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3D Proteins

An interview with Kurt Wüthrich

Nobel Laureate for Chemistry in 2002 “for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution”

by Piero Tundo

Kurt Wüthrich

T You have pioneered two-dimensional NMR spectroscopic analyses. Your work resulted in a massive contribution to the study of 3D protein structure. How many protein have you actually solved so far?

W I don’t know exactly now how many structures we have solved, it is somewhere between 100 and 150. More important, to date, more than 8,000 protein structures have been solved by NMR worldwide.

T This is a significant number! What was, at the beginning of your work on protein structure, the most difficult data to interpret and the most exciting result?

W The turning point in developing this method was to discover that the nuclear Overhauser effect could provide the data that enabled one to determine a new protein structure. As for the most exciting results, there are three outstanding events: in 1974 the observation that the aromatic rings of phenyl aniline and phenyl alanine and cytosine undergo rapid rotational motions inside proteins; in 1984 the first protein (bull seminal protease inhibitor) structure determination by NMR; in 1996-1997 the determination of the structure of the prion protein during the mad cow disease crisis in the UK.

T How do you see the future of NMR spectroscopy for the determination of macromolecular biological structures? In the past you have been working on structural aspects of genome expression and regulation and currently the main focus of your work is in structural genomics. What may be the implications of the results of such studies?

W The work on genome expression and regulation was focused on the structure of homeodomains and the interactions of homeodomains with DNA. This is a typical structural biology project and it gave new insights into the mechanism of differentiation in higher organisms. This is one example of very many projects worldwide on this sort of problem. What I am currently engaged in is to determine as yet unknown structures of gene products, with the aim of expanding the structural coverage of the protein universe.

T So moving from static structural proteins, you are now investigating dynamic interaction of proteins with DNA, that is to say proteins at work?

W There is always dynamics in NMR structures because we work in solution (as opposed to static crystal structures determined *via* X-ray crystallography).

T Your Ph.D. thesis was in the field of inorganic chemistry. You then started broadening your interest to biology and biochemistry. In which field would you suggest a chemist should now broaden his/her knowledge?

W I studied chemistry, physics and mathematics for my university degree and this was an excellent basis for all further developments. What a student learns in these three subjects is likely to be useful for a lifetime, whereas detailed biological knowledge changes more rapidly during the last 50 years. So I would recommend studies in physics and chemistry with a strong foundation of mathematics and computational methods, because this is a good basis from which to evolve into areas of biology and biomedical research.

T So you suggest that students first have a solid base of fundamental science then they can choose, with more freedom, to go where their inclination takes them?

W Absolutely! Although there is a special situation in my case in that I also have a degree in sports, which means that I also went to medical school to learn about anatomy and physiology, which had a certain influence on my later activities.

T A future challenge for chemists will be to develop cleaner processes and eco sustainability: in short, we say, to be a green chemist. What is your personal idea on how chemistry should develop in to Green Chemistry?

W I would want to make two statements here. Firstly, in the past, accidents with chemicals that led to pollution of water, soil and air, have given a very bad name to chemistry for many – politicians and lay people – and it was always very difficult to recover from such incidents. I remind you of accidents where the Rhine was largely polluted (1986, Basel), accidents in Italy where the soil was badly polluted (1976, Seveso), in India where a gas leak killed thousands (1984, Bhopal). It is obvious for the field of chemistry that every possible effort has to be made to stay clean. Even when working with what you call “green chemistry”, one must be extremely careful not to affect the environment. Secondly, the very recent accident with the oil spill in the Gulf of Mexico shows that in the future we can no longer rely on classical heavy chemistry, we will have to refine methods, we will have to make more out of less natural resources and most of all we have to use renewable sources of energy. There is a very important role that chemistry will have to play during the next decades, in solving problems along these lines.

T I completely agree with you, because now we have the means to solve the problems and to steer chemistry towards development while taking into consideration the chemical cycle of nature, which only chemists can understand and the general consensus is that only chemistry can solve these problems.

W With regard to the public image, it is actually unfortunate that much of the clean chemistry happens under a different name, like environmental sciences and similar, rather than being represented as chemistry.

T You have been secretary general of IUPAB (International Union for Pure and Applied Biophysics) and member of the ICSU (International Council for Science) General Committee. According to your personal international experience, what will be the role played by science in this era of ever growing globalization?

W ICSU and the international unions are mostly political instruments, and their main focus has been to promote the development of science in the 3rd World, which is of course a key issue. Aside from this, science has been a global enterprise long before one started to talk broadly about globalisation, it has always been a trademark of science and scientists that they were linked worldwide and that they would set up informal collaborations, independent of what politicians in their country would do at the time.

T So the role of science and chemistry in a growing world is the continuing dissemination of knowledge?

W Yes, and in many ways science has had a similar role to sport, historically speaking, in starting international interactions between countries that did not properly interact on a political level. Contacts by athletes and scientists were often followed by politicians. I may just remind you of the way mainland China came back into the International Community, this was started by sports events and by scientific contacts, before there was a political solution.

T You were born in Switzerland and you never seem to forget about your hometown where you return as often as you can. How important are your roots for the development of your international career? In this context, what advice would you offer for a student whishing to work abroad?

W Well let me answer this in two ways. The first is an emotional one, I am very much attached to my home town and my home country. I grew up on a farm and I am still managing a big forest which used to belong to this farm, I return to my home town at least twice a year to see the forest engineer to plan future work. This gives me a reference point when travelling all around the world, which I do a lot. The second is that being born in Switzerland, I was strongly encouraged to learn foreign languages. It is a trademark of our small country that we have three official languages and that in addition, we must know English in order to survive, otherwise we can not work in tourism and similar. Thus there was a very strong motivator to learn languages and this has helped me a great deal in my career later on.

T So your advice to students would be to attempt to acquire a second langue at the very minimum?

In Italy they must learn English in order to survive in a natural science career. There is a similar point to the one I made about physics, chemistry and maths: if you learn a langue in high school, you have learned that language for life. Therefore I think I was extremely fortunate to have grown up in a bilingual city, French and German speaking, and to have been pushed very hard to learn English early on.

T Finally, this is a question we have posed to all the Nobel laureates we have interviewed. Do you think ethical issues should be addressed by science? Do you believe they should be included in a student's curriculum?

W This is a difficult question for me to answer in a direct way. On the one hand, we must teach our students about fair behaviour in science and not just in science and in life. On the other hand, we must make sure that thinking about ethics and similar does not completely inhibit young people from ever doing anything new. There must be is a subtle balance between the two. We must talk to our students about proper behaviour, about ethics of science, but we must also leave free space for them to develop without being overly inhibited by constantly thinking about negative implications their results might have.

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