

12 HC12: Magnetic Nuclear Resonance



van Quantum tot Molecuul

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Magnetic Nuclear Resonance

Based on Atkins and de Paula, *Physical Chemistry* 10th edition, Chapter 14

In this final lecture of the course, we will explore the important topic of Magnetic Nuclear Resonance and show it is the basis for one of the most important applications of quantum theory in medical therapy, namely *Magnetic Resonance Imaging*.

The *learning goals* of this lecture are:

- (a) Understand that the atomic nucleus has a magnetic moment, and that upon interaction with a magnetic field its energy levels split for different values of z component of the nuclear spin.
- (b) Understand and be able to interpret Nuclear Magnetic Resonance (NMR) spectra.
- (c) Understand how pulse techniques can be employed in order to measure NMR spectra.
- (d) Become familiar with the basic principles of Magnetic Resonance Imaging (MRI).

12.1 Nuclear spin

Classically in the presence of an external magnetic field \vec{B} a particle with a magnetic moment $\vec{\mu}$ has associated an energy $E = -\vec{\mu} \cdot \vec{B}$. In quantum theory, promoting observables to operators, we find that the Hamiltonian that describes this interaction is

$$\hat{H} = -\hat{\vec{\mu}} \cdot \vec{B}. \quad (12.1)$$

An electron moving around an atomic nucleus has associated an associated *angular momentum* \vec{l} and thus a magnetic moment, so in this case the Hamiltonian operator reads

$$\hat{H} = -\gamma_e \hat{l} \cdot \vec{B}, \quad \gamma_e \equiv -\frac{e}{2m_e}, \quad (12.2)$$

where γ_e is the *magnetogyric ratio of the electron*, also known as gyro-magnetic ratio.

Considering without loss of generality a magnetic field with magnitude B_0 pointing in the z direction, the Hamiltonian will be $\hat{H} = -\gamma_e B_0 \hat{l}_z$. From our previous discussion of angular momentum in quantum mechanics, we know that this Hamiltonian will have as eigenvalues:

$$E_{m_l} = -\gamma_e m_l \hbar B_0 \equiv \mu_B m_l B_0, \quad \mu_B \equiv \frac{e\hbar}{2m_e} = 9.27 \times 10^{-24} \text{ J T}^{-1}, \quad (12.3)$$

where the constant μ_B is known as *Bohr's magneton*, and m_l is the quantum number of angular momentum in the z direction.

The result above is the contribution from the electron energy from the interaction of its *orbital angular momentum* with an external magnetic field. However, an electron also has an *intrinsic angular momentum*, its spin, which will also need to be accounted for. In this case the corresponding Hamiltonian will be

$$\hat{H} = -g_e \gamma_e \vec{B} \cdot \hat{s}, \quad (12.4)$$

with $g_e \simeq 2.002319$ is known as the *electron's g-factor*, which deviates from 2 due to relativistic quantum effects, and \hat{s} is the spin operator. As in the case of the angular momentum, for a magnetic field in the z direction, the contribution to the total electron energy of the interaction between the electron spin and the magnetic field will be:

$$E_{m_s} = g_e \mu_B m_s B_0, \quad (12.5)$$

where of course now $m_s = \pm 1/2$. Therefore, for $B_0 \neq 0$ a given energy level will split due to this effect by an amount $\Delta E = g_e \mu_B B_0$, as shown in Fig. 12.1.

The interaction between a magnetic moment and an external field can also be represented within the *vector model of the spin*, illustrated in Fig. 12.2. In this picture, the external magnetic field induces a *precession* of the electron spin, defined in general as the change in the orientation of the rotational axis of a rotating body. The magnetic moment of the electron will experience a torque $\vec{\Gamma} = \vec{\mu} \otimes \vec{B}$, and thus the magnetic moment will rotate around the axis defined by the magnetic field with frequency

$$\nu_L = \frac{|\gamma_e B_0|}{2\pi}, \quad (12.6)$$

which is known as the *Larmor frequency*, and play an important role in the following discussion.

The splitting of energy levels due to the interaction between a magnetic field and an angular momentum can be used for the so-called *magnetic resonance*. Let us first discuss we case of electrons, and then we will turn to nuclei. Since the magnetic field induces an energy splitting of $\Delta E = g_e \mu_B B_0$, a transition between these two energy levels will have associated a frequency

$$\nu = \frac{g_e \mu_B B_0}{h} = \frac{g_e e B_0}{4\pi m_e}, \quad (12.7)$$

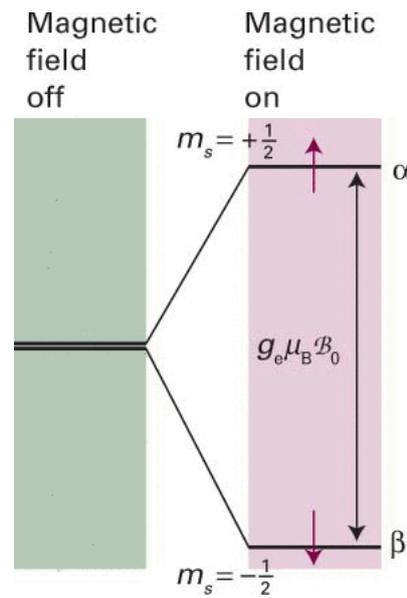


Figure 12.1: In the presence of an external magnetic field B_0 , a given electronic energy state splits into two different states due to the different contribution to the $\vec{s} \cdot \vec{B}$ coupling to the total energy. These two states are separated by an energy shift of $\Delta E = g_e \mu_B B_0$.

where we have used the definition of Bohr's magneton. Eq. (12.7) is known as the *resonance frequency* for electrons: absorption of electromagnetic radiation for this value of ν will thus be favored. For a reasonably strong magnetic field of $B = 0.3$ T, we find that this frequency is $\nu \simeq 10$ GHz, in the domain of *microwave radiation*. Note that the Boltzmann distribution predicts that the state with lower energy will have higher population, and thus the absorption of EM radiation at these frequencies will be facilitated. Note also that this transition can take place only with the condition of paired electrons between the initial and final levels.

Now, *any* particle that has associated an angular momentum will exhibit similar interactions with an external electric field. What about the *atomic nucleus* then? Atomic nuclei are composed by protons and neutrons, each of which are fermions, that is, *spin 1/2* particles. Their angular momenta will add up and in general the nuclear spin I will be different from zero. And from there on the usual properties of angular momentum follow, for instance, a nucleus with spin I will have associated an intrinsic angular momentum of $\sqrt{I(I+1)}\hbar$, and its components $m_I \hbar$ along a given axis will take the values $m_I = I, I-1, \dots, -I+1, -I$.

The resulting splitting of the energy levels will be similar to the electron case, with the only difference that now the atomic nucleus has a different magnetic moment. Therefore, we will have that the energies associated to the nuclear spin in an external magnetic field are given by

$$E_{m_I} = -\gamma \hbar B_0 m_I, \quad \gamma \hbar \equiv g_I \mu_N \quad \mu_N = \frac{e \hbar}{2m_p} = 5.051 \times 10^{-27} \text{ J T}^{-1}, \quad (12.8)$$

where we have introduced the *nuclear magneton* μ_N and the nuclear g -factor g_I . In the specific case of a $I = 1/2$ nucleus, the energy levels will split into two with an energy difference $\gamma \hbar B_0$, and now the resonance frequency Eq. (12.7) for $B = 12$ T will be $\nu \simeq 500$ MHz, in the regime of *radio-waves*. This very significant change in the resonant frequency of nuclei as compared to electrons is explained from the fact that $\mu_N \ll \mu_e$ because of the much larger nucleon mass $m_N \gg m_e$. Therefore, nuclear magnetic resonance can be achieved for radiation *much smaller energies* (longer wavelengths) than those of the electron case.

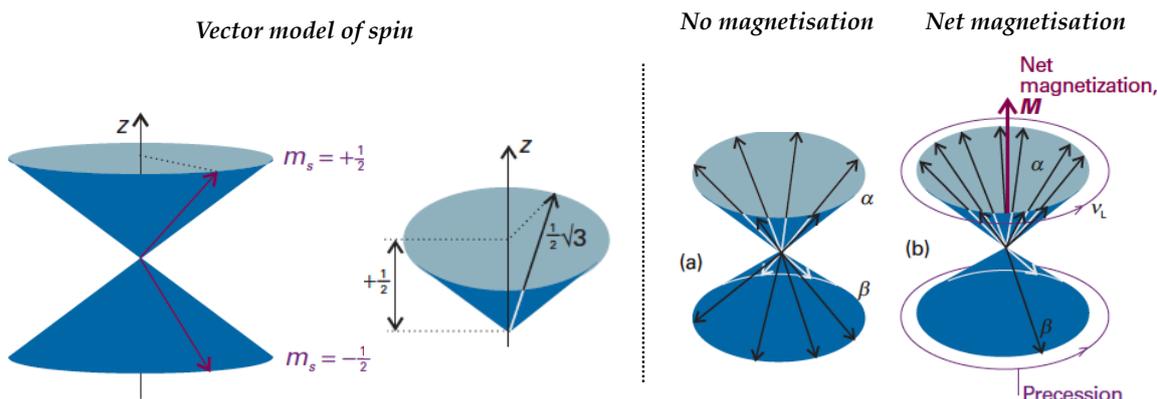


Figure 12.2: Left plot: in the vector model of electron spin, spin can be represented by a vector of length $\sqrt{3}/2$ whose component in the z direction is $\pm 1/2$. Right plot: in the absence of an external field, there is no net magnetization of the electron spin. For an external magnetic field, the electron spin develops a net magnetization, represented as a precession around the z axis.

12.2 The chemical shift

In practice, the interaction between atomic nuclei and external magnetic fields will be partially shielded due to the surrounding electrons (atomic and/or molecular), and therefore nuclei experience a smaller magnetic field,

$$\tilde{B}_0 = B_0 - \delta B \equiv B_0 (1 - \sigma), \quad (12.9)$$

where σ is the so-called *shielding constant*, and its value depends very sensitively on the specific chemical structure surrounding the nucleus. As a consequence of this shielding, for a fixed value of the external magnetic field B_0 , nuclei of different chemical identify will have associated *different resonant frequencies*. We call this *chemical shift* the measure of the differences in the resonance frequency due to the shielding effects of the electrons, which allows to discriminate not only between different chemical elements but also between the same element in different locations within a molecule.

Given that the local magnetic field experienced by the nucleus is $B_0(1 - \sigma)$, the associated Larmor frequency will also be reduced, and will be given by

$$\nu_L = (1 - \sigma) \frac{\gamma B_0}{2\pi}. \quad (12.10)$$

Then we can define the *chemical shift* δ as the shift of the Larmor frequency relative to a reference value ν_0 , that is

$$\delta \equiv \frac{\nu_L - \nu_{L,0}}{\nu_{L,0}} \times 10^6, \quad (12.11)$$

which is roughly independent of the specific value of B_0 , which cancels partially in the ratio. Therefore, if for example we have a reference Larmor frequency of 500 MHz for a given field B_0 , then a chemical shift of $\delta = 1$ ppm (parts per million) corresponds to a shift in the Larmor frequency ν_L as compared to the reference value of 500 Hz.

To illustrate the concept of chemical shift, in Fig. 12.3 we show a schematic representation of the ethanol molecule, $\text{CH}_3\text{CH}_2\text{OH}$. In the same figure we also show chemical shift δ associated to different hydrogen nucleus in the ethanol molecule. We observe that the closer to the oxygen nucleus, the larger the chemical

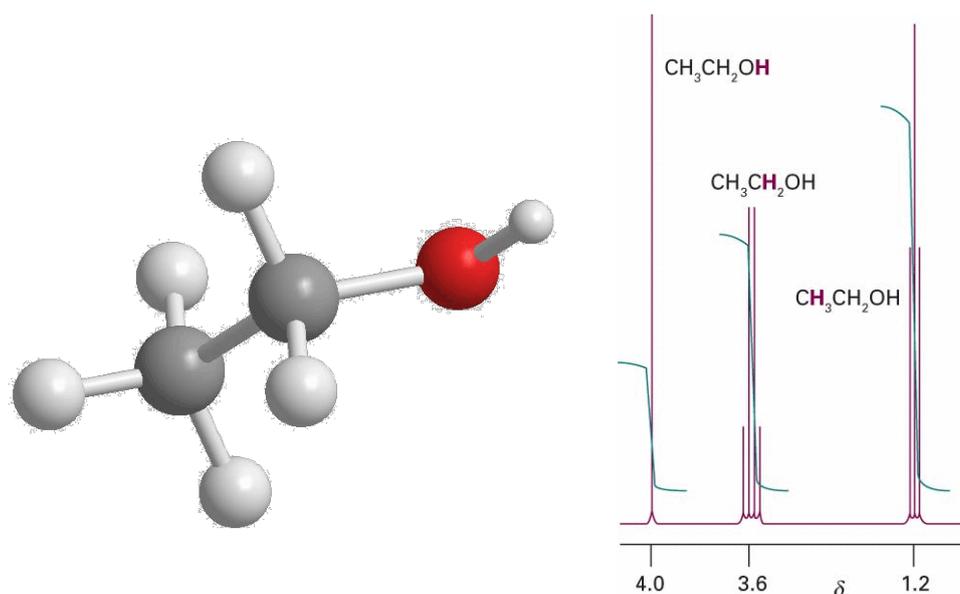


Figure 12.3: Right plot: schematic representation of the ethanol molecule, $\text{CH}_3\text{CH}_2\text{OH}$. Left plot: the chemical shift δ associated to different hydrogen nucleus in the ethanol molecule. We observe that the closer to the O nucleus, the larger the chemical shift.

shift. This can be explained since oxygen is the most electro-negative element of the molecule and thus attracts the most the molecular electron density, leading to an enhanced chemical shift of the neighboring hydrogen nucleus. From Fig. 12.3 we also see that there is a *fine structure* for the each nucleus in the ethanol molecule. This fine structure arises from the *spin-spin coupling*, where the spin from one nucleus contributes to the local magnetic field of a neighboring nucleus.

12.3 NMR spectroscopy

We now want to illustrate how we can measure NMR spectra and chemical shifts, as required for medical applications. This can be achieved by means of the *NMR spectrometer*, and requires introducing the concept of the *pulsed technique*.

The basic ingredient of NMR is the measurement of the *chemical shifts* for each atom in a molecule of the analysed sample, which then allows its identification by comparing with the reference spectra. One possibility would be to measure the *rate of absorption of radio waves* as a function of their frequency ν , which should be dominated by the Larmor frequencies of the nuclei in the sample. As illustrated by Fig. 12.1 (applied to the magnetic moment of nuclei), the value of the photon energy that induces the resonant transition $\beta \rightarrow \alpha$, $E_\gamma = \gamma B_0 / 2\pi$, lies in the radio part of the EM spectrum. This approach is however challenging, since first of all the population difference between α and β , the nuclear atomic states with different spin, is small, and second because such a frequency scan is a rather slow process. Indeed, the difference in population between α and β can be as small as $\mathcal{O}(10^{-5})$.

The alternative is to use *pulse techniques*, which are much more efficient. To understand the pulse method works, we consider a vector model for the nuclear spin, such as that shown in Fig. 12.2 for the electron. Let us assume that the nuclear spin is $I = 1/2$ for simplicity. The length of this vector is $\sqrt{I(I+1)} = \sqrt{3}/2$ (in units of \hbar), and the projection in the z direction is fixed to be $I_z = \pm 1/2$. Recall that the operators \hat{I}_x , \hat{I}_y

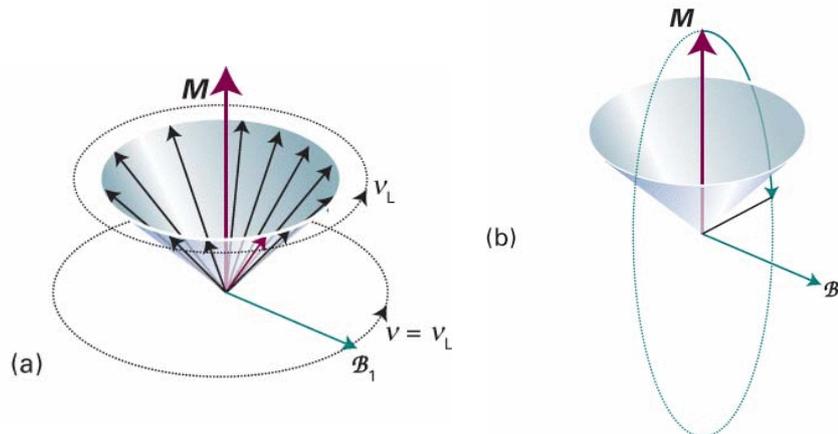


Figure 12.4: In the pulse method, a magnetic field polarized in the (x, y) plane oscillates with frequency ν_L (left plot), perpendicular to the nuclear spin. In the rotating reference frame, the nuclear spin experiences a constant magnetic field B_1 (right plot).

and \hat{I}_z do not commute among them.

For a vanishing external magnetic field, $B_0 = 0$, the energy of the two states α and β are the same, and so they have the same average population. Once we switch on the external magnetic field, $B_0 \neq 0$, the energy of the two levels splits, with $E_\beta < E_\alpha$ (see Fig. 12.1). Due to Boltzmann statistics, we know that the population of the lower energy state α will be larger than that of the higher energy one β , $N_\alpha > N_\beta$. This implies that a *net magnetization* is created in the analyzed material, proportional to $N_\beta - N_\alpha$.

The next step in the pulse method is that, in addition to the static magnetic field B_0 , we also add an *oscillatory magnetic field* in the (x, y) plane, with Larmor frequency ν_L and circular polarization so that B_1 rotates in the (x, y) plane with frequency ν_L . Recall that the static magnetic field B_0 is applied along the z direction, and is thus perpendicular to the new oscillatory magnetic field. This additional field will induce the transition $\alpha \leftarrow \beta$, that is, from the lower to the higher energy nuclear magnetic states. If we now transform to the *rotating frame* with Larmor frequency ν_L , the nuclear spins will experience a *constant magnetic field* B_1 . Therefore, in this frame, the nuclear spins will exhibit a precession with a different value of ν_L , as illustrated in Fig. 12.4. This new Larmor frequency will be

$$\tilde{\nu}_L = \frac{\gamma B_1}{2\pi}, \quad (12.12)$$

and thus the period of the new Larmor precession will be

$$T = \frac{2\pi}{\gamma B_1}. \quad (12.13)$$

In the pulse method, rather than having the oscillatory field B_1 activated the whole time, we have it on only for a small amount of time, the *pulses*. In particular the duration of this pulses should be one quarter of the total precession period, $(1/4) \cdot (2\pi)/\gamma B_1$, corresponding to an angular rotation of $\pi/2$, which typically corresponds to a duration of microseconds. Now, while in the rotating frame the magnetization M is constant in the (x, y) plane, in the *laboratory frame* it will rotate with Larmor frequency ν_L . This oscillatory magnetization can be detected in the *coil* of an *NMR spectrometer*, where it can be transformed

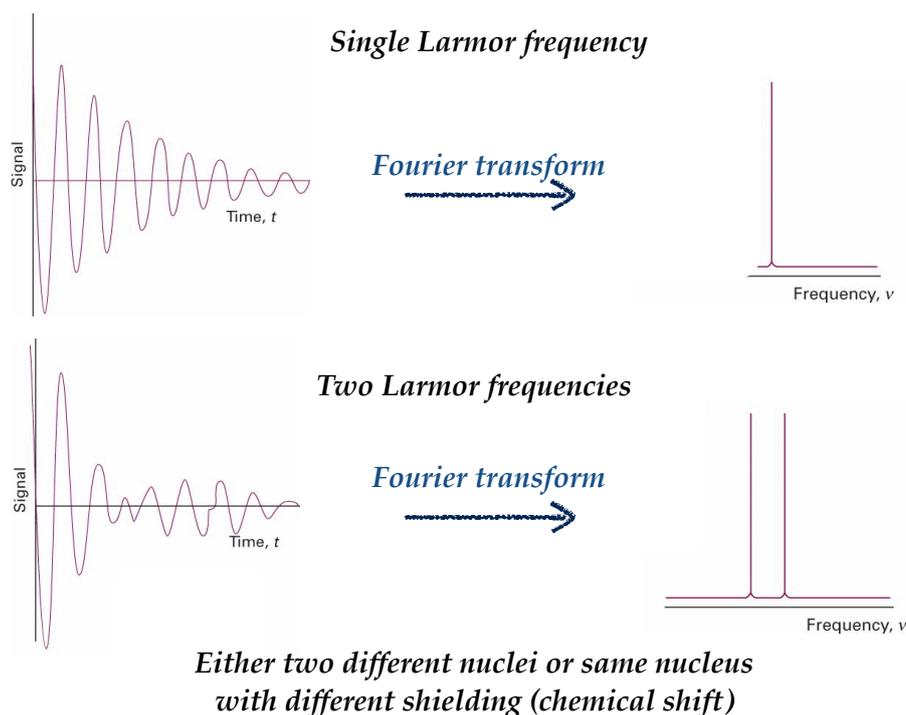


Figure 12.5: The oscillating signal measured in the MNR spectrometer can be Fourier transformed to determine the values of the Larmor frequencies present for the studied sample. In a sample with different nuclei and/or nuclei with different chemical shifts, the Fourier transform will exhibit multiple peaks corresponding to each of the relevant Larmor frequencies.

into output electromagnetic radiation in the radio spectrum.

A characteristic signal of the measured MNR signal is that it will appear as a Free Induction Decay (FID), which oscillates with Larmor frequency ν_L but whose amplitude decays exponentially due to the finite duration of the length of the pulse. The oscillating signal detected in the MNR spectrometer can then be Fourier-transformed to determine the values of the Larmor frequencies for each of the nuclei in the studied sample, as shown in Fig. 12.5. This way, in a sample with different nuclei and/or nuclei with different chemical shifts, the Fourier transform will exhibit multiple peaks corresponding to each of the relevant Larmor frequencies.

The reason why the MNR signal in Fig. 12.5 decays exponentially with time can be understood as follows. After a $\pi/4$ pulse, the magnetization of the atomic nuclei is not in thermal equilibrium with its surroundings. In particular, since β has a higher population than α , the pulse will affect more the former level and thus contradict the expected Boltzmann populations. Indeed, after the $\pi/4$ pulse the population of spins in the two levels is similar. After a some time, following the pulse, the system will be back to thermal equilibrium where

$$\frac{N_\alpha}{N_\beta} = e^{-h\nu_L/k_B T}. \quad (12.14)$$

This *longitudinal relaxation time* T_1 will be given by the time it takes for the system to recover its original magnetization M_0 along the z direction, namely

$$(M_z(t) - M_0) \propto e^{-t/T_1}, \quad (12.15)$$

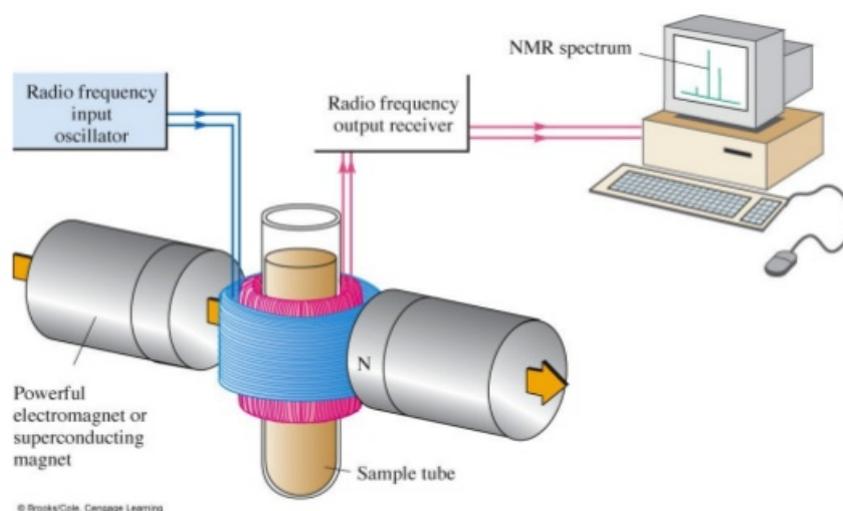


Figure 12.6: In an NMR spectrometer, a powerful magnet is used to apply a strong magnetic field to the studied sample. Then, the sample is irradiated with pulsed electromagnetic radio waves and the response of the system under this radiation (which frequencies are absorbed) is monitored to determine the resultant NMR spectra.

where we see that for $t \gg T_1$ the magnetization will be $M_z(t) = M_0$, as was the case before the pulse.

Moreover, after the $\pi/4$ pulse there will also be a new magnetization M_y along a given direction in the (x, y) plane, that is, the phase of individual nuclear spins along this plane (in the vector model of the atomic spin) will be common. Some time after the pulse, this common phase will be lost and the associated macroscopic magnetization in the transverse direction M_y will disappear. We can then define the *transverse relaxation time* T_2 as

$$M_y(t) \propto e^{-t/T_2}, \quad (12.16)$$

so that for $t \gg T_2$ we have that $M_y \rightarrow 0$, as was the case before the pulse. The longitudinal relaxation mechanism also affects the transversal one, so typically $T_1 \geq T_2$, of the order of a few seconds. The main impact of the T_2 relaxation is the *broadening of spectral lines*. Indeed, it can be shown that the *width at half-maximum* of a MNR line is given by

$$\nu_{1/2} = \frac{1}{\pi T_2}. \quad (12.17)$$

The experimental apparatus for the measurement of NMR spectra is illustrated in Fig. 12.6. First of all, in an NMR spectrometer, a powerful magnet is used to apply a strong magnetic field B_1 to the studied sample. Then, *pulsed electromagnetic radio waves* and the response of the system under this radiation (which frequencies are absorbed) is monitored to determine the resultant NMR spectra. The frequency of the pulsed radio waves is tuned to reproduce the Larmor frequencies of specific magnetic nuclear resonances, as explained above. The Fourier transform of the output radio frequency, as indicated in Fig. 12.5, indicates the Larmor frequencies of the various atomic components of the sample.

12.4 Magnetic resonance imaging (MRI)

Magnetic Nuclear Resonance is the key principle underlying *Magnetic Resonance Imaging*. This imaging method is based on the deliberate application of an *inhomogeneous magnetic field*, in other words, a *magnetic*

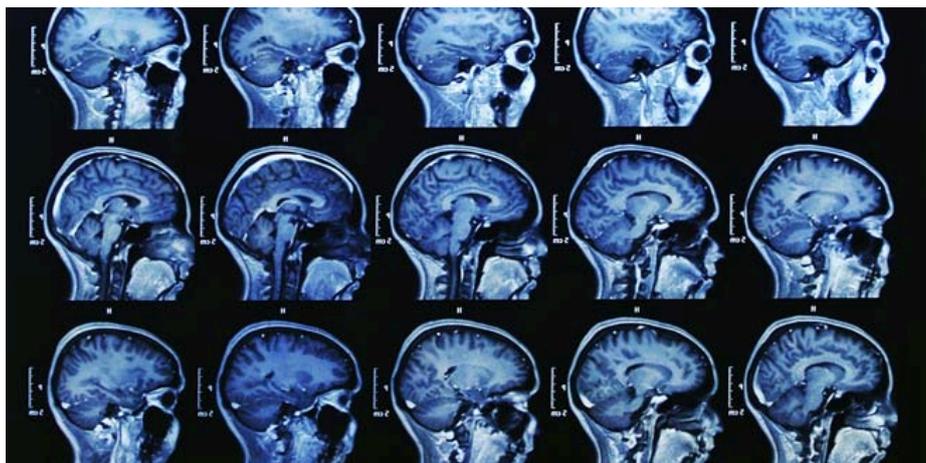


Figure 12.7: By means of Molecular Resonance Imaging, it is possible to obtain three-dimensional images of soft tissue, in this case white and grey matter inside the skull.

field gradient. As we have discussed, each molecule of the imaged sample, in the presence of a external magnetic field, will have associated a Larmor frequency of

$$\nu_L(\vec{r}) = (1 - \sigma) \frac{\gamma B_0(\vec{r})}{2\pi}, \quad (12.18)$$

which now will be different for each position \vec{r} of the sample, due to the inhomogeneity of the magnetic field. By comparing the observed Larmor frequencies with the expected values for some molecules and taking into account the magnetic field gradient applied to the sample, we can reconstruct a *three-dimensional* image of the chemical components of the sample.

The typical MRI application is based on the proton resonance, therefore the largest signal will come from those body parts with the highest concentration of water. To enhanced the contrast, it is possible to use that the longitudinal and transverse relaxation times T_1 and T_2 depend on the time of local environment, for example they are different in membranes than in bulk water. This way, it is possible to image separately using MRI different types of soft tissue such as gray matter, white matter or spinal fluid. In Fig. 12.7 we illustrate how by means of Molecular Resonance Imaging it is possible to obtain three-dimensional images of soft tissue, in this case white and grey matter inside the skull.

12.5 Summary

Let us summarize some of the important topics that have been covered in this lecture:

- A moving electric charge has an associated *angular momentum* \vec{l} , which can then interact with a external magnetic field \vec{B} .
- The interaction of the electron spin with an external magnetic field induces an energy splitting that can be proved by resonant absorption at microwave frequencies.
- Atomic nucleus also have an intrinsic angular momentum, spin, built upon the spin of its components, protons and neutrinos. Depending on the specific nucleus, this spin can be zero, half-integer or integer.

- The nuclear magneton μ_N is much smaller than the electron magneton μ_B due to the mass suppression of the atomic nuclei as compared to the electron mass.
- Magnetic resonance absorption in nuclei takes place at radio frequencies.
- The chemical shift quantifies the degree of shielding of nucleus by core electrons in the presence of external magnetic field.
- Magnetic nuclear resonances can be efficiently probed using the *pulse method*, where short pulses of $\pi/4$ angle are used to excite the magnetic resonances.
- The MNR signal decays exponentially due to the longitudinal and transverse mechanism of spin relaxation.
- Magnetic nuclear resonance is the key for Magnetic Resonance Imaging, where a magnetic field gradient can be used to obtain a three-dimensional image of soft tissues.