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An Introduction to Nuclear Magnetic Resonance Spectroscopy

by Andrew Yang

Nuclear Magnetic Resonance Spectroscopy, or NMR Spectroscopy, is a powerful non-destructive research technique that uses the magnetic properties of nuclei to investigate the corresponding molecules and their interactions. The phenomenon of nuclear magnetic resonance was first measured by Isidor Rabi in 1938 using molecular beams,¹ and in 1946 Felix Bloch² and Edward Mills Purcell³ expanded the technique to study liquids and solids, for which they were awarded the 1952 Nobel Prize for Physics. NMR Spectroscopy has become one of the most widely used spectroscopic techniques, seeing application from the investigation of organic molecules to the resolution of protein structure in studies of structural biology.⁴

NMR Spectroscopy is based on detecting transitions between nuclear spin states, where nuclei in a magnetic field absorb and re-emit electromagnetic energy at specific resonance frequencies. NMR spectroscopy can generally be reduced to two fundamental steps: (1) alignment of the nuclear spins in a constant applied magnetic field, and (2) perturbation of the alignment with an applied frequency pulse. This is possible due to the fact that nucleons possess spin angular momentum, which can give rise to magnetic moments, meaning that their energies depend on their orientation in an applied magnetic field. The energy of a magnetic dipole in an

¹ Rabi, I. I.; Zacharias, J. R.; Millman, S.; Kusch, P. "A New Method of Measuring Nuclear Magnetic Moment." *Phys. Rev.* **53** (4): 318. **1938**.

² Bloch, F. "Nuclear Induction" *Phys. Rev.* **70**: 460-474. **1946**.

³ Purcell, E.M.; Torrey, H.C.; Pound, R.V.; "Resonance Absorption by Nuclear Magnetic Moments in a Solid." *Phys. Rev.* **69**: 37, **1946**.

⁴ Wuthrich, K. "Protein structure determination in solution by NMR spectroscopy." *J. Biol. Chem.* **265** (36): 22059-62. **1990**.

applied magnetic field is given by

$$E = -\boldsymbol{\mu} \cdot \mathbf{B} \quad (1)$$

where $\boldsymbol{\mu}$ is the magnetic dipole moment and \mathbf{B} is the applied field.

The magnetic dipole moment is proportional to the nuclear spin angular momentum of the nucleus \mathbf{I} , giving

$$\boldsymbol{\mu} = \gamma \mathbf{I} \quad (2)$$

where γ is the gyromagnetic ratio, a characteristic property for the specific particle or system of concern. The angular momentum vector of the nucleus must be quantized both in magnitude and in direction,⁵ and is characterized by two quantum numbers: the nuclear spin angular momentum quantum number I and the nuclear spin magnetic quantum number m_I . The value of I is fixed for a particular nucleus, but the value of m_I spans the range between $-I$ and $+I$ in integer steps. The magnitude of the angular momentum vector \mathbf{I} is related to the angular momentum quantum number I by

$$|\mathbf{I}| = \hbar(I(I+1))^{\frac{1}{2}} \quad (3)$$

where \hbar is the reduced Planck constant, or Dirac constant. Some information of the orientation of the angular momentum vector is given by the nuclear spin magnetic quantum number m_I by

$$I_z = m_I \hbar \quad (4)$$

where I_z is the projection of the angular momentum vector along the Cartesian z-axis.⁶

Individual nucleons have half-integer spin quantum numbers,⁷ meaning that nuclei can have an integer or half-integer quantum number I . Similar to electrons, anti-parallel spin alignment in protons and in neutrons is the permitted state, so nuclei containing even numbers of

⁵ Gerlach, W.; Stern, O.; "Der experimentelle Nachweis der Richtungsquantelung im Magnetfeld" *Zeitschrift für Physik* **9** (1): 349-352. **1922**.

⁶ Slichter, C.P. *Principles of Magnetic Resonance*. Springer: Berlin, **1990**.

⁷ Pauli, W. "The Connection Between Spin and Statistics" *Phys. Rev.* **58**, 716-722. **1940**.

both protons and neutrons have overall zero spin or $I=0$. However, a parallel spin alignment between a proton and a neutron is the permitted state rather than anti-parallel alignment. Consequently, nuclei containing odd numbers of both protons and neutrons have nonzero integer values of nuclear spin quantum numbers. Nuclei containing an odd number of protons and even number of neutrons or an even number of protons and odd number of neutrons have half-integer spin quantum numbers.

The most commonly studied nuclei are that of Hydrogen-1, or protium, which consists of a single proton. A lone proton has a spin of $I = \frac{1}{2}$ and a large gyromagnetic ratio of $\gamma = 2.6752 \times 10^8 \text{ rad/Ts}$.⁸ The high natural abundance of the hydrogen-1, especially in organic molecules, and the relatively sizable gyromagnetic ratio are responsible for the popularity of proton NMR spectroscopy. However, any nuclei with an intrinsic magnetic dipole moment could theoretically be used for NMR spectroscopy.

Since $I = \frac{1}{2}$ for a proton, the magnitude of the spin angular momentum is $|\mathbf{I}| = \hbar(\frac{3}{4})^{1/2}$ with possible projections along the z-axis of $I_z = +\hbar/2$ or $I_z = -\hbar/2$ for values of $m_I = +\frac{1}{2}$ and $m_I = -\frac{1}{2}$, respectively. A proton having $m_I = +\frac{1}{2}$ is said to be in a spin-up state, and a proton having $m_I = -\frac{1}{2}$ is said to be in a spin-down state. From the above equations, it can be seen that these two states differ in energy due to the relationship between the energy and the projection of angular momentum on the z-axis:

$$E = -\boldsymbol{\mu} \cdot \mathbf{B} = -\gamma \mathbf{I} \cdot \mathbf{B} = -\gamma I_z B_0 = -\hbar \gamma B_0 m_I \quad (5)$$

if the applied field \mathbf{B} has the magnitude B_0 and is directed along the z-axis, such that $\mathbf{B} = (0,0,B_0)$. For a proton then, there is a energy difference of energy between the two spin states of

$$\Delta E = \hbar \gamma B_0 \quad (6)$$

⁸ Williams, E.R.; Olsen, P. T.; "New Measurement of the Proton Gyromagnetic Ratio and a Derived Value of the Fine-Structure Constant Accurate to a Part in 10^7 " *Phys. Rev. Lett.* **42** 1575-1579. **1979**.

which indicates that the difference in energy is proportional to the strength of the applied magnetic field. Due to the relatively small values of the Dirac constant and gyromagnetic ratios, NMR spectroscopy requires the use of strong magnetic fields to produce significant energy differences.

Applied electromagnetic radiation can induce a transition between the $m_I = +\frac{1}{2}$ and $m_I = -\frac{1}{2}$ states, resulting in a measurable absorption of energy. The nucleus is said to be in resonance when this absorption occurs, hence the name of “nuclear magnetic resonance.” This resonance can only occur when the applied electromagnetic radiation matches the energy of the transition, meaning that the resonance occurs at specific frequencies of applied radiation. Typical frequencies generally fall within the range of radio waves, making NMR spectroscopy a relatively energetically mild technique compared to other spectroscopic techniques.⁹

Though it may initially appear that all nuclei of the same proton and neutron composition would have the same resonant frequency, much of the utility of NMR spectroscopy is due to the fact that nuclei in differing chemical environments differ in their resonance frequencies. This difference is due to the electrons surrounding the nuclei, which produce a shielding effect. As charged particles, electrons moving in the applied external magnetic field generate an opposing secondary field,¹⁰ thereby reducing the effective magnetic field at the nucleus. Consequently, the energy difference between the spin states is reduced, and the resonant frequency is lowered, leading to the phenomenon known as chemical shift. Though the extent of shielding also depends on orientation of the molecule relative to the applied field, in typical liquid or gaseous spectra random motion is expected to average out oriental dependence.

Since the energy transitions are proportional to the applied magnetic field, the location of

⁹ Wang, A.C.; Bax, A.; “Minimizing the effects of radio-frequency heating in multidimensional NMR experiments” *Journal of Biomolecular NMR*. **3** (6): 715-720. **1993**.

¹⁰ Maxwell, J. C.; “On physical lines of force” *Philosophical Magazine*, **1861**.

absorption peaks in an NMR spectrum inevitably vary between spectrometers. In practice, a reference substance is often used, the most common being tetramethylsilane, $(\text{CH}_3)_4\text{Si}$, which is often treated as the 0.0 point in an NMR spectrum.¹¹ Relative frequency differences between absorption peaks in a spectrum can then be scaled by dividing out the strength of the applied magnetic field.

However, resonance frequencies can be further perturbed by interactions between nuclear spins.¹² Coupling of the angular momentum leads to mutual splitting of the signals of the interacting nuclei. This spin-spin coupling, or J-coupling, requires that the nuclei be bonded relatively close to one another, meaning that the signal splitting in the spectra provides detailed information on the conformation and structure of the studied molecule.

¹¹ Mohrig, J.R.; Hammond, C.N.; Schatz, P.F.; *Techniques in Organic Chemistry*. 2nd Ed.; W.H. Freeman: New York, **2006**.

¹² Ramsey, N.F.; Purcell, E.M.; "Interactions between Nuclear Spins in Molecules." *Phys. Rev.* **85**: 143-144. **1952**.