

# The Nobel Prize to Kurt Wütrich

## A recognition to a great man who is the founder of biological NMR

by Ivano Bertini

*The Nobel Prize in Chemistry 2002 presents various keys of interpretation. First of all it is a recognition to an extraordinary man who is the founder of biological NMR. It is also a recognition to the power of this spectroscopic technique as structural method in biology which has been growing in recent years. Last but not least, it represents also a proof of how a far-sighted policy of investments in research can lead to results of excellence.*



As soon as I discovered that Kurt Wütrich had won the Nobel prize I sent an e-mail to Kurt, together with Lucia Banci and Claudio Luchinat, saying: "It was time, congratulations!!! We are bursting with joy for you." That was the feeling at CERM (the Center of Magnetic Resonance of the University of Florence). It was time! Kurt developed the methodology to obtain the solution structure of proteins and published the first structure in 1985.

In the following year he published the solution structure of a metallothionein, correcting an earlier x-ray structure. With these papers he opened a new research field, i.e. the solution structure determination of biological macromolecules by NMR. Nowadays NMR is recognized as a methodology for structural biology and a significant share of structures deposited in the PDB (Protein Data Bank) is done by NMR. One major limitation of the methodology is the difficulty in studying large proteins. In order to obtain structural constraints for a structure, it is necessary to be able to detect all of the nuclei.

With a 800 MHz NMR instrument, proper protein labelling, and multiple dimensional spectroscopy, a protein of 30,000 Dalton can be routinely afforded. Wütrich published, 5 years ago, a new pulse sequence (TROSY) which allows for the investigation of proteins of 100,000 MW and beyond. In *Nature* this year he published an investigation of a complex between a chaperone and a polypeptide of a total MW 900 kDa. The TROSY sequence gives the sharpest signals at the field of around 1 GHz. Thus, the TROSY pulse sequence has provided the theoretical background for NMR companies to produce the 1 GHz magnet. The accomplish-

ment for which the prize was awarded is: "for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution". This is music to my ears. It is an appreciation of the work of chemists in biology. The scientific career of Kurt should not only inspire our activity but should inspire also those that govern the Italian Universities towards a policy of excellence and cooperation. Around 1975 Kurt had a 360 MHz and started a fruitful collaboration with Richard Ernst which lasted for a decade.

A paper on NOE as structural constraints by Ernst and Wütrich collects more than 1.200 citations. Richard Ernst obtained the Nobel Prize in 1991 for his contributions to NMR spectroscopy. When the collaboration ended, Kurt was already in the field of structural biology. In 1996 he took advantage of the laboratory of Adriano Aguzzi who was studying prions, and solved the first of a series of solution structures of prions. His lab was always among the first to buy the new NMR instruments. He has now the 900 MHz in Zürich. However, he is reaching 65, and in Switzerland there are no exceptions to the 65 year retirement. So he is moving to Scripps Institute in San Diego, where there is no age limit for retirement. At Scripps he also has again a 900 MHz (which was the first installed, the second being that in Zürich).

Kurt started his career with a PhD in inorganic chemistry in Basel, moved to Berkeley with Robert Connick to study paramagnetic complexes by magnetic resonance spectroscopies, then went to Bob Shulman at Bell Laboratory to study metalloproteins by NMR, and then finally in 1972 he went to the Polytechnic in Zürich as an assistant of the peptide chemist Richard Schwyzler. He has educated a large number of people, many of them being now in key posi-

tions at various places: Gerard Wagner at Harvard, Dominique Marion in Grenoble, Gottfried Otting in Stockholm, Martin Billeter in Göteborg, Anil Kumar in Bangalore, Miguel Llinás at Pittsburg, Peter Güntert in Yokohama, Thomas Szyperski in Buffalo NY, Dario Neri and Konstantin Pervushin in Zürich etc. Unfortunately, some important names may have escaped my memory, particularly because I may not be aware of all the scientists that have spent time in Zürich. Regardless, it is clear, that a number of important scientists are products of Kurt's lab. If I compare my curriculum with that of Kurt, I notice that I am not PhD (except one degree honoris causa), I obtained Libera Docenza, I could not have graduate students before 1982 (because Italy did not have graduate courses) nor could I have grant holders, because in the 80's grant holders were considered exploited workers without security...

I had the first decent spectrometer in 1989, and I consider myself lucky by Italian standards. In 1994 I solved the first solution structure of a paramagnetic metalloprotein by using and adapting Kurt's protocols. I started interacting with him in 1979 on the occasion of a NATO school in Maratea that I organized, and since then I have interacted with him at various places. A couple of times, late at night after several drinks, Kurt expressed admiration for what I have been able to do in a country like Italy. I never knew whether I should be proud or offended by this comment. Definitely, his ability to manage and organize his lab coupled with the excellent environment provided by the Polytechnic of Zürich have been helpful, but it is his extraordinary intelligence and his capability of moving the frontiers of science forward for decades that accounts for the results he has achieved. Let us wish him comparable success for the second part of his life in America.

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