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Nuclear Magnetic Resonance

by

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Nuclear Magnetic Resonance

Both protons and neutrons being fermions and having spin ½ tend to couple when forming nuclei and give nuclear spins which are integral or half-integral or zero. The interactions between the nucleic spins are much weaker than those for electron spins, and therefore the concept of bond formation and spin paring cannot be introduced. This fact introduces a principle difference between the nucleic and the electronic magnetic systems.

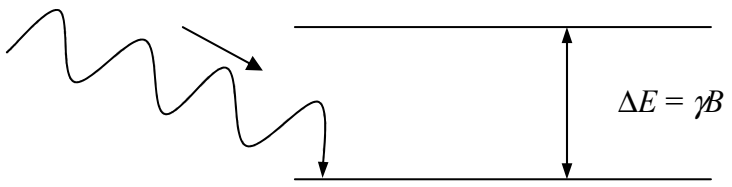
The Phenomenon

In order to model the system of nuclear spins one can consider a set of N identical spins $(h/2\pi)\mathbf{I}$ having magnetic dipole moment $\boldsymbol{\mu}$**, which** are separated well enough to justify the assumption of negligible interactions between them. The initial condition can be set to a random uniform distribution of the orientations of the individual magnetic moments, all the projections of the magnetization $\mathbf{M} = (1/V)\Sigma\boldsymbol{\mu}_i$, are zero.

On the application of static magnetic field $\mathbf{B}_0$ along the z axis the magnetic moments will start to precess around this direction. The projection of the ith moment onto the z axis will be $\mu\cos\theta_i$, and in the classical description θ_i can have any value, and since they are uniformly and distributed at random, $M_z = 0$. Moreover, because all the spins precess at the same angular frequency $\omega = 2\pi g\mu_B B_0/h = \gamma B_0$ and therefore maintain constant phase differences, the perpendicular components of **M** will remain zero. This represents the general conclusion that an isolated system of non-interacting spins cannot be magnetized. If the model system is let to dissipate energy, for example through radiation, or if the moments are coupled to a thermal reservoir (the lattice in a solid or the electron shells) the system will acquire magnetisation as the low energy states will be more populated than the high energy ones. Therefore the coupling of the system to a thermal reservoir or even only the ability of the system to dissipate energy gives rise to a net magnetization.

If the spins are not coupled among themselves, and the thermal reservoir does not couple them or introduce any kind of correlation between their phases, the transverse components of **M** will decay because the phases of the individual spins will be randomised to a uniform distribution (the magnetic field introduces non-uniform distribution only with respect to the z axis and the components of the spins are not coupled by any external means). The characteristic time of this relaxation may be referred to as the *thermal relaxation time* T_1. If we let the spins interact weekly, which is to say that every spin will feel a random component in its local magnetic field (if the spin is purely magnetic e.g., for the neutron, or in the electric and magnetic fields and their local gradients if the spin has a proton contribution), similar contribution will lead to another type of relaxation process with a different characteristic time, normally called the *spin-spin relaxation time* T_2.

When irradiating a system of spins subjected to a magnetic field, which lifts the degeneracy of the energy levels with the factor of the *Zeeman energy* $\Delta E/2$, with an electromagnetic wave (in other words photons), transitions are induced between those levels, and the system in general absorbs energy. The absorption is, of course not the whole matter, there is also emission, but if coupling exists between the spin subsystem and a thermal reservoir, only a part of the ongoing photons will be reemitted, and phonon or other quasi-particle excitations can be created.



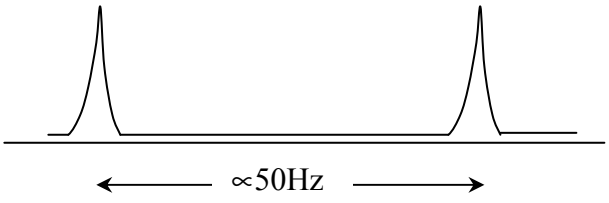
Chemical Shifts and Shielding

Let us consider the Bohr model of the atom. The electrons circulating in orbitals around the nuclei will create currents, which will tend to shield the central region of the atom from the applied magnetic field (as in the classical approach to the atomic diamagnetism). Therefore the applied magnetic induction may be decreased in the manner $B = B_0(1 - \sigma)$, where σ is a positive value analogous to the diamagnetic susceptibility.

If an explicit solution can be reached for the electrons wave functions or approximate solutions can be given by means of superposition of some basic set of atomic functions resulting for example from a Hartree-Fock procedure the value of σ can be calculated as:

$$\sigma = \frac{e^2}{3m}\left\langle 0\left|\sum_i \frac{1}{r_i}\right|0\right\rangle$$

For the case of molecules the shielding varies for different orientations of the magnetic field with respect to the axes of symmetry of the molecules, and in principle σ should be referred to as tensor. Nevertheless, due to the rapid rotation of the molecules, what is measured in the experiment is an average scalar value, which order of magnitude is 10^{-5} - 10^{-6}. Because the accuracy of control and measurement of the magnetic field is insufficient to allow for calculating of σ it is more popular to perform measurements in constant field and measure the shift in the resonance frequency for, say, protons, in different molecular environments. The shifts are usually very small of the order of 10Hz at about 100MHz, i.e. 1ppm, but still measurable because of the inherent precision of the frequency measurement.



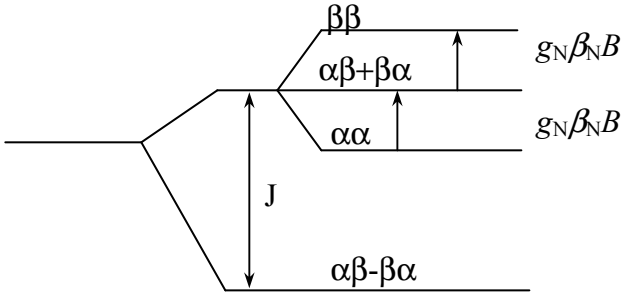
Of course, what is of general value is the frequency shift per unit applied field, and shifts resulting in a single line considerably separated in frequency from the lines of interest, therefore a standard is needed that is chemically inert, symmetrical and non-polar. A preferred standard for the proton NMR is tetramethylsilane in which, due to rapid rotation around the Si-C bonds, all protons are effectively equivalent.

Spin-spin Coupling and Splitting

Often the nuclear spin-spin interactions or correlations are expressed empirically in the form of a Heisenberg term in the Hamiltonian of a system of two identical spins, like:

$$H = -\gamma B_a I_a^z - \gamma B_b I_b^z + \left(\frac{J}{\hbar^2}\right)\vec{I}_a \cdot \vec{I}_b$$

where $B_a = B_0(1 - \sigma_a)$, $B_b = B_0(1 - \sigma_b)$. If the protons are equivalent, the solution is simple and leads to splitting of the energy levels as shown below:



However for all the spin products the transitions are suppressed and no spectral splitting can be observed.

Another simple approach is to analyse the linear case, when $\hbar^2(\omega_b - \omega_a)^2 >> J^2$. The Hamiltonian then simplifies to:

$$H = -\omega_a I_z^z - \omega_b I_b^z + (\frac{J}{\hbar^2}) I_a^z I_b^z$$

The eigenvalues for all of the possible spin products can be shown to be:

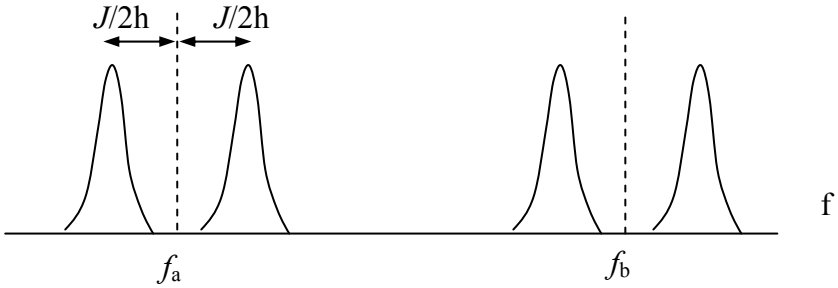
$$E_{\beta\beta} = \frac{1}{2}\hbar(\omega_a + \omega_b) + \frac{1}{4}J$$

$$E_{\alpha\beta} = \frac{1}{2}\hbar(\omega_a - \omega_b) - \frac{1}{4}J$$

$$E_{\beta\alpha} = \frac{1}{2}\hbar(\omega_b - \omega_a) - \frac{1}{4}J$$

$$E_{\beta\beta} = -\frac{1}{2}\hbar(\omega_a + \omega_b) + \frac{1}{4}J$$

Resulting in the spectrum below:



The further analysis for greater number of spins is more complicated and usually is performed numerically, but the general features are similar, e.g. the spin-spin correlation induces splitting which is related to the number and the kind of neighbouring spins, thus high-resolution NMR spectra are of great interest as they reveal information about the exchange couplings transmitted through the electrons in the chemical bonds. Such information in addition to the chemical shifts proves of significant use for the chemical structure analysis.

Chemical or Site Exchange

As we already noticed, the chemical shifts depend upon the local environment and together with the spin-spin splitting which depends on the mutual coupling, can vary if there is exchange of a nucleus from one site to another. The resulting spectrum can be

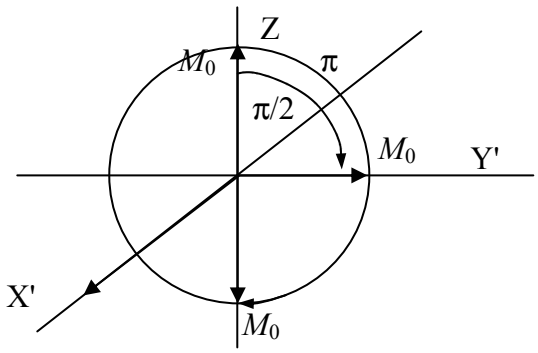
considered as a superposition of the relevant sites spectra. Using the uncertainty principle, the broadening in a particular level can be estimated as:

$$\Delta E = \hbar / T$$

Where T is the lifetime of the level, which can be shown to preserve its characteristic Lorentzian shape. Thus the broadening of the spectral lines can reveal useful information about the kinetics of chemical reactions and the molecular dynamics.

Relaxation and Damping

To further reveal the problem of spin relaxation mechanisms, let us suppose that stationary magnetisation has been achieved in the direction of *OZ*. To instantaneously define the *OX*, a rotating field of magnitude B_1 and frequency ω, is switched on. In a coordinate system of *OX'Y'Z* rotating around *OZ* at ω, B_1 is stationary and the apparent precession is as if B_0 does not exist if we satisfy $\omega = \omega_0 = \gamma B_0$. In this frame M_0 starts precessing around B_1 and as this field can be applied as pulses of appropriate duration M0 can be rotated to both *OY'* or to *-OZ*. There is an instantaneous tendency for the original direction of the moment to be restored, therefore the pulse duration should be kept less than T_1. Making this assumption, after an appropriate pulse M_0 remains initially parallel to *OY'*, and is actually rotating at ω_0 in the laboratory frame.



After the application of the radio frequency pulse, the signal in the appropriate set of coils decays generally with the characteristic time T_2 and this is called the free induction decay, since it is observed in zero r.f. field. There are methods of determination of T_1, also, e.g. by means of π/2 pulses, which when well timed can read the development of M_0 after a π pulse.

The value of the spin-spin relaxation time can be determined also, by carefully examining the widths of the absorption lines at half-heights, observed by the continuous-wave NMR:

$$\Delta f = \frac{1}{\pi T_2}$$

as of course the spectra and the time behaviour of the system are directly related.

Therefore it is often preferred that multiple free induction decays are written down and averaged before a Fourier transform is done by means of a computer, rather than increasing the precision of the frequency scan in the classical continuous wave measurement which is often more difficult and time-consuming.

Knight Shifts

Good NMR measurements in metals are problematic, due to the small penetration depth of the radio frequency radiation. Therefore, powders with small grain size should be used for which the particle size is comparable with the skin depth. Besides these

problems, large shifts of frequency from the nuclear free resonance value, often more than 10 times bigger than the chemical shifts.
According to the scientist, which name this effect bears, these shifts can be explained in terms of paramagnetic polarisation of the s-state conduction electrons, as the s-wave-functions are non-zero at the nucleus. The effective field is equivalent to the hyperfine interaction observed in the Mossbauer and other spectroscopic experiments and is given by:

$$\Delta B = \frac{\mu_0 \chi H_0 \left|\overline{\Psi(0)}\right|^2}{N}$$

where χ is the temperature-independent paramagnetic susceptibility, N is the number of atoms per unit volume, and ψ is the s-orbital wave function of interest. The calculated from first principles shifts, generally, compare well with the experimental data.

Nuclear Magnetic Resonance in Solids

A model Halmiltonian for the system of two identical spins in a solid can be constructed in the form of sum of a Zeeman term, Izing term and a term depending on the spin rising and lowering operators, which reflect the contribution of the mixed states in the total energy:

$$H = -\omega_0 (I_1^z + I_2^z) + \frac{A(\theta)}{\hbar^2}(-I_1^z I_2^z + \frac{1}{4}(I_1^+ I_2^- + I_1^- I_2^+))$$

The energy levels splitting can be deduced as follows:

$$E_1 = \omega_0 \hbar - (\frac{A}{\hbar^2})(\frac{1}{4}\hbar^2)$$

$$E_2 = 0 - \frac{A}{\hbar^2}(-\frac{1}{4}\hbar^2 - \frac{1}{4}\hbar^2)$$

$$E_3 = 0 - \frac{A}{\hbar^2}(-\frac{1}{4}\hbar^2 + \frac{1}{4}\hbar^2)$$

$$E_4 = -\omega_0 \hbar - (\frac{A}{\hbar^2})(\frac{1}{4}\hbar^2)$$

The angular dependence term $A(\theta)$ due to the quadruple moments can be substituted in the above, and the resulting splitting can be expressed like:

$$f = f_0 \pm \frac{3}{4}\frac{\mu_0}{4\pi}\gamma^2 \frac{\hbar}{2\pi}\frac{1}{r^3}$$

Besides the case in whish the spins are further away from each other, when the resulting splitting obviously tends to zero, there is one more case in which this term is small, which is when the angular part becomes zero. This can be shown to be satisfied for an angle of about 55^o. Thus valuable information about the disposition of the molecules of water of crystallisation in certain crystals can be retrieved. Rotating such a crystal, on certain positions appearance of doublets can be noted. Theoretical considerations can be made also for the case of random distribution of the water molecules, in which specific broadening of the line-shapes is involved.
The ability to obtain high-resolution NMR spectra is also helpful when the angular part in the Hamiltonian, due to the dipole-dipole and quadruple interactions, produces effects similar to those observed in liquids with rapid molecular motion, namely the motional narrowing. Nevertheless because large rotational speeds are required, this methodology

represents severe experimental difficulties, which is not the case with the intrinsic rotation of the molecules in some liquids.

NMR in Magnetically Ordered Materials

With regard to the hyperfine interactions of the nucleus with the electrons the nuclear spin Hamiltonian can be written as:

$$H = -\gamma B I_z + A\langle S_z \rangle I_z$$

Where the mean $<S_z>$ is corresponding to the polarisation of the electron spins in the applied magnetic field, and as was already noticed, can be related to the magnetization and the susceptibility:

$$\langle S_z \rangle = \frac{\hbar M(T)}{Ng\beta}$$

So the Hamiltonian finally becomes:

$$H = -\gamma(B - \frac{a\chi}{\mu_0 \hbar \gamma Ng\beta})$$

The s-conduction electrons can attribute to the spontaneous magnetization according to the RKKY mechanism if they are polarized by locally ordered spins, or partially polarized d-band. If the magnetisation of the s-electrons is taken to be proportional to the magnetisation of the whole crystal:

$$\langle S_z \rangle = \frac{1}{2}\hbar \frac{M_s(T)}{M_s(0)}$$

Which explains why NMR can be observed in magnetically ordered materials even in the absence of applied field. When talking about s-band conduction electrons, attention should be brought over all the s-electrons, which have significant density of the wave function in the region of the atomic nuclei.

Often in ferromagnets high absorption is observed, which disappears with the approaching of saturation, and is associated with oscillating domain walls. The local changes in the magnetisation in the domain walls are equivalent to modulating the local nuclear field, but the quantitative analysis is problematic because it requires information about the domain wall densities and amplitudes of oscillation.

Magnetic Resonance Imaging

Let us define an axis *OZ*, by applying a magnetic field in this direction, and consider, for the moment, vector gradients having only one component. If we take, for example, a cubic space element with magnetic field $\mathbf{B} = \mathbf{k}B$ normal to the bottom surface, and $B = \mathbf{k}(B + \delta B)$ on the upper surface, keeping $B_n = 0$ on all other surfaces. If the the gradient field can be considered small,

$$b_z = b_z(0) + x\frac{\partial b_z}{\partial x} + y\frac{\partial b_y}{dy} + z\frac{\partial b_z}{\partial z}$$

In fact, the definition of the gradient as a tensor is appropriate to be used:

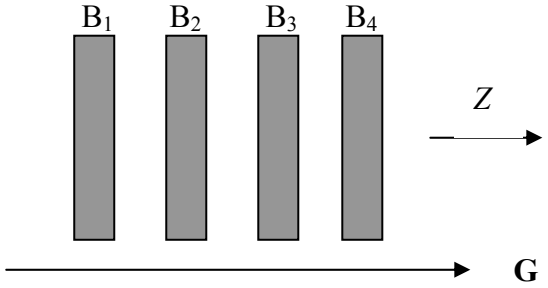
$$G_{ij} = \frac{\partial B_i}{\partial x_j}$$

And the derivative with respect to a given direction in space can be taken as:

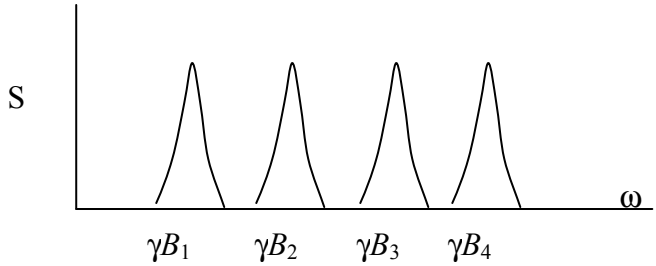
$$dB_k = k \cdot G$$

Often what is required, but practically very hard to achieve, is a controlled linear field gradient, with minimised extraneous components.

It can be shown on the simple example of a space partially occupied by water, that NMR experiments in linear field gradients can give structural information about the system. Lets suppose that a gradient field is applied to the region below:



The different layers experience different fields and therefore generate different absorption signals at $\omega_i = \gamma B_i$, and if we assume an equal spin density in each layer, the peeks will be in equal height:



If we now go to continuous approximation, stating that the spin density varies from sheet to sheet in a smooth manner, making the number of sheets infinite, since $\omega \propto B$ and $B \propto z$, the frequency scale will be easily converted into coordinate z, and the observable $S(\omega)$, will become a one dimensional image in space of the total spin density. Further on images corresponding to different linear gradients can be numerically combined to produce 2D image.

In order to define a slice in space, rather than a plane, at certain frequency and background field, an oscillating gradient G_z may be applied with a frequency of Ω. Thus it is possible to define a slice of thickness $2\Omega/\gamma$. Further field gradients define the element of space from which the information about the spin density is to be extracted. So, effectively subdividing the volume of interest into n x n x n elements, the reconstruction of the whole image would require n^3 experiments and the solution of n^3 equations, thus making the process very slow.

In order to speed-up the image reconstruction time, another approach was suggested based on the free induction decay pulse technique, which as already noted, is often much faster than the continuous wave absorption measurements.

Let us assume that a plane of spins perpendicular to the *OZ* has been selected by applying a $\pi/2$ pulse, before which a gradient with components $G_x(t)$ and $G_y(t)$ to choose a *XY* plane at the given moment of time *t*. The signal form this spin-slice can be referred to as sum of signals coming from space elements with different spin densities, giving contribution to the total like $A_i e^{i\omega t} = A_i e^{i\gamma Bt}$, where A_i is proportional to the local spin density. If we go now to continuous spin density approximation, for the signal at a given moment in time *t* we have:

$$S(t) = \int \rho(\vec{r}) e^{(i\gamma \int_0^t \vec{r} \cdot G(t')dr')} d\vec{r}$$

We can further define:

$$\vec{k} = \int_0^t \gamma G(t')dt'$$

And rewrite the expression for S as:

$$S(t) = \int_0^t \rho(r)e^{i\vec{k}\cdot\vec{r}}$$

Because k is the wave number defined by the applied gradients and not the wavelength defined by the radio frequency radiation. The above integral can be looked at as the Fourier transform of the spin density spatial distribution. By controlling the space gradients of the magnetic field applied, the whole k space can be covered, and therefore, by means of reverse Fourier transform, the original spin density distribution can be recovered.

By the appropriate set of radio frequency sine modulated pulses, selective exitation can be achieved in a whole slice on certain coordinate z. The spins in this slice can then produce free induction signals in the appropriate pick-up coils. The signal height will be proportional both to the local spin density as well to the local magnetic field gradients in a defined spatial element, therefore the applied gradients have to overwhelm the chemical shifts induced by the differences of the local atomic surroundings.

For the conventional Fourier Transform NMR the existence of two independent time scales is of great importance. The first one is associated with the characteristic time for the spin echoes and can be denoted by t_1, and the detection time t_2. The signal, therefore has to be referred to as $S(t_1,t_2)$ and is given by:

$$dS = \rho(x, y)dxdye^{i\gamma Bt}$$

The times t_1 and t_2 then can be addressed as the times during which the two gradients $G_x(t_1)$ and $G_y(t_2)$ are applied. We can now write the signal as follows:

$$S(t_x, t_y) = \iint \rho(x, y)e^{i\gamma(xG_x t_x + yG_y t_y)}dxdy$$

So the original spin density distribution can be restored by reverse 2D Fourier transform, and the reconstruction requires only n experiments for n x n element image.

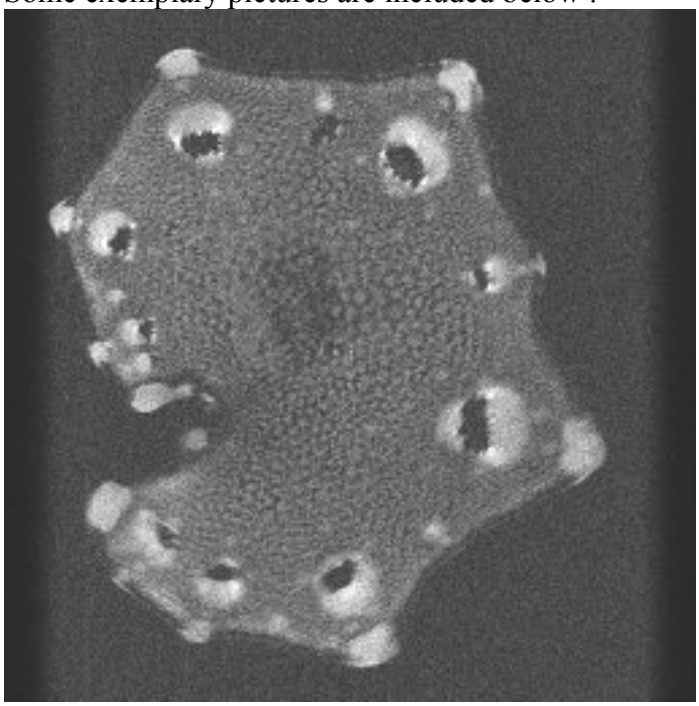
Further improvement in the image acquisition time can be achieved by another type of excitation, which involves the following switching procedure for the field gradients: first one of the gradient fields, let us say G_y is switched in order to select a point on the k_y axis, then k_x is traversed while applying G_x and that is followed by transfer to another G_y value, and so on. This excitation method is called echo-planar imaging, brought the acquisition times to the order of tens of a second while maintaining the resolution level, to compare with the times of the order of several hours for the conventional gradient-selection imaging, or that of the gradient-recalled-echo techniques, which are of the order of ten seconds.

The experimental difficulties involved are severe, namely: huge and homogenous magnetic fields in reasonable volumes and large and rapidly changing linear gradients, resulting in big eddy-current losses. Nevertheless, these difficulties have presently been overcome, letting instantaneous and precise spin-density imaging in big volumes, which is of enormous help in the medical diagnostics.

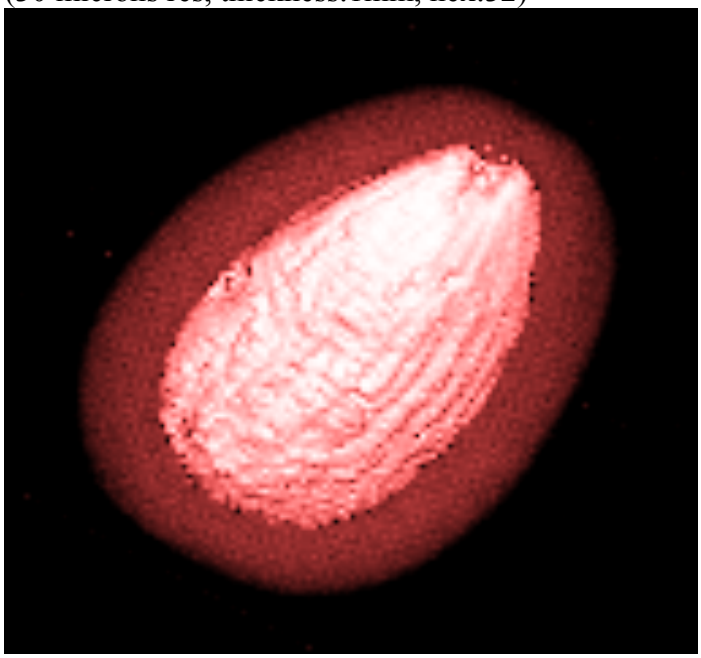
Applications of NMR Imaging

The non-medical applications include the real-time imaging of diffusion processes, mainly diffusion of water in various porous materials, as well as quality control for certain polymers and biomaterials.

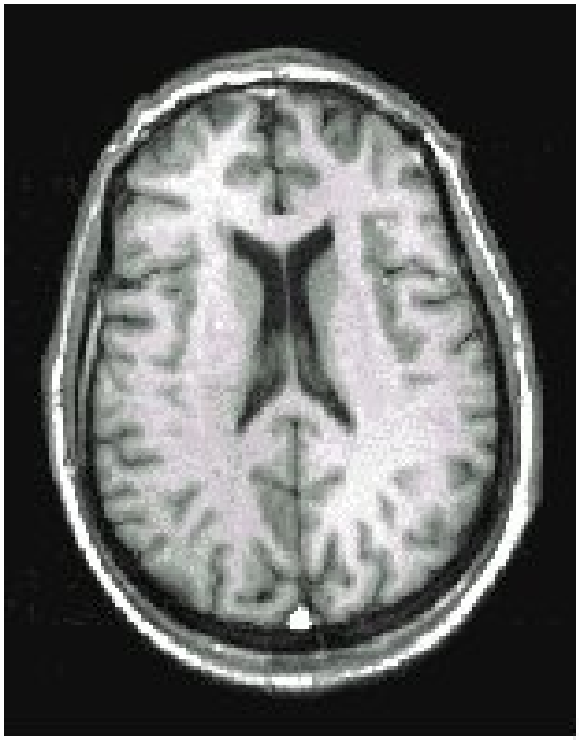
The medical applications are quite numerous and a detailed account is hard to achieve. The advantages with respect to other methods include, lower levels of ionisation radiation, excellent resolution, speed, ability to discriminate both hard and soft tissues, as well as water or fat content.
The disadvantages of the method are mainly: the application of high magnetic fields, big and rapidly changing field gradients, high-power radio frequency radiation, high levels of acoustic noise, necessity of cryogen liquids; all of which can be potentially dangerous or even lethal.
Some exemplary pictures are included below :



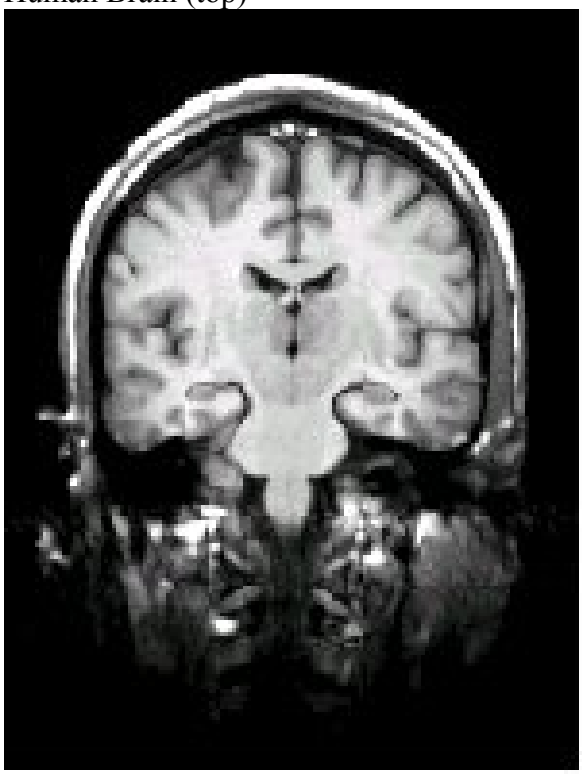
Single Slice of Cerely
(30 microns res, thickness:1mm, nex:32)



Almond chocolate-Volume Rendered



Human Brain (top)



Human Brain (front)

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