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NMR Spectroscopy

NMR spectroscopy relies on the fact that nuclei of spin $\frac{1}{2}$ align in a magnetic field and reverse direction with a precise amount of radiation (of the radio frequency). The amount of energy required to flip a nucleus' spin is characteristic of its chemical environment. Analysis of a molecule's NMR spectrum can help determine its structure in solution.

History

1890's: Peiter Zeeman observes that nuclei of certain atoms behave strangely in a magnetic field (1902 Nobel Prize, Physics). This phenomenon is later found to be due to nuclear spin.

1946: Edward Purcell¹ (Harvard) and Felix Bloch² (Stanford) independently describe NMR (1952 Nobel Prize, Physics).

1966: Richard Ernst (1991 Nobel Prize, Chemistry) discovers NMR sensitivity is improved by using short, intense pulses of radiation followed by a Fourier Transform to produce a spectrum.

1970's: Ernst helps develop multidimensional NMR.

1985: Kurt Wüthrich shows how NMR can determine structure of a protein (2002 Nobel Prize, Chemistry).

Theory

Nuclei with odd atomic number (^1H , ^{13}C , ^{15}N , etc.) have nuclear spin.

In the absence of a magnetic field these nuclei point in random directions, but in the presence of a magnetic field they will align either parallel or anti-parallel to the magnetic field.

The parallel orientation is lower in energy. When a nucleus is exposed to the right combination of magnetic field and electromagnetic radiation it flips from parallel to anti-parallel orientation.

The absorption of energy required for flipping is detected by the NMR spectrometer.

Depending on the environment of a nucleus and the interactions it makes, a specific amount of energy will be required to make it resonant.

The NMR Spectrometer

Consists of 4 parts: Magnet, RF generator, Detector, and Computer.

Magnet: surrounds sample, generating a magnetic field (1-20 Tesla)

RF generator: Emits precise frequency of light (Radio frequency)

Detector: Measures sample's absorption of RF energy

Computer: Analyzes the signal from the detector to produce a spectrum

Types of NMR Spectroscopy: ^1H , ^{13}C , and multi-dimensional spectroscopy

^1H (Proton) NMR:

Examines the characteristics of ^1H (99.9% of H)

The number of peaks = the number of chemically different ^1H

The area of the peaks is proportional to the number of ^1H absorbing at that particular frequency

The chemical shift (frequency of ^1H absorption) indicates the functional groups interacting with that ^1H

The splitting of the peaks (the number of smaller peaks a signal is split into) = (the number of other ^1H interacting with a certain ^1H) - 1

^{13}C NMR:

Examines the characteristics of ^{13}C (1% of C)

The number of peaks = the number of chemically different ^{13}C

The chemical shift indicates the functional groups interacting with that ^{13}C

Multidimensional (2D, 3D, 4D) NMR:

Allows for larger molecules to be studied

Makes it possible to determine solution structure of a protein

2D NMR (chemical shifts represented on 2 axes and intensity of a 3rd) uses a complex pulse sequence to perturb nuclear spins. It involves 4

stages: preparation, mixing, evolution, and detection. Common techniques are COSY (gives distance through covalent bonds) and NOESY (gives distance through space).
3D and 4D NMR spread the 2D spectrum out over additional dimensions

(Figure removed due to copyright considerations.)

¹Purcell, E. M., Torrey, H. C & Pound, R. V. Resonance absorption by nuclear magnetic moments in a solid. *Phys. Rev.* **69**, 127 (1946).

²Bloch, F., Hansen, W. W. & Packard, M. Nuclear induction. *Phys. Rev.* **69**, 37 (1946).

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