



HOUSE OF LORDS

Science and Technology Select Committee

Corrected oral evidence: Engineering biology

Tuesday 16 April 2024

11.20 am

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Members present: Baroness Brown of Cambridge (The Chair); Lord Borwick; Lord Drayson; Lord Jamieson; Lord Lucas; Baroness Neuberger; Baroness Neville-Jones; Baroness Northover; Lord Rees of Ludlow; Viscount Stansgate; Lord Wei; Baroness Young of Old Scone.

Evidence Session No. 2

Heard in Public

Questions 8 - 16

Witnesses

I: Professor Tom Ellis, Professor of Synthetic Genome Engineering, Imperial College London; Dr Lucia Marucci, Associate Professor in Systems and Synthetic Biology, University of Bristol.

USE OF THE TRANSCRIPT

1. This is a corrected transcript of evidence taken in public and webcast on www.parliamentlive.tv

Examination of witnesses

Professor Tom Ellis and Dr Lucia Marucci.

Q8 The Chair: I welcome the witnesses to the committee's second evidence session in its new inquiry into engineering biology. This morning we will hear from Professor Tom Ellis, professor of synthetic genome engineering at Imperial College London, and Dr Lucia Marucci, associate professor in systems and synthetic biology at the University of Bristol, who I believe is running the first doctoral training centre in synthetic biology that we heard about in the previous session. I am sure that people will want to follow up on that very important issue with you.

The session is being broadcast on parliamentlive.tv. A full transcript is being taken and will be sent to you shortly after the meeting for minor corrections. Just as a reminder, if you do not get a chance to say something in the session that you would like us to know about, or if you think there is any data or any other evidence that would be useful to us, we would be delighted to receive that as evidence after the session.

Thank you both very much. Let me kick off by asking both of you, first, to give us an idea of what areas of engineering biology your research covers. Tell us briefly about what you do.

Dr Lucia Marucci: Thank you for inviting us. It is really nice to be here today. I was trained as a mathematician, although I work in biology and have been doing this for the past 20 years. As a mathematician, my training has been very important in how I think about engineering biology. Research in my group is at the interface of mathematical modelling, computer science and engineering biology.

Part of my group works on the combination of mathematical models of cells with machine learning and genome editing, to redesign cells in a smart and intelligent way for a range of purposes. For example, we are now working on metabolic engineering. The other half of my group works at the intersection of control engineering and synthetic biology. We are basically applying the principles of feedback control to redesign cells in robust ways. One of the projects, which is the theme of my EPSRC fellowship, is about trying to apply automation and microfluidics technologies towards the design of combination therapies for cancer; this is done in collaboration with AstraZeneca.

This is about the research in my group. More broadly in Bristol, we cover the breadth of eng bio that we were discussing before, and I also co-direct the Bristol BioDesign Institute. This is also the inspiration for the new doctoral training centre in eng bio. I am sure there will be a chance to talk more about this.

Professor Tom Ellis: I am at Imperial College. I trained as a biotech student and PhD, and I have been running a synthetic biology research group at Imperial for 14 years. During this time, I have focused my group on the notion that, in engineering biology, we should start to consider DNA as a programming language, because our abilities to understand

DNA and manipulate it are getting better and better every year. I think this is a fundamental part of engineering biology.

The kind of research that my group does focuses on trying to understand how we can go to the genome and other pieces of DNA that we put into cells and write, as well as we can, that DNA sequence to instruct the cell to do specific tasks for us. A lot of it is foundational. We are trying to set the methods and get the understanding there for what will be a major technology for the rest of this century, so it is very long-term stuff. Some of the stuff we do in my group is a bit more applied and is looking for earlier applications. One area is materials, particularly trying to engineer microbes, which is mostly what we work on, to be able to produce materials with qualities and characteristics that we cannot get through other mechanisms or standard methods so that we can have new advanced materials.

I am also a co-director of our academic synthetic biology research centre at Imperial and have been involved in a lot of training, both at undergraduate and graduate level, for synthetic biology research and now engineering biology research as well.

The Chair: Approximately how many of your research team members are from the UK? Just tell me; do not expand on it, because it is an issue that Baroness Neuberger will take up with you later. I thought it would be interesting to have that piece of data—just roughly.

Professor Tom Ellis: I would say that it is now 50%.

Dr Lucia Marucci: The same—50%.

The Chair: Do you think that is good or bad?

Professor Tom Ellis: I think that is a good ratio. We will get on to this later, but if we want to compare ourselves to the US or China, we hear reference to “scientific superpower”. Our population is 60 million, so it is nice also to be able to have experts from other places to help us to be a superpower.

The Chair: It is a healthy sort of balance.

Dr Lucia Marucci: I would say the same. Compared to the past, in terms of post-docs, there are now more UK post-docs because of what we have been discussing: short-term funding and it is harder to get to the UK from Europe. In the past it was more international than now, to be honest.

The Chair: I will leave Baroness Neuberger to deal with that. I do not want to tread on her toes at this point.

Q9 **Lord Wei:** What are the major applications for engineering biology that you think have the most potential over the next five to 10 years?

Dr Lucia Marucci: I will start, given my background and the research of my group, and because it was not covered much in the previous session.

I think we now have an opportunity, given advances in AI and modelling, and with multiomics, to finally start to design cells in a smart way and make the design-build-test-learn cycles more robust, faster and cheaper. This was something we could not do 10 years ago when we were talking about synthetic bio, and this is also what I think is the key difference now that we use the new terminology of engineering biology. We can do that because we can measure lots of cells and things at a high-throughput level; we can do multiomics. We can do that because we have computers to run AI algorithms. The ones that we are using at the moment are not that new, but now we have the computer power to run them.

Finally, we also have mathematical models that describe multiscale processes of cells. I believe that, if we manage in the next 10 years to really apply CAD to design cells, as we do in many other fields of engineering, we will have a chance to speed up progress and innovation as well.

This can be applied in principle to any application. It could be applied to biomanufacturing, which we were talking about. It could also be applied to design new gene therapies and so on. This is where I think there is a major opportunity.

Another major application—Susan was talking about it before—is in healthcare. There are plenty of opportunities there. She has already talked about gene therapies, for example. In the UK, we are at the forefront. For example, the UK was the first country to allow gene therapy for sickle cell disease. The way of doing this is to use CRISPR technology so you can basically edit cells in a patient in such a way that they can produce haemoglobin.

In gene therapies, we have lots of companies working in this space. I will mention some research in Bristol. My colleague Ash Toye has been working on the development of eng bio methodologies to grow blood cells in the lab and on the development of methodologies to engineer them to be used for different diseases. There have been clinical trials with the NHS. He has founded a company. These are just examples of different applications in healthcare and personalised medicine.

There is also the design of vaccines. Eng bio can do lots in terms of vaccinations. Again, in Bristol, a company called Imophoron is developing the next generation platforms for vaccines based on nanoparticles. These are just examples of precision medicine. We could and now can apply CAD design, for example, in the space of designing vaccines or proteins in a smart way. Indeed, we can use AlphaFold, for example, to predict the function of proteins, using AI. I think there is a lot of overlap in this space between AI, machine learning, modelling, automation and precision medicine.

Professor Tom Ellis: On top of that, if we have to think about five to 10 years, that is a reasonably short timescale to be thinking about for biology. If you think about the length of time it takes to develop things and take them through clinical trials, it is a little hard to think of things

we are working on right now that will give applications within five years. But I note some of the companies named in the previous session, particularly ones working in areas of sustainability and production in the chemical space, which is where the UK is quite exciting right now. For example, mention was made of C3 Biotech with its aviation fuel and Colorifix with its approach for dyeing materials. Those are areas where we see applications working now.

From an academic point of view, we are thinking more of 10 to 20 years at the moment. That is our job. We have to set the research and the foundations for things that will come further down the line. What is particularly interesting there is the space of using engineered biology to replace our unsustainable productions in the food area, particularly the use of meat.

In the UK, I see this really interesting space taking on the really big challenges. Growing meat in a vat may have to be taken on by very large and well-funded companies in sectors such as the US, but young entrepreneurs in the UK have been much smarter. They think about whether there is a niche for something else. For example, a very young start-up company in London, Multus Media, has been thinking about who will provide the reagents to those bigger companies. How will they get vegan reagents made, growth factors and things like that required for this meat? Hoxton Farms, which was mentioned before, is looking at whether you can grow, in fermentation-style, pig cells to get pig fat from them. Rather than having to build a meatball out of cultured cells, you can build something like a meatball out of plant matter but add in pig fat that has come not from pigs but from cultured cells, which makes it taste and act a lot like that.

One other area I want to highlight, which is really exciting, is my area, which is working on writing and synthesising genomes to get entirely custom-designed cells that can do things. This is an area where, amazingly, the UK is the world leader in this space right now. Jason Chin's research group at LMB in Cambridge produced a synthesised, recoded version of the entire genome of *E. coli*, a workhorse microbe used throughout biotechnology. That is by far the biggest completed genome project in the world in terms of making a synthetic genome. It has led to a start-up company, Constructive Bio, which has all the IP to be able to design and build entire microgenomes to make custom products, particularly getting the machinery in those cells to make proteins that nature has never made before that can have the capacity to be used in all sorts of different areas: materials, medicines and other areas.

Lord Wei: Do either of you think that there will be a sort of ChatGPT moment for this domain in the coming decade or so, or do you think that there are a lot of little supply chain industrial processes behind the scenes, or in healthcare, that over time change the world but not necessarily in any big, visible, world wide web-type moment? Is it steady progress, or do you think a sudden shift might happen with one or two

verticals?

Professor Tom Ellis: At the moment, for me it is a steady shift, but we are always aware that technologies can come out of somewhere and change things. For example, 10 to 12 years ago CRISPR appeared and everyone was immediately able to jump on that and start using that. It has really given an acceleration. Something could happen, and a lot of people are pushing for custom-synthesised DNA to be made very cheaply and very quickly at scale for people to put into cells to test for many different designs. That would be a game-changer and would particularly lower prices and lower the cost of everything in this space.

Dr Lucia Marucci: I completely agree. One key issue at the moment is costs. I do not think that for some of these technologies we can prove that they are cheaper than others. This is also about scaling up. If we can somehow fill the gap between the research that we do in our labs, in academia and industry—we talked earlier about infrastructure—hopefully we should be able at an earlier stage to understand how long it will take to use those technologies.

Another mechanism is when small or spin-out companies are bought by bigger companies, and that can speed things up. In Bristol, we have a very nice story. Ziylo is a company set up by a PhD student. It developed a synthetic bio-based methodology for diabetes. It was bought by Novo Nordisk for \$800 million. That is another way in which things can move faster, but it really depends on the technologies.

Q10 **Lord Lucas:** You referred to this in part in DNA, but are there still major things that need to be sorted out before we can make progress in this technology? Can you see big obstacles in the way of this becoming a universal technology for us?

Dr Lucia Marucci: We have been talking a lot about the design-build-test-learn cycles and about using automation, machine learning and AI. We still have an issue with data. In synthetic and engineering biology, there is still a barrier to getting high-throughput data that is collected following standards, as in any other engineering discipline. I think it is important to lower the barrier to make data acquisition easier, faster and cheaper, and, at the same time, to adopt standards as we do in any other engineering discipline and in metrology. We still use a lot of arbitrary units. We should not be doing that because it is not really helpful. That is one thing that I think we need to consider.

I also believe that it is important to make platforms for data acquisition, data analysis, integration and automation more accessible to wider communities. That is really important for speeding up progress, and it allows this transition from synthetic bio into an engineering discipline.

Professor Tom Ellis: This is a very interesting question because there are so many different ways I could answer it. If we think about what we see in the software industry and people using computers, this is a technology that has been built from the bottom up over 120-odd years

since the discovery and understanding of the electron and how to move that around. We are probably 50 to 70 years behind on that in our ability to take biology, understand what the underlying code inside the cell is—DNA—and be able to manipulate it in ways that are as quick and easy as the ways people write new code for computers, for example. To be honest, it will always be more difficult and more expensive because the process of working with biology requires moving atoms around, rather than electrons. It is a level up in terms of complexity.

The big barriers for us at the moment to get to the stage where it is much more like software engineering are that the costs and the infrastructure requirements to be doing experiments and making things are still very high. I have already mentioned writing DNA. If you want to test out a DNA sequence, getting companies to synthesise and make that for you is still far more expensive than reading it. If we can get anywhere near that level, getting those costs down a thousandfold would greatly help and you would see researchers spending much more of their time writing designs and testing them.

Even then, there is the whole experimental cycle of testing out these things. This is not someone working from home with a laptop and going on a cloud server to test things out. Everything we do requires someone going through years of training and getting access to a lab where there are all sorts of safety rules and regulation. There are lab coats. Everything is slow. Everything is, "Please repeat this at least three times for it to be statistically valuable". It is still experimental and difficult. For engineering biology to get to the point where we can see electronic engineering and software and how they go on, we need to be solving all those challenges.

I would add an even further challenge there. The mindset we have in engineering biology, where we want to recreate what we can see in things like the electronics industry from what has come from basic physics, may be a little simplistic, because we know that biology is dynamic. Over time a cell will evolve; it will mutate and change its behaviour. That is an amazing superpower technology that we would like to grasp.

We may also want to consider that our own thinking on a scientific level is limiting, in that we are still very much concerned about making, let us say, a cell make something and only make that, and not change over time, whereas you could imagine saying, "Wouldn't it be great if we could build something and get a cell designed in a way that it will get better over time? It will self-repair, do things better and make products for us better". So we may also need to think about the scientific shift to thinking about biology as being something that can teach us better ways to do engineering.

Lord Lucas: What are the dangers we should have our eyes on? Are we getting towards a point where some unsupervised lab might make an aphid-mediated virus that killed all grasses, for instance? What should we be doing to make sure this does not bite us?

Professor Tom Ellis: This is a complex question. There is some effort. If we can get DNA synthesis—writing the DNA—down to a very low cost, you will see lots of people entirely relying on that. At some level, you can regulate what people are doing by being able to understand what sequences you are sending to people and being able to block those. At an early stage, over the last 10 years, the DNA-synthesis companies have formed a global consortium to try to monitor what sequences people are requesting and prevent people who should not have certain sequences having them in their labs.

Education at all levels—going to undergraduate and even at high school—about what engineering biology is and what it can do is a great way to get people thinking about and discussing mostly the benefits of it, but it is also good to educate people about the risk side of it.

It is an enabling technology that can have dual use, but a lot of non-engineered biology is very threatening and problematic. I do not see much evidence of work that people are doing in engineering biology that is immediately putting us at more risk than what can happen from people just finding natural microbes and pathogens, and doing nefarious things with those, or even just chemicals, rather than using living systems.

Q11 **Lord Borwick:** Can you expand on your work on engineered living materials? Are we talking about things like wood or something completely different?

Professor Tom Ellis: That is a good question. It is an interesting name—engineered living materials—because it immediately makes you think of a living material with living engineered cells within it, but that is about half the field. What we are doing is using engineered cells to grow and augment materials in a way. For the product that is made, we have used the engineering of cells—in our case, in my research group, mostly microbes—to try to define and customise the way the material is made and grown to have certain properties and functionalities, but then the material itself might be sterilised and used for other applications.

There are some application areas that we and others are working on that would be growing materials that then have actual living cells within them—maybe dormant cells or engineered cells—that can sense and respond or self-repair the material. That is a little more futuristic, but there is already scope for using those kinds of materials in medical or health settings, particularly things like implants with engineered cells or matter contained within people within the material that cannot escape, and they can do all sorts of sensing, actuation and acting on what they find and see within the environment.

In our research, to give you an example of the sorts of things we do, we like to work with a microbe that grows a very pure form of cellulose. It can make all sorts of different materials from this depending on how you grow it and the genetic engineering that we do to that microbe to turn systems on and off or maybe to add new genes to it so that it can make different things.

I say to my research group that the long-term vision here is to have a cell with a genome, within which we put the DNA, the instructions, that can turn on and off the production of all sorts of different material properties so that this microbe can be grown in a very easy, low-cost and low-tech environment. Depending on what DNA it has and what cues it has been given, it can make a whole plethora of different materials in different places and different times during the growth of the material, which can lead to us having much more control over the sorts of materials we get just by growing a microbe.

Lord Borwick: It is multipurpose.

Professor Tom Ellis: Yes.

Lord Borwick: Is it not inherent in this that it takes a very long time to come out with a product that is actually useful, whereas most of the microbe work that you do produces stuff within a matter of weeks? Is that not right? I am not an expert on this, so I need your help.

Professor Tom Ellis: That is true. In engineered living materials research, a lot of what people are doing focuses on proteins—getting cells to make very interesting proteins that can form material structures. That can be quite slow because proteins are expensive for cells to make, particularly at scale. If you think out there in biology of what material structures are made from proteins that are big, things like antlers can take a year—

Lord Borwick: That is the point I was making.

Professor Tom Ellis: Exactly. We are working with carbohydrate as the base material—the cellulose—and, for us, it is pretty fast. We can get a tray about a metre long with a sugary liquid in it, and this can be waste rather than a pure liquid. We seed the microbes in and we will have a full sheet of material that is probably a few centimetres thick after about a week or two. This is reasonably easy to scale, and it is producing us materials that we can play around with and do things with in a very short timescale. So there is definitely the opportunity to produce products reasonably quickly in that space.

There are start-up companies in this area, including some that I collaborate with, that are working on making materials to replace things, particularly in the fashion and textiles industries. They have microbes and engineered microbes growing these materials.

Lord Borwick: That is very exciting. To produce a new cloth, if you have to start with a new sort of sheep, it takes many years.

Professor Tom Ellis: That is right, yes.

Lord Borwick: If you can grow it in a matter of weeks or months, you could see a very rapid acceleration in the entire industry.

Professor Tom Ellis: Yes. The London based start-up company that we work with, Modern Synthesis, is using microbes that produce what we call bacterial cellulose to be able to make a material to replace leather with an alternative, vegan, non-petrochemical-based and biodegradable replacement. Obviously, in leather, it takes years to grow a cow.

Lord Borwick: It is a thoroughly nasty process to do.

Professor Tom Ellis: That is right, yes.

Lord Borwick: There is a lot of pollution and there are a lot of other problems. It is likely to be cheaper as well as better in the respects that you have mentioned.

Professor Tom Ellis: It would be hard to be anywhere near as bad as leather production is for the environment.

Lord Borwick: Is this something that is progressing very well and we could see a product from in a few years?

Professor Tom Ellis: Yes, some of these start-up companies are close to having, or have, small-scale products available. They require partnering with maybe a fashion company. In particular, high-end fashion is very interested in testing out in this space. That is quite good because then they can charge \$1,000 or so for a fancy-looking handbag, and the amount of material needed to make that at that scale is not a huge amount, so it provides a nice way to bridge towards larger-scale work further on. I would say, yes, there are products from this space within the next two to three years.

Lord Borwick: That is very exciting. Thank you.

Professor Tom Ellis: I hope so. For the field of engineering biology, as well as all these amazing things you have heard about from therapeutic sustainability, it would be good for us to have consumer products that people actually want because it will help people understand what engineering biology can do and it makes them feel part of it.

Lord Borwick: Yes, if they can go out and buy it, that is very exciting. You still have a lot of testing. You have to test that it is not poisonous. There is a chance of somebody eating their handbag or their hat.

Professor Tom Ellis: There are lots of tests that can be done. The materials industry is very good at all sorts of standardised tests. I am not sure about eating. I would definitely much rather eat our thing than chromium-tanned leather.

Lord Borwick: Absolutely. Thank you.

Q12 **Lord Drayson:** We are very interested in our inquiry in the creation of economic growth for the UK from the commercialisation of the science that we have been discussing. You were here for your colleagues' earlier statements. I am really interested in the current environment in 2024 for

academics such as you and the groups that you need in terms of the positives and negatives for you in being engaged in the commercialisation of your research and what you think should be done to significantly improve the success in providing a significant contribution to the UK economy.

Dr Lucia Marucci: I have been in Bristol for 11 years. When I joined Bristol, we did not have any spin-out companies in eng bio. Then we got significant investment in synthetic bio via BrisSynBio, for example, and now we are in the top three by the number of deals secured with spin-out companies, and we have nine spin-out companies in eng bio. First, investment is important to start commercialising things.

We are also running, via Science Creates, a deep-tech incubator in Bristol—an accelerator programme for eng bio. It is the first type of acceleration programme for eng bio and it is now the second round. That is extremely helpful. In the first round, a former PhD student of mine took the accelerator, and now a current PhD student of mine is doing so. We are now taking the first steps for a spin-out company. These things have been helping.

What do we need more of? We need more training. Lots of colleagues do not know much about what they should do if they want to translate something they do in their lab or in their group into a product. They do not know much about regulations and IP. Most importantly, it is about training early-career researchers, because in most cases they are the ones who have the time and the will to spin out something that they did during their studies. Training is really important at all levels. Training in translation and regulation is key.

Accelerator programmes are helpful to start bridging the gap sometimes between short-term funding and possibly companies. Something that has been mentioned in the previous session is deep-tech suites that enable you to start testing whether something you developed could become a product. We need more of those, and not just in the golden triangle. This is something that Susan mentioned earlier, and I want to reiterate it. We are in the south-west. We have been growing a lot, but to grow more we need investments that are made around the country as well as support for scientists who are considering setting up a company.

Professor Tom Ellis: I agree with a lot of what Lucia said as well as a lot of the comments made in the previous session. There has been a recent review and there were recommendations on university tech transfer offices and what sort of a barrier they can be to spin-outs. The standard deal at Oxford University is 20%.

Lord Drayson: How about at Imperial, seeing as you are at Imperial?

Professor Tom Ellis: At Imperial, it begins at 15%. We have done a lot of work over a 10-year period to change it—to reduce that. In particular, we have something that is very attractive initially, when you think about it, called the Founders Choice, where, if you come up with IP and you are

securing it, you say, "Actually, I want to take this to be my own and found this into a start-up company".

Lord Drayson: If you compare the atmosphere now to when you finished your PhD, although that was at Cambridge and now you are at Imperial, is the atmosphere more supportive or less supportive for academics considering making the jump to commercialisation—full time? I am just trying to get a sense. Is everything great or has it got worse?

Professor Tom Ellis: That is a good question. The answer is "both". That is not a great answer. What has got better? There is much more opportunity and it is much more in the mindset of the students and researchers. The thirst for doing a start-up now, particularly in engineering biology, is huge. We have undergraduates who turn up in London and say, "Okay, how am I going to get my start-up by the end of my first year of being an undergraduate?" Then there are all sorts of competitions, mechanisms and accelerators. None of that was there before.

The tech transfer offices are working on better deals. Underlying all this, how it seems, in my opinion, to have got worse is that there is less bandwidth for academics to spend the time. The hurdles for doing a spin-out company have become higher; there are more steps to take, more things to consider and more people to meet.

Lord Drayson: Bureaucracy.

Professor Tom Ellis: Yes, maybe because there are more opportunities. To do it well, you will have to really dedicate time to it, and academics are continually complaining about how stretched their time is.

One thing in particular that everyone complains about with the university tech transfer offices is that it is not necessarily the stake that they take; it is that by taking a stake of any sort of size they want to be involved in all the negotiation steps and all the contract steps. They are completely overstretched. Therefore, whenever an investor says, "Hey, let's move on this. Let's do this. Oh, wait, I have to get the tech transfer office's approval", it might then take months to come back. Months of waiting around for a start-up is death.

Lord Drayson: If one of your post-docs came to you and said, "I want to start a start-up, Prof. How long do you think it will take me to get the permissions from Imperial to do it?", what would you say?

Professor Tom Ellis: A year, maybe longer. It also depends on the ability of that post-doc to drop everything else they are doing and focus on this, when they are hired specifically to work on a research project if they are a post-doc.

Q13 **Lord Drayson:** That is really helpful, thank you. Can I now take you both to the other end of the process—the very large companies? We have heard how the need to shift from a petrochemical-based to a bio-based economy globally is crucial. Why is it that more industrial-scale

companies are not investing to cross the chasm from the early-stage start-up to a scaled business in this area, particularly outside life sciences? Your experience with AstraZeneca is a good example of how some do. Outside life sciences, why are more companies that are making the profits from the petrochemical industry not investing in these early-stage companies to help them bridge through to £100 million or £200 million in turnover?

Professor Tom Ellis: One thing that I notice particularly in the chemical space is a lot of what is needed for those early-stage companies to get to the next level of scale is access to fermentation facilities to scale up their stuff. To build the infrastructure to do that is incredibly expensive. People are not going to fund that unless this is a really long-term, big amount of funding. That is where CMOs—contract manufacturing organisations—come in, and there are not that many of them in the UK. Maybe there needs to be more effort to have CMOs in the UK that can ferment at scale some of this stuff.

The companies in the petrochemical space such as Ineos do not have the equipment either. They could consider repurposing the equipment or doing that. There might be a particular opportunity for some of those companies to think about building a fermentation facility and contracting it, and then eventually buying some of the best companies that are using it.

Lord Drayson: The innovators deliver. Companies such as Ineos will never do that unless they are made to do it.

Professor Tom Ellis: Yes.

Lord Drayson: Do you think that there is a case for an intervention strategy that incentivises these companies in some way to make that transition by investing in those facilities at scale?

Professor Tom Ellis: I definitely think so. If it is made clear to those companies that their way of doing things, particularly the emissions and carbon that come from it, is something that needs to be phased out, and if alternatives are provided to them for what the nation thinks is the best way for them to change how they are producing chemicals and materials, they can be part of this journey with us.

Dr Lucia Marucci: Often these big companies might not have the right equipment and they might also not have the right expertise. They often partner with us on grants. I am part of a programme grant-funded recently by the EPSRC that is about using control engineering in engineering biology. It is an eng bio grant led by Oxford. Among our partners, we have Shell and Croda. They are supporting PhD students who will be working on engineering consortia of microbes for bioremediation. When it comes to supporting spin-out companies—

Lord Drayson: I am sorry to interrupt you, but I am not really talking about the spin-out end at this point; I am talking about the scale-up challenge.

Dr Lucia Marucci: There is a gap there. We need investment and we need more facilities for the scale-up per se to fill that gap. It is true there is a gap there. Unless big companies take the risk as they did with our company in Bristol, they will not invest that much.

Lord Drayson: Professor Ellis, you used very helpfully the analogy of DNA as a code. The challenge that your industry has is the difference in terms of the software industry. You can scale a software company with pretty limited capital investment but you cannot scale your business without significant capital investment at scale. We need an economic model that addresses that. Are there any examples where you see people thinking about this to provide that level of capital investment before profitability is there to fund it?

Professor Tom Ellis: First, I want to slightly disagree with you there. In software you can scale, but the reason you can scale so cheaply and you can do these things is because Amazon has built cloud server farms in the state of Washington at huge scale and Taiwan has built superconductor factories at huge scale, so that you have a laptop, you can connect through wifi through an infrastructure, and you can access cloud computing and buy it as and when it is needed.

Where is that in engineering biology? On a global scale, it would be nice to have that—the fabrication. What does the DNA writing facility look like that is the equivalent size of the microchip manufacturing semiconductor facility? What does the cloud server look like for testing out experiments? That is the foundry network. At the moment, how does that become as big as cloud computing? How do we have the ability to be sending DNA sequences to be made somewhere, tested and run at a cloud level facility?

The Chair: Does the UK need a facility to produce DNA at scale? Is that something we need in this country?

Professor Tom Ellis: I would like to think so, yes. It is obviously a key part in the future of engineering biology. We have been talented at developing the foundational technologies around DNA. DNA sequencing is done by three methods around the world: Sanger, Illumina and Nanopore sequencing. All three of those technologies, historically, have come out of the UK. Thankfully, one of those is still a British company—Oxford Nanopore Technologies.

Synthesis—writing and constructing DNA—is where start-up companies in the UK such as Evonetix and Camena, both based in Cambridge, are using new technologies and new approaches to try to make synthetic DNA better. I would hope that, when they scale and get bigger and bigger, those facilities stay here. Having said that, Arm Holdings, which I remember as a small company in Cambridge at one point, is now not necessarily a UK company any more. Economics might eventually make these things international.

Q14 **Baroness Neville-Jones:** Stemming out of this recent discussion, I

wanted to ask you a rather speculative question. The tradition in this country on the whole has been an arm's-length relationship between the private sector and government, and it still is in the United States where private sector resources are very considerable. This is a relatively small country. I detect from some of our witnesses that we are beginning to think small as well—we just cannot do things.

Do you think that we need to become perhaps a bit more corporatist in this country, with a much closer relationship to universities and to academic research? It seems to me that we are building a new economy with an entirely different industrial base eventually. Can we do that with our traditional method, or do you think we have to move to something where the level of co-operation between public authorities and industry is much greater than it historically has been? I told you it was a speculative question.

Professor Tom Ellis: That is a complex question for a university professor.

Baroness Neville-Jones: The universities lie at the core of it.

Professor Tom Ellis: I think so. We are trying to innovate and trying to set the agenda for what the technologies are for the rest of this century that will underpin our economy and help us solve climate crisis problems, ageing problems and all the other issues. I think more strategy is needed. We definitely heard that in the last session. There is a lack of strategy. There is an element of small committees and short-term thinking: let us get these things funded, and even—

Baroness Neville-Jones: It is sort of ad hoc.

Professor Tom Ellis: Yes.

Dr Lucia Marucci: I also think it is important to take more risks in general. There is a massive opportunity for AI in eng bio. We can take the opportunity now, but we need to take more risks. Other countries are more open in the eng bio space to take risks. We are still a bit conservative. First, we want to check whether things can work before investing in them, but if we want to lead in the development of these technologies we need to take the risks.

The Chair: That is a great introduction to Viscount Stansgate's question.

Q15 **Viscount Stansgate:** I was thinking just the same thing. I will ask a question. You were present for the earlier session, so you will know what it is about. The Government's document *National Vision for Engineering Biology* sets the backdrop for their commitment to this as one of their top five priority technologies. What is it that you think the UK Government should now do in order to make the best of the opportunities that exist? I will come on to a couple of other points. You have indicated already by saying we need a strategy, but could you flesh out a bit more what you think and what your advice to the Government would be on what to do now?

Dr Lucia Marucci: To reiterate what has been said: longer-term vision and longer funds. This is also important from the point of view of staff. We are losing expertise. Post-docs leave the UK after a two-year contract. That is not great. We need longer vision and longer investment.

More risk is another thing. I mentioned DARPA. In the US, most of the engineering bio grants are funded from DARPA. That is a high-risk, high-gain kind of funder. We need more of this if we want to build new science and new products. We need more high-risk investments.

We have been talking a lot about innovation. It is important to invest more in translational research. Accelerator programmes are a great way to do this.

Training has been mentioned. I want to reiterate this. I am excited that we will have a new centre for doctoral training between Bristol and Oxford, but we need more. We plan to train at least 66 students over the next nine years. We have designed a programme that integrates automation, AI and translational training into the more traditional synthetic bio training, but we need more. We need more students who will get the training. We need more collaborations across centres, instead, as we said before, of having different places that run independently. This is what I think we need to do.

Finally, it would be great if we could work more across councils. We have the five key technologies. Can we not work more between EPSRC and BBSRC, for example? Our centre will be co-founded by the BBSRC; that is great. But if we could work more across councils and disciplines, we would have an opportunity to make the best use of the technologies we have now that could be embedded into engineering biology.

Professor Tom Ellis: In a previous session, you asked, "How would you spend the new money?"

Viscount Stansgate: I was going to come on to ask this, because the Government have indicated £2 billion. This committee is investigating this brand-new area, and at the end of our work we want to make recommendations to the Government. You are a very important first group of witnesses and we are interested in what it is that you think the Government should do. Given that there is, as you know, a certain amount of money that they have indicated they want to spend, where would you spend it? What are other Governments doing that we should be doing to safeguard our ability to make this a growth area for the future?

Professor Tom Ellis: In the UK we were the first country to have a national plan for—at the time—synthetic biology. That road map was 10 to 12 years ago. I know all my collaborators in the US were very jealous that we did that, and it took them years to persuade the leadership there to do something similar. They put in increasing investment. Many other countries followed. "How can we achieve a road map like you have in the UK?" was a question I was asked in Australia, Singapore and Korea.

Since 2017, it has all become a bit fragmented. I do not know whether the Government have been busy doing other things in the last few years. It feels like it. It was a lot more short term and there was a lack of that initial plan being followed on. It would be great to be able to revisit that now and go back to that longer vision and longer funding for the next stage of investment in engineering biology.

Assuming it is new money, where would I prioritise this kind of funding? Absolutely, my No. 1 priority is the same as what was said before. It needs to be training, because that has been a big gap. I would advocate some form of standardised training all the way down to the beginning of undergraduate level and maybe even high school. We have this wonderful thing from synthetic biology called the iGEM competition where students from many universities around the world undertake their first synthetic biology projects. They co-create. Many of these lead to start-ups or proper research papers or become research-funded grants. We have never really had a national strategy to fund there being multiple teams from the UK. It has always had to be finding money down the back of the sofa at various universities, but that has led to some amazing things. It would be nice to see some better continuation on that.

We want to keep an eye on AI and machine learning, and particularly how language models are increasingly becoming amazing at being able to understand everything about what the bases of DNA are doing by looking through DNA sequences and matching them to datasets. There needs to be a national approach to generating a lot of data from various DNA sequences. Maybe there could be an engineering biology version of UK Biobank where lots of people are collaboratively doing lots of experiments together that generate lots of data that is open for people in the UK community to train their models on to help understand how things are doing.

As we have also said, scale-up and helping companies bridge things is an area that needs investment—maybe national equivalents of contract manufacturing organisations that can take on something that is done at a 10-litre scale and do it at a 100-litre scale, optimising that and understanding all the economics of that for these smaller companies to get them to be bigger companies more quickly.

In what other areas could we work? In the US, I have seen some interesting things that they are now calling focused research organisations, where over a period of, let us say, five to 10 years a small institute is founded with a specific aim, which is something a company would not do and an academic institution would not be able to spend all its time focusing on. So it is specific goals to develop technologies or datasets.

Those have been quite successful in getting philanthropic funding in the US. The Schmidt Foundation in particular has set up several of these FROs. It would be great if the Schmidt Foundation and the UK Government could come together and set up focused research organisations on things that we see as game-changers for synthetic

biology and engineering biology. The enzymatic synthesis of DNA at low cost and high speed would be a particular favourite of mine.

Viscount Stansgate: In the last session, we heard a reference to the ministerial co-ordinating group and so on. Do you have any views on how central government should organise itself to be able to deliver on what it is that you are talking about?

Dr Lucia Marucci: Organise how the committee works, how it interacts with—

Viscount Stansgate: You think they should be something rather more high profile, organised and led from the top. I feel as though I am leading the witness. Anyway, that is my last point.

The Chair: Lord Lucas, do you want to come in and perhaps stimulate that?

Lord Lucas: In the early days of Covid, there was a plan to upscale our ability as a country to create basic pharmaceuticals—the generics that were disappearing from the market. Is your technology capable of doing that? Is this something that might replace the reliance on Chinese-based chemicals and Indian manufacture by doing something flexible here?

Professor Tom Ellis: That is definitely one of the aspects of it. That is a big driver in the US's equivalent investment and road map. It wants to be able to produce all the basic biochemicals that are used in the plastics industry within the US to become self-sufficient through being able to grow and ferment microbes that can make many of the chemicals that we are now almost entirely reliant on getting from other countries, particularly from China, where a lot of petrochemical-based production of fine chemicals is done. Engineering biology is absolutely a fundamental technology that underpins the ability to get fine chemicals and complex chemicals made by organisms rather than by the petrochemical industry.

The Chair: Might ARIA help in driving something through to a rapid conclusion? Anyway, it is one to think about. I will move on to Baroness Neuberger.

Q16 **Baroness Neuberger:** You have answered quite a lot of this area already because it is particularly about skills shortages. You have talked considerably about the need for training and, if there is real government investment, about how that is where a lot of it should be placed. Can you tell us, so that we have it for the work we will do over the next few weeks and months, which are the very specific skills shortages you are seeing at the moment? That would be quite useful to us. What should government do about it?

Dr Lucia Marucci: There is a shortage, and this is something industry told us as well. When we started to design the programme, we talked with all our partners. We have 26 industrial partners. They have a shortage of people who are trained in engineering biology—people who can write DNA, read DNA and understand what DNA does. They have a

shortage of people who can design experiments, run experiments and analyse their data. To do that you need cross-disciplinary training. On the other hand, they also need people who can understand and write code to run a machine learning algorithm and know how to interpret what they get out of this.

There is a need to train scientists in engineering biology in all its aspects—in its interdisciplinary aspects as well as in the translational aspects of eng bio. If a student can think from day 1 about the possibility of translating his or her PhD project into a product, there is a greater chance that that will happen in a natural way. It is key to allow that type of interdisciplinary training. This is something that we in the UK can do because we cover the breadth of eng bio very well.

At the same time, in terms of training, the investment made recently in AI has been much more significant compared to eng bio. As I mentioned earlier, training across different areas it might be really good. It would also generate more basic science in a natural way. We still need to invest in basic science as well.

Baroness Neuberger: You talked particularly, Dr Marucci, about post-docs leaving. This is for both of you, and I know Professor Ellis did not come in just now. Is there a specific thing we can do in terms of training, opportunity and bigging up skills that would help stop the post-docs leaving?

Dr Lucia Marucci: Yes. One issue is the length of contracts, as we discussed before. After Brexit, it became more difficult. That is something we cannot really change. Offering post-docs longer-term career opportunities is important. When I talk to my post-docs, many of them go to industry. People from abroad go back to their countries. That is a shame because we train them. We could, first, offer longer-term contracts. In Bristol, we are also trying to offer them some opportunities to get involved in teaching so that, if they want to stay in academia, they have some experience in their track record from a training viewpoint. That is important.

We already mentioned the length of time to spin out something. It is easier for students, because they own their IP, than for post-docs. That is another important element. For them, it is riskier if they want to set up a company because of their stage of life. Maybe you are at an age where you want to start a family so you need something more secure. All those aspects are important from a personal viewpoint to retain those talents in academia or more generally in the UK. That is my experience.

Professor Tom Ellis: Training is definitely the area where we really need to do the most work in the UK. As we have said, there are maybe 10 or 15 doctoral training centres for AI around the country. For engineering biology, we had one in that theme at Imperial, Manchester and UCL, and then they did not renew it. They went with Bristol and Oxford. Five years earlier, it was Bristol and Oxford that had one, and they did not renew it and they had gone to Imperial. There is just one that bounces around.

Part of that problem is at a more structural UKRI level. The Nurse report identified lots of problems with BBSRC and EPSRC being separate. EPSRC clearly has the remit for AI. It can think entirely about AI and not worry about anyone else, and it can decide that it is within EPSRC's and the UK's interests to go big on AI funding.

For engineering biology, it is in the name. Engineering biology crosses exactly two research councils, and therefore who decides to make that big investment is very undecided. EPSRC will say, "We can give money for maybe one or two training centres but probably not more because BBSRC will do them", and there are a lot of issues going on there.

We need to think a bit more about better co-ordinated training before PhD because, although it is still a complex science to do engineering biology work at these start-up companies, they would like to employ people more at undergraduate and master's level to do a lot of that work just for financial reasons. So it would be good to have more opportunities to have co-ordinated training in that space as well.

Baroness Neuberger: That is your standardised training point that you made earlier.

Professor Tom Ellis: Yes, it is about universities putting a bit more of an emphasis, if someone is doing a bioengineering degree or a biotechnology degree, on them getting experimental lab training in the key things that I look for when I hire someone to do engineering biology research in my group: whether they have used CRISPR, whether they have redesigned sequences and tested them out, and whether they have bought synthetic DNA from a company, assembled that and tested it out. If you were hiring people at a software company, you would want to know whether they have written some code, whether they have run it and whether it worked. We would like to have national training in the equivalent of that for engineering biology.

Baroness Neuberger: This is the last question from me. You both said that the 50:50 between UK and people from abroad was about right. You both in one way or another alluded to people leaving. Do you still think that the 50:50 is about right?

Dr Lucia Marucci: We could do better. I am based in engineering. Most of my colleagues are either engineers or computer scientists. Another issue, from the computational viewpoint, is attracting computational people to do research. That is another big problem. We teach our undergrads machine learning and AI. They get offers for jobs before they graduate. It is difficult nowadays to retain talent in academia. I also think it would be great if we could make academic careers—or at least PhD studies—more attractive from a financial viewpoint, especially if we want to see more interdisciplinary people coming into this field.

Professor Tom Ellis: I think 50:50 is what I would like to aim for in my research group. One of our strongest talents is that the UK is one of the best places for people to come for education and training from around the

world, and a lot of those people who come make a great success of their time here and are involved in the start-up of companies and the wealth generation in this area. Would I like more talent from around the world here? I probably would—it would be good—but, at the same time, I know that a lot of my research is taxpayer money, and we should be giving the training and the opportunities as much to our own people within the country rather than continually relying on external talent.

I said earlier that we want to consider ourselves a science superpower. If China is entirely insular, it has access to over 1 billion people. The US has 300 million people. We have 60 million people as a population, so being able to get some of the best talent in, obviously with some of that leaving and going back, is necessary as well. That is what is needed. Reasonably fluid immigration for people at this expert level to enable us to be a science superpower is definitely needed.

Baroness Neuberger: Thank you very much indeed.

The Chair: I very much thank our witnesses in this second session. It has been another interesting session and very informative for us. At this point, the meeting is now formally concluded. We really have appreciated your input. That has been extremely helpful. I am sure you will see some of the comments you have made appearing in our final report.