Face to Face

This section features conversations with personalities related to science, highlighting the factors and circumstances that guided them in making the career choice to be a scientist.

Deciphering the Gene Machine*

Face-to-Face With Professor Venki Ramakrishnan

Venki Ramakrishnan talks to Padmanabhan Balaram

Dr Venkatraman 'Venki' Ramakrishnan is the Nobel Prize-winning structural biologist renowned for his work on the atomic structure of the ribosome, among many other contributions. A trained physicist turned biologist, he is the current President of the Royal Society, London.

Venki Ramakrishnan is known for his unusual career path and is a champion of interdisciplinary research to solve complex scientific problems. He determined the atomic structure of the 30S ribosomal subunit followed by structures of the entire ribosome in many different states and in complexes with several antibiotics. This work has advanced our understanding of how the ribosome works and how antibiotics inhibit it. In the past, he has also worked on histone and chromatin structure, which help us to understand how DNA is organized in cells.

He received the Nobel Prize in Chemistry for his work on the ribosomal structure in 2009, sharing it with Thomas A. Steitz and Ada E. Yonath. He was knighted in 2012. He is a Member of the US National Academy of Sciences, Leopoldina and EMBO, and a Foreign Fellow of the Indian National Science Academy.

P Balaram (PB): Welcome to the readers of *Resonance*. As you know, *Resonance* has been conducting interviews with famous scientists. And today, we have with us, Dr Venki Ramakrishnan. I don't need to introduce Dr Venki Ramakrishnan in great detail, because he's going to tell us about himself. And, I will just lead him along with a few questions.

So, Venki, could I ask you to tell us a little bit about your early education in Baroda and the choices you made in going to the US for a PhD in 1971?

Venki Ramakrishnan (VR): I moved to Baroda when I was three, from Tamil Nadu. Initially, I couldn't even speak the local language. So, my parents sent me to the only English school in

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town at that time, which was called the Convent of Jesus and Mary High School. Well, actually, I went to kindergarten, but it was an entire school. When I was in third grade, the nuns who ran it realized that the Jesuits in town had also set up an English medium school. So, they made their own school a girl's school. But they allowed the old boys who had already registered to stay on. That way, I'm perhaps one of the few boys who graduated from a girl's school. And then I had a choice of where to go after my pre-science. In those days, you had to do a pre-science year after high school. You had K to 11, and then you went to pre-science. I did my pre-science in Baroda. And at that point, you had to choose between going to engineering, medicine or basic science. I had applied to the IITs. But of course, my parents didn't believe in coaching classes. In fact, I was probably too lazy to go to those classes anyway. I don't think I did very well in those exams; I didn't get the seats I wanted and didn't get into the IITs. I had also applied to the Christian Medical College in Vellore, which has a very tough entrance exam. The college was primarily meant to educate women physicians, and I think only about a third of the seats were for men. And, you know, this was from all over India. I didn't get that either. My mother had encouraged me to take the National Science Talent exam, and that involved doing a project and taking an exam. And I, miraculously, got that. It was almost a sign in those days that the National Science Talent Exam was only given if you went to basic sciences. So, even though I got admission to the local medical and engineering schools in Baroda, when I got through the Science Talent Exam, I really thought that I ought to do basic science. I was interested in mathematics, but many people told me that there were no jobs in mathematics. This was before the information revolution. Computing and even bioinformatics in biology is full of mathematics, but they could not predict that. So I said, OK, well, I'll do physics, that way, maybe I won't have trouble getting a job when I finish. That is how I ended up at M S University, which was a local university. I could have gone somewhere else. For example, the two choices were Delhi University and Madras University. Madras Christian College was one that was acceptable to the National Science Talent people.But I was only 15, and my parents were worried about my going off to college at that time on my own. They had also heard that students of Delhi University were indulging in drugs and getting into trouble. So, they didn't want me to go to Delhi, and I ended up studying at Baroda University, and it would have been worse. But, actually, what happened was that a few professors had returned from the US, and they completely modernized the curriculum. Hence, in the first year, we were studying the Berkeley physics course, and we were learning from *The Feynman Lectures on Physics* and so on. It was indeed a very exciting course. We were the first batch, and the professors were also enthusiastic. You know, they were trying to find their way with this new course. In the end, I think I got quite a decent education there.

PB: So, you did your bachelor's degree at M S University in Baroda. Where did you do your

Venki Ramkrishnan (left) talks to P Balaram (right).

master's degree?

VR: I didn't do a master's as such. Normally, you know, Indian students, even if they want to go abroad, do a master's in India. One option would have been to do a master's at one of the IITs or some other place. My father at that time was on sabbatical in the US, and the head of my department came to me with a letter from Ohio University, which said (it was a sort of a blanket form letter), "If you have any good students who are interested in graduate work, please encourage them to apply". I had never heard of Ohio University before. I actually asked my professor who had gone to Case Western University, which is also in Ohio, as a postdoc. He told me, "No, you shouldn't go there. That is not a serious place". But, I looked at it and I thought, you know, the professors at the University of Ohio had all been trained in very good places. So I thought, well, you know, maybe I should apply. My father at this point said, "Look, it doesn't matter where you go, as long as you work hard, you'll be fine". Actually, it isn't true at all. I think it matters a lot where you go. But of course now, in hindsight, he would say he was right. Anyway, they gave me a fellowship. The University of Illinois at Urbana accepted me without a fellowship, but then they withdrew the acceptance when they found out that I was only 19. They thought I had not done enough. They were willing to accept me as an undergraduate and give me one or two years of college credit, but I would still have to do two more years, to get a degree. Of course, no middle class Indian could afford to go to the US

in those days and pay fees and living expenses. So, I ended up going to Ohio University and started my sort of PhD in physics there.

PB: Your PhD was in physics, in nuclear physics?

VR: No, it was in theoretical condensed matter physics. I was looking at phase transitions in ferroelectrics. But, don't ask me anything about it because when I moved from Utah, I came across the only paper from my PhD work, and I don't think I could understand it at all.

PB: What propelled you to abandon physics and move into biology at a relatively critical point in your career?

VR: I think that was a key decision. You know there is a kind of snobbishness in physics. Physicists think they are better than everybody else in science, and among physicists, if you are a theorist, that is supposed to be sort of a pinnacle. And then if you are a high energy theorist, that is perhaps even more so. There is this hierarchy of arrogance. There is a famous cartoon by *XKCD* called 'Purity', which portrays this hierarchy – from sociology to psychology to biology to chemistry to physics. And then they have a mathematician standing apart. I wanted to do theory; I was sort of enamored with it. But the problem was when I started doing actual research as opposed to course work, I couldn't get a sense of what the actual problem was, and how to go about generating something really interesting.

Also, the project I was working on seemed very divorced from experiments. You know, good theorists are always very well connected with the experiments, and they are always working on theories that have some connection. Of course, that is not true with string theory because that is not capable of experimentation yet. Anyway, I couldn't make any sense of it. Then I read popular magazines like *Scientific American*, and I saw that biology was booming. I thought, well, maybe I should start over and become a biologist. In the end, I decided to finish my PhD and not just abandon it. After my PhD, I applied to graduate schools. However, many schools wouldn't accept me as a graduate student because I already had a PhD. But a few did, and one of them was the University of California in San Diego (UCSD), which had a very good biology department (still does). It was one of the top universities in the country and attracted a lot of people from the northeast, very famous people, perhaps because of the resources and California weather. And so, I ended up going there.

PB: How long did you spend in UCSD?

VR: I spent two years. When I arrived there, the first two weeks, you would get lectures by all of the professors on their work. It's a kind of survey of the research in the department. And as soon as I heard a few lectures, I realized I had no idea what they were talking about. They used all this jargon which I was completely unfamiliar with. I realized I had to take undergraduate

courses. So I asked the graduate supervisor if I could take them, and he was very supportive. You know, the thing that struck me about the US and particularly UCSD was how flexible they were. I had a PhD but they were not bothered by that. They agreed. So, I took a whole year of basic biochemistry, cell biology, and genetics. That gave me a foundation in biology. While I was doing that, I was also required to do laboratory projects, so I became familiar with lab work.

By the end of the first year, I had acquired a background in biology, and I had also become familiar with how to work in a biology lab. So, at some point, I was wondering whether I should really stay on and get another PhD. Because, I thought, well, maybe I was ready to do a postdoc. That was when I came across an article in the *Scientific American* on the ribosome by two people at Yale. It struck me because when Yale did not want to take me as a graduate student, they had circulated my application among the faculty. Two people at Yale wrote to me saying they might be interested in offering me a postdoc position. One of them turned out to be Tom Steitz, with whom ironically, I ended up sharing the Nobel Prize. The other was Don Engelman, one of the authors of the article in *Scientific American*.

So, I replied to him saying, "A Couple of years ago, you were interested in me as a postdoc when I didn't know anything about biology, and I declined and went to graduate school. But now that I have some background in biology, maybe you're still interested". And he wrote to me saying that his collaborator, Peter Moore, was going to visit San Diego. Peter Moore was really the ribosome end of that collaboration. I met Peter Moore in San Diego, and he interviewed me and then invited me to Yale and offered me a position. So, after two years, I left San Diego and did a postdoc.

PB: When did the ribosome really enter your life, and what were your earliest attempts to start in an area which must have appeared formidably difficult in those days?

VR: The ribosome was at a difficult stage because it was discovered in the 1950s. Right now, we are talking about 1978. In the early 60s and early 70s, a huge amount of work had been done on the ribosome that figured out roughly what the ribosome did and which part of the ribosome did what; which protein factors interacted with the ribosome at various stages, and so on. The next step was to ask how they did that. That turned out to be really difficult because the ribosome was huge. It is about half a million atoms, so many people, some very famous people like Francis Crick and Sydney Brenner, declared the problem solved and moved on to other fields. They felt that the rest was merely a matter of details.

That was a point of view. There were still a few people working on ribosomes, and they were trying to understand what the ribosome looked like. The ribosome is about two-thirds RNA and one-third protein, distributed among 50 different proteins. So we have about 50 proteins and

three very large pieces of RNA that somehow come together to make up this particle, which consists of two parts, a large and a small subunit. And people didn't even know where the proteins were on the ribosome. At that time, the only biological molecules that were known to carry out reactions were proteins. So they thought that the ribosomal proteins were responsible for many of the ribosomal functions, which turned out to be completely wrong. But, you know, that was the feeling at that time. What Peter Moore and Don Engelman were trying to ask was where the proteins were on the small subunit. And they were using a somewhat esoteric method called small-angle neutron scattering, which turned out to be not that useful in biology. But at that time, it seemed like an exciting new method. And I thought, well, with my physics background, I can quickly learn neutron scattering, and then I'll be working on the ribosome. By then, I knew what a ribosome was, whereas just two years earlier when I went to San Diego I had no idea what a ribosome was.

PB: So, this would be in the mid-70s, yeah, well, 1978. How did you begin to learn the techniques that you later needed to attack the structure of a ribosome?

VR: That is another complicated story. After my postdoc, I initially couldn't get any job, and then I got a job that I quit after 15 months at Oak Ridge National Laboratory to run a neutron scattering facility, which was not very satisfying. Then I moved to Brookhaven National Laboratory. So, I knew about the ribosome, I knew how to do the small-angle scattering, and I was hired there really to do neutron scattering on interesting systems. But I was given quite a lot of freedom. As a few years went by, I realized that the methods I knew were very limited. If you really wanted to understand the ribosome, you needed to at least know the atomic structure of the components of the ribosome, but preferably of the entire ribosome. But I didn't know how to solve crystal structures. Luckily, I had a couple of colleagues at Brookhaven who encouraged me. They said, you should just try to crystallize these proteins, and one of them, Steve White, said, "Well, you know, with your physics background, you won't find it hard to learn crystallography". So I started off and even took a course in Cold Spring Harbor Laboratory. It was the first crystallography course taught there. And, you know, it's been going on now since 1988, when I took the course. But then I realized that if I really wanted to learn it, I had to go away somewhere, and simply focus on learning the method. Brookhaven had a sabbatical system. You could go away for a year, and they would give you half a year's salary. I got the other half as a Guggenheim Fellowship and using that I went to the MRC Lab of Molecular Biology, Cambridge, where I now work, and which was the birth place of protein crystallography.

The lab was founded among others by Max Perutz and John Kendrew, who solved the first protein structures and got the Nobel Prize in 1962. Francis Crick was there and it's the direct successor of the MRC Unit where Watson and Crick discovered the structure of DNA. So, I wrote to Aaron Klug, then the Director, and a renowned researcher. By then, he was a

Nobel Laureate, and he would go on to become the President of the Royal Society. I wasn't sure whether he would reply, but I was working on a protein related to chromatin that he was interested in. It was a part of my lab that was separate from my ribosome interests. He replied to me saying that I could come and learn crystallography to solve that particular protein. So, I went there, and in a year, I learned quite a lot of crystallography. I ended up solving two structures while I was on my sabbatical.

PB: This was in 1988?

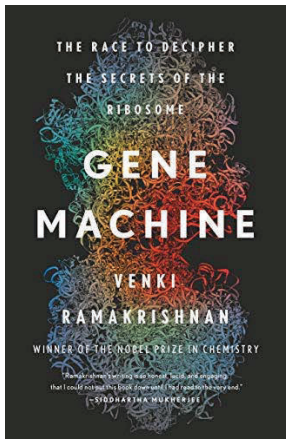
VR: No, this was a little bit later. I went there from 1991 to 1992.

PB: You have worked at many places: at Brookhaven, at the University of Utah, the MRC in Cambridge. These transitions that you made, were they the key elements in taking you forward towards the ribosome structure?

VR: I think so. They had a logic. You know, after a postdoc, you have to find a job. You can't stay forever as a postdoc. The initial job I found was not very satisfactory. It didn't allow me to do my own research. And so, Brookhaven, you just had to go there. So that move was what I would call a necessary move. Then when I came back from the MRC-LMB, Cambridge, where I was on sabbatical, I was somehow dissatisfied with Brookhaven, and part of the reason was that the Department of Energy, which was funding Brookhaven National Lab, didn't like funding individual groups who were doing their own basic research. They wanted big programs, and they wanted to fund big facilities like accelerators and reactors, and so on. So, I felt that the department didn't have the kind of environment that I wanted or rather it had it, but it was sort of declining. And, you know, it would be hard to recruit new people doing exciting new biology. I felt that if I wanted to thrive as a biologist, I probably should move before I was too old. So, I moved to the University of Utah. The University of Utah was excellent. In fact, it has several National Academy members and researchers like Mario Capecchi who won the Nobel Prize. Many of the cancer genes were first discovered there. And in my field, which is roughly speaking, RNA biology, the University of Utah was outstanding. So I went there. Then based on my sabbatical, I had an idea that I might be able to solve the structure of the entire ribosome, which other people had been trying to, especially Ada Yonath's group in Hamburg, Berlin, and Israel. But, they hadn't been making much progress towards getting a structure, and I had an idea of how to do it. So then the question was, should I stay in Utah and try to do it? And here I have to say, I was a bit afraid and worried. The reason was that in universities, you are essentially dependent on grants. These grants are about three to five years. Now, I knew that Ada Yonath's group had been working on this project for almost 15 years by this time with very large resources. She had Max Planck support in Germany and she had support at the Weizmann Institute in Israel. But even with that very large

group, she hadn't been able to crack the problem and actually, produce a structure, although she'd had the crystals for quite a long time. So, I didn't know how long it would take. And I knew that the MRC-LMB (let's just call it the LMB, because that is what everybody calls it) had this tradition of working on very long term projects. Some of the projects had taken 20 years. You know, Max Perutz's hemoglobin structure took twenty-three years from the time he started. And so they had this tradition of taking a long term view of things. So I felt, if I went there, they might not pull the rug out if things didn't work out right away. The other thing was if somebody else beat me to it, then I wouldn't be out of job. I could just switch and try and do something else. So, it seemed like a safer place. Also, there was a lot of expertise in tackling hard problems; a kind of environment for that. I was in Utah only for about two and a half years when I decided that maybe I should move again. My Chairman, Dana Carroll, with whom I'm still friends (which says something about his generosity), was not happy at all because he had hired me with a big startup, and then two years later, I went to him and said that I wanted to leave. He was understandably quite unhappy. But in the end, he was very generous. He and my colleagues in Utah were quite generous about my move. They were very supportive. It says something about the fact that they put science first and their sort of institutional ego second. They could see why I wanted to go. It wasn't for more money or more resources or anything, but it was for a particular environment to tackle this problem.

PB: You know, I realize that you've written a great deal of detail in your book, *The Gene Machine*[1] But for the benefit of the students who read *Resonance*, could you describe some of the most important moments in the solution of the ribosome structure?



VR: When we first started, there were no good crystals of the small subunit. There were good crystals of the large subunit. But that was being done, not only by Ada Yonath but also by the group at Yale, Tom Steitz, and Peter Moore. I thought the whole ribosome, for which, again, there were no good crystals, was really enormous and might be too difficult as a starting project. So I thought maybe the small subunit would be a good place to start. I didn't know how long it would take to get good crystals, but by being very careful about our preparation and making sure we had very homogeneous samples, we were actually able to get crystals relatively quickly and crystals that diffracted very well, that is, of a good enough quality to give you an atomic-resolution structure. So that was a big breakthrough, and that actually happened in Utah before I moved to Cambridge. That gave

[1]See the book review by Mahak Sharma, Illuminating the Code Reader, *Resonance*, Vol.24, No.12, pp.1471–1474, 2019.

me a sort of impetus to keep going on the project. And, it sort of motivated us at a crucial time when we were moving. Because, you know, if you're moving and things aren't working, it's really psychologically quite hard. But, if you're moving, when things are working, you're sort of excited. And then the next step was really to ask if the idea that we were planning to use to determine the phase of the structure would work. When you use diffraction to determine the crystal structures, the intensities don't contain all of the information that you need to solve the structure. For all of the spots that are produced by the diffraction pattern, one needs to know where the crest of the wave that produced one spot is relative to that of the wave that produced a different spot. This is because waves have crests and troughs, and they can be further ahead or further behind. That is called the phase problem. We had a particular way of trying to do it, which was to use anomalous scattering. That is, when you have a structure that scatters X-rays, normally when most of the atoms in the crystal scatter X-rays, the scattered ray will be related in phase to the incident ray in the same way. But, if you have anomalous scattering, it's effectively like it's absorbing the X-ray, and then re-emitting it so that there is a sort of delay. And this can be best described as an imaginary component of the scattering factor. But forget the mathematics; the practical aspect is that when you have spots that are symmetry-related, for example, if one side of the diffraction pattern looks like the mirror image of the other side, then in normal scattering, those two spots have the same intensity. But when you have anomalous scattering, there is a small difference in intensity between the two spots. And if you can measure that distance very accurately, you can get the information about the phase of the spots. And that is a very old idea. It was first thought of by a Dutch physicist named Bijvoet. And one of the first people to actually use it to solve a structure was G N Ramachandran when he was in Madras University. We thought we would use it to solve the ribosome problem. But, we weren't sure whether we would have enough signal. So one big eureka moment was when we could actually see the signal from these anomalous scatters in our data. Then we knew we could phase the structure and actually calculate it.

PB: I will turn away from the ribosome now and ask you, were there teachers, mentors, and colleagues who influenced your career in a major way?

VR: I think I had several strokes of luck. First of all, when I entered high school, I had dropped from being near the top of my class to being near the bottom of my class. In fact, I remember, in one grade, I had to get grace marks in order to pass. Otherwise, they would have flunked me. I was very good at some subjects and was just goofing off. So I went through a period when I was totally ignoring my studies. In hindsight, I was not. I was actually learning a lot. I was reading a lot, but it just wasn't my textbooks. And, preparing for exams? Maybe I was just bored. Anyway, when I went to high school, there was a very strict but somewhat motivating physics – well, science and mathematics – teacher named T. C. Patel, and he sort of

encouraged me to take more interest in science and mathematics. They told me once, "You're really a terrific student. You know what you're doing". You know, that sort of thing then made me take interest in science again. So, my scholarship recovered, or at least my exam grades improved. Then I would say probably the single biggest influence after that was my postdoctoral advisor, Peter Moore. Because he taught me what it means to be rigorous, and how to think about an experiment. He was not at all flashy. He didn't care about publishing in high profile journals or following the most trendy things. In fact, at the time I was working on the ribosome with him, the ribosome was not even fashionable. He had a long term interest in the ribosome, and he wasn't going to be distracted by fads. So, I learned a sort of attitude about that. I would say the third influence was my sabbatical year at the MRC LMB. What I found at the LMB was, nobody was working on anything trivial. They were all working on interesting and important problems. It didn't matter to them whether it was immediately solvable or not. If it wasn't immediately solvable, they would break it down into steps. But they were all directed at getting to a goal rather than just doing the next feasible experiment on something. It was a different way of doing science. I think these three things were sort of key. I mentioned the professors at M S University, who came back from the US and modernized the course. I've got to give them credit. And at Ohio University, I would say the one person who did inspire me was a person named Ron Cappelletti, who was also very strict. My own PhD advisor was not strict, and in hindsight, I think that was bad for me. I was a complete goof off again in graduate school. So, there were periods, in middle school and during my physics graduate school, when I was just not motivated.

PB: You know, you've reestablished your connections with the Indian scientific establishment after a long gap of about 30 years, and you've been coming to India over the past 18 years or so. Can you describe your impressions of science in India and the institutions that you've seen more closely?

VR: You're right. You know, for 30 years, I visited India only thrice when I was in the United States. It's sort of embarrassing to admit, but I think part of the reason was that I would only come to visit my parents. Once I got married, and they themselves moved to the US, there was not an incentive. But, I remember in 2002, I met you for the first time. I had come to give the first G N Ramachandran Memorial Lecture because he had passed away the previous year. And that was a big honor, and they were very generous. They said, "Look, we know you're going to a meeting in New Zealand around February. So why don't you tell us a date when you can stop off in Chennai and give this talk?" And I thought that was very generous of them. So I did that. It was the first time I met Indian scientists. And on that occasion, you may remember, you also invited me to come and visit IISc in Bangalore, and we flew together. I met a few scientists at the Biophysical Society meeting. And I saw that there was a fair amount of

crystallography going on. Then I came to IISc, and I saw quite a bit more science. And after that, a few years later, I thought maybe it would be a good idea to spend some time in India instead of just flying in and out, and talk to people and maybe give lectures, and so on. Partly, it was my thinking that I wanted to reconnect with India and with Indian science. So, I wrote to the Indian Institute of Science. You and Umesh Varshney arranged for a visiting professorship, which also was named after G N Ramachandran. And that started my annual or biennial visits to India. I've seen quite a few places now. The places I've seen are what I would call the elite places in India. For example, I've visited a couple of IISERs, IISc, CCMB in Hyderabad and some of the institutes in Delhi like ICGEB. These are not universities like Baroda University, which I also visited. I feel that something has changed in about 50 years. If you go back 50 years, many of the big universities were doing very good research. All the original presidency universities were centers of research. M S University used to be a notable research university. What I feel is that most of those universities have declined in relative standing. Research has been concentrated in centrally funded research institutes. And now people are trying to reverse that with IISERs. But IISERs are also centrally funded. They are not state universities, where thousands of students go to. I think that is one issue. The other issue is about the kind of science. And here, if you don't mind my being critical, I find, many scientists in India are doing what I would call extensions of what they did as postdocs when they were abroad. And they are not sort of being bold and venturing into completely new areas of research. That happens occasionally. There are individuals who are truly outstanding, and they would be considered first-rate anywhere. But as a general rule, I would say, even at the elite institutions, the science is good and it's rigorous, but it's not what I would call world-leading. When I visited China in 2011, I was enormously surprised. I had thought of China as being like India, but a little bit ahead. But actually, in China, the economy by 2011 was already extremely different. The kind of resources the institutes had was very different. I would still say that in 2011 in China, there were only a few labs that I would have considered world-class. The others were doing good science, but not, world-class science. That has changed if you go to China today. There are many labs in the top universities that are among the leading labs in the world in their fields. So, it can be done with enough resources, and with enough motivation and ambition.

PB: Now, you've been the president of the Royal Society for the last few years. Has this been a major challenge, and how have you adapted to the role of a public spokesman for science?

VR: You know, I often wonder why they even chose me as the President of the Royal Society. Because, when they elected me, I was not a mover and shaker. I was not a big institution builder. I had not overseen some great organization like a research council or something like that. I was very different from my predecessor, Paul Nurse, who was the director of the CR-UK lab and then the president of Rockefeller. So I was a bit surprised when they chose me. I

thought that perhaps I didn't have to be like Paul Nurse. There were lots of previous presidents who were very different, somewhat quieter, and maybe not as visible. So, I thought, OK, well, maybe I should accept it. It is a great honor. I felt flattered, and I thought I should give it a shot. I went in there with somewhat naive ideas. You know, I didn't really quite understand how these institutions work, and how these sort of high-level policy decisions and politics work. It's very different from doing a lab experiment within your own group. So, it was a steep learning curve. To cap it all, within six months after I got elected, the UK decided to leave the EU in the referendum. Then we had to ask how science would be affected as a result of leaving the EU. How could we maintain ties with the EU? And if all else failed, what sort of backup would we have? Now, of course, you know it is the government that has to decide this. But, in the UK, the Royal Society has enormous influence because it is the society of some of the top scientists in the country. It is taken very seriously and thus becomes a big responsibility. That was one aspect. The other aspect is, you know, looking at various science policies. I don't get directly involved in policies, but I often end up having to speak on behalf of The Royal Society, for example, on GM crops or genome editing, and issues about ethics and scientific culture, all these things. So, I feel I have learned a huge amount. I don't know how effective I've been. But, on the other hand, the Royal Society is a very well-run and very collegial organization. And it doesn't depend on any one individual.

PB: If you were starting out in biology today, which area would you choose to do research?

VR: I think I personally would be fascinated by neuroscience and especially, understanding, the principles behind brain function. I mean, we don't even understand how we remember. Say, how do I know it is you when I see you? It means in my brain, I have a map. I have a map of your face. It doesn't matter whether you are looking at me or you are looking at someone else. I can still recognize you. It means I have a complicated, three-dimensional representation of you. And then connected with that, I remember your name, and then I know who you are. I know you are in Bangalore, and that you are the former director. All these little facts about you are all connected in my brain. I can recall all that. That is an amazing thing. And we are starting to understand the little pieces of this puzzle. But I think this is going to be a sort of problem that could take a long time to solve. It will probably be solved on simpler organisms first. I think neurobiology is developing some very interesting tools to be able to look at neural circuits, and then try to go from there to understand the basis of memory and behaviour.

PB: You have had a remarkably illustrious career. Do you have any regrets?

VR: Well, I know I have had quite a lot of luck. I have to say that throughout my career, and some of it is, you know, experiments working out when they didn't necessarily have to, but often it has been meeting people who gave me ideas. Like on my sabbatical, somebody

gave me an idea that led to the use of anomalous scattering. Or Aaron Klug not throwing my letter into the wastepaper basket. There were many pieces of luck throughout. When we look back, scientists sometimes ascribe their career to a series of logical steps, but it isn't actually like that. We often make blunders, and we are often lucky. The regret I have, which will amuse you, is that I don't know enough chemistry, and I wish I had learned more real hardcore chemistry, which is to say organic and inorganic chemistry. Physical chemistry, with my physics background, is not so hard. But, actually learning about reaction mechanisms and understanding inorganic chemistry would have helped me really understand things better. As it is, what I had to do was, every time I had a little system, I had to learn enough chemistry to understand that piece of the puzzle. And, you know, that is not really satisfying.

PB: You know, the readers of *Resonance* are largely young students, although I am sure many older scientists will also read this interview. Would you have any words of advice to students on the verge of deciding a research carrier?

VR: I would say two things. First of all, when students are getting educated, they should try to stay as broad as possible for as long as possible. Because today, if you're a biologist, the frontiers of biology require physical methods. It requires chemistry, which we just discussed, and it requires mathematics. Often people will abandon subjects too soon in an effort to focus. And this doesn't mean they should sacrifice depth. But it does mean that they should keep the others going, and learn it to as high a level as possible, and get the sort of background they need so that they can be versatile when they have to tackle a problem. Finally, when they are choosing a research career, I do think it is important to go to the best institute you can, partly because your cohort will be extremely good, and you often learn from your fellow students. The professor-student interaction is one thing, but you will be spending a lot of time with your fellow students and possibly postdocs, and others. So, you want to be in the best sort of environment. You also want to be in an environment where people are aware of the frontiers of research and where things are going. That happens more at the better institutions. So trying to get into the best place is another piece of advice. And then people don't realize the importance of choosing a mentor. I would say you primarily have to be driven by your interest. You have to be interested in the problem, because in science, you know, 90 percent of the time things aren't working. And the reason is that as soon as they work, you write it up, you publish, and then move on to the next stage, which is also where you don't know what to do when things aren't working. So the period when things are actually working is quite small. So, you have to be motivated to come in every day and do the next failed experiment, and the next failed experiment, and so on. You can only do that if you care about the problem. If you're not interested in the problem, then it becomes a real drudgery. So choose something you really care about.

PB: Thank you very much Venki.

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