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Editorial

It is our pleasure to present this Festschrift in honor of Professor Kurt Wüthrich. Kurt, of course, needs no introduction, as his work has revolutionized NMR spectroscopy in general and biomolecular NMR in particular. His contributions have had impact beyond the realm of NMR, as they have transformed how scientists think about biomolecules. It seems obvious now that biomolecules are dynamic and that their motional properties can significantly influence their function. Yet, in the bygone era where static structures determined by X-ray crystallography ruled the day, the discovery that aromatic sidechains in the protein core of BPTI undergo ring flips was a shocking result that challenged the way in which proteins were viewed. Initially the implications of this work – that globular proteins undergo breathing motions, in this case allowing for rapid rotation of bulky aromatic sidechains – was met with strong criticism. Over time it has become dogma, however, foretelling the seminal role NMR spectroscopy would play in the measurement of site-specific motional parameters in biomolecules and relating these to function and misfunction. And this example is just the tip of the iceberg. Kurt and his talented colleagues pioneered the determination of three-dimensional solution structures of proteins, opening a new window of possibilities for solution NMR. New pulse sequences followed at a prodigious pace with clever acronyms and even more clever manipulations of spins to methodically dissect the specific chemical information of interest. Experiments with ever-increasing sensitivity and resolution, culminating with the brilliant amide-TROSY scheme, projected NMR into the world of large biological entities.

In his global leading laboratory Kurt has trained many of the best NMR spectroscopists in the world, who, through the years, have continued to demonstrate the power and versatility of NMR spectroscopy in structural biology, drug design and chemistry. In this Festschrift we have collected contributions from eight such renowned scientists, through which the breath and impact of Kurt's legacy are illustrated. Prof Gerhard Wagner, one of the first and most prominent members of Kurt's lab in Switzerland, tells us how to optimize Non-Uniform-Sampling (NUS) schemes for high fidelity reconstruction of either high-dynamic-range or sparsely sampled spectra. NUS expands the dimensionality of NMR spectra to facilitate Kurt's vision of NMR spectroscopy as applied to increasingly complex biological systems. Prof. Peter Guentert and Prof. Sebastian Hiller tell us about the effect of motions on NOEs, with P.G. deriving a closed formula for internuclear distance averages and S.H. addressing the influence of supra-τ_c motions on methyl-methyl NOEs. Both articles continue the tradition of Kurt, who pioneered the application of two-dimensional NOESY spectroscopy to proteins. Prof. Ramakrishna V Hosur introduces a new method that uses the concept of Mahalanobis distance to quantify differences between NMR spectra acquired under different conditions. This contribution improves one of the strongest and easiest-to-implement NMR applications: two-dimensional spectra for monitoring ligand and protein binding, as well as other biological events triggered in the NMR tube. Dr. Alvar Gossert presents a development concerning TROSY, which, introduced by Kurt, has revolutionized biomolecular NMR spectroscopy by significantly expanding its scope of application. A.G. introduces RODA, a new way to achieve spin-state selection with improved sensitivity. In his contribution, Dr. Oliver Ohlenschläger shows how to use heteronuclear cross-polarization to achieve transfer of magnetization between Cα spins of neighbouring residues during assignment of intrinsically disordered proteins. This class of polymers has been gaining enormous importance in biological processes and intermolecular interactions and represents a playing field where NMR can make unique contributions. A fundamental aspect of biomolecular NMR is sample preparation. Prof. Hideo Iwai presents how to engineer a salt-inducible intein to be used for protein trans-splicing with the split-intein technology. This technique enables the generation of segmentally labelled proteins, which helps enormously in the application of NMR to complex macromolecular systems. And, last but not least, Prof. Gaetano Montelione writes on how to organize and store NMR data to make them accessible by machine learning algorithms. This contribution projects biological NMR into the future, when, with the help of artificial intelligence, we may be able to determine protein structures by the shear comparison of NMR spectra with those of known proteins and folds.

One may wonder why we choose to celebrate Kurt now, as typically celebrations are held when one reaches an age that is divisible by five or ten and Kurt is 83 years young. Kurt has been celebrated on many occasions, including for his Nobel Prize in Chemistry in 2002. However, there is some significance with 83 as well. According to the Jewish tradition a person celebrates a coming of age when they reach 13 and a second such celebration is held when they reach 83. In both cases the celebration encourages the individual to continue learning and discovering – contributing to the world at a high level. Kurt, this is our hope for you, that in the years to come you continue to share with us new and exciting NMR contributions.

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