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Principles of NMR Imaging

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## PRINCIPLES OF NMR IMAGING

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### 1 INTRODUCTION

NMR spectroscopy has been used since 1946 in the study of condensed matter. In the last years it has also been applied to researches in fields related to medicine. The main applications are NMR Imaging and NMR High Resolution "in vivo" spectroscopy. In this paper we will be concerned only with the first topic. An immediate comparison with traditional radiography allows one to see the first difference between the two techniques: whilst X-ray images are simply absorption maps of the system under examination, so that they can show only the electron density of the sample, a NMR image includes, besides the morphology of the body, also chemical and physiological informations. A second difference is the fact that the two techniques use frequencies which lie in ranges very far from each other: in fact NMR makes use of radiofrequencies (r.f.), so that it is non-ionizing; moreover, at the present moment, no harm was found to be produced by NMR images. Before analyzing the basis that have allowed the study of heterogeneous systems, it is necessary to give a brief description of the NMR spectroscopy principles.

### 2 NMR SPECTROSCOPY

Nuclear Magnetic Resonance is based on the principle that all the nuclei with non zero spin have

also a magnetic moment  $\mu$ . If we restrict ourselves to the case of nuclei with spin one half, when they are placed in a static magnetic field  $H_0$ , usually directed along the  $z$  axis of the reference frame, they will align along the direction of the field, in a parallel or antiparallel state, following a Boltzmann distribution. The energy difference between these two levels is  $\Delta E = \hbar \omega_0$ , where  $\omega_0$  is the classical Larmor angular frequency given by  $\omega_0 = \gamma H_0$ , with  $\gamma$  the gyromagnetic ratio. The population of nuclei oriented in the parallel state will be greater of the other because this state corresponds to a lower energy. The difference between populations results in a net macroscopic magnetization  $M_0$  aligned along  $H_0$ . The equilibrium situation can be modified by applying a r.f. electromagnetic wave, with energy equal to the separation between the two levels. The effect of this perturbation is to change the distribution of the populations. When the perturbation will end, the return to equilibrium of the system will be characterized by two relaxation times: the spin-lattice relaxation time  $T_1$  and the spin-spin relaxation time  $T_2$ . The last one is the time constant with which the spins loose their phase coherence, while the realignment along the direction of the main magnetic field is characterized by the time constant  $T_1$ . These relaxation times can be measured using suitable sequences of pulses. The return to equilibrium can be detected with a coil that surrounds the sample; the variation of the component of the magnetization in a plane perpendicular to the  $z$  axis, called Free Induction Decay (FID), induces in the coil a efm signal. The Fourier Transform (FT) of this signal is the frequency spectrum of the system.

The spin-spin relaxation time gives informations on the local fields experienced by the nuclei: these fields are related to the environment which surrounds the nuclei under examination. On the other side, the spin-lattice relaxation time gives information about the energetic exchanges between the spins system and the lattice. This relaxation process is due, in fact, to the fluctuations of the local magnetic fields; the molecular motions tend to reestablish the thermodynamic equilibrium and to reorient the spins in the direction of the static magnetic field.

From a classical point of view, the effect of the r.f. pulse is to rotate the magnetization of a flip angle around an axis, that will be denominated as  $x'$ , of a reference frame rotating at the same frequency of the r.f. pulse.

F.C. Lauterbur (1) was the first to suggest a way to obtain spatial images of the NMR parameters. His original idea was to correlate the resonance frequency of the spins in different parts of the sample and their spatial positions, by means of the induced interaction between them and a linear magnetic field gradient, superposed on the homogeneous field. The effect of the gradient is to change the Larmor frequency of the spins linearly with the position, so that it becomes possible to assign each frequency of the spectrum to a given coordinate.

### 3 GENERAL PRINCIPLES OF NMR IMAGING

When the magnetization is a function of the coordinates, as in the heterogeneous systems, the Bloch equation can be written (2):

$$\frac{\partial \vec{M}(\vec{r}, t)}{\partial t} = \gamma \vec{M}(\vec{r}, t) \times \vec{H}(\vec{r}, t) - \{M_x(\vec{r}, t) \hat{i} + M_y(\vec{r}, t) \hat{j}\} / T_2(\vec{r}) - \{M_z(\vec{r}, t) - M_0(\vec{r}) \hat{k}\} / T_1(\vec{r}) \quad (1)$$

where  $M_0(\vec{r})$  is the local equilibrium magnetization,  $T_1$  and  $T_2$  are functions of the spatial coordinates, and

$$\vec{H}(\vec{r}, t) = H_x(t) \hat{i} + H_y(t) \hat{j} + [H_0 + \vec{r} \cdot \vec{G}(t)] \hat{k} \quad (2)$$

In eq. (1) and (2)  $\hat{i}$ ,  $\hat{j}$  and  $\hat{k}$  are unit vectors of the lab. reference frame,  $H_x(t)$  and  $H_y(t)$  are the components of the r.f. magnetic field,  $H_0$  is the static field and  $\vec{G}(t)$  is the magnetic field gradient, defined by

$$\vec{G}(t) = \frac{\partial H_x(t)}{\partial x} \hat{i} + \frac{\partial H_y(t)}{\partial y} \hat{j} + \frac{\partial H_z(t)}{\partial z} \hat{k} \quad (3)$$

After the r.f. pulse, the magnetic field will be given by

$$\vec{H}(\vec{r}, t) = [H_0 + (\vec{r} \cdot \vec{G})] \hat{k} \quad (4)$$

and the solution of the Bloch equation for the transverse component of the magnetization  $M_{\perp}(\vec{r}, t)$ , defined as

$$M_{\perp}(\vec{r}, t) = M_x(\vec{r}, t) + i M_y(\vec{r}, t) \quad i = \sqrt{-1}$$

is given by

$$M_{\perp}(\vec{r}, t) = M_0(r_0) \exp(i\omega t - i\gamma \int_{t_1}^{t_1+t} \vec{r} \cdot \vec{G}(\tau) d\tau - t/T_2(r_0)) \quad (5)$$

where  $t=0$  corresponds to the end of the excitation pulse and  $t_1$  is the time when the gradient is turned on. Equation (5) is referred to a set of monochromatic spins for which

$$M_0(r_0) = \int_V \rho(x, y, z) dx dy dz \quad (6)$$

is the equilibrium magnetization in the plane specified by  $\vec{r}$  in the direction of the gradient  $\vec{G}$ , where  $\rho(x, y, z)$  is the density of the resonant spins.

The total equilibrium magnetization  $M_0$  is given by the sum of the various  $M_0(r_0)$  carried over all the isochromats

$$M_0 = \int_{L_G} M_0(r_0) dr_0 \quad (7)$$

where  $L_G$  is the maximum extension of the sample in the direction of the gradient. In the same way the FID produced by the whole sample will be given by:

$$S(t) = \int_{L_G} M_{\perp}(r_0, t) dr_0 \quad (8)$$

From the expression (8) it is possible to obtain, with a suitable choice of the parameters that characterize a measure process, all the informations from a heterogeneous sample. An imaging experiment will be defined by the sequence of excitation and by the temporal behaviour of the gradient vector because they both strongly affect the whole measure process and the information available. In particular, the use of the gradients distinguishes many different imaging methods among them. We now discuss the techniques applied in almost all the practical cases.

### 4 NMR IMAGING METHODS

#### 4.1 Projection - Reconstruction (PR)

The Projection - Reconstruction technique is the first NMR imaging method that has been realized (1,3). In 1973, F.C. Lauterbur proposed to apply a linear,

time independent magnetic field gradient over the homogeneous magnetic field. In this case the expression for the gradient  $\vec{G}$  is:

$$\vec{G} = \frac{\partial H_z}{\partial x} \hat{i} + \frac{\partial H_z}{\partial y} \hat{j} + \frac{\partial H_z}{\partial z} \hat{k}$$

with

$$\frac{\partial H_z}{\partial x} = G_x = \text{const}; \frac{\partial H_z}{\partial y} = G_y = \text{const}; \frac{\partial H_z}{\partial z} = G_z = \text{const}$$

and the integral which appears in the expression (8) can be easily solved in the following way:

$$\int_{t_1}^{t_1+t} \vec{r} \cdot \vec{G}(\tau) d\tau = \int_0^t \vec{r} \cdot \vec{G} d\tau = (\vec{r} \cdot \vec{G})t \quad (9)$$

From expressions (5) and (9) it can be shown that all the spins with

$$xG_x + yG_y + zG_z = \text{const} \quad (10)$$

generate a single frequency of the spectrum; hence the relation (10) represents a plane, normal to the direction of  $\vec{G}$ , which contains the monochromatic spins.

The FT of eq. (5) will give the amplitude of the spectral component associated to the plane which satisfies the condition (10). The real part of the FT is:

$$m_1(r_0, \omega) = 2m_0(r_0) \cdot T_2(r_0) \cdot (1 + T_2^2(r_0) [\omega - (\omega_0 + \gamma \vec{r} \cdot \vec{G})]^2)^{-1} \quad (11)$$

To obtain the whole spectrum, it is necessary to sum the expression (11) over all the planes orthogonal to  $\vec{G}$ , each resonating to a single frequency. Hence:

$$S(\omega) = \int_{L_G} m_1(r_0, \omega) dr_0 \quad (12)$$

Equation (11) represents a Lorentzian line produced by the plane defined by the relation (10), centered at the frequency

$$\omega = \omega_0 + \gamma \vec{r} \cdot \vec{G} \quad (13)$$

with half height width given by  $1/T_2$  and amplitude

$$2m_0(r_0) \cdot T_2(r_0) \quad (14)$$

Equation (12) represents the whole spectrum; it is a superposition of Lorentzian lines, and if the strength of the gradient  $|\vec{G}|$  is sufficient high, so that

$$\gamma |\vec{G}| L_G / N > 1/T_{2min} \quad (15)$$

where  $T_{2min}$  is the minimum  $T_2$  exhibited by the sample, eq. (15) becomes the spin density projection along the direction of  $\vec{G}$ . In the expression (15),  $\gamma |\vec{G}| L_G$  is the spectral width of the sample in the direction of the gradient, and  $N$  an integer which defines the dimension of the reconstructed image, so that  $L_G/N$  is the achievable spatial resolution.

The FR method consists in obtaining a set of projections, each one in a different direction. The procedure which allows one to reconstruct the image is called "back-projection", and it is similar to that one used in the Computerized Tomography (CT). The NMR images, although are called "density images", represent a spatial distribution of the product  $m_0 T_2$ , as it is evident from eq. (11).

The simpler excitation technique makes use of a r.f. pulse which turns the magnetization by  $90^\circ$  around the  $x'$  axis of the rotating reference frame. The mostly used sequences are generally based on a  $90^\circ$  pulse followed by a  $180^\circ$  pulse. This forces the spins that have dephased with the characteristic time  $T_2$  to refocalize after a time  $2\tau$  from the beginning of the sequence. This procedure is called "spin-echo". The time delay  $\tau$  between the pulses is much shorter than  $T_2$ , if one wants to reduce the dependence of the image on this parameter.

If a contrast in  $T_1$  and  $T_2$  is desired, the parameters that define the sequence must be changed or other pulse sequences are needed. A  $T_2$  contrast can be obtained with a longer time delay between the  $90^\circ$  and the  $180^\circ$  pulses. A sequence that was given the name of "inversion-recovery" allows one to obtain a contrast depending mainly on  $T_1$ . It is made of a  $180^\circ$  pulse, followed after a time  $t_i$  by a spin-echo sequence. The time interval  $t_i$  should be comparable with  $T_1$ . Also a variation of the repetition time of the sequence influences the dependence of the image on  $T_1$  and  $T_2$ .

The acquisition of data from a whole 3D sample would require a very large memory and a long time to

reconstruct all the image, although in many cases the region of interest represents only a part of the body. For this reason a reduction of the sample to a chosen slice is desired. This is operated in the following way: the sample is excited with a pulse whose shape in the frequency domain is a square of width  $\Delta\omega/2\pi$ , centered around the Larmor frequency, i.e. a sinc function. If the sample is irradiated in the presence of a gradient, let us say in the z direction, only the spins belonging to planes with z satisfying the relation

$$-\frac{\Delta\omega}{2\pi G_z} < z < \frac{\Delta\omega}{2\pi G_z}$$

will contribute to the signal.

#### 4.2 Fourier Zeugmatography

This technique has been proposed by A. Kumar et al. (4), and is derived from a general class of experiments, that goes under the name of 2D NMR spectroscopy. It makes use of pulsed field gradients after the excitation pulses, in the following way: immediately after the  $90^\circ$  pulse, a magnetic field gradient  $G_x$  is applied along the x direction for a time  $t_x$ , followed by a gradient  $G_y$  applied for a time  $t_y$  along y. The FID is finally recorded during a time interval  $t_z$ , under the influence of a gradient  $G_z$ . Mathematically, the behaviour of the z component of the magnetic field is described by

$$H_z(\vec{r}) = \begin{cases} H_0 + G_x x & \text{for } 0 < t < t_x \\ H_0 + G_y y & \text{for } t_x < t < t_x + t_y \\ H_0 + G_z z & \text{for } t_x + t_y < t \end{cases} \quad (16)$$

Obviously the phase of the FID at a time  $t > t_x + t_y$  is a function of the previous time intervals  $t_x$  and  $t_y$ , hence we shall define it as  $S(\vec{r}) = S(t_x, t_y, t_z)$ . The tridimensional FT of the NMR signal  $S(\vec{r})$  is a measure of the spin density function  $\rho(\vec{r})$ , and can be interpreted as a tridimensional image of the sample.

The observed signal  $S(\vec{r})$  is formed by the contribution from the various sample parts, and can be written as

$$S(\vec{r}) = \iiint \rho(\vec{r}') s(\vec{r}, \vec{r}') dv \quad (17)$$

where  $s(\vec{r}, \vec{r}') dv$  represents the contribution of the volume element  $dv = dx dy dz$  identified by the vector

$\vec{r}$ . The function  $s(\vec{r}, \vec{r}')$  can be easily found as a solution of the Bloch equation. After a phase sensitive detection at a frequency  $\omega$ , the cosine component of the signal will be given by:

$$s(\vec{r}, \vec{r}') = \cos(-\gamma G_x x t_x - \gamma G_y y t_y - \gamma G_z z t_z) \exp(-(t_x + t_y + t_z)/T_2) \quad (18)$$

The tridimensional FT of  $S(\vec{r})$ , that will be written as  $S(\omega) = S(\omega_x, \omega_y, \omega_z)$ , will be given by:

$$S(\omega) = \iiint S(\vec{r}) \exp(-i\omega \cdot \vec{r}) dt_x dt_y dt_z \quad (19)$$

and can be expressed as a sum of the contribution from the various volume elements:

$$S(\omega) = \iiint \rho(\vec{r}) \cdot s(\vec{r}, \omega) dv \quad (20)$$

where  $s(\vec{r}, \omega)$  is the FT of  $s(\vec{r}, t)$ , and is given by:

$$s(\vec{r}, \omega) = 1/2 L(-\gamma G_x x - \omega_x) \cdot L(-\gamma G_y y - \omega_y) L(-\gamma G_z z - \omega_z) \quad (21)$$

where

$$L(\omega) = A(\omega) + iD(\omega) = \frac{1}{1 + \omega^2 T_2^2} + \frac{i\omega T_2}{1 + \omega^2 T_2^2} \quad (22)$$

From eq. (21) we can demonstrate the validity of the following identity:

$$S(\vec{r}, \omega) = S(0, \omega + \gamma \vec{G} \cdot \vec{r}) \quad (23)$$

Substitution of eq. (23) into eq. (20) gives:

$$S(\omega) = \iiint \rho(\vec{r}) S(0, \omega + \gamma \vec{G} \cdot \vec{r}) dv \quad (24)$$

If at this point we rewrite the frequency variable  $\omega$  in terms of a spatial variable  $\vec{r}'$ , i.e.:

$$\omega = -\gamma \vec{G} \cdot \vec{r}'$$

eq. (24) becomes:

$$\begin{aligned} S(\omega) &= S(-\gamma \vec{G} \cdot \vec{r}') = \tilde{\rho}(\vec{r}') = \\ &= \iiint \rho(\vec{r}) S(0, -\gamma \vec{G} \cdot (\vec{r} - \vec{r}')) dv \end{aligned} \quad (25)$$

This integral represents the tridimensional

convolution between the "true" spin density  $\rho(\vec{r})$  and the natural lineshape  $L(\omega)$  through the function  $s(\vec{r}, \omega)$ . Writing it explicitly:

$$S(\omega) = \tilde{\rho}(\vec{r}') = 1/2 \iiint \rho(\vec{r}) [L(-\gamma G_x(x-x'))] \cdot [L(-\gamma G_y(y-y'))] \cdot [L(-\gamma G_z(z-z'))] d\vec{r}$$

The function  $\tilde{\rho}(\vec{r}')$ , which we could define as "filtered density", is a complex function. Its real and imaginary parts both contain the functions absorption and dispersion, which can hardly be distinguished. Hence it is better to calculate its absolute value  $|\tilde{\rho}(\vec{r}')|$  which, under the assumption that the line shape be sufficiently narrow and the intensity of the gradients be strong enough, is a good measure of the density  $\rho(\vec{r})$ .

The advantages of this method on the backprojection technique can be found in the fact that no reconstruction process to obtain the image is needed, the 3D FT of the FIDs being itself a map of the sample. As it is the case for the PR method, the need for a too large memory obliges to a reduction of the technique to two dimensions.

In practice, the NMR imaging method mostly used nowadays is a derivation of the Fourier Zeugmatography, which was named "spin-warp" (5). The difference between the two techniques can be explained in the following way: the effect of the first gradient, for example  $G_y$ , is to change the phase of the spins in a plane characterized by a value  $y_0$  of the  $y$  coordinate of an amount

$$\gamma y_0 \int_0^{t_y} G_y(t) dt$$

as can be easily seen from eq. (18). The value of such integral can be modified either varying the time interval  $t_y$  while keeping  $|G_y|$  constant, or varying the amplitude of the gradient  $|G_y|$  with  $t_y$  fixed. This second way is usually preferred for practical reasons: it is simpler to maintain fixed the timing of the sequence and to change time by time the amplitude of the gradient than to change the length of the encoding gradient. The sequence we use on our machine is a spin echo, in which both the pulses are selective ones.

In fig.1 the sequence for a transverse section of the body is shown.  $G_z$  is the selection gradient, and it is turned on only during the selective pulses.

$G_y$  is the gradient which operates a phase encoding in the  $y$  direction. Its intensity is varied following the integral relation:

$$\gamma L_y \int_T G_y dt = 2\pi n$$

where  $L_y$  is the maximum sample length in the  $y$  direction,  $T$  is the duration of the gradient pulse and  $n$  is an integer which takes on the values:

$$-N/2, -N/2-1, \dots, -1, 0, +1, \dots, N/2-1$$

if it has been assumed to sample each echo in  $N$  points. The bidimensional FT of  $N$  echoes will give a  $N \times N$  image of the object.

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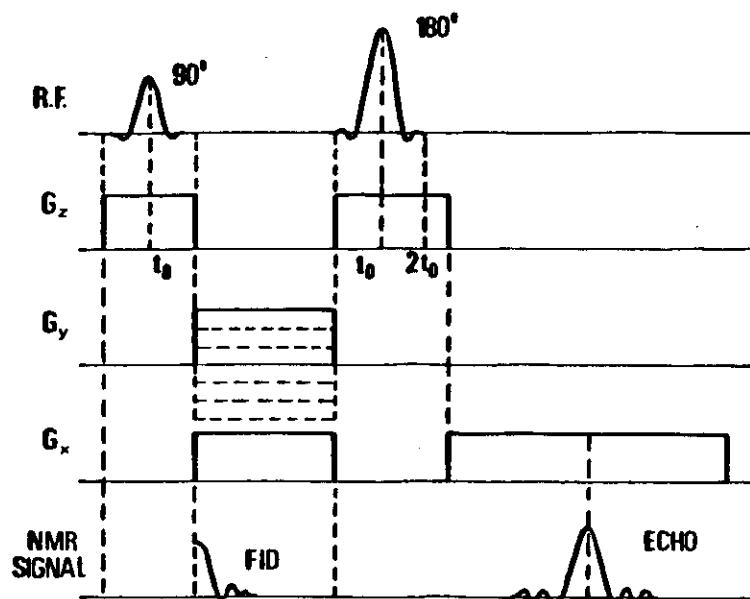


Figure 1. Typical 2DFT sequence. It is a spin echo with both selective pulses. The gradient  $G_z$  is switched on to select a x-y slice during r.f. irradiation. The  $G_x$  gradient is the reading gradient, which is on while the echo is recorded.  $G_x$  introduces the frequency spread along the x axis. The phase encoding gradient  $G_y$  is applied with a whole set of amplitudes and for each one the echo is sampled. The 2DFT of the recorded signal gives the spin density map.  $T_1$  contrast can be generated by applying an extra selective  $180^\circ$  pulse before the spin echo sequence (IR).

