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"Bacteria can think too"

Interview with Alain Prochiantz

Ariane POULANTZAS

Alain Prochiantz, a professor in the Morphogenetics Department at the Collège de France, retraces the twists and turns – what he calls "accidents" – in his scientific career. One such "accident," a major unexpected discovery, has redrawn the theoretical contours of his discipline and paved the way for new therapeutic approaches. Prochiantz speaks here as a scientist, but also as a philosopher of science and as an artist, all of which he feels are mutually complementary pursuits.

Books & Ideas: Alain Prochiantz, you've been a professor at the Collège de France since 2007. You hold the Chair of Morphogenetics and you also work in a laboratory at the École Normale Supérieure on the evolution of the nervous system. Can you tell us about your career path and, most importantly, the turning-point in your career?

Alain Prochiantz: Yes, there were plenty of twists and turns because I actually began in 1971, working on vegetable viruses, especially the one in turnips. I know that sounds funny but it's a very interesting virus. And then after that I decided to go into neuroscience in 1976.

Books & Ideas: You went from turnips to neuroscience without any transition?

Alain Prochiantz: Yes, people generally go from the brain to the turnip, but I decided to go in the opposite direction. At the time I was working in a Collège de France laboratory, by the way, on the development of the nervous system before leaving for the United States. I think the turning-point you're referring to is the one that occurred 30 years ago, when I came across a phenomenon that I was not expecting, that nobody was expecting. We realized that certain molecules that are supposed to remain inside the cell cross its membranes and invade other cells. It was so unexpected that the scientific community, including myself, felt there was every reason to believe it was an artifact[1]. But it turned out it wasn't. And that was to decide the rest of my scientific career.

Books & Ideas: Do you remember the moment you made this discovery, when you came across this perplexing fact? What did you say to yourself? Did you redo the experiment several times? What did your colleagues say?

Alain Proschiantz: I said to myself that it wasn't possible. But at the same time I immediately considered the theoretical consequences that had to be drawn from this

[1] I.e. "a spurious observation or result arising from preparatory procedures" (*Random House Kernerman Webster's College Dictionary*) – Translator's note

observation if it was true. That happened very fast in my head. What we were observing was of course an astounding phenomenon. But there were nine chances out of ten that it was what we call an "artifact."

Books & Ideas: There's a line by Claude Bernard that you quote in your book *The Darwin Variations*. I'll read it aloud because it seems a very apt description of your own story: "When you come across a fact that conflicts with a reigning theory, you have to accept the fact and abandon the theory even if the theory is defended by big names in the field and generally accepted." To which you add: "The worst thing would be to see only what matches and dispense with whatever might derail the paradigm. Science gets stuck in its initial algorithm. Accidents become impossible."

Alain Prochiantz: Yes, I think we had an accident. In fact, I myself am a casualty of science, just as there are casualties of road accidents, but I survived!

Books & Ideas: In your inaugural lecture at the Collège de France, you also said the fact that you had observed and defended this paradoxical finding probably had to do with your being so young at the time.

Alain Prochiantz: Actually I was already 40. I'd begun in 1971 and that was in 1987. So I already had 16 years of scientific work under my belt. But I was young within this particular field. When you change fields (and that happened to me several times: plant biology, neuroscience, developmental biology), you see things with eyes that are not blinkered by the reigning received ideas quite simply because you don't know them. At the time I didn't realize the extent to which this observation might rock the boat. But I went right ahead – a bit too much, I must admit, and in a pretty provocative style. We did serious work though.

Books & Ideas: Has this discovery shifted – or actually exploded – the established paradigm?

Alain Prochiantz: I think this discovery wrong-footed several paradigms. First of all, the transcription factors (which are in the cellular nuclei and regulate the expression of genes) are not supposed to wander between cells. It was all the more surprising at the time as we thought these factors didn't have the sequences needed to leave a cell or to penetrate another, that is to say to cross membranes. Everyone thought membranes could not be permeable to proteins. So all of a sudden I think I got on the wrong side of a certain number of dogmas of cellular and developmental biology.

Books & Ideas: Were you the first to observe these transcription factors leave the cell?

Alain Prochiantz: Yes, I think so. It seems to me it had been suggested by someone working on an HIV virus transcription factor, who had showed that this transmission factor could cross membranes. It was an interesting experiment, but it was never taken to its logical conclusions. You know, you make an observation and then you transform that observation into a discovery. The observation takes a few weeks and the transformation a few years. The beginning is easy, the rest a lot harder.…

Books & Ideas: And nowadays no-one challenges this theorized fact?

Alain Prochiantz: I don't know everybody. There may be people who call it into question, people are skeptical in any case. I know a few myself. Let them do the experiment and then they'll be convinced.

Books & Ideas: How did your peers react at the time?

Alain Prochiantz: That depends. The reactions were pretty mixed. Some said "this isn't possible," others "this is interesting if it's true." Still others backed me up and helped me out.

Books & Ideas: You say one of the problems is precisely that when you happen upon a fact like this which isn't generally accepted, "you're putting yourself in an awkward position vis-à-vis the reigning theory – a theory so widely accepted that even questioning a detail elicits disproportionate reactions from the scientific community, from the whole papal enclave? and other guardians of the temple."

Alain Prochiantz: Because it's disconcerting to us scientists, you know, in a sort of paradigm that is relatively comfortable. Suddenly some "ninny" shows up and tells you "no, that's not the way it works." That's downright nerve-racking. We touched a pretty interesting nerve here because scientists are conservative by nature, which is perfectly normal, because we're better off being conservative. I'm conservative too. The problem is that at some point something just doesn't make sense anymore. And at that point, we have to be able to accept the fact that it doesn't make sense.

Books & Ideas: You're better off being conservative because otherwise it would be too easy to challenge the prevailing theory?

Alain Prochiantz: Yes. In fact, I'm quite respectful towards the peer review process. The more bizarre something is, the more you need to come up with solid proof. And this conservatism in the scientific community forces us to come up with proof and more proof…. At the end of the day, that actually shores up the discovery.

Books & Ideas: In your inaugural lecture you also talk about the initial skepticism of scientific journals, which in a certain sense forced you to refine your arguments.

Alain Prochiantz: Yes, of course, but scientific journals are the scientists themselves.

Books & Ideas: And are you still working on that discovery today?

Alain Prochiantz: Yes, I am, because the fact itself has never been questioned. It has even led to the creation of new tools, new vectors. I think people accepted the fact very quickly. Now, at the physiological level, that's something else. Once you've demonstrated that transcription factors can penetrate certain cells, that doesn't mean they necessarily do that in an animal or in a plant. Hence the need to show it actually does happen like that in an animal. Then we need to understand what purpose that serves: why, what is the function of this process? And so once we'd demonstrated that it's possible, which we did pretty fast, it still took us twenty years to find some physiological functions. We did that in collaboration with other laboratories.

Books & Ideas: Can you tell us a little more about that?

Alain Prochiantz: These transcription factors, these molecules, which are normally on the nucleus, are position markers. Imagine I take any cell from your brain or elsewhere: if I knew the combination of these factors in your brain and the quantity of each of these factors in that cell, I could tell you exactly where that cell is in your brain. It's as if you had a little flag saying "I'm a cell from Strasbourg," for example. When you walk around, when you migrate, for example to go to Paris, you can change transcription factors the whole way there. That's called "guidance." It's a very important phenomenon in guiding axons[2], especially during the development of the nervous system. I'm also sure that all this could give rise to applications in certain pathologies.

Books & Ideas: Yes, because you do basic research, but this basic research will most probably have practical applications soon. You mentioned pathologies, could you tell us a little more about that?

Alain Prochiantz: Yes, I do basic research, but there isn't one physics for building bridges and another physics for bridges that collapse. It's the same science. So from the moment you discover a new mechanism for the transmission of signals (which is what happened), that necessarily has a physiopathological counterpart. So yes, I think there are pathologies that are associated with defects in this signaling through the transfer of proteins, which we called messenger proteins. Especially pathologies of the nervous system that are linked to what is called the "critical period," that of learning in particular.

Books & Ideas: Which occurs at what age?

Alain Prochiantz: That depends. For binocular vision, for example, it's at the age of 4. For languages, or motor system development, it's a different age too. All of this is accompanied by changes in the system. And if those changes don't go well, that is if the brain doesn't adapt to its environment, you are left dysfunctional. My colleagues and I think this transfer of transcription factors plays a big part in controlling this period in which one is capable of learning. So thanks to these transcription factors, we're trying to open up periods of cerebral plasticity again in adults and thereby cure certain pathologies linked to defective acquisition during the so-called critical period.

Books & Ideas: What types of pathologies are you working on?

Alain Prochiantz: For the time being, we're working on binocular vision in mice…. I don't work on humans, I'm not a doctor. I work on chickens, zebrafish, mice, which have lots of things in common with *Homo sapiens*, of course.

Books & Ideas: In your various books you talk a lot about the scientific revolution ushered in by the discovery of development genes. What are development genes?

Alain Prochiantz: If you dissect my hand, you'll get the same cells you would if you dissected my foot. And yet as you can see, the shape of the hand is not at all the same as that of the foot. Development genes are the genes that make the same cells join forces to make a shape A, the hand, in one part of the body and another shape B, the foot, in another. And that goes for all the organs, too. This is morphogenesis. I'm a morphogeneticist. So development genes are basically the genes that decide the shape according to the position.

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[2] An axon is the long threadlike extension of a nerve cell that conducts nerve impulses from the cell body (*Collins English Dictionary – Complete and Unabridged*, HarperCollins Publishers 2003) – Translator's note

Books & Ideas: You do some awful experiments on flies in this regard. They have eyes all over, they've got wings instead of eyes…

Alain Prochiantz: Yes. You can force a fly to have a wing in lieu of eyes, legs in lieu of antennae, eyes at the tips of their antennae or at the ends of their legs.

Books & Ideas: So could these development genes be said to be more essential than many other genes?

Alain Prochiantz: All genes are important, but there are genes and there are genes, that's for sure. A gene that decides whether you have blue or black eyes, curly or straight hair, is important for certain people, but that's not the same thing as whether you have an ear in the "right" place, for example. So yes, there are two categories of genes. Transcription factors, including this family that wanders from cell to cell, are products of development genes. So they're a type of gene that is particularly important if we want to understand what shape is, that is to say development as well as evolution. Evolution is also the creation of new shapes. So yes, these are very essential genes.

Books & Ideas: In what way do development genes shed new light on evolution?

Alain Prochiantz: These development genes were discovered quite recently: the first development gene was cloned in 1984. That was a milestone in the history of biology because this type of gene made it possible to connect up genetics, development and evolution. In fact mutations of these genes permit huge morphological changes in living beings. This is the basis of evolution. Consequently, development genes are the key to understanding both ontogeny and phylogeny. Thanks to them, a new discipline called "evo-devo" was born. And we find ourselves faced with what could be called a real theory of life. This theory cannot be reduced to a physical theory, even though we are made of matter. We *are* made of matter. From the moment you take an interest in development, in reproduction and evolution, you need concepts that are specific to your object of study: that is basic physiology. The discovery of these genes is, in my opinion, a milestone in the history of our discipline.

Books & Ideas: Are development genes fundamental to understanding what is special about human beings? You insist a great deal on the specificity of human beings vis-à-vis other living species.

Alain Prochiantz: Yes, because you aren't talking to a monkey. And you're not a monkey either. You're capable of reading a book. I know that nowadays there's a crazy notion that we are a branch of monkeys. That's completely wrong. It's an accounting exercise that produces this illusion. It has been found that there is a 1.23 percent difference between the genomes of chimpanzees and those of *Homo sapiens*. But that means nothing because living beings for the most part all have the same genes: we're 80 percent mouse. In cerebral terms we're very different from monkeys. While a monkey has 400 cm^3 of cortex, we have on average 1400. That's 1,000 cm^3 too much. And it is that excess 1,000 cm^3 that makes us *sapiens*. What's what makes for poets, suicides, scientists and scholars….

Books & Ideas: Getting back to genetic considerations, you talk a lot about the importance of epigenesis in human beings, the fact that in the human being the phenotype is far less restricted by the genotype than in other animal species.

Alain Prochiantz: First of all, epigenesis is important in all animal and plant species, that is to say: for a given genome you have an infinite number of possible phenotypes because living beings are incredible machines when it comes to adapting to the environment. Now there are different ways of adapting. When you look at invertebrates, the approach is I'd say rather clonal: they reproduce very fast. If you are such a creature, you make a thousand others within the space of a few days, a few hours. Over the course of evolution, what ultimately happens is you reproduce less and less. Now we come to us, *Homo sapiens*: we couple up and produce two more of our kind. That takes us forty years. Now at this rate natural selection is going to be complicated even if we keep on evolving, which is indeed the case, genetically speaking. The strategies employed, the ones genetically selected, are strategies that permit adaptation at the individual level, what is known as individuation. As it turns out, I think we've reached the peak of this ability to adapt through individuation. This phenomenon whereby it isn't so much the individual who adapts to the environment as the environment that makes, that fashions, the individual, is epigenesis.

Books & Ideas: This is where you came up with the concept of "*anatural*" man.

Alain Prochiantz: Yes, in a book you can't find anymore because the publisher refuses to reprint my writings.

Books & Ideas: Well, while we're at it, at least tell us the title.

Alain Prochiantz: *La biologie dans le boudoir* ["Biology in the Boudoir"], published by Odile Jacob. Yes, I put forth the concept of man's "anature" (with a privative "a"). An "anature" by nature. It's not a religious concept at all. I'm a staunch atheist. It is precisely by nature that man is "anatural." It is due to the very nature of our development genes and the way evrything was designed that we have, in a manner of speaking, left nature. And that's a fact: we are technological animals. We wouldn't be here otherwise.

Books & Ideas: And in saying that, you are also asserting the mutual independence of the various scientific disciplines. You are a staunch advocate of non-reductionism as well, of whatever form it may take: whether it's a matter of attempting to humanize the natural sciences or to biologize anthropology, which brings to mind sociobiology and E.O. [that's what everybody calls him in America!] Wilson's book *Consilience: The Unity of Knowledge*.

Alain Proschiantz: Yes, but I don't confuse the object in and of itself and the scientific object. These are two different things. A scientific object is an *object* more than a *theory*. So I can think about you. Your brain can very well be an object of study in physics. I can take your brain, fling it around the room and calculate its trajectory as a function of its convolutions, of its *drag*.... After that, I might approach the brain from another point of view, as a biological object. It must be borne in mind that a scientific object is the object plus the theory that takes into account what we're going to study about that object. From this point of view, I am indeed a staunch advocate of the independence of the disciplines. That doesn't mean things can't shift, that there is no interaction, that one cannot take an interdisciplinary approach. Precisely because these theories are not objects in and of themselves, they are fragile objects that shift, that evolve as well. That is precisely why there are interactions and things are not frozen in place. But if I study man from a sociologist's viewpoint, I'm not going to have the same body of theoretical knowledge as an anthropologist or a biologist or a physicist….

Books & Ideas: We always aspire to cover everything through our own particular discipline, to encompass all the other approaches, to do life science using a physico-chemical approach, or sociology or psychology using biology.

Alain Prochiantz: Nothing is off limits in science. I think everything's possible. But theories are things that exist and have a history. They are human constructs, of course, they don't just appear out of the blue. They may be wrong, there may be room for improvement. But for the time being, physics and chemistry are, to my mind, tools – tools we need for our study of living beings. But on the theoretical level, an organism is alive insofar as it is a living object and is subsumed as such under a theory of living beings. On this head, I am very loyal to Claude Bernard, whom I've read and admired a great deal. If I go into nature with my friend Philippe Descola, who's an anthropologist, he'll look at the animals and *Homo sapiens* differently from the way I do. When an Indian says this panther is my sister, this is not at all the same way a biologist would say it.

Books & Ideas: Don't sociobiologists have not only a tendency to co-opt objects of study, but also a way of saying things about them that goes beyond a purely biological approach?

Alain Prochiantz: But of course, some biologists exhibit a certain imperialism towards the humanities, similar to the imperialism of physics towards biology, and mathematics towards physics. We don't have to approve.

Books & Ideas: And that's precisely it, I was trying to elicit your disapproval.

Alain Prochiantz: Well I don't approve at all. I can't conjecture about what's going to happen in five, ten or thirty years. But today I don't think economics, for example, is a science based on the nervous system. One can try to find out what's going on in a nervous system at the moment an economist is about to make a decision, which becomes neurobiology, but that no longer has anything to do with the science of economics. And yet that doesn't mean there is no science of economics.

Books & Ideas: You have a very special definition of thinking in which you stick to your place as a biologist.

Alain Prochiantz: In other words, I never, or almost never, leave my discipline.

Books & Ideas: So what is thinking for a biologist?

Alain Prochiantz: For me, it is the ability to adapt at the individual level and at the level of the species. It is the relationship that obtains between myself, for example, and the environment. There you go, that's what thinking is. So this is a very biological definition. But it means that everything thinks: bacteria think, plants think. Even if it isn't thinking at the same level of complexity, of course. This is a biological definition, which differs from any other definition of thinking that may come from another discipline and is completely justified in its theoretical domain. As a biologist, I think that bacteria think, in their tiny way.

Books & Ideas: You've taken a lot of interest in Alan Turing's work?

Alain Prochiantz: Yes, a lot. I have great admiration for this great 20th-century poet.

Books & Ideas: You talk about thinking. And yet your approach to thinking differs a great deal from his.

Alain Prochiantz: From his approach in his first writings, yes, but not those at the end. At the outset he thought the brain was a logical machine. He was a very great mathematician who solved some very hard problems in mathematics. He was a great computer scientist, too, who was after all, in a certain sense, the inventor of computer science and computers. He was also a very great philosopher. I think the article ["Computing Machinery and Intelligence"] he wrote in the [British academic] journal *Mind*, opening with the words "Can machines think?," is one of the key articles in philosophy. Plus he was a very great biologist, who invented the concept of the morphogen. I am a morphogeneticist. And his book was very useful to me, by the way, in understanding what I was doing myself. In fact, I think we discovered something that is related to Turing's theory in biology. He wrote three or four articles. But every one of them was a success – a success in three different disciplines. Nowadays, people write 500, 800 articles and nobody will remember them in ten years' time. He wrote three and we're still discussing them. I'm sure we'll still be discussing them in fifty years.

At the end of his article "Can Machines Think?" he says we need to understand how a child's brain is able to form over the course of its development to ultimately apprehend its environment. In a certain sense, he abandoned that idea of a mechanical brain. He thought human beings would be able to come up with an answer, later on, to how to design machines that think. But I have never said anything different; that is to say, there is a machine that thinks: the brain. Yet we need to give up on computer models that are a bit asinine and can't account for human thinking. And that is how Turing became a biologist, and came to pursue morphogenetics, that is to say the development of forms. That is how he laid the foundations for a theory of morphogenetics and morphogens that is, in my opinion, crucial.

Books & Ideas: How did you discover Turing?

Alain Prochiantz: I had read a lot about him when I was a "kid," that is between 1974 and 1980. I rediscovered him in some drama work – which was a pleasure by the way – I did with my friend Jean-François Peyret. Jean-François had put on two beautiful productions about Turing. At the time I wasn't working directly with him yet, in other words I wasn't writing directly with him. At the time he had this mania for inviting scientists to talk to actors. The way Peyret works is quite interesting: he has a text he calls "Score No. 1," on which the actors improvise. And then in the evening he rewrites. Through this process, he undertakes a sort of natural selection of the text. To help the actors understand what it's all about, he invites people to a round-table discussion with the actors. And when he did his work on Turing, he knew I was pretty interested. So he asked me to come and talk. Consequently, I was obliged to re-read Turing. He forced me to re-read, and in really re-reading Turing, not as a student but as someone who wants to understand, I realized that what I was doing collided head-on with his theory of morphogens.

Books & Ideas: Did that help you move forward in your theoretical work?

Alain Prochiantz: Naturally, that really gave me some ideas. Not long ago we published a totally Turingian article in the *Journal of Theoretical Biology*. It's what I call "nocturnal science." Yes, I think you've got to take time out to do that sort of thing. Reading the thinkers of old is never a waste of time. You know, science is a conversation between friends, with

people who are, fortunately, alive, of course, but also with people who are dead. And it's a conversation that keeps going. When you read Darwin nowadays, you learn all sorts of stuff.

Books & Ideas: Do you still work with Jean-François Peyret?

Alain Prochiantz: We're going to. At any rate, we still get together, we talk about it.

Books & Ideas: So have you done plays with him?

Alain Prochiantz: Yes, I wouldn't put it that way, let's say Jean-François and I fashioned some slightly bizarre objects that were performed in Avignon at the TNS [*Théâtre National de Strasbourg*] in Strasbourg, Chaillot, Caen and Toulouse.

Books & Ideas: And if we wanted to read these strange objects, these booklike objects?

Alain Prochiantz: *La génisse et le pythagoricien* ["The Heifer and the Pythagorean"], *Les variations Darwin* ["The Darwin Variations"], which were published by Odile Jacob and which demonstrate a bit of my conception of science. For at the outset the idea wasn't to do theater, but science, a different way of doing science. I think it's indispensable if you really want to understand.

Books & Ideas: You're 60 years old and yet you're quite young.

Alain Prochiantz: Yes, well, that depends. You haven't seen the engine.

Books & Ideas: I haven't seen the engine, but I see what it produces.

Alain Prochiantz: My days are numbered now.

Books & Ideas: So how do you intend to use the time you have left?

Alain Prochiantz: To pursue my work, I have about ten years in the laboratory ahead of me, if I live that long. You can do a lot of things in ten years in the lab. I'm going to try to do the best I can. It goes fast.

Books & Ideas: Shall we get together again in ten years?

Alain Prochiantz: Maybe…. Let's hope so.

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