educate people in a way that it's really understandable. I think trying to make comparisons is helpful.

We kind of force evolution in our own ways and have done that for many years, with agriculture; it's not as if we didn't selectively breed things and try and do as much as we could to take advantage of things that we saw as beneficial.

In the area of medicine, it's really difficult, because on the one hand, you can achieve so much by really understanding genomes and being able to edit those. Like you can prevent people having these awful diseases for the rest of their lives, you can cure you can cure all sorts of conditions that really make someone's life difficult.

The ethics around the boundaries on that is difficult as well because we're as a society starting to see that like things that we used to think of as severe disabilities and they're just people like us and shouldn't have their right to be who they are changed.



I think there's so many mixed feelings about that because we love seeing the progression in the field of "look at all these amazing things we can do," and we can grow this and change that and help that person. But it's scary when you're like, who's actually pushing the pints on this, like who is who's driving what gets done.

And if it gets in the wrong hands, who's going to be able to stop that. There's a really interesting series called <u>"Unnatural Selection"</u> which involved quite a lot of people from the SynBioBeta community. What that really tries to unpack is like the democratization of genetic modification, really.

And like, how much power should we actually have to change these things either, in plants or in other people or in ourselves; if I inject myself with a gene therapy, where do I stop what could I change about myself? I don't know if you've seen these like muscly pigs that were, from a few years ago and you can change the, I think it's like the muscle cells in pigs to make them really hench.

And it's just are we happy about living in a society where that thing is something that everyone can do? But then is that the only way that you'll get people to be less afraid of synthetic biology; if they can buy a kit off Amazon so, instead of buying steroids, you buy some sort of gene therapy instead.

Maybe then people care less about that whole element of things. And it's hard with the recent vaccine hesitancy. I think it's not fair to demonize those who are frightened of it. And I think it is just a case of it needs to be understandable and people need to also see as you said, Kary, what are the benefits and what could this change for you?

But also realize that, in some of these cases, it isn't perfect. And all we can do is try and say we're doing what we can to mitigate the risks. And this is the alternative, and with a lot of this stuff, it's like the alternative is unfortunately worse. And just being able to communicate that and bring people in.

So, it's, I would say science communication is something that could definitely improve. A lot of the companies who are trying to, get their products out, really need to invest in that. I wish I saw more of that. And as the scientists need to realize that, as much as it's important for us to find these cool things, like it's only as good as how you can explain it.

I think there's a quote from Einstein about that. And, we can't just say, "oh, we know what's best because we are the people doing the science," and we don't. And that's the point I made earlier: you can't, you need to bring in people who really understand the stakeholders.

Kary Bheemaiah: Yeah, there's definitely a lot more vulgarization that we're seeing. And the topic is, like I said, it's coming to having its reemergence all over again.

It's definitely going to be a series of transitions, which need to happen one on top of another, in order for this to start becoming like a new kind of jargon and vocabulary that everyone uses. So, every time a new technology comes in, you realize when it's reaching a certain point in which everyone understands it, when it moves from being some kind of technical jargon, to just becoming like a verb that everyone just uses in certain kinds of ways.

We still haven't found a cool verb for synthetic biology. I'm hoping that happens in the next couple of years or so, but we're already seeing that gradual vulgarization and people starting to get into it in more and more detail. So, I'm still optimistic, even though I would, I was a bit acerbic in terms of my opinion in the way people think about it, but I'm still optimistic in the way that it's future is going to be accepted in markets.

Ollie Judge: Running with that optimism, I want to end with a bit of a unique question. So, we know, obviously, synthetic biology has a lot of applications and different ways that people can use it, but it's not applicable for everyone. If you're building like a little software as a service thing, probably you don't need a synthetic something to help you out.

We have a lot of listeners from a lot of different industries and all that kind of stuff. What's the one thing that, and this can be technology process, whatever, that you think would be applicable and useful in the way of thinking that people could apply to their own work? So, it could be for example, that the way that you guys think about data in this world, because obviously you need it to be very clean and you need to manipulate it in good ways and understand what's good.

So, if you were talking to someone from any industry, what would you say would be super important that they could get their head around and potentially use in their day-to-day life?



Kary Bheemaiah: I'll go with what I'm more used to talking about, which is if you've got all these different kinds of data, which are in different kinds of formats and need to communicate with different devices so that you can get something coherent out of it, we are seeing the same thing right now with all the conversations we're having in terms of intelligent sensors, IoT, 5G, Edge AI, and Cloud.

So, we've created these new technologies, which are going to have transformative effects on multiple industries. But the problem is because the data is in different formats and it needs to be converted and be used by different kinds of APIs and then be used by different kinds of automation devices, whether they're hardware or software, it's creating a real pig's breakfast when it comes to MLOps.

So, I see a lot of people who are working on it, and they're definitely trying to solve that. If you want to actually think about how you could apply your stuff from a SAS world or an AI world into synthetic biology, this is something that we could use, because there's even more complexity that's happening if it's synthetic biology.

So that, that's definitely an easy one. And then secondly, and I'll finish up with that. As you've probably seen during this podcast, synthetic biology is made up of so many different technologies mixing up together. And I think what it offers in a much more framework sense, is how an actual technology evolves and how an actual technological leap that happens.

Every technological leap happens when you have different kinds of technologies mixing together in different ways to create something novel. And if the invention that comes out of it becomes successful, then you call that innovation. So, you can use this framework of the way that, how synthetic biology is actually mixing all these technologies together to create something new as a reference framework for yourselves in whichever industry that you work with.

Ollie Judge: Nice point. Ellen, what do you think people could learn?

Ellen Simmons: I think actually some useful verbs for translating synthetic biology is just bio-manufacturing or bioprocessing, and those apply to a lot more industries then, when you think of it that way.

I would say that generally, yes, If I'm just thinking of any industry you think of, is there anything that we are using or producing and is there any way that some organism could get involved? I think that's cool. And maybe it's that you use a lot of paper where's that paper coming from, or maybe you produce a lot of waste of this type of gas, but what could that gas maybe feed into that could be useful then to make? Just those sorts of thoughts might be, interesting.

But also one thing I've, been thinking about a lot is the fact that when we talk about this creating models and simulations, and then using them as inference and predictive predictions for our processes, that applies to so many things. And I think the principles that are used for converting these like data lakes of wherever you're getting your data from.

And bear in mind, like in a bio-reactor you could be measuring all sorts of different types of data with different structures and modalities and everything. So being able to take like unstructured or different types of data and then do something useful with that and create models, which can then feed into something else. I think that doesn't have to just be biology.

That's one of the really interesting sides of like Industry 4.0 in general. And actually, a lot of those principles are cross-sector. And I think everything that we can do to try and think of smart ways to do experiments, whether those experiments are with organisms or with chemicals or with computers in general, can we do cool stuff there?

And as I said before, like all sorts of different skills are required to actually push forward this ecosystem. I really liked the idea that, the fourth industrial revolution is about pooling knowledge and trying to push everyone up together. And a big outcome of that fourth industrial revolution would be that we can do way cooler things with biology that we wouldn't have even thought of.

And it won't be super hard, and it won't even be a big thing that we talk about. I hope that in five years, no one's even talking about it as a cool thing anymore because it'll just be so normal.

Ollie Judge: It is easy to see how synthetic biology is a crucial area for solving problems in both our present and future. And it presents unique opportunities for businesses.

A big thank you to today's guests, Kary, and Ellen for sharing their insights and expertise.



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