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PULSE AND FOURIER TRANSFORM NMR

Introduction to Theory and Methods

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Preface

NMR techniques have developed during the last 25 years along two rather different lines—continuous wave (cw) or "ordinary" NMR, and pulsed NMR. The vast majority of users of cw high resolution NMR are, in our experience, only vaguely aware of the potentialities of the pulse methods. The recent commercial development of Fourier transform techniques for obtaining high resolution spectra with a tremendous potential for savings in time has, more than any other event, convinced chemists using high resolution NMR that a knowledge of the fundamentals of pulse methods is essential. Sensing this need among some of our colleagues, we organized a one-semester course in the NIH Graduate Program on "NMR Pulse Methods." That course, in turn, led to the present volume.

In writing this book we set as a goal a 100 page volume addressed to chemists and others familiar with high resolution NMR but with no background in pulse techniques. Our objectives were to describe as simply as possible the various types of pulse experiments that are commonly employed, to provide the theoretical background necessary for understanding these techniques, and to evaluate the practical application of pulse methods and the necessary instrumentation. We have often sacrificed mathematical rigor in order to use classical pictures that, we hope, will make the concepts easier to grasp.

The first two chapters review NMR fundamentals and introduce the basic pulse methods. Chapter 3 summarizes the salient features of pulse spectrometers, while Chapter 4 explains—in words, as well as equations—why nuclei relax. Chapter 5 is devoted to the rationale, the advantages, and the limitations of Fourier transform NMR methods. Chapter 6 shows how the idea of the "rotating frame" can be used to understand certain experiments that extend the range of application of pulse techniques. And the final chapter treats briefly a few important special uses of pulse methods.

We hope that this introduction to pulse NMR theory and techniques will provide the reader with a foundation for further study of more advanced texts, such as the elegant and lucid works by Slichter and by Abragam, and will help stimulate further application of pulse techniques to a wide range of chemical problems.

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Symbols and Abbreviations

Symbols

$\mathbf{A}$ spin-coupling tensor

A_{BX} B–X spin-coupling constant in radians per second

A_{∞}, A_{τ} amplitudes of FID signal after 90° pulse at times $t = \infty$ and $t = \tau$ in a 180°, τ, 90° experiment

C capacitance

C_{eff} effective spin-rotation constant for molecules in liquid state

$C(\omega)$ Fourier cosine transform

$C_{||}, C_{\perp}$ components of $\mathbf{C}$ parallel and perpendicular to symmetry axis

C_{3v} threefold axis of symmetry

c velocity of light

$\mathbf{C}$ spin-rotation tensor

D separation between field gradient pulses

d duration of field gradient pulses

$\mathfrak{D}$ diffusion coefficient

$\mathfrak{D}_{||}, \mathfrak{D}_{\perp}$ components of $\mathfrak{D}$ parallel and perpendicular to symmetry axis

ΔE separation between two energy levels

E_{a} activation energy

E_{c} interaction energy

e charge of the electron; also a constant (~ 2.718)

e^2qQ quadrupole coupling constant

$F(\omega)$ Fourier transform of $f(t)$

$f(t)$ Fourier transform of $F(\omega)$

f_o center frequency

G dc or steady field gradient

g pulsed field gradient

H_0 dc magnetic field

ΔH_0 inhomogeneity of H_0

H_1 macroscopic rf field

H_{eff} an effective magnetic field, defined by equation 1.37

H_t total magnetic field at a nucleus

H_{loc} magnetic field at a nucleus due to neighboring nuclei

H_d local field arising from static magnetic dipoles

h microscopic rf field

h Planck's constant

h_0 incremental dc magnetic field

h_x, h_y, h_z components of h

$\mathcal{H}_Q, \mathcal{H}_{cs},$ Hamiltonian operator for quadrupole, chemical shift, spin

$\mathcal{H}_{sr}, \mathcal{H}_d$ rotation, and dipolar interactions, respectively

I spin quantum number; also moment of inertia

i unit vector along x axis

i square root of minus one; also an index

J_{BX} B–X spin coupling constant in hertz

$J_i(\omega)$ spectral density function defined by equation 4.8

J rotational quantum number

j unit vector in y direction

K 1024 (referring to computer memory)

$K_i(\tau)$ correlation function defined by equation 4.5

k Boltzmann constant

k unit vector in z direction

L inductance

M macroscopic magnetization vector

M_0 value of M at equilibrium

M_x, M_y, M_z components of M

M magnitude of M, also nuclear mass

m_i magnetization due to nucleus i

O a general operator

P power

P_a fractional population of site a

p angular momentum vector

Q quadrupole coupling tensor

Q_{ij} components of Q

Q quality factor of tuned rf circuit

R	resistance; also spectral resolution
R_1	spin–lattice relaxation rate ($R_1 = 1/T_1$)
R_2	spin–spin relaxation rate ($R_2 = 1/T_2$)
$R_2{}^0$	R_2 in the absence of scalar relaxation
$R_1{}^I, R_1{}^S$	R_1 of nuclei I and S, respectively
$R(\tau)$	cross-correlation function
r	coordinate in spherical coordinate system
S	spin quantum number of nucleus S
$S(\omega)$	Fourier sine transform
S/N	signal-to-noise ratio
T_1	longitudinal or spin–lattice relaxation time
T_2	transverse or spin–spin relaxation time
$T_2{}^*$	time constant for decay of FID in presence of magnetic field inhomogeneity
$T_1{}^I, T_2{}^I$	T_1 and T_2 of nucleus I, respectively.
T_r	rise or fall time of a signal
$T_{1\rho}$	T_1 in the rotating frame
$T_{2\rho}$	T_2 in the rotating frame
$T_2{}^0$	T_2 in the absence of scalar relaxation
T_n	nutation relaxation time
t_p	width of time duration of a pulse
t_{cp}	time between 180° pulses in a Carr–Purcell experiment
t_{ij}	components of T
$t_{ij}(l), t_{ij}(m)$	t_{ij} in the laboratory and molecular frames, respectively
t	time
t_n	time for rf field to rise from zero to final value
T	a second rank tensor
u	u-mode, or dispersion
V	volume; also molecular rotation frequency
v	v mode, or absorption
W	power
x	x axis in laboratory frame
x'	x axis in rotating frame
Y_i	spherical harmonic of order i, defined by equation 4.4
y	y axis in laboratory frame
y'	y axis in rotating frame
z	z axis in laboratory frame
z'	z axis in rotating frame
β	bandwidth
γ	magnetogyric ratio
Δ, Δ'	chemical shift range
δ	small quantity
$\delta\omega$	chemical shift difference

$\epsilon_{1/2}$ width of spin echo at half height

η asymmetry parameter

ζ filling factor

θ angle

μ magnitude of μ

$\boldsymbol{\mu}$ nuclear magnetic moment vector

μ_J molecular magnetic moment of molecule in Jth rotational state

μ_N nuclear magneton, a constant

ν_0 resonance or Larmor frequency in hertz

$\nu_{1/2}$ line width at half-maximum intensity

π constant ($\sim$3.14); also 180° in radians

σ chemical shift (magnitude)

$\boldsymbol{\sigma}$ chemical shift tensor

$\sigma_{||}, \sigma_{\perp}$ components of $\boldsymbol{\sigma}$ parallel and perpendicular to symmetry axis

τ the time between pulses in a pulse sequence

τ_c molecular correlation time

τ_e correlation time for chemical exchange

τ_J angular momentum correlation time

τ_S correlation time for spin state of nucleus S, usually $\tau_S = T_1{}^S$

Ω a precessional frequency, defined by equation 1.42

ω_0 $2\pi\nu_0$, resonance frequency in radians per second

Abbreviations

CP   Carr–Purcell

CPMG   Carr–Purcell–Meiboom–Gill

cw   continuous wave

DEFT   driven equilibrium Fourier transform

FFT   fast Fourier transform

FID   free induction decay

FT   Fourier transform

SEFT   spin-echo Fourier transform

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Basic Concepts in NMR

The early work of Bloch *et al.*[1] showed that nuclear magnetic resonance in bulk materials can be observed in several ways. The *slow passage* experiment consists of slowly sweeping the radio frequency (rf) applied to a sample in a fixed magnetic field (or, alternatively, slowly sweeping the field with a fixed rf). The resonant signal is observed as a line of approximately Lorentzian shape. High resolution NMR studies, and some broad line experiments as well, are carried out under conditions that approximate the requirements for slow passage. *Adiabatic rapid passage* requires that the sweep rate of either frequency or magnetic field be between certain limits. Adiabatic rapid passage is now used only infrequently in chemical applications—principally in the search for resonant frequencies of nuclei that give weak signals. The slow passage and rapid passage methods are usually referred to as *continuous wave* (cw) techniques, since the rf is applied continuously while the spectrum is observed.

A third method of observation, suggested by Bloch *et al.*[1] and put into practice initially by Hahn[2] makes use of short bursts, or *pulses*, of rf power at a discrete frequency. The observation of the nuclear spin system is made after the rf is turned off. Such techniques are called *pulse methods* or *free precession* techniques. Combination methods, in which rf pulses are applied but the transient behavior of the spin system is studied while the rf pulse is on, have also been developed[3]; we comment further on such methods in Chapter 6.

In this book we describe the basic phenomena of the various pulse methods, the experimental techniques needed for their study, and some of the more important chemical applications of the methods. Although pulse methods were introduced almost as early as cw methods and have been

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improved in sophistication and versatility, they have until recently attracted only limited attention from chemists. Within the last few years, however, technical innovations have begun to permit the study by pulse methods of the complex molecules of interest to most chemists; in fact, we show in Chapter 5 that it is possible to obtain the same spectral information from a pulse experiment and subsequent mathematical analysis (principally Fourier transformation) as can be obtained by an ordinary slow passage experiment. However, pulse methods are often much more efficient, thus producing a very significant saving in time or improvement in signal/noise.

As we shall see in Chapter 2, relaxation plays an important role in pulse experiments, and as a result pulse techniques provide the most generally useful method of measuring relaxation times. In the past, relaxation has often been dismissed as of no real importance in chemical problems, but with the advent of pulse methods that permit measurement of relaxation times for individual NMR lines in complex molecules, a whole new dimension is opened that promises to complement measurements of chemical shifts and coupling constants in providing information about molecular structure. In Chapters 2 and 5 we describe these pulse methods and give examples of their use, while in Chapter 4 we try to provide some insight into the origin and mechanisms of relaxation. Relaxation times, as measured by pulse methods, can also provide direct information on such important processes as chemical exchange, conformational changes in macromolecules, binding of small molecules to polymers, and molecular diffusion. In Chapters 6 and 7 we discuss methods for making such investigations over a wide range of experimental conditions, together with examples of their use.

In this introductory chapter we review some basic NMR properties and attempt to provide a conceptual framework for visualizing how nuclear magnets behave in pulse experiments. Of fundamental importance to our entire treatment in this book are two simple mathematical procedures: (1) the use of a rotating coordinate system to simplify the equation of motion of precessing nuclei, and (2) the use of Fourier transformation to establish the relation between the time course of certain processes and the basic frequencies characterizing those processes. We review the necessary background for these topics in Sections 1.5 and 1.7; examples of their use occur continually through the book.

1.1 Relaxation and Nuclear Magnetic Energy Levels

It is well known from elementary NMR theory[4] that a nucleus of spin I has $2I + 1$ energy levels, equally spaced with a separation

$$\Delta E = \mu H_0/I, \tag{1.1}$$

where H_0 is the applied magnetic field, and μ, the nuclear magnetic moment, is given by

$$\mu = \gamma h I / 2\pi. \tag{1.2}$$

Here γ is the magnetogyric ratio, a constant for a given nucleus, and h is Planck's constant. From the usual Bohr relation, the frequency of radiation that induces a transition between adjacent levels is

$$\nu_0 = \Delta E / h = \gamma H_0 / 2\pi \quad \text{(Hz)} \tag{1.3}$$

or

$$\omega_0 = 2\pi\nu_0 = \gamma H_0 \quad \text{(rad sec}^{-1}\text{).} \tag{1.4}$$

At equilibrium, nuclei are distributed among the energy levels according to a Boltzmann distribution. Following any process that disrupts this distribution (e.g., moving the sample into or out of the magnetic field, or absorption of rf energy), the nuclear spin system returns to equilibrium with its surroundings (the "lattice") by a first-order relaxation process characterized by a time T_1, the *spin–lattice relaxation time*. We shall discuss relaxation processes in Chapter 4; for the present it is sufficient to note that T_1 may vary over a wide range (approx. 10^{-4}–10^4 sec) but for small diamagnetic systems is typically of the order of 0.1–10 sec.

Since a nucleus remains in a given energy level *no longer* than T_1 on the average, we can estimate the *minimum* width of the NMR line from the Heisenberg Uncertainty Principle:

$$\Delta E \, \Delta t \gtrsim h, \tag{1.5}$$

where ΔE and Δt are the uncertainties in measurement of energy and time, respectively. For the case we are considering, with a line of full width at half maximum intensity $\nu_{1/2}$, this becomes

$$(h\nu_{1/2})\, T_1 \gtrsim h, \qquad \nu_{1/2} \gtrsim 1/T_1. \tag{1.6}$$

Often lines are broader than indicated by equation 1.6. For example, in solids or slowly tumbling molecules in liquids, magnetic dipole–dipole interactions between nuclei lead to appreciable line broadening, sometimes several kilohertz, as compared with the width of about 1 Hz expected from equation 1.6 for $T_1 = 1$ sec. To account for processes that cause the nuclear spins to come to equilibrium with each other, a second time T_2, the *spin–spin relaxation time*, is defined so that

$$\nu_{1/2} \approx 1/T_2. \tag{1.7}$$

To agree with the more precise definition of T_2 that we shall introduce in Section 1.3, we relate T_2 to the width of a Lorentzian line by the equation

$$\nu_{1/2} = 1/\pi T_2. \tag{1.8}$$

In this discussion we have been referring to the "natural" width of the resonance line determined by molecular processes. If the magnetic field is not perfectly homogeneous, nuclei in different parts of the sample experience slightly different values of the field, hence by equation 1.3 resonate at slightly different frequencies. This leads to a contribution to the line width due to inhomogeneity (ΔH_0) of

$$\nu_{1/2} \text{ (inhom)} = \gamma \, \Delta H_0/2\pi. \qquad (1.9)$$

By analogy to equation 1.8, we can define a time T_2^* in terms of the *observed* line width as

$$\nu_{1/2} \text{ (obsd)} = 1/\pi T_2^*. \qquad (1.10)$$

Thus T_2^* includes contributions from both natural line width and magnetic field inhomogeneity:

$$1/T_2^* = 1/T_2 + (\gamma \, \Delta H_0/2). \qquad (1.11)$$

1.2 Some Basic Properties of Vectors

Since we shall find it convenient to use vector notation in describing many aspects of pulsed NMR, we digress briefly from our discussion of NMR fundamentals to review a few of the basic properties of vectors.

A vector, denoted in this book by boldface type, has both magnitude and direction. It is customary to describe a vector by giving its components along three mutually orthogonal directions. For example, we can write

$$\mathbf{A} = A_x\mathbf{i} + A_y\mathbf{j} + A_z\mathbf{k}, \qquad (1.12)$$

where $\mathbf{i}$, $\mathbf{j}$, and $\mathbf{k}$ are vectors of *unit* length along the x, y, and z axes, respectively. From the Pythagorean theorem, it follows that the length of $\mathbf{A}$ is given by

$$|\mathbf{A}| = [A_x^2 + A_y^2 + A_z^2]^{1/2}. \qquad (1.13)$$

When there is no ambiguity, we may write A, rather than $|\mathbf{A}|$ to denote the length or magnitude of the vector $\mathbf{A}$.
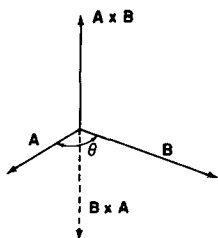
The scalar product (or dot product) of two vectors, $\mathbf{A}$ and $\mathbf{B}$, inclined at an angle θ relative to each other, is defined as

$$\mathbf{A} \cdot \mathbf{B} \equiv |\mathbf{A}|\,|\mathbf{B}| \cos \theta. \qquad (1.14)$$

From simple geometric relations, one can show that

$$\mathbf{A} \cdot \mathbf{B} = A_xB_x + A_yB_y + A_zB_z. \qquad (1.15)$$

Figure 1.1. The vector (cross) product of two vectors. The vector $A \times B$ is perpendicular to the plane formed by A and B. Note that $B \times A$ points in the direction opposite $A \times B$.

The scalar product is, as its name implies, a scalar quantity—possessing magnitude but not direction. The *vector product* (or cross product) of two vectors inclined at an angle θ with respect to each other is a vector quantity whose magnitude (length) is given by

$$| A \times B | = | A || B | \sin \theta. \qquad (1.16)$$

The direction of the vector product is perpendicular to the plane defined by A and B, as indicated in Figure 1.1. Note that the three vectors, A, B, and $A \times B$ form a right-handed system. The vector $B \times A$ would point downward in Figure 1.1; thus

$$B \times A = -A \times B. \qquad (1.17)$$

It is shown in elementary treatments of vector analysis[5] that the most convenient way of expressing the vector product in terms of the components of the individual vectors is the determinental relation

$$A \times B = \begin{vmatrix} A_x & B_x & i \\ A_y & B_y & j \\ A_z & B_z & k \end{vmatrix}. \qquad (1.18)$$

We shall use these relations in the classical treatment of NMR.

1.3 Nuclear Precession

Although many features of NMR spectra can be understood only by quantum mechanical considerations based on the energy level approach of Section 1.1, a number of properties are more easily visualized through a classical treatment. Most of the pulse experiments that we shall consider fall into this category; hence we shall use the classical treatment almost exclusively.