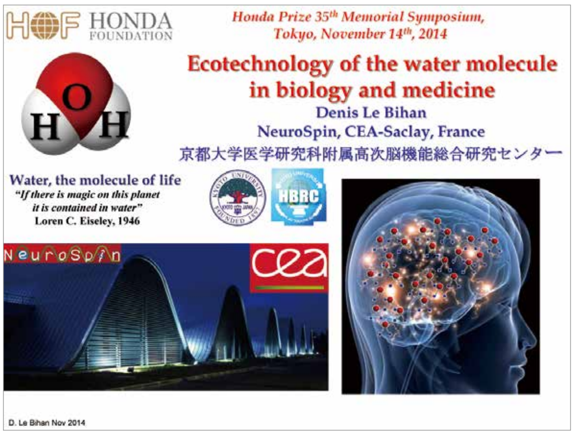
Dr. Denis Le Bihan

Born in France in 1957.
The 33th Honda Prize laureate in 2012.
Director of NeuroSpin, CEA Saclay, France

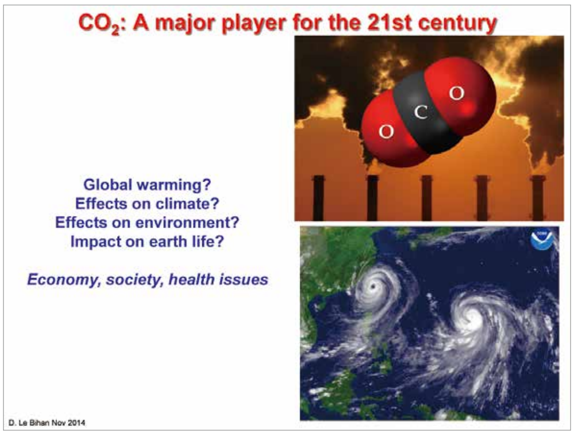
Life Frontier

Ecotechnology of the Water Molecule in Biology and Medicine

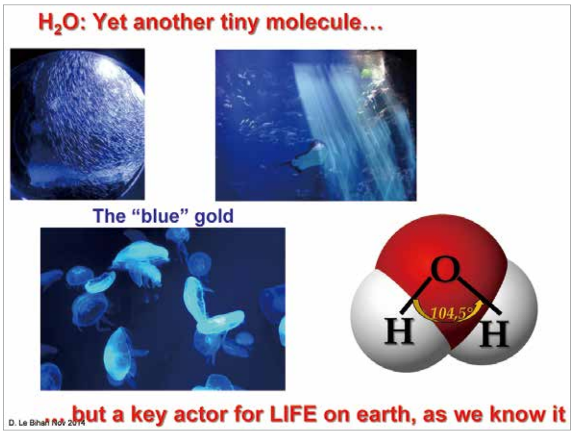


Thank you very much. Good afternoon, and it's a great honor to be with you today. I'm very, very thankful to the Honda Foundation for inviting me again to share with you some of my views about how I can see the future regarding eco-technology.

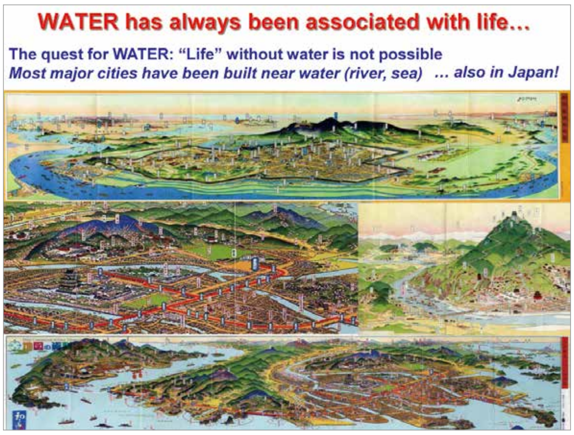
As you know, we are doing a lot of thinking about a tiny molecule, CO_2, because of the predictions of global warming, the effects on the climate, the effects on the environment, and so on. Of course, these changes in the climate also have very large consequences on water, for instance, typhoons, and that's what I'd like to show you today.



My talk will focus mostly on this other tiny molecule, H_2O, so just water, the "blue gold" as we know it, which is of course very beautiful, and I'd like to remind all of us that water is really a key actor for life on earth as we know it. And I'll show you that it is even more important than what you think.



Water has always been associated with life. Without water we cannot have any life, as we know it today at least. And most of the cities in the world have been built next to water like rivers or seas, and of course, Japan is no exception.

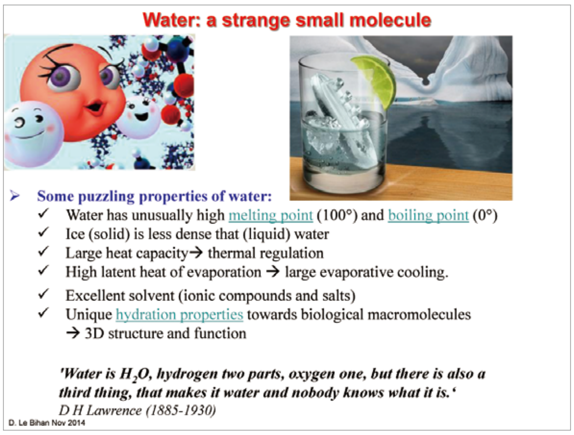


Unfortunately, water may also be associated with death, for instance when we lack water, and this is of course, terrible but that may happen in the future if we don’t pay attention. Too much water is not good either, for instance, tsunamis and flooding, and water, although it is a very small molecule, has a lot of power and can cause mechanical destruction. So I think that while CO_2 is very important, H_2O might play a bigger role than CO_2 in the current century and people may fight to have access to water.

But maybe not all waters are equal. I’m lucky to live sometimes in Kyoto, and Kyoto’s water is very important. In Buddhism water has a sacred value, but I think that this is not by chance. Most religions have incorporated water into their thinking, probably because humankind has to have a very strong connection to water. And, of course, Kyoto water is so good that we can make beautiful Kimonos and we can make good sake. So I guess now you are convinced that water is very important.

Water is a very strange molecule. It has very interesting properties that cannot be completely explained today. Of course, you know very well that the temperature for water to boil is 100°C and for freezing it’s 0°C, but I’d like to point out something very special: ice floats when really it shouldn’t. For other molecules, when they become solid they drop to the bottom of the liquid.

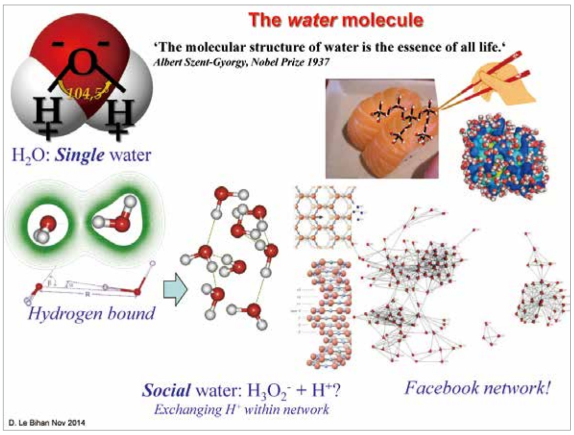
Unfortunately, this is responsible, for instance, for tragedies such as the Titanic, which was a big tragedy, but it also explains why ice floats on your whisky. Why is that? It’s not clear.



Another very important property is that water is very helpful to control temperature. This is why we sweat a lot during the summertime and this is why babies are so sensitive to heat because they have a large surface and they have evaporation, which could be dangerous for them if it becomes excessive.

Water also is very important if we consider all the molecules we have in the body such as proteins and other macromolecules. The shape of these molecules comes from their interaction with water.

These are the facts we know, and we also know that water is H_2O, two parts hydrogen and one part oxygen, but D. H. Lawrence said that there is a third thing that makes it water, but still we don't know what it is, so I have to say that the water molecule itself remains a mystery.

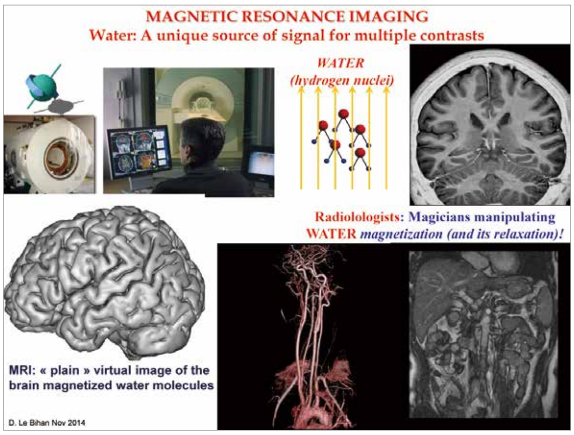


Let's see in more detail what the water molecule is about. Again, one oxygen atom and two hydrogen atoms. I call it a single water molecule, but this is dynamic, everything is moving all the time. Let's take sushi for instance. If you press sushi with chopsticks water will come out even though the fish is dead and even if it is very fresh sushi. How is that possible?

Well we have to remember that there is what we call the hydrogen bond. Water molecules are sticky, not only between themselves, but also to the proteins that are present in the fish, so all those molecules of water are always bound to other macromolecules. This is very crucial to explain life as we know it. Without those hydrogen bonds, without the special angle, 104º, between the two hydrogens and the oxygen there would be no life on earth.

But water is also social. A single water molecule doesn't exist. Water molecules have to be related. They have to communicate. They are organized like that and if we take now the statistics supporting those networks, water may not be H_2O anymore. Some physicists think that we may describe water as H_3O_2 because the molecules are sharing hydrogen atoms between themselves. If you look at the Facebook network and the water network, you can see some analogies, so we have to consider that water in tissues is organized as a network.

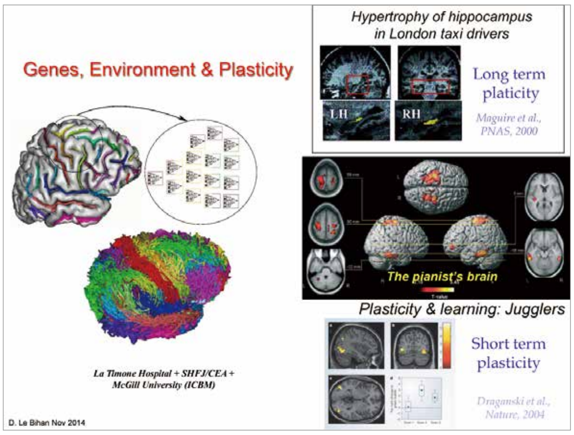
We should also never forget that we are water. Sixty to seventy percent of our body is made of water, and 75% of our brain, maybe 80% of our brain, is just water, so we think with water, and that's what I'd like to show you soon.



Let's go to my own research, which is using magnetic resonance imaging to investigate the human body and especially the brain. Magnetic resonance imaging, or MRI, uses a very strong magnet and with this magnet we will magnetize water, or more precisely the hydrogen nuclei of the water molecule, but let's say water.

This is, for instance, a slice of the brain (upper right/previous slide), a vertical slice of one of my colleagues who is very much alive, very healthy, and you can see beautiful contrast between the gray and white matter, you can see some details such as vessels, and all of this comes from the magnetization of the water molecules, which is different between grey and white matter. Why? We have no idea, but it's beautiful.

With MRI technology we can see the vessels coming out of the heart and going to the brain, we can see what's going on after we have a meal with digestion and so on (lower right/previous slide), and, of course, we can see beautiful images of the brain (lower left/previous slide). But this is not a brain, this is an artificial brain, it is a virtual brain, sometimes I call it an avatar of the brain, but this will give us many, many details about how the brain is made.



Let me give you some examples. Our brains are very similar. There is only one humankind, so all of our brains are about the same. But if you look at the details, look at this red line here (left figure), which is the limit between areas linked to the motor system and areas in the back linked to how we sense things, for instance when we touch our fingers.

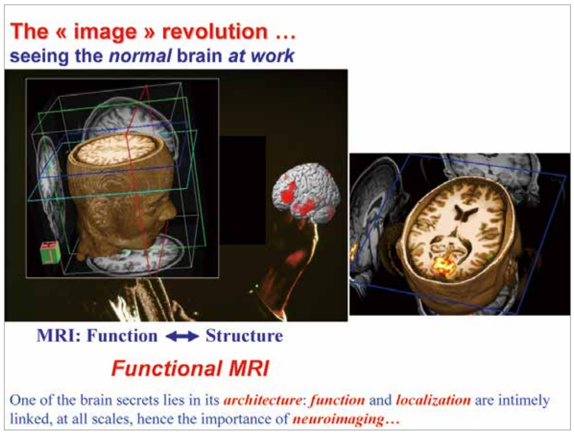
Everybody has such a structure in the brain, but the location, the exact location, and the exact shape is highly variable. So what I want to say is that we make what we want of our brain.

If we look at the hippocampus, a very small area we have in the brain, well, it's not that small, it is linked to memory. In fact, the Nobel Prize in Medicine this year was given to the people who discovered that. If we look at London taxi drivers, who are very good taxi drivers, Japanese taxi drivers are very good, also, but the study was done with English taxi drivers, they have shown that the hippocampus is bigger in size in taxi drivers than in normal, non-taxi driver people (upper right/previous slide). Just because taxi drivers use their memory to navigate, they have increased the size of their hippocampus.

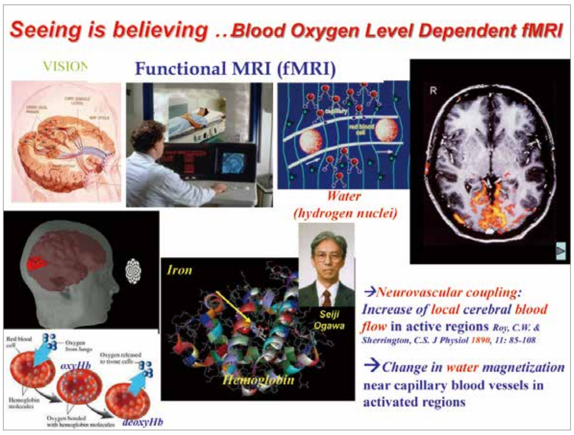
Pianists also. Pianists and other musicians also have over-developed regions of the brain, which are, for instance, used for coordination between the hands (right center/previous slide).

This plasticity is occurring very fast. In this example here, young people, students, were taught how to juggle every day for 10 minutes (lower right/previous slide). After just a few weeks, we can see that some parts of the brain are developing because they have to make an effort about spatial localization.

And this is going on all the time. I'm sorry to say that at the end of my talk I will have modified your brain a little bit, and I will have modified my own brain because there is already some interaction going on.



This is about the shape and anatomy of the brain. Now we can do even more and that's what I call image resolution. We would like to see what's going on in our brain when we think. In fact, we know very well that there is a link between function and localization. Each part of our brain is dedicated somewhat to a function, so if we can image the brain and see which parts of the brain are activated, we will have some clues about what the brain is doing.



With MRI it's possible to do that now, to look deep into your brain without any **invasive techniques***, without any surgery, just normal people can go to a magnet and we can discover many things. This is called functional MRI.

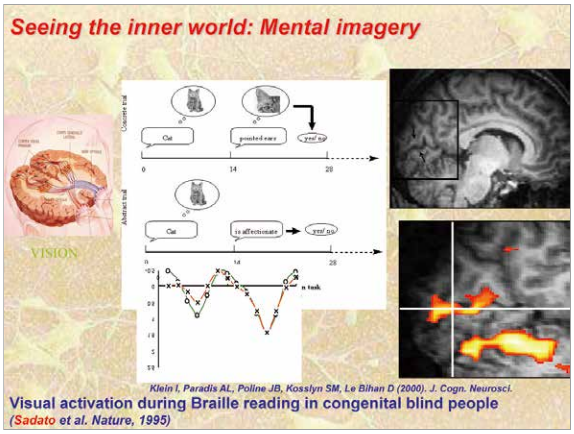
* Any surgical or exploratory activity in which the body is pierced by a device or instrument

When you look at this screen, the image comes from your eyes to the back of the brain and then it is shipped to the front part of the brain so that you can recognize what you have on the screen. Prof. Seiji Ogawa, a good friend of mine, developed a method to do that. Let me explain briefly what it is about.

We know, and this was known back in the 1880s, so a long time ago, that in the regions of the brain that are active, there is an increase in blood coming up. There is more blood in activated regions. Now, blood is red because there are red blood cells inside the blood, and red blood cells are red because inside there is a very important molecule called hemoglobin.

Hemoglobin carries oxygen from the lungs to the tissues, not only the brain, and the hemoglobin molecule contains an atom of iron and, as you may guess, in the strong magnetic field of the magnet this iron atom can be magnetized. So it's not only water but also iron.

So in brief, the small vessels we have in the brain have to be seen as containing tiny magnets. The red blood cells could be seen as tiny magnets circulating in the small capillary vessels. The water molecules that are there will sense the presence of flowing blood, so in the regions that get activated there is an increase in the blood flow and this will translate into a tiny change in the magnetization of the water molecules, which we can detect with MRI and sophisticated algorithms.



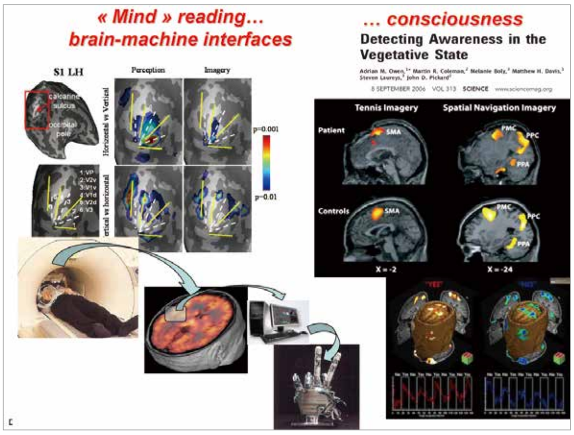
So let's do a simple experiment. If you close your eyes, and you think about a cat, you see a cat in your brain somewhere, but my question is where is that cat? There is no real cat and my question is whether the regions of the brain that are used to see the real world also used to see virtual images?

So I did this experiment. Here you say to somebody in the magnet of the MRI system the word "cat," you can say it in Japanese, it works also, and they have to think about a cat. Forty seconds later a question, "Are the ears of the cat pointed?" and they have to think again.

This is an image of the brain (right/previous slide), this way, and the back here is the visual cortex, the region we use when we see the real world. What we see in our images is that when we just think about a cat, there is a change in the magnetization of the water molecules. Thinking has an effect on the magnetization of water. This is huge.

The reason, again, is that there is an increase in blood flow in this area because it has been used by thinking of an image. So what we showed in this very simple experiment is that looking at the real world or looking at the inner world shares some networks.

Next, Prof. Sadato in Okazaki, at that time he was in the United States, did an experiment where he asked people blind from birth, people who have never been able to see, to read braille with their fingers, and he discovered that by reading braille those people were activating the visual cortex.



So it's fantastic. That means that even if you don't use your brain as it has been designed, you can somewhat use it in a different way. In fact, my own view is that there are some circuits in the visual cortex that are shared by real vision and virtual vision, or reading braille. Reading braille is just connecting dots in space to recognize letters so it's a visual function and we can say from these experiments that blind people can see with their fingers.

But we can do something even fancier. If you think about an object, for instance, vertical or horizontal, we have to consider that at the back of the brain we have a direct projection. Of course, it's distorted, but if you see something vertical you see for instance that the regions that are activated have this shape, while if you see a horizontal object, the regions are a little bit different (upper left/previous slide).

Now if you ask people to think of a vertical or horizontal object, you can read their mind by looking at the images. For instance, here, this person is thinking about a horizontal bar. Here, this person is thinking about a vertical bar. And nowadays we can even ask people to think about letters, "H," "E," "L" and so on, and we can decode that this person is saying "Hello." So this is where we are now.

You can even measure signal activities in the brain to drive robots. This person here is playing this famous game in Japan, well, not only in Japan, but rock-paper-scissors that children like to play. He is moving his hand or just thinking about moving his hand without moving at all and the computer will pick up the signal in the motor areas, decode the signal, and send some electrical current to tiny engines in an artificial hand. And you see at a distance, it could be 1,000 km away, a hand moves just driven by the thought of the person in the magnet (lower left/previous slide).

Even maybe more challenging is this story of a young lady, 26 years old, who is in a vegetative state after a car accident. Of course, there's no reaction when you pinch her, nothing. When you ask her "What's your name?," nothing. So the group of Dr. Owen said let's put this lady in the MRI machine.

They asked the lady, "What's your name?" and there was no response; however, the MRI images showed that the regions of language, like the Broca area, light up, meaning that this lady in a vegetative state was understanding the question and was even responding to the question.

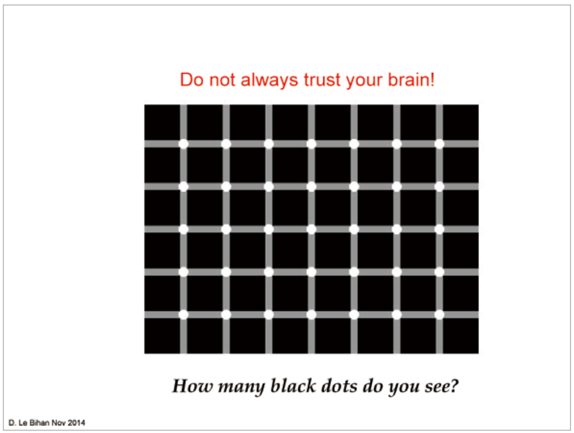
So they were very, very intrigued and said, "Could you think that you are playing tennis?" and of course the lady did nothing but they saw a response in the regions of the brain that are activated when a normal person thinks about playing tennis (right/previous slide).

"Madam, could you think that you are moving in your house and exploring the rooms?" Again, no response; however, the MRI images showed that the regions that get activated are the same as those that a normal person would activate by doing the same thing.

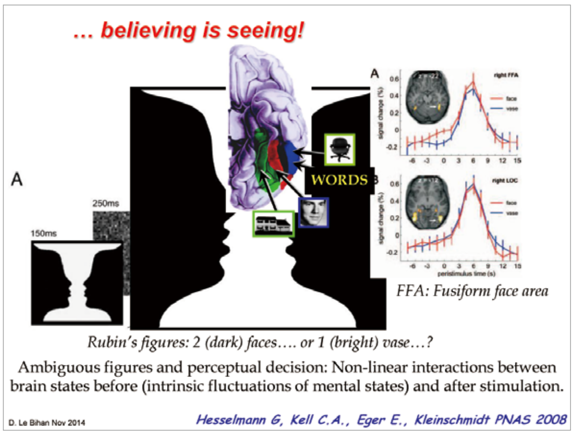
So basically, some communication was possible in this lady who was in a vegetative state. Today, it has been shown that about 20% of people in such vegetative states are in fact able to communicate thanks to this kind of experiment.

Today, we can use even EEG (electroencephalogram) just to pick up signals on the surface of the skull, so there is no need for MRI. So I think that's where imaging is driving us.

However, our brain is like a piece of software, I will not name any names, but with bugs. Here you will probably see dots that are black but in fact there are no dark dots on the image. This is an artifact created by your brain, so we are not perfect. This is also very famous: you can see a vase or you can see two faces, right (next slide)? How do you decide what you want to see?

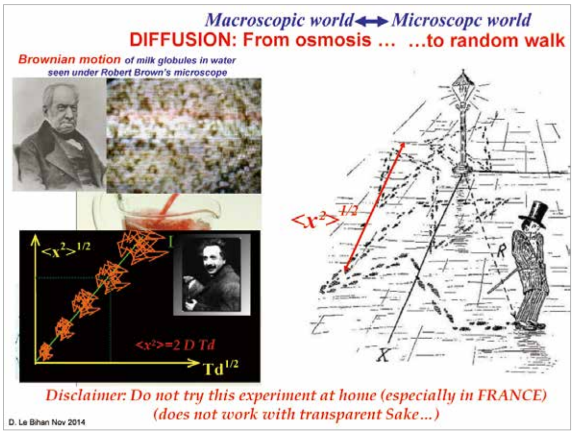


What I want to show you is that you don't decide. The brain decides before you're aware of it. So the image is shown in the MRI magnet for a very short time, 150 ms, and then you press a button. If you want to say, "I saw a vase," you press left, and if you want to say, "I saw two faces," you press right.



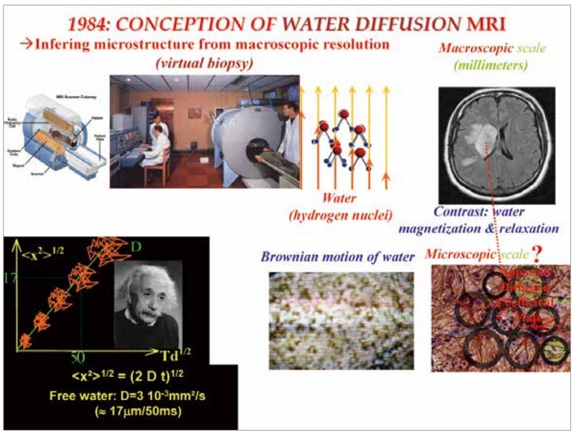
Under the brain there is one area, in red, here (center), that is dedicated to the recognition of faces, and we have to consider that the brain activity is changing all the time but we are not conscious of it. It is fluctuating. That's what we call "intrinsic fluctuations of mortal states."

At time zero you have an image, but look here (upper right graph), two seconds before the image is projected, this area could be spontaneously activated or spontaneously un-activated. If it's activated two seconds before the image comes, you will see faces. If the region is not activated two seconds before you see the image, you will say, "I see a vase." So you feel and believe that you decide but you don't decide anything. The brain is deciding for you in advance.



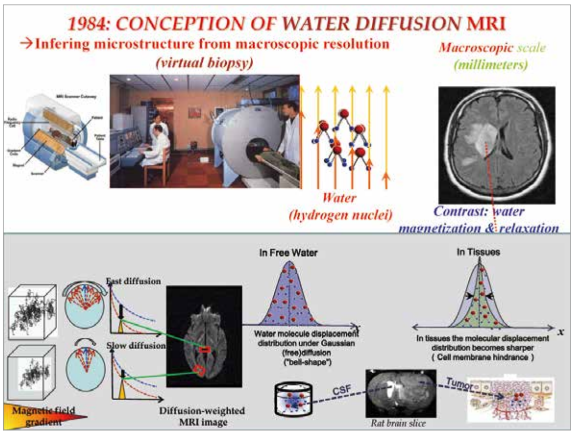
Let's switch now to something else, just to show you that water is even more important. This is an experiment that you should not do, although it doesn't work with sake anyway. If you mix red wine and water, at some point it gets mixed. This is called diffusion. The reason for diffusion was shown by Albert Einstein through his PhD thesis.

He explained this mixing by the fact that molecules, for instance water molecules, had a random walk like a drunken man trying to go home. It's just random. He made a very sophisticated model with an equation, which maybe is not as famous for you as the relativity equation $E = mc^2$, but to me it's a very important equation because it's a way to link the macroscopic world, you see the red wine being mixed, with the microscopic world, the molecules that you can't see.



So let's go back to MRI. There is a patient with a lesion here and as a doctor the question is what is it? Is it a tumor? What is it? I'd like to know, but the resolution of the image is only macroscopic, millimeter-scale, so you cannot see anything. Your dream is to have a virtual biopsy to be able to see the cells that are in this lesion, and this is what I developed back in '84 with diffusion MRI.

The idea, using Einstein's theory, was to consider that water molecules, because they diffuse, will fill obstacles such as membranes and so on. I used Einstein's model, Einstein's equation, and I made a method that can give us images of this diffusion of water. We don't see the water molecules one by one, what we see at the macroscopic scale is a message transmitted by the microscopic motion of the water molecules.

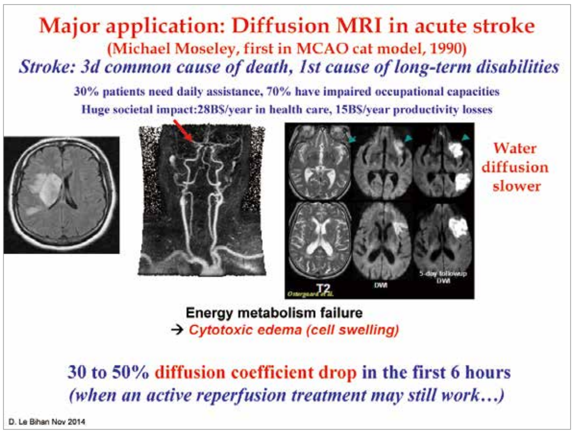


If you take water in a bottle like that, it's free of displacement (bottom), so that means that the molecules can explore a big area. In tissues such as the brain, because it's compact and there are many fibers and cells, the displacement of the molecules is reduced.

Again, I don't want to disturb you with the physics but on the image I made it was possible to have a contrast from grey to white, from black and white, showing how much movement the water molecules have. In a tumor with many cells, diffusion will be reduced. If there is cyst with a collection of water, then diffusion will be higher.

So the very first application of this came in 1990. This patient, in fact I showed you him before, had an acute stroke. That means he had a clot in an artery of the brain, as we can see here, and all the **neurons*** in the territory of this artery were dying. He was losing several millions of neurons per minute, so it was terrible.

* A nerve cell that carries information between the brain and other parts of the body



Many patients will die from this, and unfortunately even those who do not die will suffer from being severely handicapped. In fact, acute stroke is the very first cause of long-term disabilities. People will stay paralyzed for life or they will not be able to speak for life. Once they have a stroke, you have to consider it's for life.

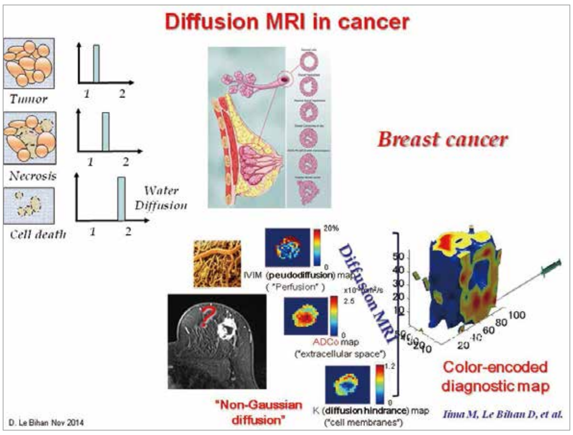
What has been shown is that in the acute phase, the diffusion of water slows down. The water movement is decreasing. Why? It's a little bit difficult to explain, but it has been shown even in patients developing a stroke. You see the white areas and even though you are not a doctor you can see that something is abnormal.

With conventional, plain MRI we don't see anything, we only see it with diffusion MRI, but the miracle is that now we have drugs called thrombolytic agents, which if given to the patient will dissolve the clot, re-establish blood circulation, the patients are saved, and the paralysis disappears and they can speak again.

But this has to be done very quickly, within the first six hours; otherwise, it is too late because we are losing several million neurons per minute. So this is what diffusion MRI can allow, and in fact this is why I got the Honda Prize in 2012.

Water diffusion is also very important in cancer.

For instance, if there are many, many cells in a tissue, as in cancer, water diffusion will decrease. If the tumor is benign or if the tumor has disappeared, for instance, diffusion will increase again. In breast cancer, especially, this is very important. Many, many women are concerned because they have mammography for screening and sometimes we see something abnormal and we don't really know what it is.



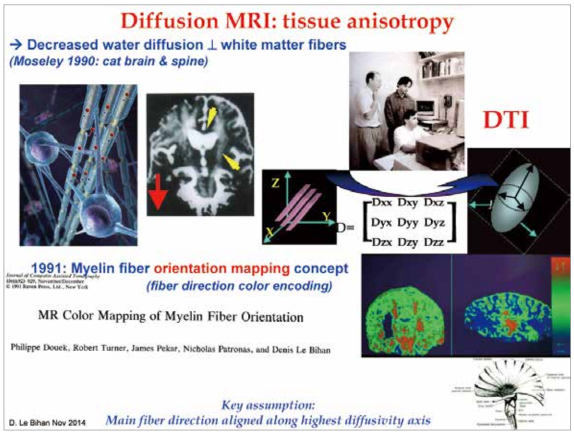
For instance, this lady had a lesion, even if you are not a doctor you can see that there is a lesion, and so she was injected with something to create contrast and this is why we can see the tumor so well. But this doesn't tell us if it is a malignant lesion or a benign lesion.

With diffusion MRI, we can obtain information with colors telling us what is the probability of each part of the lesion to be malignant. For instance, we can see that in the center of the lesion there is nothing wrong, but at the periphery it becomes very malignant, and from this we can decide where to put the needle for biopsy.

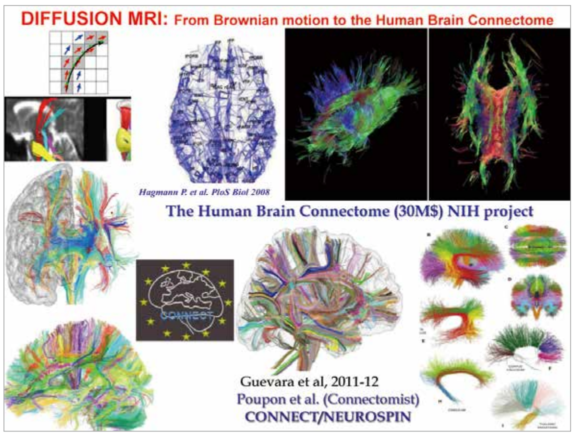
And we can even, by using computer software, isolate the lesion and see inside like the surgeons will do when they operate on the patient, but this can be done without any invasion just by measuring diffusion.

The next application is that it has been shown that in white matter, diffusion was anisotropic. What does that mean? Gray matter contains neurons at the periphery of the brain. Everything else is white matter, which are the wires that are connecting the different parts of the brain.

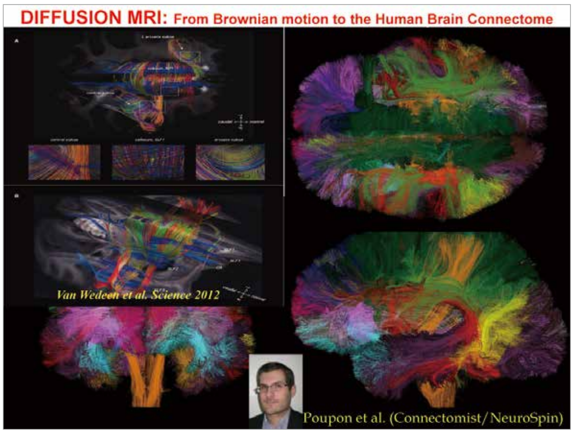
It was shown that the diffusion of water is faster along the fibers than perpendicular to the fibers. So my idea, long ago in '92/'94, with my colleagues such as Peter Basser at NIH, was to develop a mathematical framework whereby measuring the diffusion of water in several directions we can obtain point-by-point estimates inside the brain of the orientation of the fibers. In the direction that the diffusion is higher, we know that the fibers must be parallel to this direction.



This was done in the 1990s and the idea, of course, was to obtain some connections between those voxels, those points. This is now very easy to do and this is what we call the human brain connectome. We can make beautiful images of the connections in the brain.

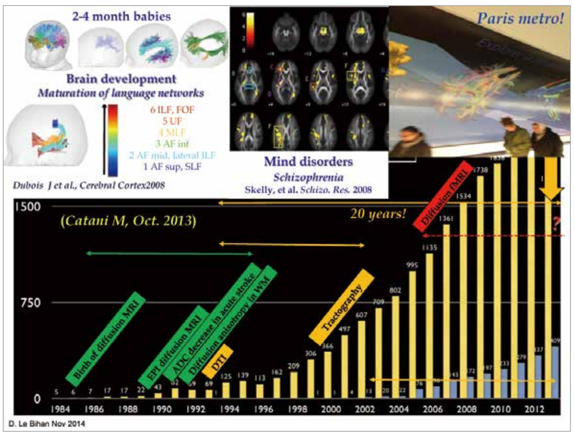


In the United States they dedicated 30 million dollars to make an atlas of the connections in the human brain. In Europe, we have a little bit less money, so we got only 2 million, but we worked with 12 partners to make images like that, which were the first images of the connections in the human brain.



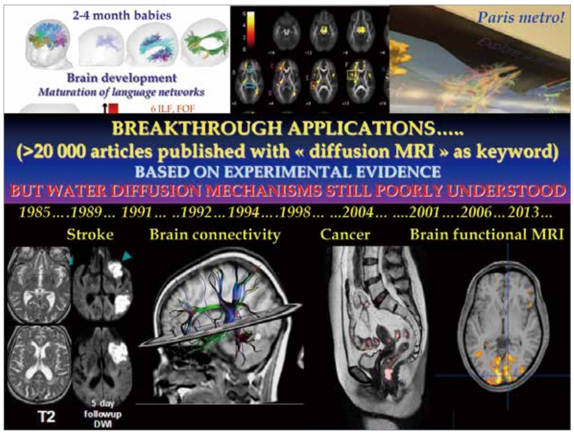
We have now more than 100 brains like that. It takes 15 to 20 minutes. You just go into the magnet, you don't even have to think about a cat, nothing, you can just sleep, and we obtain these gorgeous images of the connections in the brain.

So a very important message here is that from new idea to application in real life takes a long time, 10 to 15 years. I invented diffusion MRI in 1984 with application in stroke in 1994. For DTI, this method for the connections of the brain, 1994 was when it was invented, and it's only now that it's being used.

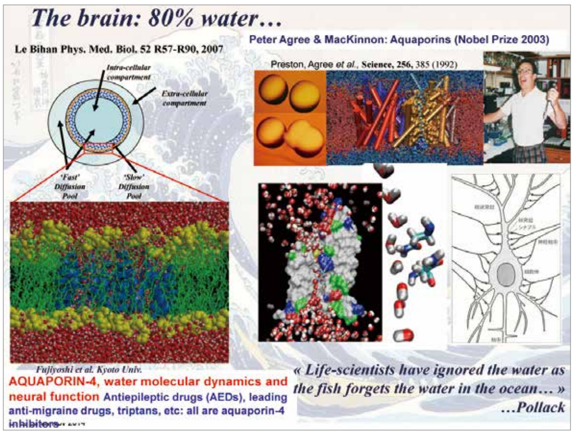


It was used for instance to see that in babies who are only two months or four months old, before they can speak, the fibers in the left hemisphere, in the future areas linked to language, are more numerous. There are more fibers already so the brain of the baby is ready on the left hemisphere to deal with language.

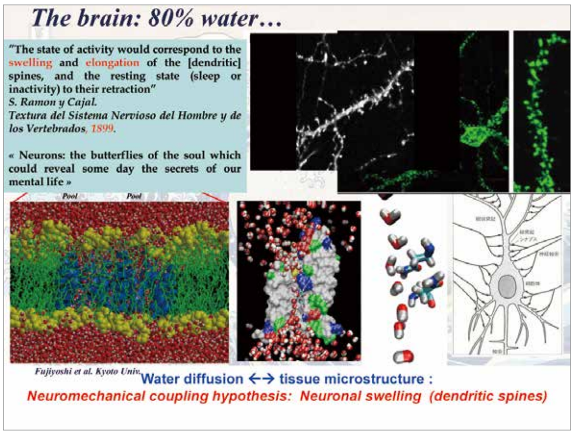
In some schizophrenic patients, we can see that the fibers connecting the frontal areas and the areas involved with sounds, audition, are faulty. The connections are not so good, and you know schizophrenic patients usually hear voices, so that may explain it.



Now this technique is so popular that in one of the Paris Metro stations, they put as art a figure of the connections of the human brain. I think that it is becoming very, very popular.



So diffusion MRI has been used for many applications, for stroke, for orientation mapping of the fibers in the brain, for cancer detection, and it's used now for detecting activation in the brain. I don't have time to explain everything, but I would just like to convey the message that we should not forget water. Water is very important and Pollack said that life scientists have ignored water as fish forget water in the ocean.



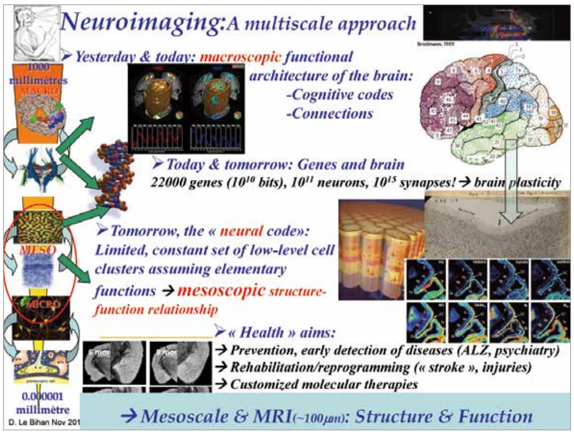
Water for instance, like in the sushi, may not be organized in the same way next to membranes, next to proteins, or elsewhere. And it's known now from the discovery of Peter Agre and MacKinnon, who got the Nobel Prize in 2003, that water molecules can cross cell membranes by using specific channels called aquaporins.

There are specific molecules that are dragging the water molecules one by one, breaking the hydrogen bonds, so nature has capitalized on water and is doing tricks to the water molecule, for instance, to break the hydrogen bond. Cells can say they want so many water molecules in or so many water molecules out. This is heavily controlled and some drugs now are designed to use those features, for instance to treat patients with epilepsy or migraine.

If we consider neurons, they have many, many dendrites, which are like antennas for the neurons but they have hundreds of them. And on each of those antennas we have some connections with other neurons. One single neuron can be connected to 10,000 other neurons.

Think about your cellphone, your cellphone connected with 10,000 contacts, it's huge. We have 100 billion neurons so the connections are huge. Ramon y Cajal, who discovered or invented the concept of neurons, said that neurons are the butterflies of the soul that could reveal someday the secrets of our mental life. I think he was completely right.

He also said that the swelling and contraction of all those structures was probably a key element to understand how the brain works, and this is what diffusion MRI can reveal also. This is what I call the neuro-mechanical coupling hypothesis, where the changes in the size of the parts of the neuron's linked to water movement can be detected by diffusion MRI, and they are pointing to maybe how the brain works.

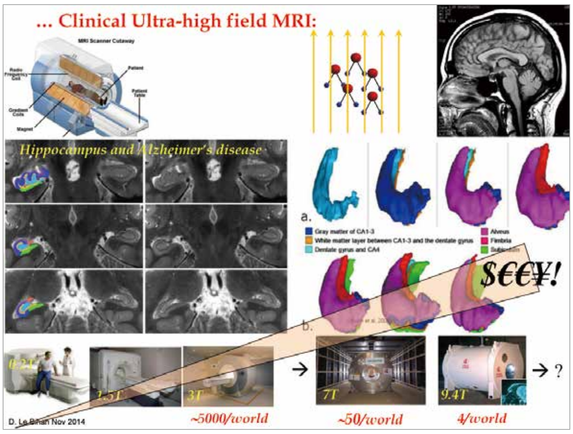


So this is where we are today (MRI image at the top). We can obtain images of brain activation, even in people in vegetative states, and we can obtain beautiful images of the connections in the brain, but that's not enough. We need to understand more. We have about 20,000 genes, but as I said 100 billion neurons with each of them connected to up to 10,000 other neurons. So genes cannot explain our brain.

We have language areas, all of us, but genes cannot say if I use this area for French or English or Japanese. This is the environment. So this is what we want to understand, what I call the neural code, how the organization in space of the neurons along the cortex make it specific for language, for vision, for motoricity. This is completely unknown today.

To do this we have to address the right scale. We have to go now to very high-resolution images so that we can understand better and have early detection of diseases. Maybe we can reprogram the brain after some injuries, that would be a dream, but I think it's possible. We will have to wait.

So how to do that? Well, MRI is about magnetization of water molecules using a strong field, so just to give you an idea, this is a magnet that you have on your fridge, 0.005 Tesla, which is the unit for magnetic fields.



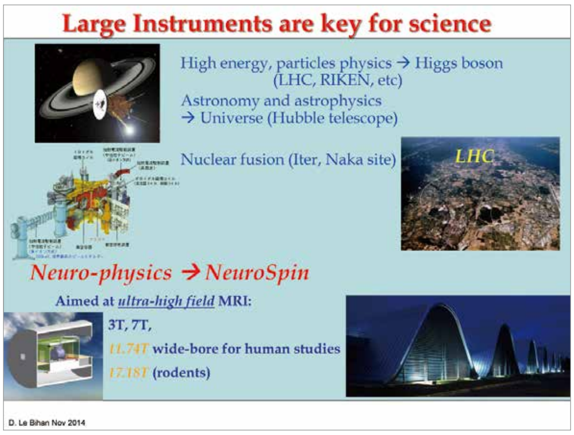
In hospitals, magnets are usually 1.5 T, so 30,000 times the earth's field. Nowadays, including in Japan, we can find machines working at 3 T or 60,000 times the earth's field, and there are a few machines, you will have five this year, in Japan working at 7 T or 140,000 times the earth's field. There are even a few machines working at 9.4 T. So you see there is a race for high field. Why?

For instance, look at the hippocampus (left center/previous slide). This area of the brain that is over-developed in London taxi drivers. In fact this area, which is linked to memory, is the first to be hit in Alzheimer's disease, so if you have a way to see this area very well in great detail in patients at the early stage we think that we may help them with diagnosis and then be able to slow down disease progression. We don't have a treatment, but at least we can delay symptoms.

These are images, for instance, of the hippocampus obtained at 7 T (right center/previous slide), but our dream is to go to an even higher field. The problem is that to see it costs a lot of money, so we have to share and physicists know very well how to share their instruments.

That's the LHC where the Higgs boson was discovered recently, and at Riken in Japan I also know there are huge facilities. For nuclear fusion, you know that in France we have the ITER site to produce energy from nuclear fusion. Japan is also one of the leaders for this.

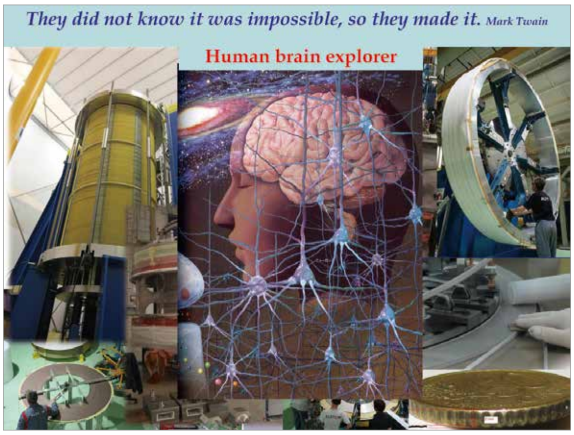
So this is how I decided to convince my bosses and the administration, the politicians, if you like, to build in France a place where we could have a very high-field MRI system, and the target is 11.7 T, so 220,000 times the earth's field.



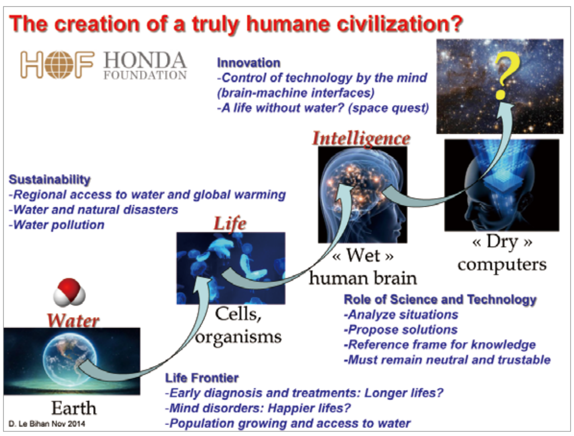
This is the magnet (next slide). It's huge: 5 m in length and 5 m in diameter. It will be the first in the world of this intensity to scan the brain. It was designed by the physicists at my institution, the Atomic Energy Commission. It's under completion now and it will be installed in NeuroSpin. It will be cooled down to -271°C, so 1.8 K, in order for this magnet to get the right field strength.

So it is today being built in a factory called Alstom in France where they make the French TGV and where they are also making for you in Japan some special magnets for nuclear fusion. This is how the magnet looks (left). It's almost finished now. It's incredible.

And just to show you the precision, this is a coin, this is a French coin (lower right/next slide), a European coin, and the black line here is the position of each of the 170 pancakes that we have to put in the magnets. The location is extremely precise and this is crucial. We are building what I sometimes call the "Human Brain Explorer," and we will get these magnets in about one year from now. Many people thought it was not possible so I like that they didn't know it was impossible, so they made it. That's our case.



To finish I'd like to comment on the motto of the Honda Foundation, which I like so much: "Creating a truly humane civilization." Sustainability is crucial. I hope I've convinced you that water is absolutely necessary. Global warming might change access to water, people may fight, and wars could be started because of access to water. Water is also connected to natural disasters.



Water appeared on earth and this is how life could be created. Life came thanks to water, cells, organisms, so the life frontier is about this kind of life.

We need to have early diagnosis and treatment of diseases to have longer lives, but longer lives are good only if we have happy lives, so we have really to understand mind disorders and see how we can cure them.

The population will be growing so access to water will be even more of a challenge. Water has permitted life and life has permitted intelligence to come and this is what I call the "wet" human brain; brain works with water. And in science and technology, of course, we use our brain to analyze situations and to propose solutions.

I think scientists should be considered as a reference frame for knowledge but only if they remain neutral and trustworthy. This is not always easy, but the next step, which is a little bit scary, is that from water to life to intelligence, we are steering to what I call "dry" intelligence, dry computers.

Maybe dry computers at some point will not need us anymore so we have to be extremely careful about how we control these technologies and how we interface with water. But maybe this life without water will be necessary if we want to explore the universe, and with those words I'd like to show that the vision of the Honda Foundation is really, really timely.

In English, maybe it is not so easy to go deep into the roots of this vision, but if we consider that life, the heart, is very important, this is something we cannot find in dry computers. We will have to be sure that we are able to preserve our emotions and our way of living. This is our direction, this is where we are going, this is not something we have achieved, this is what should drive our research.

Diversity, biological, that's very clear, but now we have to respect cognitive diversity, how people have different ways of thinking. We should respect them and we should focus on young people because they are our future. We have to show them that diversity is important.

We should also invest and protect old people because they have a huge quantity of knowledge that we can learn from, and they have to be able to share it with us, so we should do our best to protect the well-being of old people.

Thank you very much for your attention.

Q & A

MC: We would now like to take your questions. Does anybody have a question?

FUKUNAGA: I am Fukunaga of the Tokyo Abduction Research Group. I would like to thank you for that extremely interesting talk. My question is, does the hydrogen bonding process that makes a water molecule separate from or stick together with another water molecule create a network that makes atoms or molecules other than oxygen and hydrogen within the living organism stick together or separate in the interaction of, for instance, protein? What kind of non-water molecule or atom in the living organism makes such a fluctuating interaction with water? My question is in regard to this point.

LE BIHAN: I'm not sure I understood everything you wanted to address, but I have to say that, of course my talk was mainly on the water molecule, but water molecules in fact are responsible for the shape of many other molecules. With MRI, especially with high field, we are now trying to see ions such as sodium and we are also trying to see metabolites, neurotransmitters. In the brain, it's very important also to see how the different molecules activate neurons.

My vision is that water molecules are responsible for the shape of those molecules, and as you pointed out, there are a lot of dynamics in all these problems, and I think this is something we forget.

People usually have a fixed view of the system. For instance, the brain, neurons, connections but people don't realize that everything is moving all the time and water molecules have a very crucial role.

Maybe that's not exactly the question you wanted to cover but we have not enough time for me to go through everything.

FUKUNAGA: I understand what you just said. But what I would like to ask is whether the hydrogen and oxygen atoms of H_2O, or the H_2O molecule—components of water—have a fluctuating interaction with other atoms and molecules, i.e., separating from or sticking to them, for example, when they form the shape of atoms or molecules inside the organism such as nitrogen, phosphorus, magnesium, and potassium. Is there a direct interaction?

LE BIHAN: I still don't understand.

MC: Thank you very much. In the interest of time, let us take just one more question.

Questioner: Thank you very much. The development of medical equipment and medicine plays a tremendously significant role in prolonging human life. On the other hand, recently, the issue of death with dignity concerning a woman in the United States brings to light the question of balance with how one lives, whether a long life is everything or not, and that is a difficult question to resolve. I would like to ask your opinion about striking a balance between development in medical equipment and medicine, on one hand, and death with dignity and life support, on the other.

LE BIHAN: So are you talking specifically about breast cancer or other kinds of cancers as well?

Questioner: Not only in regard to cancer, but medicine in general.

LE BIHAN: So the problem today is, I think, and I'm talking about breast cancer because I think it's a very important issue, women when they have something abnormal on the mammography they may have surgery or they get invasive treatment. But sometimes there is nothing wrong.

This is very costly, psychologically for the women, of course, but also for the economy because they have to go to the surgery and they have to get invasive treatment. Sometimes we have to remove the breast, or maybe there is no cancer.

With these imaging techniques we think that we can help surgeons make decisions. For instance, in our images, if it is red, it's cancer and we have to operate. If it's green, it's not cancer so we may only have to monitor for maybe six months or one year. If it's orange then we are not completely sure so this is when you have to do a biopsy and use a needle to take a sample.

The problem is that if you use a needle there will be a trace later, so when the lady has a mammogram one year later, you see a trace of the needle and sometimes it's difficult to sort out if it is cancer coming or just a trace of the needle. We believe that such diffusion MRI methods have the potential to sort the women who have cancer from those who have no cancer.

The problem is that MRI is very expensive so we cannot use MRI as a screening modality. So the idea is to reserve this diffusion MRI for women who are at high-risk genetically because we know that they have a high chance to develop a cancer so maybe they could have his technique available, or for women who have suspicious lesions on ultrasounds or mammograms.

MC: Is that okay?

Questioner: Thank you very much.

MC: Then that concludes Dr. Le Bihan's lecture. Thank you very much.

MC: Thank you very much.