1. BASIC NMR

Nuclear magnetic resonance is a spectroscopic method that is used to investigate some of the characteristic frequencies of molecular systems. The basis of NMR is the existence of a nuclear spin. The nuclear spin is a quantum number that arises due to a relativistic effect in the quantum mechanical treatment of spectroscopy. There is no classical description that predicts the existence of nuclear spin. A classical analogy, however, is constructed by assuming that the electrical charge of a physically spinning nucleus (a convenient fiction) induces a nuclear magnetic field. The nucleus can then be thought of as being a small bar magnet. If the nuclear magnet is placed in the magnetic field of a stronger magnet, the nuclear magnetic moment will tend to align with the external field just as the magnetic needle of a compass aligns with the earth's magnetic field. To force a compass needle to point "south" requires some effort (energy). Likewise, it requires energy to anti-align the nuclear magnetic field with respect to the external field. Nuclear spins that are aligned with the external field (α spins) have a lower energy than those that are anti-aligned (ß spins).

In the absence of a magnetic field there is no difference in energy between α and ß spin states (in fact separate states do not exist), but as a magnetic field is applied, the nuclear spins relax over time (i.e. lose energy to the surroundings) to a state in which there are more spins in the lower energy state. At thermal equilibrium, the excess population of spins in the lower energy level gives rise to a macroscopic magnetization (Figure 1.1).

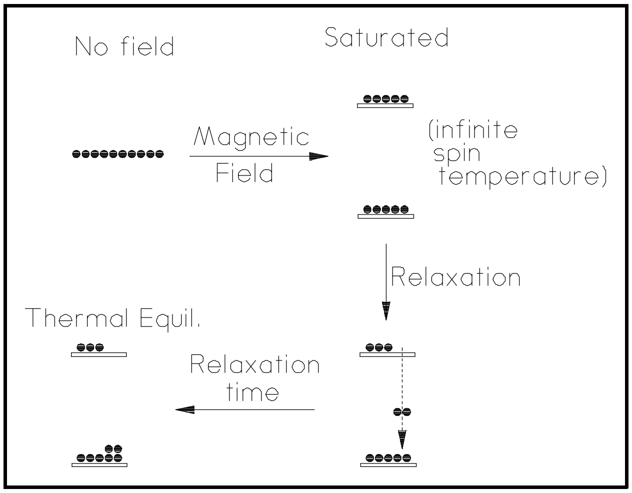

Figure 1-1.1. Relaxation of nuclear spins in a magnetic field to create a bulk magnetization. This process is characterized by a exponential relaxation rate, $1/T_1$.

The energy for a spin 1/2 nucleus with a magnetogyric ratio of γ in a magnetic field of magnitude H_0 is:

$$E = -\gamma\hbar H_0 I_m \qquad \text{(1-1.1)}$$

where ħ is Plank's constant divided by 2π and I_m is 1/2 for an α spin and -1/2 for a ß spin. The difference in energy between the nuclear spin states is very small. For a proton in a 14.1 Tesla field (600 MHz) the difference between the α and ß states is only about 60 millicalories/mole. The populations of the two energy levels is governed by a Boltzmann distribution which in turn depends on the ratio of the energy differences between states to the temperature of the system. At equilibrium the population ratio is:

$$\frac{n_\beta}{n_\alpha} = e^{\frac{-\Delta E}{kT}} \tag{1.2}$$

$n_ß$ is the population in the higher energy state and n_α is the population of the lower energy state. ΔE is the difference in energies and kT is the Boltzmann constant times the absolute temperature. Since the thermal energy (kT) at 25 °C is about 600 calories/mole even for ^{1}H nuclei, which are the second most sensitive nucleus after ^{3}H, the excess of spins in the α state is only one part in about 10,000 at the highest magnetic fields (14 Tesla [600 MHz]) available for NMR. Detecting the small magnetic moment arising from population difference in the α and ß energy states is the fundamental task of NMR spectroscopy.

In optical spectroscopy, the energy differences between electronic states are large (6000 cal/mole for blue light) compared to thermal energies (~600 cal/mole). Therefore, the occupation of high energy states in optical spectroscopy due to thermal energy is extremely rare (one part in 20000) and therefore every absorbed photon causes an electron transition from the lower energy state to the higher energy state. The absorption of photons by the electronic system are easily measured by comparing the input light intensity with the intensity of light after it has traveled through the sample. This is a very sensitive technique when compared to NMR spectroscopy. In NMR, both of the energy levels of a spin 1/2 nucleus in a magnetic field are essentially equally populated. An absorbed photon can cause transitions of the spins from the lower to the higher energy level or just as easily cause a stimulated emission of a spin from the upper energy state. The net absorption of photons in the sample is very small since the excess population in the lower energy level is small. The input intensity of photons is equal to the intensity of the output to 1 part in 10,000. Observing small NMR signals in the presence of a large irradiation signal is very difficult, NMR spectroscopy requires very careful design of instrumentation to eliminate the excitation energy from the desired signal.

The NMR experiment is performed as a resonance technique. Resonance is a phenonemon that is well known to mechanical engineers. All buildings, bridges, cars, and other structures have natural characteristic vibrational frequencies or eigenvalues that depend on the design and materials. Natural forces on the structures such as winds or earthquakes may have frequency components that could drive the building into damaging oscillations. One goal of the designer is to make the characteristic frequencies of the structure far from any naturally occurring frequency. At the characteristic frequency, energy is efficiently transferred into and out of the system.

The frequency at which the transfer of energy is most efficient is the resonance frequency. The equation for a Lorentzian (resonance) absorption lineshape is:

$$A = k \frac{T_2}{1 + T_2^2 \Delta\omega^2} \tag{1.3}$$

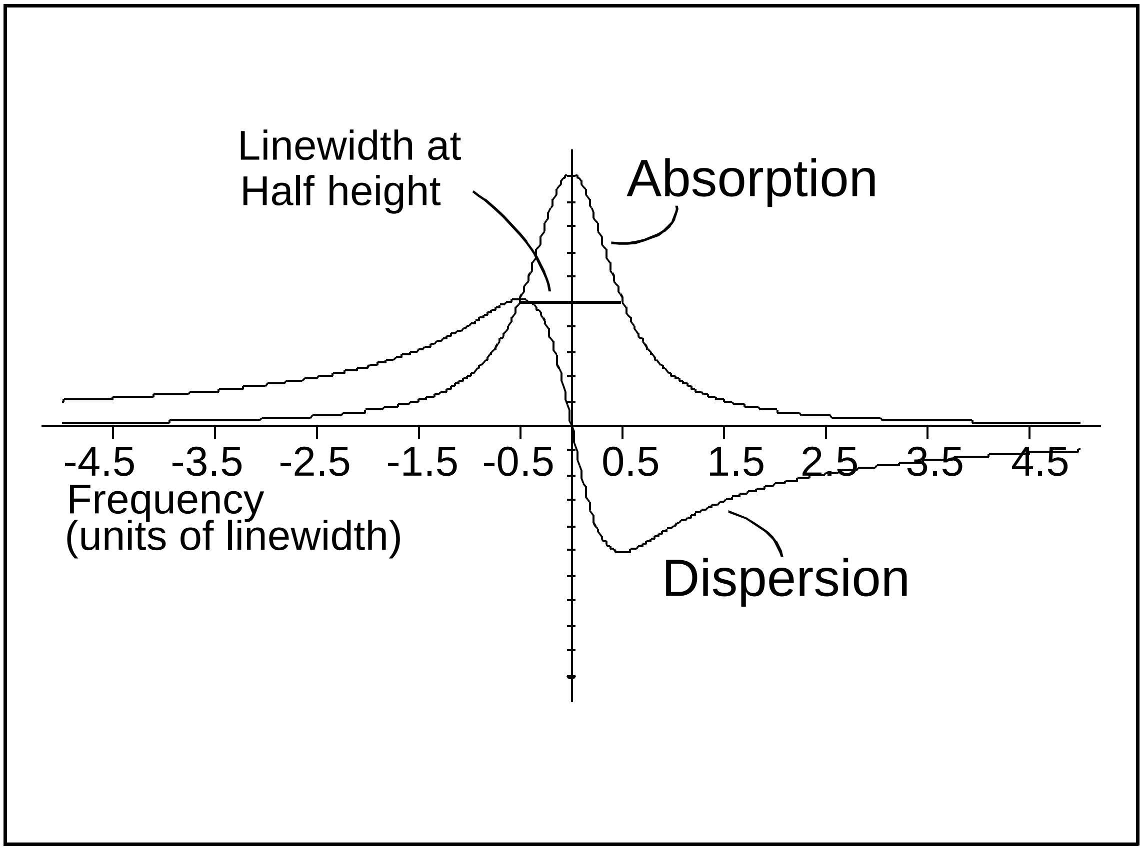

Figure 1.2. Lorentzian absorptive and dispersive lineshapes. Note that the dispersive line has finite amplitude over a much wider range than the absorptive line. This is important to remember in setting spectral widths.

A is the absorption amplitude, Δω is the difference between a reference frequency and the resonance frequency, k is a constant that depends on the magnetic properties of the nucleus and the static magnetic field, and $1/\pi T_2$ is a the linewidth in Hertz at half height. Resonance also has a dispersive component that is described by:

$$D = k \frac{\Delta\omega T_2^2}{1 + T_2^2 \Delta\omega^2} \tag{1.4}$$

D is the dispersive amplitude.
Plots of Δω versus the absorptive and dispersive amplitudes are shown in Figure 1.2.

At the resonance frequency, $\Delta\omega=0$, the absorption line is at a maximum and the dispersion line is at zero. The area under the absorption peak, the frequency at the absorption peak maximum, and the width of the absorption line at 1/2 maximum amplitude, are the parameters that define the Lorentzian line.

The natural frequency of nuclear spins in a magnetic field is termed the Larmor precession frequency. When a nuclear spin is placed in a magnetic field, the external field produces a torque on the nuclear magnetic moment that causes the spins to precess about the direction of the applied field (the Z axis by convention) at a frequency that is proportional to the product of the magnetogyric ratio of the nucleus and the applied field strength.

$$2\pi\nu = \omega = \gamma H_0 \tag{1.5}$$

Larmor precession frequencies for NMR active nuclei are in the range of tens to hundreds of megahertz. The energies of the photons required to induce transitions between aligned and anti-aligned magnetic spin states correspond to frequencies in the radiofrequency portion of the electromagnetic spectrum.

Technically, the pulsed NMR experiment is performed by placing a sample into a magnetic field, exciting the nuclear spin system in some controlled manner with one or more pulsed radiofrequency (RF) fields, and then detecting the response of the spin system to the excitation. The experimental hardware is very similar to the equipment used in radio broadcasting. A radio transmitter in the console produces a signal at a given frequency. These signals are transmitted through an antenna (the probe coil) to excite the spin system. The transmitted RF signal is a pure, single frequency which excites the spin system away from the equilibrium state. The excited spin system "dirties" the pure signal by adding modulations corresponding to resonance frequencies characteristic to the spin system. The excited system transmits the modulated RF signals which are picked up by the probe coil and detected by a radio receiver. The received signal is "demodulated" and the frequencies of the spin system are obtained.

The only direct contact that the spectroscopist has with the spin system is through the application of RF fields (and the static magnetic field). Among the possible manipulations are the control of the strength and frequency of the of the RF field and the timing between successive excitations. In multipulse NMR experiments, the spectroscopist relies on interactions within the spin system in order to manipulate the evolution of the spin system. Knowledge of the internal interactions in the spin system and the manipulations of the RF fields are the key to spin gymnastics, whereby one can deduce molecular structure by interrogating the enslaved nuclear spins. The experimentalist can force the spins to dance only until the great saviors, T_1 and T_2 relaxation, come to release the spins from their bondage. As always, thermodynamics wins in the end.