BIOLOGY 2.0
Engineering life
SCRIPT

NARRATOR
01:00:05
From cells to fully-fledged organisms... from molecules to eco-systems... life exists in a myriad of forms.
01:00:15
Until now, biology has sought to observe and understand it, perhaps even to control and exploit it...
But today scientists are looking to invent and manufacture new living beings; basically, to synthesize life.
01:00:29
This is the challenge of a new techno-science, synthetic biology.
Biology 2.0, which promises to solve all our problems.
Is this a new, and ultimate, industrial revolution?
01:00:43
Or is it just the opposite? By affecting life in such proportions, are we not taking unprecedented risks?
01:00:54
To find out, I travelled the world to meet the field's leading figures... to learn and discover more... and sometimes getting completely lost!

RON WEISS
01:01:03
Synthetic biology is almost like genetic engineering on steroids. We wanna be able to program cells as easily as we program computers.

CHRIS VOIGT
01:01:14
Every product of synthetic biology is something that hasn’t existed, every genome that we engineer hasn’t existed before.

ELEONORE PAUWELS
01:01:23
Synthetic is really not a word that sounds great these days. There are concerns about long term implications, government failures: failure to control, failure to ethics.

NARRATOR
01:01:36
My first surprise was to discover that with synthetic biology, it's not only biologists who can work on living beings now, but engineers too. After bridges, buildings and machines, now they're interested in life! Welcome to the era of engineering life
Astonishing! That, tickles my curiosity right away.
01:02:01
Apparently there is an American professor who transforms bacteria into a form of calculator that can be re-programmed, like a computer.

01:02:11
How? Well, to find out, I head for the east coast of the US.
01:02:18
The man in question is one of the discipline's pioneers, and apparently one of the most brilliant new bio-engineers... as well as one of the most unusual.
I have an appointment with him in Massachusetts, on some marshland.

CHRIS VOIGT
01:02:38
My name is Christopher Voigt and I'm the professor of biological engineering at the Massachusetts Institute of Technology and I'm the co-director of the synthetic biology center.

IN 01:02:57
N: Hello !

NARRATOR
01:03:01
Chris Voigt's laboratory is in Cambridge, but he's opted for another setting to explain how his work started.

CHRIS VOIGT
01:03:11
One of my hobbies or guilty pleasures is to go crabbing, they're one of the most delicious things that you could imagine eating.
When we look out at the natural world, we see all of the sophistication that living biology can perform.
In synthetic biology… we're trying to build new biology that hasn't before existed.
But we're so far behind that that's what's motivating me in my career.
The crabs are the essence of what biology can do. And even though you think of a crab as being kind of a dumb animal, when you see it in its environment, you can see it's making decisions, it's thinking about what it's doing, it's being very careful and cautious. It can survive incredible conditions, its ability to act as a defense, to swim. The materials that are on the crab are incredible. Everything is just perfect.
01:04:13
In my own journey towards biology one of the most remarkable things has been understanding that cells make decisions. And it's not something that we think of, cause we think - Well, we make decisions that's part of our consciousness.
01:04:26
If you cut your finger and you bleed onto a coverslip. And you look at all the cells, you'll see white blood cells. Those cells have the capability to chase after invading bacteria, hunt them down, consume them and then look for additional bacteria.
So you'll see your own cells, chasing after this bacteria. If it runs that way, it makes the decision to follow. And all that's encoded in its DNA. So you can have circuitry and decision making capability, sensing capability within individual cells, all encoded in the DNA.
01:05:28
What crabbing does is you have to be so focused at the moment that it clears your mind. And so I have a lot of the ideas for what we do in my lab immediately after

crabbing. Sometimes on the drive back home, I'm thinking very carefully about new ideas and that's where a lot of that can occur.

NARRATOR
01:05:54
Unfortunately, the catch wasn't as good as we'd hoped. But Chris Voigt invites me to appreciate another local specialty as he explains a little more about this new discipline which engineers life, as one might do with a machine.
01:06:16
It's possible... Because we have to understand that every organism, every living cell, has one or several functions.
Certain cells aid in digestion, others convert light into energy for plants, or transform sugar into alcohol, like yeast, a surprising little unicellular fungus.
But how do these cells know the nature of the work they have to accomplish? They quite simply have a manual, or a program, inscribed in their nucleus, their genome.
01:06:49
The genome is an organism's instruction book for life. It describes all of a life-form's functions. The book is made up of several chapters - which we call chromosomes. Chromosomes themselves are composed of genes. They form the sentences in the book. Each gene, or each sentence, is read like an instruction. All the genes together tell the cell what it has to do.
All of this is written using an alphabet, DNA, made up of the well-known molecules A, G, T and C... for Adenine, Guanine, Thymine and Cytosine, which are always organized in pairs: the A with the T, and the C with the G, known as base pairs.
Genes are transmitted from one generation to the next, identically, or are modified to respond to essential new functions or new requirements for the cell to survive. This is what we call evolution.
If we know how to modify them, and put them together, we can then change very simple functions into more complex ones.
Approaching life in this way radically changes scientists' work. Seeing life-forms as a sum of different functions, as a system, is no longer the starting-point of a biologist, but that of an engineer.
Chris Voigt is, among other things, an engineer. This time he invites me to MIT. For him, living organisms are machines, which can be put to use to serve mankind.
I'm looking forward to seeing his lab.

IN 01:08:27
Charles: Hi Chris
CV: Welcome to MIT
Charles: Thank you!

NARRATOR
01:08:31
I wonder if there are crab machines here in his office?

IN 01:08:34
CV: This is the Synthetic Biology Center
Charles: Has all the area been built recently, or…?
CV: The Synthetic Biology Center is about three years old.

CHRIS VOIGT
01:08:46
What we're trying to do in my lab is really create the foundation of tools that allow you to think bigger with respect to how to use cells in order to create new materials or new chemicals or to create a living system that's able to think and respond to its environment in a way that we find useful.
01:09:08
Every product of synthetic biology is something that hasn't existed, every genome that we engineer hasn't existed before.

NARRATOR
01:09:16
In order to build these new genomes, it's clear that Chris Voigt looks at life very differently than I do. His vision is that of a designer, of a system architect.

CHRIS VOIGT
01:09:28
To synthetic biologists cells are like machines. They contain all of these different working parts that collectively work together so the biology can do all the things that we see around us.
01:09:48
And one of our roles as engineers is to be able to get in and understand how to manipulate these machines so that we can re-engineer it with them to do other things. Everything that's in that cell is encoded in the DNA sequence. And so if we want to go in and design it to do something new it always comes down to manipulating the genes that are required in order to have the code that does that new thing.
01:10:21
So there's a real pleasure in being able to engineer biology. Trying to create an algorithm that runs inside a living cell where it's alive and doing all of the things that it has to do to survive but in the background it's just running one of these programs that you've put inside. It is an incredibly challenging problem.
01:10:44
For a long time in synthetic biology you had to do it by hand, it was very low tech. It was just trying to break down genetics into these more fundamental functions. In the last couple of years we've been able to develop some computer-aided design techniques that allow us to have new algorithms apply to the problem so that the computer can design the DNA sequence.
For example, a big part of the effort in my lab is to design the computer software where somebody can go in and using a high-level language, the same language that's used to design a computer chip, they can create an algorithm where instead of having it turn into an Intel processor, it actually, automatically takes that and turns it into a DNA sequence.

NARRATOR
01:11:38
Very well... Basically, Chris Voigt and his colleagues are using a computer program to create new DNA sequences, which is still engineering. But how do they switch from the computer, to reality?

Chris tells me that the virtual sequences he designs are physically assembled on another continent. He orders them by email from a specialist German company called GeneArt. Companies of this kind are known as gene foundries. They make DNA from simple jars of chemical products which each contain one of the 4 basic molecules.

CHRIS VOIGT
01:12:16
When we order a sequence of DNA, we send a file that can be tens of thousands of base pairs of A, Ts, Gs and Cs. And they have a number of robots just dedicated to physically build a DNA sequence. And they guarantee that they'll send back that exact DNA sequence, where every single base pair is exactly as you ordered it.

NARRATOR
01:12:54
So we have DNA, which is sometimes virtual and sometimes real, travelling round the world, electronically or in little vials, by mail... I have to admit, it sounds pretty scary. Can Chris Voigt, or any other synthetic biologist, simply order any genetic sequence they want? Even a virus or some other pathogen?
Chris reassures me. Apparently all the companies that synthesize genes are regulated by strict internal and external controls and rules. On the other hand, he is concerned about other potential issues linked to synthetic biology.

CHRIS VOIGT
01:13:33
One of my biggest concerns is around illicit economic interest. Currently it's relatively straightforward for a student from one of these labs to be able to build an organism that can make illegal drugs for example. So if you can make yeast, make heroin or make methamphetamine or any of other of these compounds you're really looking at an innovation that completely changes globally the way that we think about drug propagation and affects politics and world conflict and everything, that's a capability that's gonna come online very soon, like in the next five years.
And I don't necessarily see people really engaging that risk or thinking through what the implications are gonna be.

NARRATOR
01:14:23
This is a real problem, and I can only hope Chris Voigt’s message will be heard.
For him, in any case, whatever the uses or mis-uses, the 21st century will be "bio-technological".

CHRIS VOIGT
01:14:39
We're just scratching the surface as to what's possible if you can engineer biology. And the real question is when are we gonna get to the point where we can design and build an entire genome from scratch using fundamental principles, just understanding how the different genetic components click together.
01:15:07
I think it's one of the biggest challenges right now in science.
01:15:16

The last century in large part was defined by electronics and computers and so on, I think this century and the economy of this century, are gonna be around the possibility of engineering biology.

NARRATOR
01:15:32
Chris Voigt talks about what the future holds, and I can see the dramatic progress that's been made since DNA was first discovered in the 1950s, and the first experiments in genetic engineering were made in the 60s and 70s.
It was at that point that the word engineering in this context took on a new meaning, as engineers began to work in biology for the first time. Their contributions were also crucial to the amazing adventure of the first sequencing of the human genome in the early 21st century.
Today, computer technology enables scientists to progress even faster, increasing calculation capabilities and speed, and extending the possibilities for designing new genomes.
As I listen to Chris Voigt explaining how it's possible to construct an entirely new living organism in a laboratory, I have a strange feeling of déjà vu...
I think back to an announcement made in 2010, the effects of which resounded like a bombshell well beyond the boundaries of the scientific community.

Archives - Craig Venter
01:16:37
We're here today to announce the first synthetic cell. This is the first self-replicating species that we've had on the planet whose parent is a computer.

NARRATOR
01:16:47
At the time, the story was that scientists had succeeded in making a form of synthetic life from 4 bottles of chemicals and a computer program.
Certain observers immediately contradicted this version of the facts. Like Jim Collins, who I meet in Boston.
He too is an engineer, or more exactly, a professor of bio-medical engineering.

JIM COLLINS
01:17:12
I'm concerned by the hype that surrounds synthetic biology. The hype is problematic at times. We, for example, have seen many, many more media pieces on synthetic biology than we have original papers. I don't think we need to generate buzz to generate funding. I think the media needs to generate buzz to sell magazines and sell newspapers.

NARRATOR
01:17:38
Jim Collins tells me that, in his opinion, synthetic biology can only work with already-existing organisms, and that it is quite incapable, for the moment, of creating life from scratch.
He gives me his version of what Craig Venter's team actually did in 2010.

JIM COLLINS

01:18:00
They had taken a natural mycoplasma bacteria and they sequenced its genome; they've made some slight modifications to the genome on the computer, they synthesized it chemically and introduced this synthesized natural genome into a related mycoplasma and were effectively able to reboot it so that organism was able to take up that genome.
I think that what Craig's team has done is a technological marvel. They did not create from scratch a new organism or life, they modified an existing one.

NARRATOR
01:18:45
If it had been presented in that way at the time, the story would definitely not have made the international headlines in the same way.
But beyond the publicity the story brought to synthetic biology, I once again note the relevance of engineering. Research now involves constant toing-and-froing between biology and computers.

JIM COLLINS
01:19:05
Synthetic biology has been dominated by analogies from information theory and computer science. So you'll hear people talking about the cell as a programmable unit, you'll hear about DNA as being the software for a cell. I think this helps engineers to understand where they can actually impact molecular biology, but these analogies can only go so far, in that a naturally evolved organism is not an engineered system.

NARRATOR
01:19:41
It’s no doubt for this reason that before he talks about results, Jim Collins reviews where the field actually stands now. He emphasizes the difficulties that he has to confront every day as someone who’s engineering life.

JIM COLLINS
01:19:56
In synthetic biology we've got pretty good at coming up with the circuit schematics pretty quickly, we've gotten pretty good now at finding the parts, we've got pretty good at putting together and making them. Where we're not very good is that invariably the circuit is not behaving the way you like and it typically takes many months if not years, to get even a simple circuit to behave at the level of quality of function that you like.

NARRATOR
01:20:25
This lack of reliability and results in no way prevents further research. There’s no need to understand every aspect of a machine’s inner workings in order to use it.
01:20:39
For several years now, Jim Collins has been working on medical applications. As I’ve seen with other scientists, he has been influenced in his choices and decisions by his background.

JIM COLLINS
01:20:54
I was a collegiate runner and in my junior year, my third year in college, I actually had a persistent strep infection and it more or less ended my running career. My lab recently has actually been motivated to use engineering approaches to address persistent infections; And we were able to use an engineering approach to actually figure out how do persistent bacteria behave, and how we can actually then exploit that to change its state, to make it vulnerable to the antibiotic.

NARRATOR
01:21:28
Through his ability to understand, at least partially, how the machinery in certain bacteria works, Jim Collins knows how to destroy them. His research focuses in particular on organisms that can be seen almost everywhere, in a formidably resistant form: biofilms.

JIM COLLINS
01:21:44
Biofilm is a community bacteria that is surrounded by an extracellular matrix and they're attached to a surface. So the stuff on the side of a ship is an example of a biofilm. Most bacteria exist in biofilms and are not free-swimming. Why a bio-engineer like myself is interested in biofilms is that bugs in biofilms are a thousand times more resistant to antibiotics.
And bugs love to form biofilms on anything we put inside somebody's body and so now, if you're going to get an artificial knee or artificial hip, a pacemaker for your heart, the risk is not the surgery, the risk is that you're going to get a biofilm infection. And if that happens, they then just open you back up, remove your device, let the infection clear and then reintroduce the device.

JIM COLLINS
01:22:38
We decided we wanted to take a synthetic biology approach to eradicate biofilms. And what we did was we re-engineered bacteriophage. Bacteriophage viruses that specifically infect bacteria. We engineered the bacteriophage so that they would express enzymes that would break up the biofilm.

NARRATOR
01:23:01
Jim Collins' organisms don't just attack bacteria, but also the very structure of biofilm: a thick matrix that provides a highly resistant coating. By attacking this matrix, Jim's organisms manage to eliminate the bacteria, layer by layer. This new approach is extremely effective.

JIM COLLINS
01:23:18
The phage infects the bacteria, they'll make multiple copies of themselves using the machine of the bacteria and then they explode the cell. Our approach is able to go in and allow the phage to penetrate and infect the top layer of the biofilm but then break down the biofilm to expose more and more bugs and we're able to show that this

approach could eradicate greater than 99.99 percent of the biofilms in various settings, be they clinic and/or industrial.

NARRATOR
01:23:57
Wonderful. Bravo...
But I do have a doubt... Could this highly destructive bacteriophage be the precursor of other, equally virulent, modified organisms, and end up being completely uncontrollable?
Jim reassures me... more or less…

JIM COLLINS
01:24:12
We don't have extensive capabilities to re-engineer organisms just yet. Most of the organisms that we make are much weaker than anything you'll find in nature and one of my points to the public is they really should be concerned about what nature has out there, because it is incredibly powerful and it's going to get us.

NARRATOR
01:24:34
It's true - the sheer power of some of our natural predators, microscopic or otherwise, is chilling. One of the greatest feats of the 20th century was certainly to limit or control their effects. Could bio-engineers go even further?
01:24:52
Meanwhile, I've learned from Chris Voigt that cells can make decisions. And by modifying the genome of these cells, we can modify their decisions and their behaviors.
Jim Collins has told me that we can't do everything: despite the enormous possibilities afforded by computers in terms of simulations and calculations, we're still a long way from knowing how to create a living organism out of nothing. On the other hand, we are able to work on relatively simple living systems, which enables us - no small feat - to conceive of cells that be of service to medicine, for example. But what about more complex systems, combing a variety of functions?
01:25:34
This very subject is the research field of the engineer I'm about to meet on Manhattan Beach in Los Angeles.

RON WEISS
01:25:46
My name is Ron Weiss, I'm a professor in biological engineering at MIT.

IN 01:25:54
Charles: Hi!
RW: Hi, How are you?
Charles: Nice to meet you.
RW: Nice meeting you too
Charles: so we go this way?

NARRATOR
01:26:01

Ron Weiss is the co-director with Chris Voigt of the Synthetic biology department at MIT. Like Chris is also enjoys doing things in the open air.

RON WEISS
01:26:11
Ever since I was a little kid, I was interested in programming things and computers. Halfway through my PhD I was working on this project called "Amorphous Computing". And the notion was that we'd like to be able to program very small entities that might be even the size of a grain of sand and get them to do things.
I was looking at biology as a way to get inspired, because you have millions or billions of little computing elements that interact with one another and are working towards a particular task or a set of behaviors.

NARRATOR
01:26:50
For Ron Weiss, the analogy between his two passions, computers and biology, works perfectly.
His objective is therefore to ultimately be able to program a cell as simply as an information technology engineer can program a computer to give it several tasks.

RON WEISS
01:27:06
So when we wanna design behavior in a cell, usually what we do is we first come up with some kind of a high level idea. There's some specific behavior that we want a cell to be able to accomplish and then we start decoupling them, meaning we start decomposing it to smaller pieces that we may be able to then genetically engineer inside the cell.

NARRATOR
01:27:31
Ron Weiss makes an analogy between his own objective and the local surfers.
He breaks it up into several sub-problems.
In order to surf, you need 1: to float and slide on the wave. 2: to control your trajectory. 3: to adhere to the board, and 4: if you fall off, don't lose it in the waves.
To put each of these sub-functions into practice, you need to use and combine several specific tools.
In order to explain how to give these different functions to a surfer/cell, Ron invites me to accompany him on the quest for various parts required for its construction. In other words, it's time to go shopping.

IN 01:28:18
RW: How's it going?
Surf shop employee: How's it going?

NARRATOR
01:28:24
If I pursue his analogy: for the 'float and slide' function, the tool is a surfboard. To 'control your trajectory', you have to choose from among a range of fins. To 'adhere' to the board, there are various waxes; and to be sure not to lose it, you use a leash.

RON WEISS
01:28:44
We say, we have this gene, which can do something, and we have this other part that can regulate the production of this protein, and then we can glue together, for example, ten pieces to create a large DNA circuit.
What we do is we usually go to the freezer and we look to see what parts, what generic circuit we have available to build something.
One of the important goals in synthetic biology is to be able to have a huge library of parts in circuits that are just available for us and for everyone else in the world to be able to engineer with.
01:29:29
There has been really an explosion in the number of parts and devices and circuits that are available. So for example, the « Registry of Standard Biological Parts » is the world's biggest collection of genetic parts, and I think it has on the order of 10 000 or 15 000 parts that are available for people to experiment with, and to build other circuits and components with.

NARRATOR
01:30:01
The basic parts, or pieces of DNA used as construction modules, are naturally known by synthetic biologists as bio-bricks.
When their equivalents are applied to the ideal surfing scenario, they enable Ron Weiss to use the most cutting-edge technology to float and slide and keep stable.
All that remains is the human factor, and this is much more difficult to control.
For Ron, the fact that not every aspect of life is understood in no-way hinders engineers in their research.

RON WEISS
01:30:35
We definitely want to be able to program the cell before having a full and complete understanding of it. In as we're programming the cell, we're also trying to discover more about it to refine and re-optimize the programs. So it's a continuous cycle of programming-learning-programming-learning programming-learning.

NARRATOR
01:31:01
So what can Ron Weiss achieve using this technique today? In his lab, he can manufacture 300 biological circuits in parallel in 3 or 4 days, with each one containing up to 15 genes. But this is nothing compared to what he will have to be able to do in order to build the circuits for a cell with more complex functions. The circuit in a bacteria requires 4000 genes. In a human cell, this would be 80,000 genes.

RON WEISS
01:31:29
For simple behaviors, we now are able to engineer the cells to be able to perform them reliably. But what about more complex behaviors?
01:31:41
My dream in Synthetic Biology is to be able to type for example a genetic program or use some kind of a 3D modelling tool that allows me to think about the behavior that I

want, and press a button, and then a few hours later get a tube of DNA that contains a genetic circuit that will exactly carry out that program when I put it inside the cells. It's not quite there yet. We haven't quite reached this scenario, that we can program the cell to do anything that we want.

NARRATOR
01:32:23
As I leave Ron Weiss and the MIT campus, I can't help remarking that synthetic biology research is essentially North-American. There are quite simply more resources here: more labs, more capital... The prestige, and the money, of American universities attract students and PhDs from around the world, and many of them settle here.
However, in Europe, and in France, there are several centers devoted to synthetic biology, as well as a number of independent teams.
Jerome Bonnet runs such a team. After a long stay at Stanford, he returned to southern France to pursue his research, thanks to private funding. He too wants to master the complexity of cellular circuits, and sees living beings as instruments... instruments he wants to control.

JEROME BONNET
01:33:12
My name is Jerome Bonnet. I'm a synthetic biology scientist at the Structural Biochemistry Centre at the CNRS in Montpellier. What I'm interested in is applying engineering principles, particularly electronics principles, to cells. We could basically say it means programming cells like as we program a computer.

IN 01:33:30
Charles: Hello Jérôme
JB: Hello Charles Antoine
Charles: Are you well?
JB: Fine and you?
Charles: Yeah...

JEROME BONNET
01:33:37
In West African music, there are some very simple rhythms, with certain clearly-defined elements which intertwine in a complex way. We can compare a cell to this sum of small actions, which are ultimately simple, but which combine to form something complex. In synthetic biology, we're limited by the complexity we can manipulate, because of the various contextual effects we might find; like interactions between the components we don't understand. So we're obliged to start with really very simple systems, and once we've understood a simple system, we can add other parts and make it more complex.

NARRATOR
01:34:19
A former disciple of Drew Endy, one of the founding fathers of synthetic biology, Jerome Bonnet has decided to apply his mentor's maxim to his own work: "complexity sucks".

He relies on the notion that if one is able to build something, one will soon be able to understand it. And what he wants to build should be of use to the complex biological systems conceived by Chris Voigt, Ron Weiss, and Jim Collins.

JEROME BONNET
01:34:53
My research involves manufacturing genetic components which enable cells - bacteria, as it happens - to perform logic operations : additions and multiplications, and also to store information ; to have memory that we can program. The aim is to manage to program a cell using a language that's close to a computer language.
Certain functions are much more difficult to obtain in electronics, but we manage to obtain them in biology, where the architecture is much more simple. Notably because in electronics, we have motherboards, where we install components, and it's a two-dimensional system. In biology, we're working with a kind of molecular soup, in 3 dimensions, and so this enables different interactions.
What I initially developed in my work, were genetic switches, which are based on the manipulation of DNA molecules in cells.

NARRATOR
01:35:48
The switches designed by Jerome Bonnet enable the expression of a gene to be controlled. This means the implementation, or not, of a particular genetic function.
But as I'm not sure I really understand...

IN 01:36:03
Charles: A logic gate is several…
JB: Transistors
Charles: Transistors, right…

NARRATOR
01:36:09
Jerome risks an analogy with the nearby canal...

JEROME BONNET
01:36:18
What we've done with these sequences, these switches, is to control the DNA. Like we control the flow of water in a canal with locks.
What we've built is the genetic equivalent of a transistor.

NARRATOR
01:36:37
I've bearly grasp that the transistor is like an on off switch for the current and Jerome Bonnet already bombards me with a number of poetic terms, such as 'RNA polymerase', 'logic gate', 'ribosomal subunits', 'enzymes'...
What I do understand though is that, like with computers, by combining transistors, increasingly complex functions can be created within a cell.

JEROME BONNET
01:37:00

It lets us introduce calculation into biology. The world has completely changed. Whereas it costs 3 million to sequence the human genome 15 years ago, today we can do it for 1000 euros in a day.
We're making huge progress, but compared with electronics, we're still back in the 50s, when people started building computers, or even before the transistor was invented.
We provide people with tools, and then they apply them to their particular problem. This could be for making a therapeutic molecule, for example, like an anti-malaria molecule, or for programming a cell: like a lymphocyte, for detecting cancer biomarkers... things like that.

NARRATOR
01:37:46
Tools like those developed by Jerome Bonnet first of all have to fulfill a function. In synthetic biology, like with all research, applications are needed, and as soon as possible. And so it is naturally in the health-care sector that these bio-engineers have concentrated their efforts.
If there's one place in Europe to see the biggest pharmaceutical laboratories, it's Basel, at the junction of 3 countries.
01:38:14
It is here that I meet Martin Fussenegger, a professor of biotechnology and bio-engineering at ETH, the federal polytechnic. He also uses and assembles bio-bricks, but with very precise medical applications.

IN 01:38:29
MF: Hi Charles…
Charles: Hi Martin, nice to meet you

MARTIN FUSSENEGGER
01:38:38
Here in Basel, people produce blockbuster drugs, which are on the market saving thousands of people's lives.
It what came knows natural to expand this technology using designer cells, those cells which are engineered at multiple levels.

NARRATOR
01:39:08
On the way to his laboratory, Martin Fussenegger shows me something that has become a symbol of the city, and which, in his mind, also symbolizes the logic behind his work. The fountain created by Jean Tinguely.

MARTIN FUSSENEGGER
01:39:23
What Tinguely did is he took rubbish parts, parts which people threw away and from these components he reassembled machines, which are not useful but they are beautiful.
So, the analogy with synthetic biology is take the parts, biology parts, we reassemble them so they can work like machines. Unlike Tinguely who does something beautiful, synthetic biology's also a piece of art but has the ambition by assembling new components to do something useful, for example in a treatment strategies. I think

artists and scientists, they're pretty similar, they need to be the crazy guy, the creative guy who invents and innovates to put ideas which are not common sense.

NARRATOR
01:40:25
There's nothing extraordinary about the ETH offices. Scientific work-places and labs all over the world tend to look the same. We're supposed to be at the forefront of research here... but the real innovation lies inside the heads of those who work here. And Martin Fussenegger has a truly unique approach...

MARTIN FUSSENEGGER
01:40:51
What we're trying to develop is a so-called prosthetic networks. Now, we are very familiar with the word prosthetics: if we have a problem with the heart, we get a prosthetic heart, if we have a problem with our arms, we have prosthesis for that.
So, meaning mechanical prosthesis which replace a mechanical part of our body.
Now we transform this complex form of mechanical world into the metabolic and molecular world.
We call it designer cell and we engineer the bio-sensor which constantly senses the metabolite in the blood. If it's obesity, it's blood fat levels and if it's diabetes, of course, it's glucose. So, in any of these cases, the designer cells can precisely sense the metabolite in the blood, it processes this information and produces a protein, which is then released back into the bloodstream.
So, if your blood fat levels are too high, the sensor recognizes that, produces a satiety hormone what tells your brain you've eaten enough, you should stop feeding.
There's nothing artificial behind that. The sensor which looks at the blood fat levels constantly is actually just a derivative of a sensor which we have in the liver. So, it's just the linkage and the fact that this was engineered into cells which are then implanted into the body, which makes this device unique.

NARRATOR
01:42:38
Martin Fussenegger shows me the mice in which his designer cells have already been implanted. These cells prove the progress that's already been made, and prefigure the next step: implanting them in the human body.
In order to attain this objective, the cells have to be produced according to procedures that are strictly regulated.

MARTIN FUSSENEGGER
01:43:07
We need to control therapeutic transgenes very precisely. So, we thought about the best way to control transgene in your implants, was to control transgenes in your body through the skin just by shining light onto the skin.

NARRATOR
01:43:26
In future applications, the blue light will be replaced by an organic trigger within the body. For the moment, the blue light only serves as proof of concept. Martin tells me how it works.

MARTIN FUSSENEGGER
01:43:41
The technology we found was blue light which penetrates the skin, reaches your designer cells implanted onto the skin and can fine-tune the expression of a gene inside your body, inside the implant. So, the censor we used at that time was just a blue light sensor we all have in our eyes; it's called melanopsin, and this reacts to the blue light we shine onto the skin.
So, this again is a beautiful example on how synthetic biology has nothing to do with being synthetic or artificial, it's just by placing a natural human receptor from the eye into another cell.

01:44:33
Prosthetic networks cannot only get the regulation dynamics right, it can already detect the onset of a disease. So, which means it automatically diagnoses a problem and already counteracts it. Your implant will supervise your body at any time and you don't need to do anything, it takes care of diagnosis and first intervention.

NARRATOR
01:45:02
When we listen to the scientists, the arrival of such applications seems imminent. In reality, this is not really the case, as imminent in everyday parlance, means ten years, at best.
I still have time to eat chocolate, unless I'm subjected to blue light...
But perhaps now is the time to worry about the secondary implications, or side effects, of such work and applications. In this context, we have to take other factors into account, such as economic issues, and political action.
01:45:47
One good place to start could be Washington DC, and so I head there to find out more.
01:46:01
I meet Eleonore Pauwels, a Belgian who's been in the States for many years. She works at the Woodrow Wilson Center, a think-tank and discussion forum for academics, scientists and politicians.
01:46:19
The first thing Eleonore works on is public perception. She wants to know how people regard this new techno-science. If they have heard of it

ELEONORE PAUWELS
01:46:30
Synthetic biology. It's a big term. « Synthetic » is really not a word that sounds great these days.
Why are people more comfortable with some technologies and really scared of other ones? I think, in the case of synthetic biology, first of all, there was a problem with playing with something that's alive, something that's similar to our genetic code. You know, it's close to our identity in a way.

NARRATOR
01:47:01

To get a better idea of how people perceive what these engineers of life are doing, Eleonore regularly invites citizens' panels to take part in focus groups. The first question to be raised concerns what they know about the subject.

ELEONORE PAUWELS
01:47:18
Most of the time, people don't know about synthetic biology.
They don't know the term. They usually don't like it. But, you know, they are actually able to make quick analogies, quick heuristics to notions like cloning, stem cells and genetic engineering.
15% of our participants are concerned about the risk of synthetic biology before information, and it moves to 33% post information.
Which means that when you start to explain to them what you do with biology on a computer, DNA is the software of life, what kind of application we could have for the energy system, for the food system… The discussion becomes more complex.
They are concerned about long term implications, they are concerned about governance failures. Failure to control, failure to anticipate, failure to ethics.
They want oversight regulation transparency. But if you look at our technological history there is always failures to control and failures to anticipate. A great humanist said that technology gives you a gift in one hand and stabs you in the back with the other. And that's kind of what happens.
01:49:05
I'm not really afraid of the technology itself. The problem is that science is part of an economic enterprise. It's supposed to produce growth, you need to go fast, as fast as possible, to the market with great applications. I think we should sometimes go fast, when it comes to health research, for example. But we need to be mindful each time, it's gonna have implications on larger systems. And policy-making is definitively behind. So from the lab, to the federal agencies, we need to get better at anticipating potential bio-safety and bio-security implications, before commercialization. But we have time to do risk research, because most of the promises are gonna be realized only in 10, 15, 20, 30 years.

NARRATOR
01:49:58
Eleonore Pauwels also looks at other issues that maybe of less interest to the general public and less worrying; but they're equally important.
All of these discoveries affect our common asset: life itself. Who will own this "Biology 2.0"?

ELEONORE PAUWELS
01:50:14
You have 2 obvious cultures that are actually fighting each other, in synthetic biology.
So you have the culture asking for much more open source systems. They come from computer design, and they know that innovation comes from sharing, comes from openness. And you have the most traditional culture that comes from molecular biology, they are used to patents.
Some companies are actually keeping huge libraries of genetic variations, closed from the public and from other universities. That's a huge problem, I think. It could definitely stifle innovation.

NARRATOR
01:50:56
Can individual interests outweigh the common interest? Energy, health, food... the implications are so important, and potentially lucrative, that we're entitled to have reservations. In considering living beings in a radically new way, assembling their components like building blocks, and modifying them at will to be useful and profitable, engineers have initiated a technological revolution that goes far beyond anything that has happened before.
I can see that some of my own fears, shared by Eleonore Pauwels, are legitimate, but others often come from my lack of understanding about what synthetic biologists are actually doing: what do they intend to make, and what are their methods? Are they getting results? Are applications already on the market? And will these applications, now or in the future, dramatically change our daily lives?

My journey into the world of synthetic biology continues...

END CREDITS 01:52:02