BIOLOGY 2.0
Making Evolution Evolve
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 something getting completely lost.

FRANCES ARNOLD
01:01:03
I applied the algorithm of evolution to create new biological things.

LAURIE ZOLOTH
01:01:10
My concern is you could be the creator of a new entity who has not doesn’t exist

GEORGE CHURCH
01:01:18
Most of limit that people see is there imagination

NARRATOR
01:01:24
It took me a while to figure out where to start...
The first lead I followed up was evolution itself. Because in synthetic biology, scientists want to "evolve evolution"...
A surprising notion... which immediately made me curious...
01:01:44
For example, I found one Canadian who wants to produce morphine without growing poppies...
How? To find out, I set off for Quebec, and its untouched wastelands.
01:01:59
I thought I'd find myself in a hi-tech, climate-controlled research laboratory. But instead, I'm in a rather different environment, where my host likes to see things with a cool head!

VINCENT MARTIN
01:02:11
My name is Vincent Martin. I'm a biology professor at the University of Concordia in Montreal. I do a great deal of genetic manipulation, particularly with micro-organisms.

IN 01:02:20
Charles: Shall we get dressed?
VM: It's minus 20°. Let's get dressed.
01:02:28
Charles: You're quicker than me. We can see you're more experienced.
VM: Definitely.

NARRATOR
01:02:35
Vincent Martin specialises in genetic manipulation. He tells me about the directions man has always tried to make evolution take: directed evolution.
We can see what this means quite clearly in a real-life situation.

VINCENT MARTIN
01:02:50
When you find yourself in an environment like this, you can see biological life much bigger. There are several examples of the domestication of all sorts of organisms on the planet, which are a direct result of man.

01:03:27
The characteristics of sled-dogs are that they are very resilient, and more docile, etc. We would have started with a wolf, and I imagine we began by selecting a wolf with a more docile nature, and with greater stamina. Through subsequent breeding, and the selection of offspring that were increasingly docile and resilient, the wolf ultimately evolved into a sled-dog.

01:03:54
Obviously, between the wolf and the dog, you'd have to be quite patient to see the wolf's evolution, as it takes a certain amount of time.
01:04:15
Evolution is always directed by a selective pressure. Society has carried out directed evolution for a very long time.

VINCENT MARTIN
01:04:52
In the laboratory, we can do exactly the same thing, except that we can accelerate the process, particularly with micro-organisms as they reproduce much quicker. We can therefore have several generations in a very short time in the lab. And by applying some form of pressure, we can introduce the characteristics we want into the evolutionary process.
My precise field in synthetic biology is the synthesis of natural products among micro-organisms.
There are many natural products that we can extract from the environment, but that's not the best way to do things. What we're trying to do is to reproduce the molecules in question in a more controlled artificial environment.

In my lab, we work a lot with a family of molecules called alkaloids. Examples of alkaloids that many people know would be morphine and codeine. These molecules are produced in opium, or the opium plant.

IN 01:05:47
*VM**:** What's incredible is that all the active molecules in question accumulate in the latex here. They're molecules which are used in the pharmaceutical industry, but they're often quite difficult to synthesize chemically, or even to find via a natural source, in a plant.*

NARRATOR
01:06:06
Through synthetic biology, Vincent is trying to manufacture new molecules by using life-forms like a factory, using their principal characteristic, evolution, as a tool. It's the key challenge in this new discipline. To understand the main principles that govern it, Vincent Martin first of all reminds me that each organism, each living cell, has one or more 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.

01:06:49
But how do these cells know the nature of the work they have to accomplish? They quite simply have a manual, or a programme, inscribed in their nucleus, their genome.
01:07:05
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 organised in pairs: the A with the T, and the C with the G, known as base pairs.
Let's take man as an example. My book, or my genome, was first decoded in 2001. It's made up of 23 chapters, 23 chromosomes, and contains around 3 billion base pairs, which form about 30,000 genes.
Quite a tome.Well not exactly…

The biggest book we know belongs to a small plant, "Paris japonica", with 150 billion base pairs. The smallest, or shortest book, is that of a bacteria called "Carsonellarudi", which has just 160,000 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.
01:08:52
Am I an expert now? Not really, this is just the basics of life.
What's new is that the evolution of genes is just like everything else: we don't have the patience to wait for years to get a result...

Everything's moving ever faster, and we want to accelerate the process even further. We want to male evolution evolve.
I therefore rush off to see someone who has done more than most to promote this idea. She's waiting for me at her home in California, in her vegetable garden.

FRANCES ARNOLD
01:09:25
I'm Frances Arnold, I'm a professor at the California Institute of Technology, where I teach chemical engineering, bioengineering and biochemistry.

I love biology. I think that biology is the best engineer and has created a whole array of beautiful, fascinating and highly efficient objects, life forms, even the molecules are beautiful.
01:10:00
I was trained as an engineer, but when I discovered that biology engineers all these things by the algorithm of evolution, I wanted to go in there and start building new biological things myself.

NARRATOR
01:10:16
I might quite simply have spoken about the successive steps necessary for evolution, but Frances Arnold talks about an algorithm. The word clearly reflects the engineer's thinking that characterizes her approach.

IN 01:10:28
Charles: Hello
FA: Hello. Welcome
Charles: Nice to meet you Frances. Shall we go over there?
FA: Yes

NARRATOR
01:10:35
For the moment however, before she tells me how she uses evolution, she too wants to take me to a calm, natural environment.

FRANCES ARNOLD
01:10:41
All living organisms, ecosystems, every level of complexity in nature comes from evolution. Everything from the simplest molecule, that can convert sugar to a fuel, to the whole cell, to the multicellular organism like you, me or a cat or a dog.
To all these organisms working together, all the microbes that live in your body are the products of evolution and coevolution with you. To the whole ecosystems, and in fact the whole planet that's connected through this process of trial and error and natural selection.

IN *01:11:30*
FA: Look at all there little horns. He’s got a helmet full of horns

01:11:36
I have images on my computer of the craziest, wildest, most wonderful creatures you can imagine.
And these aren't products of our imagination, these are projects of nature's imagination and they are fabulous.
Insects that look like sticks. Fabulous orchids that have the faces of monkeys, they've all evolved in order to survive and reproduce.

NARRATOR

01:12:07
Spending time with a scientist like Frances Arnold helps me to evolve too, and to see the world rather differently...

IN 01:12:27
FA: Coyotes and bears. It’s just completely wild, all the way to… out to the Mojave.

NARRATOR
01:12:33
All around us, and inside us too, living organisms evolve: some are visible, others invisible... but in practical terms, how does observing all this diversity help her?

FRANCES ARNOLD
01:12:47
The molecules that biology makes, the organisms, they all solve tremendously difficult problems. They can extract energy and materials from their environment and convert those into self-replicating, living, breathing organisms. That's pretty smart. Humans don't know how to do that.
It's a pretty smart machine. They are programmable machines in a sense. And what we're trying to do is learn how to reprogram them so that we can take some of their functions and attach them to other things, like curing disease or making materials.
We pump oil out of the ground and turn it into plastic. And not very efficiently. So if we could use sunlight and carbon dioxide or renewable resources in the form of waste agricultural products or even garbage, and convert that into the things we need in our daily lives, like biology does, we would be much better off.

NARRATOR
01:13:54
Frances Arnold underlines the urgency of producing and consuming differently, as this is her chief preoccupation when she works every day in her laboratory at Caltech. And the main reason she's seeking to evolve evolution.
01:14:12
On the way, she explains how the past 70 years have profoundly affected our knowledge in the field of biology, with the discovery of DNA by Crick, Watson and Franklin in the 1950s, the manipulation of the first genes, and more recently, the work on sequencing the genomes of all living beings.

FRANCES ARNOLD
01:14:34
What's changed is that we had the DNA revolution, we understand a lot more about how biology works. We know the code of DNA, we can write DNA, we can read it.
01:14:54
Instead of just studying biology, we can now bring engineering into that. And build it ourselves. We're understanding the building blocks well enough that we can put them together in new ways.So that we can explore parts of the biological world that nature couldn't go to.

NARRATOR
01:15:23
It all seems so simple, to hear her explain it. She says it's sometimes possible to modify less than 1% of DNA in order to obtain a new species.

I admit I'm not necessarily comfortable with the idea of heading in that direction... And in my opinion, I'm not the only one...

FRANCES ARNOLD
01:15:41
Natural selection has dictated what exists on this planet. But we're no longer constrained by the limits of biology.
Artificial selection, our choices can start to dictate what exists on the planet. It already has, right? We've been doing it ever since we walked on this planet. We've been gifted with the intelligence to learn how to use agriculture for our benefit. We breed pets that can enhance our lives. You get to choose the mother and father but not a whole lot else.

FRANCES ARNOLD
01:16:26
But in the laboratory when you're doing it at the level of DNA, I can have three parents, I can have 33 parents. I can introduce mutations, fast or slow. I can make a billion progeny and then I have to choose what properties to look for in this progeny and I have to explore what are those pathways by which new features can come about.
01:17:06
So in synthetic biology, I applied the algorithm of evolution in the laboratory to create new biological things.
There're too many different ways for evolution to go, to think that nature tried everything, it's just impossible. Nature tried but the tiniest fraction of all possible DNA sequences. So that means there's plenty for me to try.

IN 01:17:32
FA***:*** *You can see those tiny little spots there. You can seethat. Those are bacteria that are growing.*

FRANCES ARNOLD
01:17:39
I learned how to breed molecules, like you breed cats and dogs. Recombining their DNA, mutating it. And then seeing what those new DNA sequences encode. And if I like them, I keep them. And if I don't, I throw them away. And I keep iterating, generation by generation. Until I have something that's useful.We can do it in days now.

NARRATOR
01:18:09
My head is spinning, caught between enthusiasm and dread...
But Frances Arnold cuts short my dilemma. She tells me that scientists are still a long way from matching what evolution can do...

FRANCES ARNOLD
01:18:33
Evolution has done this for 4 billion years. And as a result the music that evolution created, that composition, that sequence of DNA, is beautiful. It's perfect. But when a human goes in and tries to build DNA like that, we're just learning how to hold the pencil. We're just beginning to explore these things.
01:19:15
We are definitely limited by a profound ignorance of how biology works. The knowledge blocks us. The understanding of the relationship between the DNA sequence and what it does. How that DNA sequence encodes function. We do not understand that.

If you put DNA from a monkey into a microbe, it may or may not read that DNA. We don't know why that is. We will, some day, know that.

NARRATOR
01:19:58
There seems to be a strange paradox... Could it be the complexity of life that make scientists ever more ambitious?

FRANCES ARNOLD
01:20:09
It's in our DNA to learn about biology and to manipulate biology. I just hope we don't destroy our planet at the same time we learn all these things. But it's in our DNA to invent it’s who we are, it’s what evolution has made us.

NARRATOR
01:20:40
It's no doubt my own DNA that makes me want to find out more, and to hit the road again.
The idea of making evolution evolve, of mastering living codes and sequences in order to create biological machines capable of solving our problems, means that most scientists have their eyes firmly fixed on the future, but some of them are also interested in solutions that have been forgotten and overlooked in the mists and meanders of the past.
I therefore decide to visit a man whose name became famous well beyond the boundaries of the scientific community when it was wrongly suggested he wanted to revive Neanderthal man.

GEORGE CHURCH
01:21:31
I'm George Church, professor of genetics at Harvard Medical School and director of the personal genome project.
01:21:47
When I was very young, I lived on the water and there was a dragonfly nymph, which (looks like)...which is a wingless water creature (that) turns into a winged air creature. And I thought that metamorphosis was remarkable. And it made me want to not only watch, but influence. From very early on we learn how to manipulate biological systems. My mother and I did breeding of flowers and other grafting of branches on the trees. So I was introduced to the idea that biology isn't all natural, gardening is unnatural. And that's a good thing.
When later I realized that you couldn't just watch and think, you had to actually test ideas,
I got introduced to real technology where you can read and write DNA completely arbitrarily and so manipulate biological system… this is synthetic biology.

GEORGE CHURCH
01:23:04
My motivations in synthetic biology are that many problems in the world either ARE biological problems or HAVE biological solutions. Food, distribution and the quality of nutrition, infectious disease, aging, cancer, all these are inherently biological.
But there are other things where biology can be used for non-biological things - to purify water, to provide the next generation of molecular computing, DNA storage, and so forth, and so... So biology represents a lot of solutions.

NARRATOR
01:23:41

When a scientist with the stature of a Greek god predicts so many miraculous solutions to save the planet, I'm just stunned.
Transform life into a global factory? A universal machine that can manufacture anything and everything? Synthetic biology suddenly appears to be a goose that can lay golden eggs...

GEORGE CHURCH
01:24:01
Can any organism make any chemical? I think probably yes. Life can make just about anything. It's not limited 'life making life. You can probably make plants and animals make anything. The interesting question is - what CAN'T you do. Every day it seems less and less like. Living systems will take salts and turn them into metals, like gold-salt into gold-metal or turn them into semi-conductors.

IN 01:24:34
Charles: good girl!

GEORGE CHURCH
01:24:36
The beauty of biology, is that it can make atomically precise thing, and it self-assembles. So instead of having to individually screw in every bolt, you give it the basic idea and it will do the rest for you. This is wonderful, this is truly new.
Synthetic biology is the next industrial revolution.

NARRATOR
01:25:03
As I watch George Church work, I see that he uses his computer more than his microscope. His vision of the living world, once again, is primarily that of an engineer, rather than a biologist.
And his "revolution" is already "industrial", in that it enables him to assemble and test millions of newly-designed cells.

GEORGE CHURCH
01:25:27
Synthetic biology is an effort to introduce engineering principles into biology to implement more automation in the process of making large genetic constructs.
We use computer-aided design, very similar to the computer-aided designs used for making cars and cell phones.
We apply that to design millions of genomes to specification. Each slightly different, each testing out a different design concept.

NARRATOR
01:26:02
What's interesting about biological matter is that it multiplies very easily, by itself, and so scientists are not restricted to a single conceptual prototype.
George Church explains how he makes cells that are equipped with these genomes, and then tests them.
His selection process makes me think of a competitive sport... where each genome is competing against the others.

GEORGE CHURCH
01:26:24

It will be intentionally 'hit and miss', intentionally 'trial and error'.
So it will be like “I’m going to have a billion go in, have a selection that says 'Only those that make that chemical in that amount are going to make it through to the end' and one winner comes out.

NARRATOR
01:26:51
But that's not all: the prototypes can also be modified, even as they're being used and tested.

GEORGE CHURCH
01:26:59
You can actually do surgery on a cell while it's 'awake', while it's running. I mean, it's like repairing a car or a boat while it's in a full operation. And that has the advantage that if you do anything wrong, it will immediately break and you can do many of these things in parallel and watch all the ones that break and then you can fix those independently and the ones that didn't break - you can build those up into something more complex.
Very often we can build a nice model and it behaves in the computer the way it should but you get your surprises, you're gonna make many, many errors. Every time we fail as an engineer, we succeed as a scientist, we make a discovery.

NARRATOR
01:27:51
It has to be said that George is more than enthusiastic about the discoveries and progress that synthetic biology can bring...
I even feel obliged to remind him why I have come: to talk about the past.
Because ever since I first heard about his work, I've been excited by the notion of "retro-evolution": the idea of going back, of exploring evolutionary history, in order to bring old species back to life... species whose characteristics could well be useful today.

GEORGE CHURCH
01:28:19
DNA is the oldest book, the oldest story and we can recover information from the past from things they were extinct by 2 main methods: one is looking at the family tree of living species, really ancient trees that go back to the beginning of life, and we can say, oh the grand great great grandfather must have looked like this.
And then the second way is we can actually find DNA out in the environment, let's say in the tundra, which is up to 700.000 years old. So it's, the organism is dead, but the DNA is still intact enough that we can sequence it, or we can reconstruct pieces of animals that have been extinct. As it turns out, my lab does do research on mammoths and their relationship to elephants. And we're doing synthetic biology to bring back some of the DNA we find in mammoths and make cold-resistant elephants.

NARRATOR
01:29:20
In actual fact, making elephants look like mammoths isn't really the main reason George Church wants to bring back species from the past.
It's because certain species, be they simple cells or complex mammals, could provide solutions to our problems. Certain organisms from the past could help to combat contemporary diseases. And why not reinforce the 3% of the tough old Neanderthal that still survives inside me to compensate for my homo sapiens fragility?

I have to say, however, that once again, I'm not really at ease. How can we be sure that these new or revived genomes won't proliferate or interact uncontrollably?
George Church reassures me. Scientists have imagined various responses, including one that may seem odd, but which for them is irrefutable: the creation of a new DNA, that would be totally different from the one that's existed in nature for 3.6 billion years. A new molecule, offering the same possibilities, but using new components. The T for thymine, for example, could be replaced by a new chemical element symbolized by an X.

GEORGE CHURCH
01:30:33
With xenobiology, we can create lots of alternative universes today. We can create new organisms with new genetic codes, you can make a new base pair of DNA that doesn't exist in nature.
So instead of A base pairing with T, and G with C, you'd now have a new base pair of X with Y, but you can now incorporate it. And the organism will replicate it as it was one of the standards.
That's terrific. And we can see what the pros and cons are. If we get something that's better than life in some way, replicates faster, or you know, is more adaptive, more diverse, then we can genuinely ask « Why didn't that happen before? ».

NARRATOR
01:31:22
Better than life? Pretty heady stuff... so let's keep our feet on the ground.
Xenobiology wants to reassure people by promising to make uncontrolled hybridization among modified organisms impossible... and claims there would be another advantage too: increasing the diversity of life-forms. But it still all remains to be proved...

GEORGE CHURCH
01:31:44
The beauty of biology is that it's complex at every scale, from atoms all the way up to ecosystems.
Every now and then you do need to simplify things briefly to do an experiment. But we're interested in generating diversity, not reducing diversity.
If the human population becomes too mono-cultural, if we're too much alike one another historically that's a risk. We can become extinct because we all have the same resistance or lack of resistance to infectious agents. So there is a great advantage of complexity and diversity...

NARRATOR
01:32:29
Evolving evolution, increasing diversity, using genomes from the past, industrially producing medicine or energy from living beings, creating organisms whose DNA is based on a new chemical formula...
The on-going revolution that George Church and Frances Arnold are talking about is developing everywhere, and so I prepare to continue my exploration of the USA and head for a tranquil residential neighborhood of San Francisco, in order to meet another ardent and tireless advocate of synthetic biology.
A number of questions are still intriguing me: how do engineers actually procede when they work on such complex organisms? And who had the weird idea of putting fur on my skate-board?

The man waiting for me here is a straightforward chat, and his candid observation, " complexity sucks", has upset many of those who accuse synthetic biology of wanting to over-simplify life.

DREW ENDY
01:33:26
My name is Drew Endy. I'm a bio-engineer at Stanford University.

IN 01:33:32
Charles: Hi!
DE: Charles! Good morning, how are you?
Charles: Good morning sir.
DE: Nice to see you. Welcome.

DREW ENDY
01:33:44
Synthetic biology for me is both a science and a technology

IN 01:33:50
DE: Let's see. Get this out of the way.

DREW ENDY
01:33:54
From a scientific perspective what we're trying to understand and discover how natural things that already exist work. We can learn by taking things apart and biology as a science has worked for a long, long time at taking things apart.

We can also learn by putting things together. It's very hard but you learn a lot by trying to put things back together. So synthetic biology is the science of learning by building and seeing what happens.

IN 01:34:21
DE: Let's see how it goes, huh?

DREW ENDY
01:34:31
I am an engineer. So I like to build things. And practically what that led me to as an engineer working in the science of biology, trying to understand how things work is, I could make predictions in my mind, using the tools of an engineer, how a natural biological system might behave differently if I changed it.

NARRATOR
01:34:54
Stanford University, where Drew Endy takes me, has one of the most renowned engineering departments in California.
The university now has a synthetic biology department too, a major achievement for Drew, a prominent figure in the battle for the discipline to be finally recognized. The premises are brand new.

DREW ENDY
01:35:16

One of the fundamental engineering goals in synthetic biology is to make biology easier to engineer.

IN 01:35:24
DE: go to the left!

DREW ENDY
01:35:27
How? We don't know.
Initially, we get our ideas by looking at the history of humans working with material and making things more engineer-able.
So if I'm in Segovia, Spain, and I look at the aqueduct that's over 2 000 years old. One of the things I noticed is they used standard rocks. They're square. They actually spent energy to make rocks that were easy to stack.
That allows multiple people to coordinate their labor. So they can anticipate what it is that they're building.

IN 01:36:09
DE: I'll show you one more thing…

NARRATOR
01:36:10
The idea of building with genes is not new.

IN 01:36:13
DE: Why don't we go see something else, huh ? We're going to go out here.

NARRATOR
01:36:19
From the early days of genetic studies, scientists sought to modify cells in order to give them useful functions. To manufacture insuline for diabetics, for example. But it was almost as easy as stacking rocks.
The challenges for synthetic biology, however, are much more complex: like building a bridge. And this requires a vast quantity of standardized rocks.
Step by step, Drew Endy decomposes the instructions that make up the program of a synthetic cell designed to treat a certain pathology.

DREW ENDY
01:36:50
Let's say I wanted do make a program like, you know for a cell that I might want to engineer to treat a tumor in my brain.
I'm going to need to put a composition into that cell which is of the following. Go into the patient, don't cause trouble, sample your environment, see if you can find these molecular signals that indicate you are near a glioblastoma, a brain tumor. If you find yourself in such an environment where multiple signals are present all together, execute a logic function known as AND, A and B and C must be present and if so, engage the capacity to proliferate, make more copies of yourself. Begin to invade the tumor.
While you're inside the tumor, make a therapeutic chemical. Meanwhile, every time you divide keep track of how many times you've divided because we don't want this therapeutic cell to divide too many times and become a synthetic tumor. And if you divide too many times then destroy yourself.

Wow, all of a sudden you can see this is a much more complicated composition than make lots of this drug. It's a whole character with a lot of sophisticated programming.
How do we do that?

NARRATOR
01:38:26
Drew Endy had the idea of working on standardization, by creating a kind of catalogue of genes that are useful and easy to assemble, depending on their functions, just like the standard rocks in Segovia.
Knowledge of such genes has greatly increased. Drew tells me that the cost of sequencing a genome has been divided by 10,000 in the past 10 years, and scientists have undertaken the systematic decoding of life-forms, trying to discover which instruction corresponds to which gene.

DREW ENDY
01:39:04
We are creating a new virtual organism in which parts are being brought from all over and we are figuring out how to make them composable with each other.
There's no doubt we're going to be able to do it. The question is how much work will it be.

NARRATOR
01:39:29
The sooner the better, perhaps, as there's a crying need for cells that can destroy cancers. But Drew Endy outlines the three obstacles that have to be overcome.

DREW ENDY
01:39:47
Number one, even for the best studied natural systems, when you look at the parts on the DNA, we only know about what half of them do for any organism.
It'd be like lifting up the lid in the trunk of your car and you'd look at the engine compartment. I don't know what half of those things do. And it's not just you as the owner of the car, nobody on the planet knows.

NARRATOR
01:40:12
It's true, many people don't know how a motor works, and yet they still drive. Scientists do the same thing: they use living beings, without fully understanding them.

DREW ENDY
01:40:25
The second thing that was strange was, when you look at how the components are organized. Like one part is connected to two functions. You might have the steering wheel for the car over here and then you'll have another wheel - it might be the radio volume knob.
And they're all separate wheels, and the wheel, when you turn it might also change the volume of the radio. When I go to change the volume on the radio maybe the steering wheel moves a little bit.

NARRATOR
01:41:12

And there's a third problem too: a problem of scale. On the scale of a cell, the laws of physic and chemistry - which determine the behavior and interactions inside each cell - are very different.
Scientists can therefore have to face rather odd and unexpected behaviors, known as emergence phenomena.

DREW ENDY
01:41:32
If you go and run off a cliff, do you fall down or do you jump and fly away?
This is a modest form of emergence...
In synthetic biology, there we are, we're trying to realize constructive emergence and prevent surprises that are destructive.
When I design a cell, I have to anticipate that it's capable of evolving which then begs the question "How would I like it to evolve?" And could I program its evolution? That's new.
If I wanted to engineer a system to not evolve, I'm gonna have to work against a lot of intrinsic properties of the material.

NARRATOR
01:42:36
Working against nature... does synthetic biology really believe that anything and everything is possible? And Drew Endy doesn't dodge that question.

DREW ENDY
01:42:48
We, as humans, as we continue to learn more about nature, including biology, what should we be doing?
What's our plan, how do we make this all work? How do we make it safe? How do we make it secure? How do we keep being human?
I think what's honestly missing is thoughtfulness. A different way I think about it is what I call … skate-boarding, a half-pipe, where a skateboarder in a half pipe will go back and forth, and a lot of the early buzz in synthetic biology is we're gonna save the world, no, no, no, we're gonna destroy the world, no, no, no, we're gonna save the world and I call this the half-pipe of doom.
We're growing something that will be very, very big, and everybody should have a voice on that.

NARRATOR
01:43:39
If you ask me all I can say it that synthetic biology is responsible for a few bruises and sore muscles.
As for the political and social issues raised by synthetic biologists, I wonder if it's a real case of soul-searching or merely playing to the gallery.
I need an expert's view on these ethical questions. And I have an appointment with one at a castle in Germany, a place that inspired one of the most enduring myths in bio-engineering.

LAURIE ZOLOTH
01:44:22
My name is Laurie Zoloth, I am a professor of bioethics, medical humanities and religious studies at Northwestern University.

IN 01:44:33

*Charles**:** Hi Laurie. So here is the Frankenstein castle*
*LZ**:** Yes, it is. With its towers pointing to the sky*

LAURIE ZOLOTH
01:44:50
What's interesting to me is that synthetic biology has a way of seeing the world, that the world could be a series of choices.

IN 01:44:59
Charles: question of direction… we have…
LZ: the first obvious one
Charles: This one or this one… I think I'm gonna choose this one
*LZ**:** I like this one*

01:45:12
And, of course, as a moral philosopher, everything I see, every act is a moral gesture.

NARRATOR
01:45:19
Laurie Zoloth underlines a key characteristic among scientists working in synthetic biology: just like Drew Endy, Frances Arnold or George Church, they all have the same scientific background, which conditions the choices they make.

LAURIE ZOLOTH
01:45:33
People who work on synthetic biology, more than half, were trained as engineers. And the discipline of engineering is different from the discipline of the basic biological scientist whose inquiry is 'how does this work? An engineer is trained to make something, to make a bridge, for instance, and not really think 'who's gonna go over this bridge? 'is it an army? Right? is it a caravan for food?', it's just 'will the bridge hold this amount of bearing weight?' What's important is efficacy.

NARRATOR
01:46:08
Laurie Zoloth also points out that most of these synthetic biologists are from: North America. Is this a coincidence? Is technology less frightening in the US than elsewhere? There may well be a cultural factor to take into account here.

LAURIE ZOLOTH
01:46:22
People I think are optimistic about science in the United States. I think, I think the American idea that you can fix something, that technology makes things better and not worse, is a powerful idea for us.
You can point to failures in science. But by and large, you should be optimistic about the fact that scientists actually made our lives better. We live longer, our children don't die of terrible infectious diseases, our water is cleaner.
And that use of science to make the world a safer world, a cleaner world, a healthier world, has got to be applauded. You can not always be suspicious. BUT it is always possible that the entire project is a failure. That's what makes it science, by the way.

NARRATOR

01:47:13
I'm constantly surprised by the extent to which North-Americans manage to remain positive, even in the face of failure. So how do they do it? Laurie has her own thoughts on that...

LAURIE ZOLOTH
01:47:24
This has to do with the history of American pragmatism, a uniquely American way of thinking about problems. And especially by the way about technology.
Americans, after the Civil war, were faced with the carnage of what it looks like when you have a huge fight about ideologies.
And so it created a willingness in American philosophy and for Americans generally, which is 'Let's not start with principles', and try out empirical solutions to see how we go.

NARRATOR
01:48:10
American pragmatism therefore functions like this: first of all you build something, then you test it as you go. Problems are solved as you advance, not beforehand.
Trial and error is the fundamental approach to synthetic biology.
01:48:37
Of course, Laurie is just like anyone else. She's concerned about scientists working on dangerous bacteria or deadly viruses. What’s more, she's worried about something much more basic.

LAURIE ZOLOTH
01:49:02
What's interesting about synthetic biology that’s really different from genetic engineering is this one ontologically different part, which is - you could possibly make something that did not exist ever before.
You could be the generator, the creator of a new entity that has just doesn't exist.
It pulls us right into the Mary Shelley story, Frankenstein's monster. Mary Shelley writes that story after the loss of actual children, one after another. And she yearns actually for a doctor that could overcome death.
01:49:56
Doctor Frankenstein needed more than an ethics course, he needed the unfailing commitment to always love and care for his creature. That’s the part we have to pay attention to. You should make things that you have responsibility for.

NARRATOR
01:50:12
So, scientists around the world: be responsible. This is Laurie Zoloth's leitmotif. She doesn't want to leave them alone, she wants to help them, and accompany them.
She travels the world, from one conference to the next, to raise awareness among scientists, and those who fund them.

LAURIE ZOLOTH
01:50:28
They're responsible for their mess. Completely responsible. Utterly responsible.
If you spill oil in the Gulf then you have to stay there until it's clean.
Unless we're sure that people will stand by the messes they make, then we have failed in our efforts. So can you set up an education for them? Is it possible for them to understand the power that they have and to really learn to self-regulate it.Accident will happen? of

course accident will happen. There is no question that there will be accidents, there will be mistakes, there will be failures, and there will be accidents because again it is not a certainty, it is just science. Are we ever ready for mistakes?

NARRATOR
01:51:16
As they regard living beings in a radically new way, assembling their parts like building blocks, and modifying them at will to be more useful and profitable, engineers inevitably arouse a curious sentiment, combining fascination, enthusiasm, and concern.
I can see that some of my own fears, as Laurie Zoloth emphasizes, are legitimate, but others often come from my lack of understanding about what synthetic biologists are actually doing: what are their methods? What are their aims and ambitions, and what applications are they working on? How will progress in computer technology help them to dream of ever-more original creations, which could profoundly change our daily lives, in terms of health-care, energy and basic materials?
This is what I shall discover as I set out to meet other bio-engineers, scientists of a new type, often a new breed of audacious entrepreneurs.
My journey to explore the world of synthetic biology has only just begun.

END CREDITS 01:52:12