

CURIOSITY-DRIVEN RESEARCH

Keynote by Daniel Zajfman, Berlin, 9/11/2018

Thank you very much for your kind words. And thank you very much for inviting me to this impressive meeting and to the impressive Helmholtz Association. The Weizmann Institute has many ties with the Helmholtz Association. And given the relative size of the Helmholtz Association and the Weizmann Institute - which you might know is a very small institute - and the fact that you're still taking new members, maybe you should take this one as well? That would actually add something to you. I would not be against it, actually, given the value and the quality of the Helmholtz Association.

What I would like to talk to you about is the strategy of scientific research. When we are running scientific institutions, and also scientists, we always have to ask ourselves, "Where do I put the emphasis?" Or for those who are holding the money, "Where do I put the money?" How do I invest so that scientific research will move forward one way or another, for something we all want, which is for the benefit of humanity, ultimately? Because this is really what scientific research is all about: for the benefit of humanity. There are of course many strategies, and if we needed to decide what topics to invest in, I don't think we would agree because science can touch so many issues of life from disease, technology, ecosystems, climate change, and so on. There are so many topics in which we could actually make a difference, that if you had to decide in which topic to invest, I don't think we could get a group of people sitting around a table to all agree on one single topic. That of course is the privilege of countries and associations to make their own decisions. But what I'd like to show is that there is always another option. An option that has existed for hundreds of years and somehow has been pushed aside for the last, I would say, few decades or so. And that is curiosity-driven research. The one where we don't try to

choose a topic, where we don't try to choose a science, but where we choose a scientist. And I want to remind all of you that ultimately scientific discoveries are not made in the lab. They are made in the brain of the scientist. That's where things happen.

So the title of my talk is "Curiosity-Driven Research". The question mark of course is: Is that really a curious strategy? Just to remind you how good we are at predicting the future of technology, I want to remind you for example that in 1895, a very famous physicist made a very strong statement saying that, "Heavier-than-air flying machines are impossible." That was of course a few years before we had airplanes. And a little earlier, if we really talk about even today's technologies, Ken Olson - who was the CEO and chairman of a very famous company that was competing with IBM at the time, Digital Equipment Corporation - said that there is no reason anyone would want a computer in their home. That was in 1977, I had a PC in my office in 1983, six years later. This is actually the reason that company disappeared. And, of course, I could quote a lot of these sentences showing you that it is not only hard to make predictions about the long-term future, but as you can see, even short-term. Think about the internet and think about 1990. Did someone really know that the internet market would be billions if not trillions of dollars today? Actually nobody. So it's very hard to make predictions, and the question is: If it is really hard to make predictions, then how do we invest? How do we make decisions?

I just want to remind you a little bit of how scientific research basically works. In a very simple way, and it's oversimplified of course, but just to make it clear. Usually ideas start from scientists who are very passionate about some topic of scientific research, and their goal is to fill the bucket, what we call a reservoir of knowledge. This is what all scientists are doing. They are publishing papers and they add to the knowledge, universally speaking, because anyone and everyone can read these papers. Then usually, when the bucket of knowledge is being filled up - and it's not by one scientist but usually by many of them contributing to the same bucket - these things will move to the market and someone else - not usually the scientist, but someone else in the market - will think that these ideas are quite good. There is even a market for it. Why don't

we change and use these ideas to make them something which can be useful for, as I said, for humanity, and creating a market or answering a problem and providing a solution for the market. And that of course leads then to many products we know today. If you really think about the history of the last hundred years, perhaps even thousands of years, there are very few things that we as human beings have done, but scientific research has changed so much the way we are living. Think about how we lived thousands of years ago and how we live today. And you realize it is because we as human beings have been wise enough or smart enough or curious enough to understand what this world is made of and to engineer it in a way that would be useful for us. That is what scientific research is all about. The question is: What drives the initial scientific research at the very beginning so that we can really create a market? What I would like to show to you is that the most important tool we have is - curiosity. Because as I have shown to you, it's very hard to make predictions.

I'll start by just showing you some examples. But again, I like to be very precise about what I'm trying to do here. You might remember this famous gentleman [Donald Rumsfeld]. He was not a scientist, just to remind you. But he made a very famous statement about something unrelated to science. He said, "There are known knowns. There are things we know that we know." That's also true in science: "There are known unknowns. That is to say, there are things that we know we don't know." For example, what's dark matter? We know it exists, but we don't know what it is. "But there are also unknown unknowns. There are things we don't know we don't know." The question I'm going to ask is: How do we discover things we don't know we don't know?

Let me give you some examples of what I'm talking about. So here's a discovery that was made in Germany more than 150 years ago. X-rays. I'm sure you all know what X-rays are. They're very useful. But I want to remind you that X-rays were not discovered because there was a program. What kind of a program would you establish back in 1875 if you don't even know that X-rays exist? How do you make a decision to invest money in something that you cannot even dream exists? You cannot dream in 1875 that radiations can go through your body and make pictures of

your bones on a piece of plastic. So what's the program? How do you invest? So just to remind you, this gentleman, Röntgen, back then was doing very boring experiments, the kind of experiments that probably nobody would invest in today. He was basically measuring the current between two electrodes in a flask of gas. He was producing graphs that were quite boring. There was no interest in it. But then one day in his lab, he found some light on the wall, some scintillations, and he was curious enough to ask the question, "What is the light on the wall here?" I want to remind you that these kinds of experiments were made for more than 20 years already. He was not the first one to make the experiment. But he was the first one to be curious about it - not the result of his experiment, but what was happening in his lab. And then he did something that as you know all men do when they don't know what is happening: he called his wife. And she put her hand on it and that's how we got our first X-ray. You can see the wedding ring of the lady here. Now, remember, there were no programs here. There was no way to set up a program that would make that discovery. You could say it's lucky. Well, I'll show you that being lucky is actually a talent. It doesn't happen to everyone. So the point that I'd like to make is that there are no scientific strategies or scientific programs to discover X-rays.

Let me show you another example which is a bit more cumbersome but you'll get it. I'm sure that at least those who are not from Berlin, people like me, have been using GPS to come here. It's a very easy tool, you put in the address and it drives you all the way. For you to understand the technology of GPS, you might know it's based on a lot of satellites that are orbiting around this planet, more than 35, to cover the whole planet. Inside of each of these satellites, there is an atomic clock. The first atomic clock was developed in 1955. In order for the whole system to work, we also need to understand magnetic resonance, which was discovered in 1945 by Isidor Rabi. And your GPS would not work, it would give you the wrong position, if it wasn't for the theory of relativity of Albert Einstein in 1905 and 1915. That's all fine. That's backwards. When we look back at the history of science, we're all very smart. Here's what we need: we need the atomic clock, we need magnetic resonance, we need relativity ... But let me ask you a question.

Do you know the way forward? Could you actually guess in 1905, from Einstein to go to Isidor Rabi, from Rabi to go to the atomic clock, for the clock to go to GPS satellites, and the GPS satellites to go to your GPS device? There is no track like this. Nobody has ever started with the theory of relativity to have your GPS working. And Einstein of course didn't even drive a car. So there's just no way to make a prediction here. It took more than a hundred years for a beautiful - but some people would call it useless - theory, the theory of relativity, to actually become a market of billions of dollars. Yes, it takes a long time. But without the theory of relativity, all GPS would not work. And I want to remind you that the theory of relativity was not the solution to any problem. It was just the curiosity of some physicist who was very curious about the universe and tried to understand what it is made of and how it works. And all that led to something we use today, easily, and of course makes our lives way better.

The last example, and then I'll go on. Electricity. If we would have been sitting here 200 and some years ago ... Well, of course there would be no projectors, no microphone, but also no light. And in any room that we would have been sitting, there would have been a lot of candles. About 200 years ago, actually mostly in the UK but also in Germany, there was a lot of R&D for candles. People were investing a lot of money to get better candles, producing more light, different colors, different perfume. Cheaper ones or expensive ones. A lot of R&D, and there were a lot of discussions. You can read about it. About how one should invest to get a better candle. Then came this gentleman named Michael Faraday and he invented electricity. Now I want to remind you of something. It doesn't matter how much money you're going to invest in developing new candles - you will never get electricity. The solution to your problem is not always where the problem is. It can be in a different place. If you look at the history of science, and here I have really looked into the details, you'll see that in fact the vast majority of major discoveries that really changed our lives were never made by people who were trying to solve a problem. This is not the story of science. Science is about curiosity and an open mind. That's

how it all happened. Truly, it took many years for all of these ideas to get on the market. But these are the ideas that really changed humanity.

If you think this is all history, then let me show you some statistics about today's drugs. Here is a paper which was published in "Science" about the fundamental science behind today's important medicine. These gentlemen, these scientists went back to look at the source of the ideas of the most important drugs. And I'm going to show a list of 28 drugs on the market. A market of billions of dollars today, but more importantly, saving the lives of millions of people. Here's the list. In the first column is the name of the drug. And in the second column there are 28 drugs. This one shows you if the ultimate discovery was part of a basic discovery program. And the answer is that out of 28, 23 were found in basic discoveries. Namely, people were not actually trying to create a drug, but rather to understand how the disease works, and perhaps not even the disease, as you'll see. The third column shows you if it was actually a program which was disease-oriented. And what you find is that out of all of these 28, 16 were actually fundamental research and were not focused on the disease itself. Then if you go to the fourth column, you'll find that 23 of these were not part of a drug discovery program either. And even more, you'll find – and that's of course where the problem is, perhaps – that the time between the basic discovery and the market is, on average, 25 to 30 years. Can we make it shorter? I believe we can. How can we make it shorter? Invest more in curiosity-driven research, because this is where a lot of the time is being spent. Of course, the other part is spending on clinical trials which is another business and that's of course more for the applied part of science. But I also believe some changes need to take place. Even in the modern world of today, where we really try to solve the problem of finding a drug for Alzheimer's, perhaps the solution is not in the hands of those who are dealing with Alzheimer's, but just like the candle and the electricity, it is on your neighbor's table. It is somewhere else that we need to look. Not under the light, but perhaps in the dark. In the unknown unknowns.

So, scientific strategy? Let's put it this way: I'm a scientist and I can tell you: Scientists, and I believe also governments – sorry to say that – are very bad at looking into a crystal ball and trying to determine directions. And if we do it, we actually already know what the answer is. When we start looking at the scientific strategy, we already know what's out there. But to really find the truly original solutions, it is going to be mostly curiosity which will help us. And in scientific research, as I said, strategic paths, if they exist, should provide a compass but not control the journey. I know you lost in the football tournament last time. So I'm just showing you the tactics ... [Zajfman grins]. I knew this would wake you up. Science is one thing, but I learned that football in Germany is something which everyone loves. So you could see the strategy was fine, but if you don't have the right players, you're not going to go very far, right? That's the issue. Same thing in science.

So, if there's no strategy, how do you create new and valuable scientific knowledge? As I said, there's a very simple strategy to do that. The first and most important thing is to hire excellent scientists who are knowledgeable, curious, and passionate about their own ideas. Not about the ideas of the president – about their own ideas. Not about the ideas of the institute – about their own ideas. The second thing is to offer them top-quality human and physical infrastructure. There's no science without microscopes, sequencers, and accelerators ... The third part is to provide them with the opportunity to take risks, which means failing a lot. And fourth, protect their freedom to think. This is a key factor and perhaps the most expensive one. So that's how we've done things at the Weizmann Institute for the last 70 years. We basically invest in excellent people with excellent ideas. We are purely curiosity-driven. And we hire scientists with four very important qualities. They have to be knowledgeable, but not too much because scientists who know a lot can sometimes be a problem. Because they feel like they know everything. And if you know everything, then there are no unknown unknowns, right? And that's not true. There are a lot of unknown unknowns. As a physicist I do believe that there's much more we don't know that we don't know. I can demonstrate it to you. The universe is 100%. We

physicists know what 4% of it is. 96% is dark matter and dark energy, think what we have done with 4%, think what we could do with 96%. So that's very simple, right? But knowledgeable is important but not that much. Secondly, they have to be very curious, because that's what takes your knowledge into the minefields where things are dangerous and risky and failing. They have to be passionate because it is difficult. Because it's going to take time. And only passionate people would spend 30 years of their life focused on an issue which might not actually succeed and seems to have no application today. And last but not least, they have to have the talent to be lucky, which we might think is not a talent, but we all know that some people are luckier than others. Like Röntgen, it's not a matter of being lucky, it's a matter of having an open mind and what we call recognizing opportunities. Which is sometimes one of the most important things we can do as scientists: recognizing opportunities happening in our lab in what we are doing.

The Weizmann Institute culture is basically based on what I said: the fact that excellent people require an environment that is just as good as they are. You cannot hire outstanding people without providing the right environment. Discovery is like learning, it's a phenomenon that takes place in the human brain. It doesn't happen in the lab. It's not because you have the best microscopes in the world that you're going to make the best discoveries. Microscopes are nothing, it's only the brain that sees something. And last but not least, what you have to do is get the platform for scientific discoveries and breakthroughs. Such a platform is the Weizmann Institute, where you have the four basic sciences: mathematics, physics, biology, and chemistry, with mathematics including computer science. Put them together so that you have an embedded multidisciplinary approach. Then create a framework with high-level education programs because one goal of scientific research is also to educate future scientists. These are all students and postdocs. And embed everything into a very strong intellectual property and technology transfer and I'll show you the results of it. The Weizmann Institute today has 250 research groups, 4,000 individuals including our students, and a budget of about 420 million dollars operation. So that's what I said could become a little partner to the Helmholtz Association.

What people ask me then: "If it's all curiosity research, then what is the role of the industry?"

There is a very important role. All that I've described today, or so far, is about creating ideas. But someone must take these ideas and transform them into an application. And that is in fact the role of industry. And as far as I'm concerned, and as far as the Weizmann Institute is concerned, we make a big difference between the role of academia and the role of industry. In a very simple term, we believe that the university should transfer money into knowledge. End of story. And we believe that industry should transfer knowledge into products, market, and of course more money. And so as far as the Weizmann Institute is concerned, we produce knowledge and then we really transfer the knowledge to the industry. We never create any company, we don't create startups, we don't create industries, we don't sit on the board of any company. We are scientists, and the goal and the job of a scientist is to create new scientific ideas, and the goal and the work of industry is to pick up these ideas and to transform them into products.

Does it work? Well just last year, "Nature" produced an index of the most innovative institutes based on research for more than 30 years. And this is the ranking of institutions worldwide for the last 30 years – so it's not just one year because ranking for one year doesn't mean anything in this business – that have provided the most insight into new ideas that have made changes in science and technology for the last 30 years between 1985 to 2015. And among the 10, actually first 15 institutions in the world, the Weizmann Institute is number six. And all that we do is curiosity-driven research, and fundamental research, and basic science. That's what we do. We never create a single product. We only provide the ideas. And you can see how much an impact this can have for the benefit of humanity, which is what scientific research is all about. How do we do that? As I said: Hire the best scientists, create the needed infrastructure, and provide the scientists with the freedom to think. That's what we have been doing for the last 70 years.

Does it really work? I know people like numbers and that at the end of the day they like to say, "Okay, it's a nice story, (but) for the last 70 years, what have you done?" Well, here's a graph. This is the sales of products, 35 billion dollars last year, 2017 is about the same as in 2016. This

is the sales of products worldwide, of all products based on license agreements made by the Weizmann Institute and companies worldwide. 35 billion dollars of products. That's not bad for "no strategy". And not bad for a curiosity-driven strategy. Of course, this is not the money that the institute is doing. That's the money that the industry is doing. We do get our royalties. It's fine, we are good at it. But most important for us is not the money. Not the money that the companies are doing and not the money that we're doing. But the fact that we have succeeded, through curiosity and fundamental research, to impact the world in a major way. Because I think that's really what, I say that again, the role of science is all about. We know how to provide knowledge, and industry knows how to transform that knowledge into money.

So let me finish by going back to the question that everyone has been asking me for the last 12 years that I've been the President of the Institute. What will be the next scientific revolution? And I always answer the same thing: I have no idea. I just don't know. The only question I can really answer is who will make the next scientific revolution. This I know very well because it has been shown for hundreds of years: The next scientific revolution will be driven by scientists who have a multidisciplinary view of science, the opportunity to take risks, the infrastructure to work, and the freedom to think.

Thank you very much.