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Introduction: Biological Nuclear Magnetic Resonance

NMR began as a curiosity of physics. Apart from pre-WWII studies of molecular beams, which provided the first evidence of the absorption of radio-frequency energy in the presence of magnetic fields, the first detection of nuclear magnetic resonance due to the formation of a Boltzmann population difference in the energies of certain nuclei, notably hydrogen, in the presence of a magnetic field was reported by Bloch (for liquid water) and Purcell (for paraffin wax) in 1946. The potential chemical applications of nuclear magnetic resonance were only discovered in the early 1950s, when a number of workers noticed that the resonance frequency of a nucleus is strongly dependent on its chemical environment. Explosive growth in the utility of the NMR technique to chemists occurred in the next few decades, but it remained generally useful only for small molecules until the advent of pulse techniques in the 1970s. These, together with higher magnetic fields (with increase in both sensitivity and resolution of the NMR signals) and better electronics, allowed increasingly larger molecules to be studied—into the molecular weight range of biological interest. The advent of multidimensional NMR and the employment of ^{13}C and ^{15}N labeling truly ushered in the era of biological NMR. Solution structure determination has taken its place beside X-ray crystallography as a means to obtain high-resolution structures of biomolecules. NMR imaging has become a standard diagnostic tool in medical practice, and new applications of magnetic resonance are finding a place in the diagnosis of disease. NMR also plays an important role in the industrial setting, providing diagnostic data for new pharmaceuticals. On the research front, innovations in NMR techniques continue to open new vistas and indeed to establish new fields of study. Major advances have recently been made in the study of biological macromolecules in the solid state, and we now have techniques for high-resolution structure determination in solids and membranes. Residual dipolar couplings, obtained with partially oriented samples in liquid crystal or similar media, have become a popular means of establishing long-range structural constraints in biological macromolecules. NMR relaxation studies have almost single-handedly transformed the study of molecular motion, enabling the acquisition of site-specific information on the motions of individual atoms and groups within large molecules and complexes, and, together with structural information, are providing important insights into the intimate mechanisms of biological processes such as binding and catalysis. Insights obtained from NMR have also opened up an entirely new field—the study of biomacromolecules that include unfolded states in their active repertoire. The study of conformational preferences for unfolded states is really only possible by NMR.

In this thematic issue, we have tried as much as possible to gather together a set of experts in their respective fields, to give a flavor of the wide range of new methodology now available in biological NMR, and to introduce the reader to a number of the newest techniques and developments, as well as some of the newest results, in this rapidly evolving field.

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