

Basic Theory

This section presents a basic overview of the theory of modern NMR. Readers interested in more in-depth treatments of this subject are encouraged utilize the resources listed in the reference section at the end of this document. The embedded animations in the web book <http://www.cis.rit.edu/htbooks/nmr/> authored by Professor Hornak makes this site especially useful for students learning about NMR.

Outline: Basic Theory

1. What is spin?
2. How does absorption of energy generate an NMR spectrum?
3. Why is NMR less sensitive than UV-visible spectroscopy?
4. What is chemical shift and how does it relate to resonance frequency?
5. What is precession?
6. How does precession produce the macroscopic magnetization (M_0)?
7. How can the nuclear spins be manipulated to generate the NMR spectrum?
8. What is the tip angle?
9. What is a Free Induction Decay?
10. How do T_1 and T_2 relaxation affect NMR spectra?
11. Where should I look to learn more about NMR?

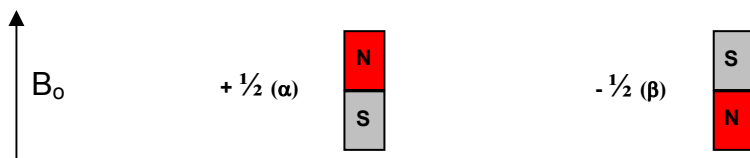
What is spin?

The fundamentals of NMR begin with the understanding that a nucleus belonging to an element with an odd atomic or mass number has a nuclear spin that can be observed. Examples of nuclei with spin include ^1H , ^3H , ^{13}C , ^{15}N , ^{19}F , ^{31}P and ^{29}Si . All of these nuclei have a spin of $\frac{1}{2}$. Other nuclei like ^2H or ^{14}N have a spin of 1. Nuclei with even atomic and mass numbers like ^{12}C and ^{16}O have spin of 0 and cannot be studied by NMR. The following introductory discussion of NMR is limited to spin $\frac{1}{2}$ nuclei.

Nuclei that possess spin have angular momentum, ρ . The maximum number of values of angular momentum a nucleus can have is described by the magnetic quantum number, I . The possible spin states can vary from $+I$ to $-I$ in integer values. Therefore, there are $2I + 1$ possible values of ρ .

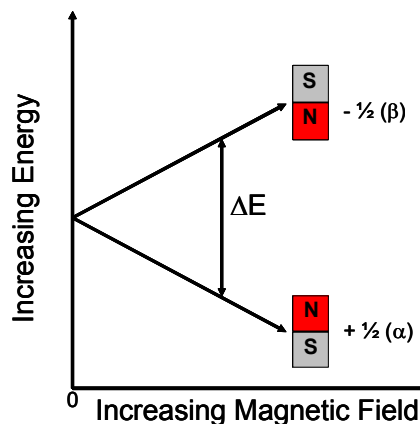
Question 1: How many spin states would you predict for ^2H ?

For spin $\frac{1}{2}$ nuclei, the angular momentum can have two possible values: $+\frac{1}{2}$ or $-\frac{1}{2}$. Since spin is a quantum mechanical property, it can be difficult to visualize. One way to imagine spin is by thinking of spin $\frac{1}{2}$ nuclei as tiny bar magnets that can have two possible orientations with respect to a larger external magnetic field. It is important to note that in the absence of an external magnetic field, these discrete spin states have random orientations and identical energies.



2. How does absorption of energy generate an NMR spectrum?

In the absence of an external magnetic field the two spins in the figure above would be randomly oriented and their energies degenerate, in other words they would have identical energies. However in the presence of an applied magnetic field, the energies of the two spin states diverge and the spins orient themselves with respect to the applied field. The larger the magnetic field, the greater the difference in energy between the spin states. For most spin $\frac{1}{2}$ nuclei, the $+\frac{1}{2} (\alpha)$ spin state is of lower energy and corresponds to having the spin aligned with the applied field while the $-\frac{1}{2} (\beta)$ spin state can be thought of as having the spin opposed to the applied field.



The difference in energy between the states, ΔE , depends on the strength of the applied magnetic field, B_0 , according to Eq. 1. In this equation γ is the gyromagnetic ratio, a fundamental property of each type of nucleus and h is Planck's constant. Table 1 shows values of the

gyromagnetic ratio for several common NMR nuclei.

$$\Delta E = \frac{\gamma \hbar B_0}{2\pi} \quad \text{Eq. 1}$$

Element	Atomic Number	Mass Number	Spin	Natural Abundance	Gyromagnetic Ratio γ ($10^7 \text{ rad}\cdot\text{s}^{-1}\cdot\text{T}^{-1}$)	Reference Compound
Hydrogen	1	1	$\frac{1}{2}$	99.985%	26.7522128	Me ₄ Si
Deuterium	1	2	1	0.0115	4.10662791	(CD ₃) ₄ Si
Carbon	6	13	$\frac{1}{2}$	1.07	6.728284	Me ₄ Si
Nitrogen	7	15	$\frac{1}{2}$	0.368	-2.71261804	MeNO ₂
Fluorine	9	19	$\frac{1}{2}$	100	25.18148	CCl ₃ F
Silicon	14	29	$\frac{1}{2}$	4.6832	-5.3190	Me ₄ Si
Phosphorus	15	31	$\frac{1}{2}$	100	10.8394	H ₃ PO ₄
Selenium	34	77	$\frac{1}{2}$	7.63	5.1253857	Me ₂ Se
Cadmium	48	113	$\frac{1}{2}$	12.22	-5.9609155	Me ₂ Cd

1. R.K. Harris, E. D. Becker, S. M. C. De Menezes, R. Goodfellow, P. Granger, Pure. Appl. Chem. 73:1795-1818 (2001).
<http://www.iupac.org/publications/pac/2001/pdf/7311x1795.pdf>

The signal in NMR is produced by absorption of electromagnetic radiation of the appropriate frequency. Energy absorption causes the nuclei to undergo transitions from the lower energy (α) to the higher energy (β) spin states. If we think about the spins as bar magnets, absorption of energy at the right frequency causes the spins to flip with respect to the applied field. As is the case with other spectroscopic methods, the difference in population of these two quantized states can be expressed by the Boltzmann equation, Eq. 2 where k is Boltzmann's constant, $1.38066 \times 10^{-23} \text{ J}\cdot\text{K}^{-1}$, and T is the temperature in degrees Kelvin.

$$\frac{N_{upper}}{N_{lower}} = e^{\frac{-\Delta E}{kT}} \quad \text{Eq. 2}$$

Equation 2 relates the ratio of the number of nuclei in the upper (higher energy) spin state and the lower energy spin state to the energy difference between the spin states, ΔE , and therefore, the magnitude of the applied magnetic field, B_0 (Eq. 1). In NMR the difference in energy in the two spin states is very small therefore the population difference is also small (about 1 in 10,000 for ¹H in an 11.74 T magnetic field). Because this population difference is the source of our signal, NMR is inherently a less sensitive technique than many other spectroscopic methods.

Question 2: Given the same magnetic field and temperature, how would the difference in population for ¹H and ³¹P compare?

3. How does the population difference in NMR compared to the difference between electronic ground and excited states?

Up to this point in our discussion, the theory of NMR seems similar to that for other common spectroscopic methods. However there are some differences that should be considered. For example in UV-visible absorption spectroscopy, which occurs as a result of electronic transitions, at room temperature essentially all of the molecules will be in the ground electronic state because the energy difference between the ground and excited states is large. However, in NMR the difference in energy in the two spin states is very small, therefore the population difference is also small (about 1 in 10,000 for ^1H in an 11.74 T magnetic field). Because this population difference is the source of our signal, NMR is inherently a less sensitive technique than many other spectroscopic methods.

Let's think now about the energy difference between the nuclear spin states in NMR. Do you recall the relationship between energy and frequency? Say we are interested in a compound with an absorption maximum at a wavelength, λ , of 600 nm. What would be the frequency, ν , of the light absorbed?

The frequency of light absorbed is inversely proportional to the wavelength as shown in the equation below, where c is the speed of light, 3.0×10^8 m/s.

$$\nu = \frac{c}{\lambda} \quad \text{Eq. 3}$$

Therefore, light with a wavelength of 600 nm has a frequency of 5×10^{14} Hz (cycles per second). The energy, E , of this light is directly proportional to the product of its frequency and Planck's constant (h), 6.626×10^{-34} J·s.

$$E = h\nu \quad \text{Eq. 4}$$

Our 600 nm light has an energy of 3.31×10^{-19} J. The energy of the light absorbed by our molecule roughly corresponds to the energy difference between the ground and excited electronic states of our molecule. How does the energy absorbed in NMR compare with this value? We already indicated that we expect the energy difference between the ground and excited spin states in NMR to be much less than for absorption of visible light. We can calculate the energy of the NMR transition using Eq.1 for a particular nucleus in a given magnetic field strength. Let's do this calculation for the protons (hydrogen nuclei) in a sample placed in an 11.74 T magnet, using the value of γ for hydrogen (normally referred to as proton) in Table 1. We can now calculate the energy difference of the spin states, as in Eq. 5.

$$\Delta E = \frac{26.75222127 \times 10^7 \text{ rad} \cdot \text{s}^{-1} \text{T}^{-1} \times 6.626 \times 10^{-34} \text{ J} \cdot \text{s} \times 11.74 \text{ T}}{2\pi} = 1.054 \times 10^{-25} \text{ J} \quad \text{Eq. 5}$$

This energy may not seem like it is that much less than the energy of our visible absorption transition at 600 nm, after all the numbers only differ by a factor of 10^6 . However, if we think about the thermal energy of our sample in terms of kT ($1.38066 \times 10^{-23} \text{ J}\cdot\text{K}^{-1} \times 298 \text{ K} = 4.11 \times 10^{-21} \text{ J}$) we can see that the thermal energy of our sample is about 100 fold less than the energy of the visible absorption of 600 nm light but is about 10,000 times greater than the energy of our proton NMR transition. This is why there is only a very small difference in population between the ground and excited states in NMR.

Having compared the energies of these two spectroscopic methods we might now ask how do the frequency and wavelength in NMR compare with our 600 nm light? We can calculate the NMR frequency, known as the Larmor frequency, using Eq. 6

$$\nu = \frac{\Delta E}{h} = \frac{\gamma B_o}{2\pi} \quad \text{Eq. 6}$$

For our example of protons in an 11.74 T magnetic field, ν is $500 \times 10^6 \text{ Hz}$ or 500 MHz. This is in the radio frequency range of the electromagnetic spectrum. It is common to refer to NMR instruments by the frequency of protons in the magnetic field associated with a given spectrometer, therefore a spectrometer with an 11.74 T magnet is referred to as a 500 MHz instrument.

Question 3: Calculate the wavelength of electromagnetic radiation corresponding to a frequency of 500 MHz.

4. What is chemical shift and how does it relate to resonance frequency?

If each type of nucleus (e.g. all protons) gave a single resonance frequency, as implied by Eq. 6, NMR would not be of much use to chemists. The actual nuclear resonance frequency is highly dependent on the local chemical environment. The effective magnetic field, B_{eff} , felt by a nucleus differs from that of the applied magnetic field, B_o , due to shielding by the motion of the electron clouds surrounding the nucleus. The greater the electron density around the nucleus, the larger is this shielding effect. The amount of shielding is expressed as the shielding constant σ , where $B_{\text{eff}} = (1 - \sigma)B_o$. Therefore the resonance frequency of each nucleus differs depending on the value of B_{eff} .

$$\nu = \frac{\gamma(1 - \sigma)B_o}{2\pi} = \frac{\gamma B_{\text{eff}}}{2\pi} \quad \text{Eq. 7}$$

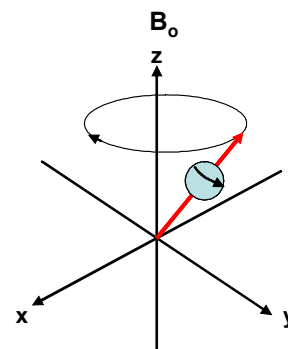
The chemical shift of a nucleus reveals much about the structure of a molecule as shielding constants are well correlated with local chemical environment. For example I can know whether a molecule contains a methyl group or an aromatic ring depending on the chemical shifts of the protons in my NMR spectrum.

Early NMR spectrometers were scanning instruments in which the radio frequency was

scanned through the proton chemical shift range until a frequency was reached at which energy was absorbed by the sample; this is the resonance condition. Modern instruments irradiate the sample with a broad band, or range, of frequencies and excite all of the protons at the same time.

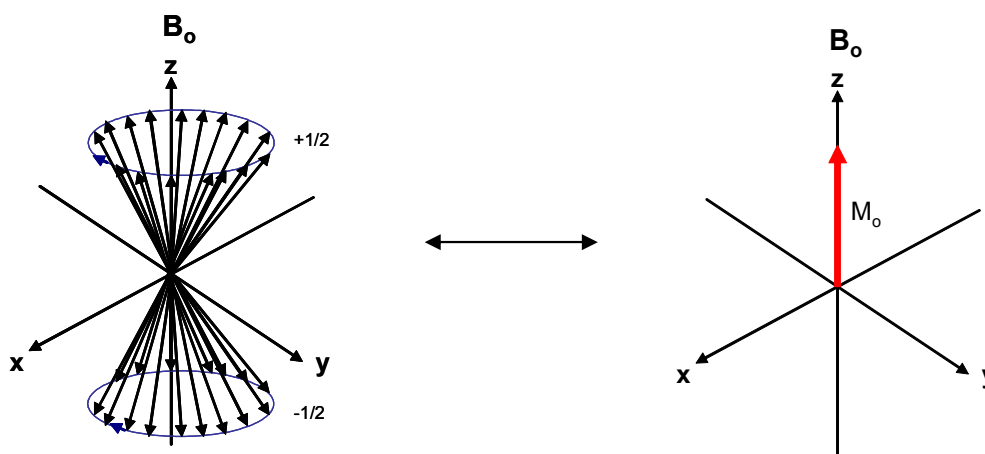
5. What is precession?

A spinning charged particle creates a magnetic field, called the magnetic moment, μ . This magnetic moment is a vector quantity that is proportional to the angular momentum: $\mu = \gamma p$. Because our nucleus has angular momentum, the magnetic moment, depicted as the red vector in the figure below, will appear to precess (or rotate) about the applied magnetic field B_0 . This precession is analogous to the motion of a spinning top. The frequency of precession is dependent only on the type of nucleus (defined by the gyromagnetic ratio, γ) and the value of B_{eff} , as defined in Eq 7. The precession of a single nucleus, depicted as a blue sphere spinning about its axis, is shown here.



6. How does precession generate the macroscopic magnetization (M_0)?

If we now examine what we would expect for an ensemble of nuclei, the magnetic moments of the $+1/2$ spins will be aligned with the applied magnetic field, while the moments of the higher energy $-1/2$ spin state will be opposed to B_0 . However, all the spins in our sample will be precessing randomly about B_0 at their Larmor frequency as illustrated in the figure below. Because slightly more of our nuclei are in the lower energy $+1/2$ spin state, if we take the vector sum of all the magnetic moments we will realize a single vector pointing in the direction of the applied magnetic field called the macroscopic magnetization, M_0 . The macroscopic magnetization then provides a way to visualize the population difference of our spins. It is this macroscopic magnetization vector that is manipulated in the NMR experiment.



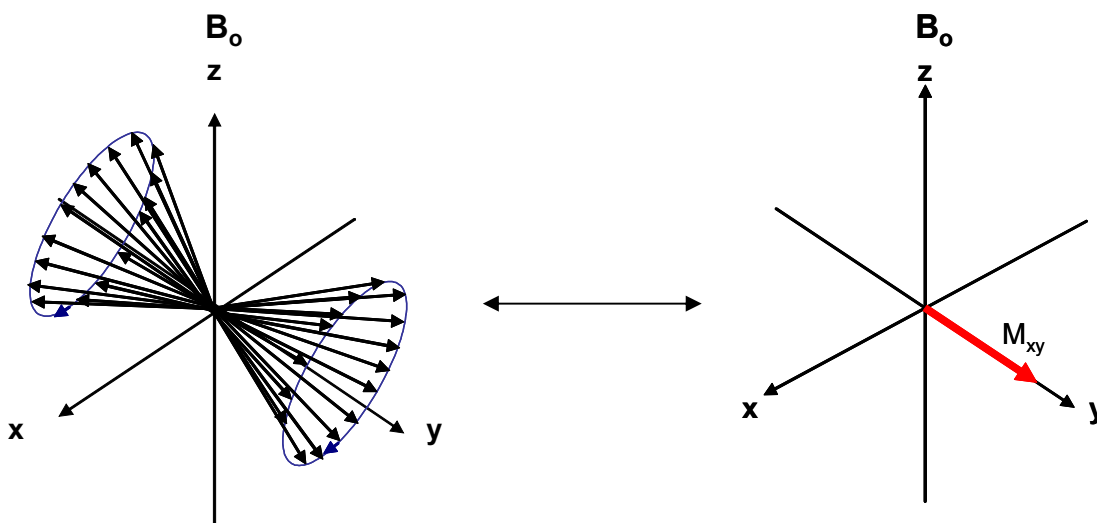
7. How can the nuclear spins be manipulated to generate the NMR spectrum?

The figure above shows the system at equilibrium. In order to generate a NMR signal, we must do something to perturb the populations of our spin states. As in other spectroscopic measurements, this is done through the absorption of radiant energy (light) of the appropriate frequency. In NMR, this transition is in the radio frequency (rf) range, corresponding to the Larmor frequency of the nucleus we are interested in. We cause this transition by irradiating our sample at a single radio frequency. An AC current oscillating at the desired rf frequency is applied to a coil wound around our sample. This oscillating current creates an additional magnetic field (called the B_1 field) that acts upon our macroscopic magnetization vector and tips it away from its equilibrium position aligned with B_0 . This B_1 pulse creates the signal that we detect in NMR. In order to excite all of the different types of a single nucleus in our sample (e.g. all of the different types of protons or carbons), this pulse of rf radiation is kept short (typically $\sim 10 \mu\text{s}$). By the Heisenberg uncertainty principle, a short pulse will excite a broad range of frequencies; $\Delta f = 1/\Delta t$.

Question 4: What range of frequencies would be excited by a $10 \mu\text{s}$ rf pulse?

8. What is the tip angle?

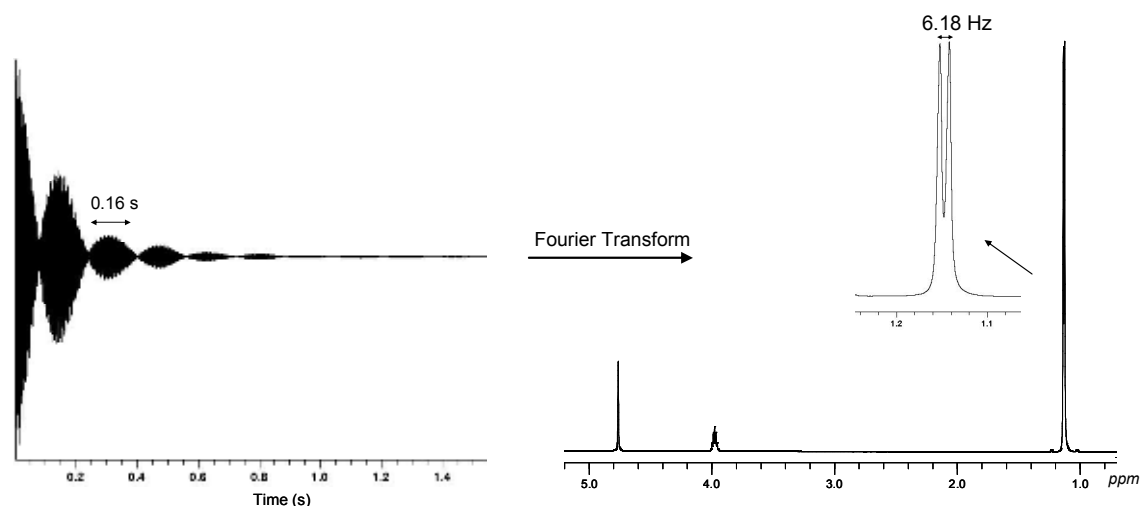
The angle that the B_1 pulse tips the magnetization through depends on the power of the pulse and its length. For a given power setting, a tip angle, θ , (in radians) can be defined as $\theta = \gamma B_1 \tau$, where γ is the magnetogyric ratio and τ is the length of time the pulse is on. What we detect in the NMR experiment is the projection of the macroscopic magnetization vector, M_{xy} , into the xy plane of the NMR coordinate system. A 90° pulse will produce the greatest signal in the xy plane. The Figure below shows the effect of a 90° pulse on the spins.



9. What is the Free Induction Decay?

The signal we detect is called a Free Induction Decay (FID). The FID is produced by the

macroscopic magnetization after the pulse. The magnetization will undergo several processes as it returns to equilibrium. First immediately after the pulse, the transverse component of the macroscopic magnetization, M_{xy} , will begin to precess at its Larmor frequency. This precessing magnetization will induce an alternating current in a coil (the same one used to generate the rf pulse) wound round the sample. This induced AC current is our FID, such as the one shown below.



The FID contains all of the information in the NMR spectrum, but it is difficult for us to discern the information in this format. Fourier transformation of the FID, a time domain signal, produces the frequency domain NMR spectrum. The resonance frequencies of the signals in the transformed spectrum correspond to the frequency of oscillations in the FID. In this FID measured for isopropanol, the 0.16 modulation of the FID is due to the 6.18 Hz difference in frequency of the resonances of the intense methyl doublet. The intensity information of each component is contained in the intensity of the first point of the FID. The signals that comprise the FID decay exponentially with time due to relaxation processes discussed in the next section. The rate of decay for each component of the FID is inversely proportional to the width of each NMR resonance.

10. How do T_1 and T_2 relaxation affect NMR spectra?

The decay of the FID corresponds to the loss of intensity of the macroscopic magnetization vector in the xy plane (called the transverse plane) by a process called spin-spin relaxation (or transverse or T_2) relaxation. T_2 relaxation occurs when a nucleus in a $-1/2$ spin state transfers its spin to a nearby nucleus in a $+1/2$ spin state, and vice versa. Since T_2 relaxation occurs through mutual spin flips, the energy of the system is unaffected, it is an entropic process. In terms of our vector model, T_2 relaxation corresponds to a loss of coherence or dephasing of the magnetization vector. The recovery of magnetization along the z (longitudinal) axis (aligned with B_0) to its equilibrium position occurs by a process called spin lattice (or longitudinal or T_1) relaxation). T_1 relaxation occurs through interactions of the nuclei with the lattice (or the nuclei that surround our sample). Lattice motions at the same frequency as the Larmor frequency stimulate the magnetization in the higher energy $-1/2$ spin states to lose this excess energy by transferring it to the lattice via a process called radiationless decay.

Since T_1 relaxation involves a loss of energy by the system as the spins return to their equilibrium populations, it is an enthalpic process. These relaxation processes are first order processes characterized by the relaxation time constants T_1 and T_2 . The width at half-height of a resonance is inversely related to the T_2 relaxation time of the nucleus, $w_{1/2} = (\pi T_2)^{-1}$. Because the magnets we use are not perfectly homogeneous, there is a secondary contribution to the line width that comes from magnetic field inhomogeneity. Therefore, the apparent spin-spin relaxation time constant or T_2^* observed in the FID includes both the natural T_2 relaxation time of the nucleus as well as the effect of magnetic field inhomogeneity, $w_{1/2} = (\pi T_2^*)^{-1}$. If you want to know the real T_2 value for a nucleus, a special experiment, called the spin echo can be used.

Question 5: What are the resonance line widths of nuclei that have apparent T_2 relaxation times (i.e. T_2^* values) of 1 and 2 sec.

The effects of T_1 relaxation are more difficult to observe directly, because it corresponds to the return to equilibrium populations following the pulse. However, if several FIDs are coadded, as is usually the case in NMR, and if the time between successive pulse and acquire steps is insufficient for complete T_1 relaxation, the resonances in the resulting NMR spectrum will be less intense than they would otherwise appear. Because quantitative NMR measurements rely on resonance intensity, understanding the effects of T_1 relaxation is very important for obtaining accurate qNMR results. Therefore this subject is treated in greater depth in the Practical Aspects section of this module.

Summary

It is hoped that this brief tutorial has provided sufficient background for you to understand the next section, focusing on practical aspects of quantitative NMR measurements. For further insights into NMR, the following websites and books are recommended. Many students find the e-book written by Professor Joseph Hornak at RIT to be especially useful since it contains embedded animations that illustrate many of the concepts introduced here.

11. Where should I look to learn more about NMR?

“The Basics of NMR” by Joseph P. Hornak, <http://www.cis.rit.edu/htbooks/nmr/>

“Georgetown Graduate Course on NMR Spectroscopy” by Angel de Dios, <http://bouman.chem.georgetown.edu/nmr/syllabus.htm>

“2D NMR Spectroscopy” by Marc Bria, Pierre Watkin and Yves Plancke, http://www.univ-lille1.fr/lcom/RMN2D/resum2D_us/index1.htm#index_us.htm

“Understanding NMR Spectroscopy” by James Keeler, John Wiley & Sons, 2005

“High-Resolution NMR Techniques in Organic Chemistry” by Timothy D. W. Claridge, Pergamon, Oxford, 1999.

“Spin Choreography: Basic Steps in High Resolution NMR” by Ray Freeman, Oxford University Press (1999).

"Modern NMR Spectroscopy: A Guide for Chemists", 2nd Edition, by Jeremy K. M. Sanders and Brian K. Hunter, Oxford University Press, 1993.

"200 and More NMR Experiments: a Practical Course" by Stephan Berger and Siegmund Braun, Wiley-VCH, 2004.

"Basic One- and Two-Dimensional NMR Spectroscopy" by Horst Friebolin, Wiley-VCH, 2004.

"Experimental Pulse NMR: A Nuts and Bolts Approach" by Eiichi Fukushima and Stephen B. W. Roeder, Perseus Publishing, 1993.