Contents

Chapter 1 Introduction to Nuclear Spin Cross-relaxation and Cross-correlation Phenomena in Liquids 1
Daniel Canet

1.1 A Survey of Nuclear Spin Relaxation Mechanisms and the Concept of Spectral Densities 2
1.1.1 Interaction with Local Randomly Fluctuating Magnetic Fields 3
1.1.2 Dipolar Interactions 6
1.1.3 Chemical Shift Anisotropy (CSA) 8
1.1.4 The Spin-rotation Relaxation Mechanism 9
1.1.5 Correlated Mechanisms 10
1.2 An Introduction to Spin 1/2 Quantum Mechanics 11
1.2.1 Operators for a Single Spin 1/2 11
1.2.2 Product-operators for a System Involving Several Spins 1/2 15
1.2.3 Product-operators for a Two Spin 1/2 System and Relevant Spin States 16
1.2.4 The Density-matrix and the Density-operator 20
1.3 Evolution Equations 23
1.3.1 The Interaction Representation 23
1.3.2 Solving the Density-operator Evolution Equation within the Bloch–Wangsness–Redfield Theory 24
1.3.3 Evolution Equations of Quantities Associated with Product-operators 26

New Developments in NMR No. 12
Cross-relaxation and Cross-correlation Parameters in NMR: Molecular Approaches
Edited by Daniel Canet

© The Royal Society of Chemistry 2018

Published by the Royal Society of Chemistry, www.rsc.org

1.4 Spin Relaxation in a Single Spin 1/2 System 28
1.4.1 Relaxation by Random Fields 28
1.4.2 Relaxation by Chemical Shift Anisotropy (CSA) 29
1.5 Spin Relaxation in a Two Spin 1/2 System Involving Dipolar Interaction 32
1.5.1 The Dipolar Relaxation Hamiltonian 32
1.5.2 Longitudinal and Transverse Auto-relaxation Rates Including the Dipolar Contribution 34
1.5.3 Cross-relaxation Rates 36
1.5.4 Cross-correlation Rates 37
1.6 The Fundamental Relaxation Equations in the Case of a Two-spin 1/2 System 41
1.6.1 The Nuclear Overhauser Effect (nOe) and the Simple Solomon Equations 41
1.6.2 The Extended Solomon Equations 45
1.6.3 The Goldman Equations 47
1.7 Multi-spin Systems. Occurrence of Dipolar–Dipolar Cross-correlation Rates 48
1.7.1 Longitudinal Relaxation 49
1.7.2 Transverse Relaxation 52
1.8 Conclusion 57
References 57

Chapter 2 Homonuclear Cross-relaxation and Cross-correlation in Small Molecules and in Soft Matter **61**
Kavita Dorai

2.1 Introduction 61
2.2 One-dimensional Cross-relaxation Experiments in Homonuclear Systems 62
2.2.1 Steady-state Nuclear Overhauser Enhancement 62
2.2.2 Transient NOE Experiments 63
2.2.3 2D Cross-relaxation Experiments in Homonuclear Systems 71
2.2.4 Distance Measurements from NOE Experiments 77
2.2.5 Selected Examples of the Usefulness of Cross-relaxation 80

2.3 Experiments to Measure Cross-correlated Relaxation Rates 94
2.3.1 Experimental Observation of Longitudinal Cross-correlations 94
2.3.2 Experimental Observation of Transverse Cross-correlations 105
2.3.3 Cross-correlations Under Spin-lock Conditions 112
2.3.4 Experimental Dynamic Frequency Shifts 116
2.3.5 Cross-correlations in Paramagnetic and Quadrupolar Systems 121
2.4 Motional Models and Cross-correlated Spin Relaxation 125
2.4.1 Spectral Densities for Different Types of Motion 125
2.4.2 Interpretation of Cross-correlation Motional Parameters 134
2.5 Molecular Information from Cross-Correlated Spin Relaxation 135
2.5.1 Structural Parameters from Cross-correlations 135
2.5.2 Estimating the CSA Tensor 136
2.5.3 Information about Carbohydrates and Nucleotides from Cross-correlations 137
2.5.4 Information about Small Ligand Conformations from Binding Studies using Cross-correlations 140
2.5.5 Motional Information from Cross-correlation Rates 145
2.6 Conclusions 148
Acknowledgements 149
References 149

Chapter 3 Heteronuclear Cross-relaxation **166**
Bernard Ancian

3.1 Introduction and Basic Concepts 166
3.2 The Heteronuclear Overhauser Effect (HOE) 170
3.3 HOE's Measurements and the Information they Provide 174
3.4 2D Heteronuclear Overhauser Spectroscopy (HOESY) 179

3.5 The 1D HOESY Experiment 187
3.6 An Improved HOESY Experiment: The P.HOESY Sequence 188
3.7 Inverse HOESY Experiments 190
3.8 Filtered-HOESY Experiments 192
3.9 1D HOE and 2D HOESY in Intermolecular Interactions 193
3.10 Using Intermolecular HOESY in Chemistry and Biology 198
3.10.1 Chemical Structure, Reactivity and Chiral Recognition 198
3.10.2 Solute–Solvent Interactions 200
3.10.3 Ion Pairs and Ionic Liquids 206
3.10.4 Metallic Bonds and Aggregates 214
3.10.5 Biology 217
3.11 Conclusion 220
Acknowledgements 221
References 221

Chapter 4 Cross-correlation in Biomolecules 239
Fabien Ferrage and Kavita Dorai

4.1 Introduction 239
4.1.1 Definitions 240
4.1.2 Span of Uses 240
4.1.3 Presentation of This Chapter 241
4.2 Theory 241
4.2.1 The Homogeneous Master Equation 241
4.2.2 Frame Transformations of Liouvillian Superoperators 243
4.2.3 Average Liouvillian Theory: Discrete Averaging 244
4.2.4 Application of Discrete ALT: Measurement of CSA/DD CCCR Rates 246
4.2.5 Average Liouvillian Theory: Continuous Averaging 246
4.2.6 Application of Continuous ALT: Measurement of CSA/DD CCCR Rates 248
4.2.7 Note on the Secular Approximation 249
4.3 Measurements of Cross-relaxation at the Steady-state Effects 249

4.4 HSQC-type Experiments to Measure Cross-correlated Cross-relaxation Rates 253
4.4.1 Measuring CSA–Dipolar Cross-correlation (1D Experiments) 253
4.4.2 2D Experiments to Measure CSA–Dipolar Cross-correlations 254
4.4.3 Multi-dimensional Experiments to Measure Dipole–Dipole Cross-correlations 269
4.4.4 2D Experiments for Measuring CSA–CSA Cross-correlations 271
4.5 Motional Models and Cross-correlated Spin Relaxation 274
4.5.1 Model-free Formalism and Large Biomolecules 275
4.5.2 Dipole–Dipole Cross-correlation in Biomolecules 278
4.5.3 Correlated Internal Motions 280
4.5.4 3D Gaussian Axial Fluctuations Model 281
4.5.5 Extraction of Cross-correlation Parameters From Dynamics 284
4.5.6 Motional Information From Cross-correlation Rate 285
4.6 Local Chemical Properties of Biomolecules 286
4.6.1 Estimating the CSA Tensor 286
4.6.2 Hydrogen Bonds and Cross-correlated Cross-relaxation 290
4.7 Chemical Exchange and Cross-correlations 292
4.8 Information About RNA and DNA Nucleic Acids from Cross-correlations 296
4.9 Ligand-binding Studies Using Cross-correlations 303
4.10 Transverse Relaxation Optimized Spectroscopy: Tailoring Auto-relaxation with Cross-correlated Relaxation 304
4.10.1 Interference Between Relaxation Mechanisms 304
4.10.2 TROSY From CSA–DD Cross-correlated Relaxation 305
4.10.3 TROSY From DD–DD Cross-correlated Relaxation 307
References 310

Subject Index **316**