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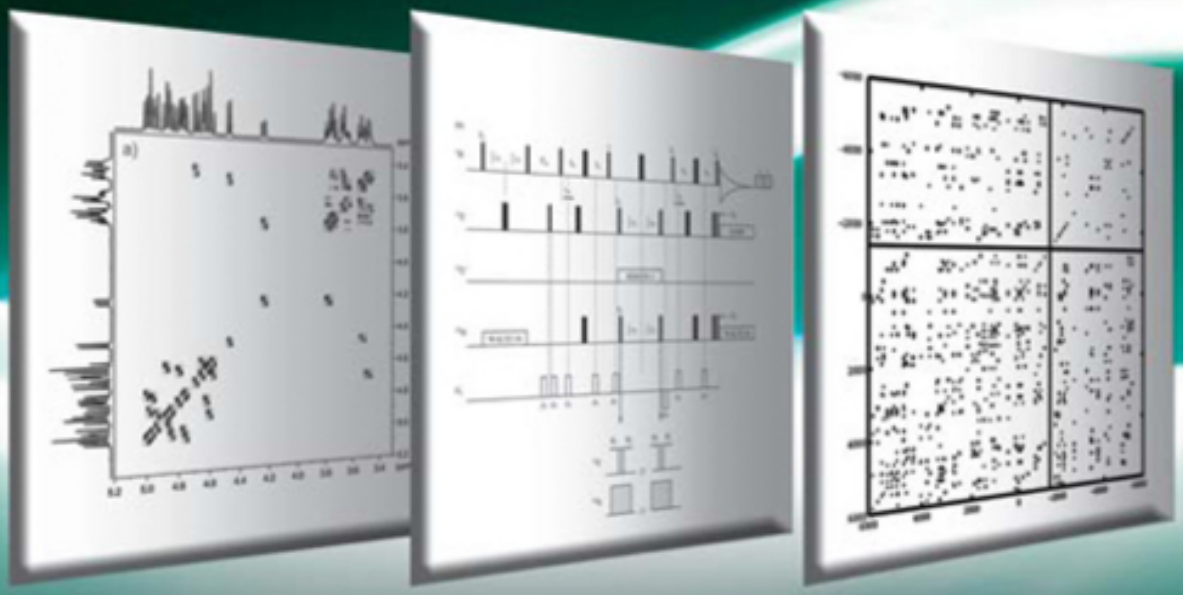
MULTIDIMENSIONAL NMR METHODS FOR THE SOLUTION STATE



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Multidimensional NMR Methods for the Solution State

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Contents

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Chapter 15: Relayed Coherence Transfer Experiments

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Chapter 34: Structures of Larger Proteins, Protein–Ligand, and Protein–DNA Complexes by Multidimensional Heteronuclear NMR

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Chapter 2: Multidimensional Spectroscopy: Concepts

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Chapter 30: 2D NMR of Molecules Oriented in Liquid Crystals—Recent Developments

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Chapter 4: Fast Multidimensional NMR by Hadamard Spectroscopy
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Chapter 21: 2D Methods of Monitoring Exchange

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Series Preface

The *Encyclopedia of Nuclear Magnetic Resonance* was published in eight volumes in 1996, in part to celebrate the fiftieth anniversary of the first publications in NMR in January 1946. Volume 1 contained an historical overview and ca. 200 short personal articles by prominent NMR practitioners, while the remaining seven volumes comprise ca. 500 articles on a wide variety of topics in NMR (including MRI). Two "spin-off" volumes incorporating the articles on MRI and MRS (together with some new ones) were published in 2000 and a ninth volume was brought out in 2002. In 2006, the decision was taken to publish all the articles electronically (i.e. on the World Wide Web) and this was carried out in 2007. Since then, new articles have been placed on the web every three months and a number of the original articles have been updated. This process is continuing. The overall title has been changed to the *Encyclopedia of Magnetic Resonance* to allow for future articles on EPR and to accommodate the sensitivities of medical applications.

The existence of this large number of articles, written by experts in various fields, is enabling a new concept to be implemented, namely the publication of a series of printed handbooks on specific areas of NMR and MRI. The chapters of each of these handbooks will comprise a carefully chosen selection of Encyclopedia articles relevant to the area in question. In consultation with the Editorial Board, the handbooks are coherently planned in advance by specially selected editors. New articles are written and existing articles are updated to give appropriate complete coverage of the total area. The handbooks are intended to be of value and interest to research students, postdoctoral fellows, and

other researchers learning about the topic in question and undertaking relevant experiments, whether in academia or industry.

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November 2009

Volume Preface

Over ten years passed between the first recognition of the potential of NMR methods based on Fourier transformation of the response to a radiofrequency pulse and the practical realization of that potential, by Ernst and Anderson, in 1966. The effect on the practice of NMR was rapid and profound, with pulse-Fourier transform equipment quickly supplanting continuous wave spectrometers. The great improvement in sensitivity achieved by this method opened up areas of the periodic table that had until then been largely unexplored by NMR, and the chemical application of multiple pulse experiments such as inversion recovery and the spin echo began in earnest.

It was only five years later, in 1971, that Jean Jeener proposed another technique, two-dimensional or 2D NMR spectroscopy, that was to have equally far-reaching implications. This time it took just four years for the first successful experiments to be reported, again by Richard Ernst and his colleagues, and once again the new methods were rapidly and widely adopted. Multidimensional NMR methods have since transformed the way NMR is used in chemistry, biology, physics, and medicine, to the extent that they are now part of the routine vocabulary of chemistry and of structural biology.

One of the most engaging features of NMR is its continuing ability to surprise. Despite over half a century of intensive study of the phenomenon of magnetic resonance, new discoveries and new developments in technique are still being made, and the flow of new ideas continues unabated. One of the most fruitful areas of development in recent years has been in methods for speeding up 2D and high-dimensionality experiments. Thus it is now possible in some

cases to acquire a complete 2D spectrum in a few seconds, or to acquire data correlating five or six spectral dimensions overnight, with time savings of several orders of magnitude. Thus while this handbook contains authoritative accounts of techniques such as COSY, NOESY, and TOCSY that have acquired the status of classics, it also includes a range of articles on techniques that have been developed within the last few years, each written by the leader of the relevant field.

This handbook is structured in four parts. The first opens with a historical introduction to, and a brief account of, the practicalities and applications of multidimensional NMR methods, followed by a definitive survey of their conceptual basis and a series of articles setting out the generic principles of methods for acquiring and processing multidimensional NMR data. In the second part, the main families of multidimensional techniques, arranged in approximate order of increasing complexity, are described in detail, from simple J-resolved spectroscopy through to the powerful heteronuclear 3D and 4D methods that now dominate the study of structural biology in solution. The third part offers an illustrative selection from the very wide range of applications of multidimensional NMR methods, including some of the most recent developments in protein NMR. Finally, the fourth part introduces the idea of multidimensional spectra containing nonfrequency dimensions, in which properties such as diffusion and relaxation are correlated.

The literature of multidimensional NMR began with three papers in 1975, then nine in 1976, and fifteen in 1977, and now contains many tens of thousands of papers. Any attempt to survey the field must therefore necessarily be very selective, not to say partial. In assembling this handbook, and the *Encyclopedia of Magnetic Resonance* with which its component articles are shared, we have

sought to provide both the new researcher and the established scientist with a solid foundation for the understanding of multidimensional NMR, a representative if inevitably limited survey of its applications, and an authoritative account of the latest progress in the development of multidimensional techniques.

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April 2010

Abbreviations and Acronyms

AR	Autoregression
BIRD	Bilinear Rotation Decoupling
BPTI	Bovine Pancreatic Trypsin Inhibitor
CAMELSPIN	Cross Relaxation Appropriate for Minimolecules Emulated by Locked Spins
CP	Cross Polarization
CPD	Composite Pulse Decoupling
CPFO	Cesium Perfluorooctanoate
CPMG	Carr-Purcell pulse sequence, Meiboom-Gill modification
CRINEPT	Cross-Relaxation Enhanced Polarization Transfer
CRIPT	Cross-Relaxation Induced Polarization Transfer
CT	Constant Time
CTEF	Coherence Transfer Echo Filtering
CW	Continuous Wave
DAPT	Dipolar Assisted Polarization Transfer
DFT	Discrete Fourier Transformation
1D	One-dimensional
2D	Two-dimensional
DNA	Deoxyribonucleic Acid
DQC	Double Quantum Coherence
DQFC	Double Quantum Filtered COSY
E.COSY	Exclusive Correlation Spectroscopy
EXSY	Exchange Spectroscopy
FDM	Filter Diagonalization Method
FFLG	Flip-Flop Lee-Goldburg
FID	Free Induction Decay
FSLG	Frequency-Switched Lee-Goldburg
FT	Fourier Transform
FTA	Fluid-Turbulence-Adapted
FWHM	Full-Width at Half-Maximum Height
GEXSY	Gradient-Enhanced Exchange Spectroscopy
GFT	G-matrix Fourier Transform
GHZ	Greenberger-Horne-Zeilinger
2′-GMP	2′-Guanosine Monophosphate