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The NMR View of Proteins

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Kurt Wüthrich is the Cecil H. and Ida M. Green Professor of Structural Biology at The Scripps Research Institute, La Jolla, CA, USA, and Professor of Biophysics at the ETH Zürich, Zürich, Switzerland. He also directs research groups at the Universidad Federal do Rio de Janeiro in Brazil and at the iHuman Institute of ShanghaiTech University in China. His research interests are in molecular structural biology and structural genomics. His specialty is nuclear magnetic resonance (NMR) spectroscopy with biological macromolecules, where he contributed the NMR method of three-dimensional structure determination of proteins and nucleic acids in solution. The Wüthrich groups have determined a large number of macromolecular NMR structures, including the immunosuppression system cyclophilin A–cyclosporin A, the homeodomain–operator DNA transcriptional regulatory system, and prion proteins from humans, cattle and a variety of other species.

Kurt Wüthrich was born in Switzerland on October 4, 1938, is married to Marianne Briner, and has two children, Bernhard Andrew and Karin Lynn. He studied chemistry, physics and mathematics at the University of Bern from 1957–62. He then moved to the University of Basel , where he obtained the "Eidgenössisches Turn- und Sportlehrerdiplom" and a Ph.D. in inorganic chemistry (Prof. Silvio Fallab) in 1964. He was a postdoctoral fellow in Basel (Prof. S. Fallab) and at the University of California in Berkeley, CA, USA (Prof. R.E. Connick), and a Member of Technical Staff at Bell Telephone Laboratories in Murray Hill, NJ, USA (Biophysics Department, Dr. R.G. Shulman). In 1969 he joined the ETH Zürich (Privatdozent 1970, Assistant Professor 1972, Associate Professor 1976, Professor of Biophysics 1980, Chairman of the Department of Biology 1995–2000). Since 2001 he shares his time between the ETH Zürich and The Scripps Research Institute. Kurt Wüthrich's achievements have been recognized by the Prix Louis Jeantet de Médecine, the Kyoto Prize in Advanced Technology, the Nobel Prize in Chemistry, and by other awards and honorary degrees.

The Wüthrich group started work toward the NMR method for structure determination of biological macromolecules in solution in the 1970s with systematic studies on NOE (NOE: nuclear Overhauser effect) build-up and spin diffusion in proteins (1), the sequential assignment strategy for proteins (2) and, in joint projects with Richard R. Ernst, the development of two-dimensional NMR with biological macromolecules (3). A framework for

NMR structure determination of proteins was formulated in 1982 (2). Among the three-dimensional protein structures in solution solved by the Wüthrich laboratory, the bull seminal proteinase inhibitor (BUSI) was the first NMR structure of a globular protein (4). In the further development of the method, the structure determinations of metallothionein (5), the amylase inhibitor tendamistat (6), the Antennapedia homeodomain–BS2 operator complex (7), and the cyclosporin A–cyclophilin A complex (8) were of special interest. Prion proteins (PrP) have become a major research focus of the Wüthrich laboratory since 1994 (9–12).

Beyond three-dimensional structure determination, the Wüthrich team worked on additional methods developments. NMR was used to study biomacromolecular dynamics, solvation and function-related conformational equilibria (13–16). The introduction of transverse relaxation-optimized spectroscopy (TROSY) in 1997 (17) has made a wide spectrum of novel NMR experiments available for studies of larger biomacromolecular structures in solution. Applications in the Wüthrich laboratory include structure determinations of integral membrane proteins and studies of their solvation in water-soluble micelles (18), and characterization of the conformational states of individual macromolecular components in supramolecular structures with molecular weights up to 900 kDa (19).

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