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Topics in Current Chemistry

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Aims and Scope

The series *Topics in Current Chemistry* presents critical reviews of the present and future trends in modern chemical research. The scope of coverage includes all areas of chemical science including the interfaces with related disciplines such as biology, medicine and materials science.

The goal of each thematic volume is to give the non-specialist reader, whether at the university or in industry, a comprehensive overview of an area where new insights are emerging that are of interest to larger scientific audience.

Thus each review within the volume critically surveys one aspect of that topic and places it within the context of the volume as a whole. The most significant developments of the last 5 to 10 years should be presented. A description of the laboratory procedures involved is often useful to the reader. The coverage should not be exhaustive in data, but should rather be conceptual, concentrating on the methodological thinking that will allow the non-specialist reader to understand the information presented.

Discussion of possible future research directions in the area is welcome.

Review articles for the individual volumes are invited by the volume editors.

Readership: research chemists at universities or in industry, graduate students.

Henrike Heise · Stephen Matthews
Editors

Modern NMR Methodology

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Preface

Nuclear magnetic resonance (NMR) spectroscopy is an extremely versatile and powerful analytical tool, which is indispensable in many research fields within chemistry, physics, biology, and medicine. Applications of this technique range from routine chemical analysis to materials science and from biological structure determination to biomedical imaging. Although the technique itself is almost 70 years old, it is far from being fully exploited, as novel developments in hardware technology, pulse sequences, and hyperpolarization techniques have expanded its applicability to ever more complex systems and demanding questions. In this volume, we give the reader a flavor of the large and multifaceted range of applications of NMR spectroscopy by highlighting the recent advances in a variety of areas.

While improvements in superconductor technology have facilitated high-resolution NMR spectroscopy at ultra-high magnetic fields with B_0 strengths up to 23.5 T (corresponding to a ^1H Larmor frequency of 1 GHz), improvements at the other end of the scale, i.e., NMR spectroscopy at ultra-low magnetic fields, also offers intriguing opportunities. NMR spectroscopy at the Earth's magnetic field is an extremely attractive option for field applications, as no large superconducting magnets are required. Furthermore, at ultra-low magnetic fields the scalar coupling becomes the major interaction which leads to a novel type of NMR spectroscopy. In the chapter "NMR Spectroscopy for Chemical Analysis at Low Magnetic Fields," the underlying principles, recent applications, and state-of-the-art hyperpolarization techniques used for pre-polarization of nuclear spins are reviewed.

A major limitation for NMR spectroscopy is the intrinsically low sensitivity due to the rather unfavorable Boltzmann distribution for nuclear spins at thermal equilibrium. Thus, considerable effort in magnetic resonance spectroscopy is made towards sensitivity enhancement by hyperpolarization techniques, such as optical polarization, para-hydrogen-induced polarization enhancement, and dynamic nuclear polarization (DNP), a method which exploits the magnetization of unpaired electrons in stable radicals or transition metals to enhance nuclear polarization beyond the Boltzmann limit. In the chapter "Dynamic Nuclear Hyperpolarization in Liquids," the fundamental theory for different polarization transfer

mechanisms in DNP is explained, and the experimental background for DNP applications is described.

Structure determination of soluble proteins of moderate size (up to 30 kDa) by multinuclear multidimensional NMR spectroscopy is now fairly standard with well-established protocols. In the chapter “NMR with Multiple Receivers,” an acquisition scheme employing multiple receivers is described which allows for faster structure determination in small molecules. Further, recently employed fast acquisition schemes such as Hadamard spectroscopy, projection-reconstruction techniques, and reduced dimensionality experiments are explained.

The most severe limitation towards structure determination by solution NMR spectroscopy of proteins larger than 50 kDa is the line-broadening due to restricted molecular tumbling. Transverse-relaxation optimized spectroscopy (TROSY), originally developed by Wüthrich for amide-protons, relies on the selective detection of the spin state for which dipolar coupling and chemical shift anisotropy relaxation mechanisms compensate each other, thus leading to reduced line-widths. In the chapter “TROSY NMR Spectroscopy of Large Soluble Proteins,” the application of TROSY methodology to extensively deuterated proteins with selective protonation in methyl groups is reviewed.

For even larger proteins, protein aggregates, protein complexes, or proteins embedded in a lipid bilayer, where the molecular tumbling is further reduced, solid-state NMR spectroscopy may become a viable alternative for structure elucidation or even high-resolution structure determination. In the chapter “Solid-State NMR Spectroscopy of Proteins”, basic principles of biological solid-state NMR spectroscopy as well as fundamental techniques for isotope labeling, sample preparation, and some selected applications are reviewed. In addition, recent developments in polarization enhancement by DNP for solid-state NMR spectroscopy are outlined.

Paramagnetic centers in molecules are often considered an inconvenient obstacle towards characterization by NMR spectroscopy. However, in the past decade, great effort has been made towards the exploitation of paramagnetic centers in small organometallic compounds, stable radicals, or even proteins with paramagnetic centers for elucidation of chemical or structural properties. In the chapter “Paramagnetic Solid-State Magic-Angle Spinning NMR Spectroscopy,” the application of NMR spectroscopy to paramagnetic solids is reviewed: The theory of major interactions between electrons and nuclei such as the hyperfine shift, the pseudocontact shift, and paramagnetic relaxation enhancement is explained in detail. Experimental details are described and some illustrative recent examples are given.

The dynamics of nuclear spins in magnetic fields and their manipulation are the underlying common theme in many new developments in NMR. We hope that the reader will enjoy the range of aspects covered in our book. Furthermore, we would like to thank all the contributing authors for their valuable contributions.

London
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