Preface

A plethora of techniques developed in the last decade has dramatically advanced solid-state nuclear magnetic resonance (SSNMR) spectroscopy as a unique tool for amazing applications into such diverse realms as analytical chemistry, bioengineering, material sciences, and structural genomics. Recent studies have shown that SSNMR is one of the most valuable techniques providing high-resolution details on the structural and functional aspects of many important biological solids (viruses, fibril-forming molecules such as amyloidogenic peptides, silk, collagen, cell walls, and molecules embedded in the cell membrane, such as lipids, cholesterol, proteins, and carbohydrates). The increasingly broad spectrum of developments and applications continues to glorify the intrinsic beauty and wealth of SSNMR. As a result, the number of research laboratories making significant contributions to solving problems related to biological solids has also increased considerably in the last decade. Therefore, I decided that publishing a book comprising all the recent developments in SSNMR and its applications to biological systems would benefit the scientific community. The goal of this book was not to provide an exhaustive compendium of information relevant to SSNMR but rather to provide a critical selection of SSNMR methods with demonstrated utility in the investigation of structure and function of biomolecules in solid-state.

Because there are no intrinsic limitations to the size and tumbling rate of molecules, SSNMR is applicable to all non-isotropic systems such as single crystalline, polycrystalline, amorphous, and semi-solids. While NMR parameters of these systems are tensorial in nature, they can be reduced to scalar parameters under magic-angle spinning (MAS), which provides solution-like spectra, but without any chemical modification. This unique advantage has been utilized thoroughly to measure accurately anisotropic interactions such as chemical shift anisotropy (CSA) and dipolar and quadrupole couplings. These anisotropic interactions contain a wealth of information about molecules: for example, chemical bonding, molecular shape and geometry, local and global molecular dynamics, folding and intermolecular interactions. In addition, the ability to measure both isotropic (chemical shift and scalar couplings) and anisotropic (mainly coherent homo- and heteronuclear dipolar couplings) from the same sample provided avenues to determine high-resolution structures of biological molecules in a non-soluble state. As a result, it is possible to determine three-dimensional structures of proteins in a microcrystalline state using SSNMR experiments under MAS. This topic is elaborately discussed in several chapters of this book. These techniques can also be extended to obtain information about the three-dimensional organization of molecules in nano (and pico) crystalline states, which could ultimately yield atomistic-resolution pictures of molecules in solid-state.

Another powerful and rapidly growing dimension of NMR spectroscopy is the study of aligned systems. In these systems, high-resolution spectral lines are rendered by the macroscopic alignment of molecules while the NMR parameters are still anisotropic. The art of preparing aligned molecules provide systems with various degrees of alignment defined by order parameters that vary from 0 (isotropic and completely unordered as in liquids) to 1 (rigid and completely ordered as in frozen solids). The last few years have witnessed tremendous progress in the development of multidimensional SSNMR methods to study aligned molecules. As discussed in several chapters of this book, significant strides have been made with respect to studying the structure and topology of membrane proteins using static SSNMR experiments on mechanically or magnetically aligned lipid bilayers. Such studies are important not only because they help us to understand basic issues related to protein folding in membranes but also to understand protein-induced damages to the cell membrane. Thus, these studies provide basic information about the mechanisms of action of a variety of biologically active molecules such as antimicrobial peptides, fusion peptides, toxins, ion channels, metal transporters, and signaling and receptor proteins.

It is important to note that the above-mentioned SSNMR studies are increasingly aimed at solving biological problems that have so far been considered nearly impossible. For example, the biogenesis of biological membranes is one of the most significant unresolved problems of biochemistry and cell biology. It should be apparent from recent biophysical studies that membrane proteins yield their structural secrets grudgingly. Therefore, it has been of considerable importance to develop a variety of biophysical techniques capable of solving, initially, the structure of membrane proteins and the host lipid bilayer within the membrane in as much detail as possible and, ultimately, of obtaining the response of each of these structures to a perturbation.

For the foreseeable future, progress in determining high-resolution structures of membrane proteins will depend greatly on SSNMR techniques. Poor sensitivity, resolution, and sample stability are some of major issues in this field and are addressed in this book. This volume also covers the theoretical and computational analysis of NMR experiments and experimental data.

I hope that *NMR Spectroscopy of Biological Solids* provides an answer for students and researchers with an interest in biological solids. I thank all the authors who contributed to this book, despite many other pressing obligations, for their understanding and patience during the prolonged birth of this project.

The cover picture of the book is a gift from Dr. Marassi (Burnham Institute) and was adapted from *Protein Science* (12, 403, 2003).

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