The spatial mapping of translational diffusion coefficients by the NMR imaging technique

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Preliminary communication

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1. Introduction

With the recent development of nuclear magnetic resonance (NMR) imaging it is important to characterise and understand the NMR response of tissues. There are several reasons why such characterisation of tissues using NMR parameters would be useful. It may provide a helpful diagnostic guide and could lead to a deeper understanding of the underlying processes responsible for many pathological and physiological states of tissues. For several years, hydrogen density, spin-lattice relaxation and spin-spin relaxation maps of objects have been obtained using the NMR imaging technique. We have developed a method for the spatial mapping of an additional NMR parameter, the molecular translational diffusion coefficient D. In addition the technique will permit the measurement of perfusion and blood flow rates.

2. Theory

The analysis of the measurement of diffusion and flow by the conventional NMR spin echo has been presented by a number of authors (Stejskal 1965, Packer 1969, Hayward 1972). We outline the essential features of this analysis and then demonstrate how the imaging technique may be introduced. Consider the simple diffusion sequence consisting of a $\pi/2$-τ-π spin-echo pulse pair with a magnetic field gradient $\boldsymbol{G}$ applied continuously. Further, let us assume that there is translational motion of molecules due to both uniform flow and diffusion processes. The equation of motion of the magnetisation following a $\pi/2$ RF pulse, in a coordinate frame rotating at the resonance frequency $\omega_0 = \gamma B_0$, and where the only field present is in the z direction is

$$\frac{\partial M_x}{\partial t} = \gamma B_{\text{eff}} M_y - \frac{M_x}{T_2} + D\nabla^2 M_x$$

$$\frac{\partial M_y}{\partial t} = -\gamma B_{\text{eff}} M_x - \frac{M_y}{T_2} + D\nabla^2 M_y$$

where $B_{\text{eff}} = \boldsymbol{G}.\boldsymbol{r} + \boldsymbol{G}.\boldsymbol{v}t$ and $\boldsymbol{v}$ is the velocity of the flow. D is the diffusion coefficient, neglecting field inhomogeneities.

Writing this in terms of the complex magnetisation $M^+ \equiv M_x + \mathrm{i}M_y$

$$\frac{\partial M^+}{\partial t} = -\mathrm{i}\gamma \boldsymbol{G}.\boldsymbol{r}M^+ - \mathrm{i}\gamma \boldsymbol{G}.\boldsymbol{v}tM^+ - \frac{M^+}{T_2} + D\nabla^2 M^+$$

There are four possible situations.

(1) No flow or diffusion. Consider the simplest case first, that in which there is no flow ($\boldsymbol{v} = 0$) and no diffusion ($D = 0$).

$$\frac{\partial M^+}{\partial t} = -\mathrm{i}\gamma \boldsymbol{G}.\boldsymbol{r}M^+ - \frac{M^+}{T_2}$$

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The solution for this after an initial $\pi/2$ pulse can be easily seen to be

$$M^+(\boldsymbol{r}, t) = M_0 \exp(-t/T_2) \exp(-\mathrm{i}\gamma \boldsymbol{G}.\boldsymbol{r}t) \tag{1}$$

The π pulse leaves M_y unchanged and changes M_x into $-M_x$. If a $\pi/2$ phase shift is employed with the π pulse then M_x is unchanged and M_y changes into $-M_y$. The two sequences produce identical results except for a change in sign of the echo.

Using equation (1) we can describe the development of the magnetisation after the π pulse

$$M^+(\boldsymbol{r}, t') = M^+(\boldsymbol{r}, \tau^+) \exp(-t'/T_2) \exp(-\mathrm{i}\gamma \boldsymbol{G}.\boldsymbol{r}t')$$

where $t' = t - \tau$.

At $t = 2\tau$

$$M^+(\boldsymbol{r}, 2\tau) = M_0 \exp(-2\tau/T_2) \tag{2}$$

since the complex phase factors cancel leaving the familiar expression for the magnetisation at the echo.

(2) Diffusion only.

$$\frac{\partial M^+}{\partial t} = \mathrm{i}\gamma \boldsymbol{G}.\boldsymbol{r}M^+ - \frac{M^+}{T_2} + D\nabla^2 M^+ \tag{3}$$

We expect that diffusion will not affect the phase of the development of the magnetisation at $\boldsymbol{r}$, but will affect the magnitude (Slichter 1978). As long as we are not near a boundary, every plane $\boldsymbol{r}$ has planes symmetrically $\Delta\boldsymbol{r}$ above and below with phase lead and lag respectively, from which magnetisation diffuses to $\boldsymbol{r}$. The phase lead or lag depends on $\Delta\boldsymbol{r}$ and is independent of $\boldsymbol{r}$. Thus we expect that the diffusion induced decay will be independent of $\boldsymbol{r}$ and therefore try the solution

$$M^{+(\boldsymbol{r},t)} = M_0 \exp(-t/T_2) \exp(-\mathrm{i}\gamma \boldsymbol{G}.\boldsymbol{r}t) A(t)$$

Solving equation (3) gives

$$A(t) = A(0) \exp(-D\gamma^2 |\boldsymbol{G}|^2 t^3/3)$$

The constant $A(0)$ is incorporated into M_0, giving for the magnetisation following the initial $\pi/2$ pulse

$$M^+(\boldsymbol{r}, t) = M_0 \exp(-t/T_2) \exp(-\mathrm{i}\gamma \boldsymbol{G}.\boldsymbol{r}t) \exp(-D\gamma^2 |\boldsymbol{G}|^2 t^3/3) \tag{4}$$

At $t = 2\tau$

$$M^+(\boldsymbol{r}, 2\tau) = M_0 \exp(-2\tau/T_2) \exp(-D\gamma^2 |\boldsymbol{G}|^2 2\tau^3/3) \tag{5}$$

as the complex phase factors cancel, giving the familiar diffusion equation.

(3) Flow but no diffusion.

$$\frac{\partial M^+}{\partial t} = -\mathrm{i}\gamma \boldsymbol{G}.\boldsymbol{v}tM^+ - \frac{M^+}{T_2} - \mathrm{i}\gamma \boldsymbol{G}.\boldsymbol{r}M^+ \tag{6}$$

Unlike the diffusion case it is no longer expected that the phase will be invariant, due to the unique direction of motion.

Solving for M^+, the magnetisation at time t after the $\pi/2$ pulse, gives

$$M^+(\boldsymbol{r}, t) = M_0 \exp(-t/T_2) \exp(-\mathrm{i}\gamma \boldsymbol{G}.\boldsymbol{r}t) \exp\left(-\gamma \boldsymbol{G}.\boldsymbol{v} \int_0^t t \, \mathrm{d}t\right)$$

and at $t = 2\tau$

$$M^+(\boldsymbol{r}, 2\tau) = M_0 \exp(-2\tau/T_2) \exp(-\mathrm{i}\gamma \boldsymbol{G}.\boldsymbol{v}\tau^2) \tag{7}$$

(4) Flow and diffusion.

$$\frac{\partial M^+}{\partial t} = -i\gamma \boldsymbol{G}.\boldsymbol{r}M^+ - i\gamma \boldsymbol{G}.\boldsymbol{v}tM^+ - \frac{M^+}{T_2} + D\nabla^2 M^+ \tag{8}$$

Try a solution

$$M^+(\boldsymbol{r}, t) = M_0 \exp(-t/T_2) \exp(-i\gamma \boldsymbol{G}.\boldsymbol{r}t) \exp\left(-i\gamma \boldsymbol{G}.\boldsymbol{v} \int_0^t t \, dt\right) A(t)$$

Substituting into equation (8) and solving gives

$$A(t) = \exp(-\gamma^2 |\boldsymbol{G}|^2 D t^3/3)$$

Thus the complete solution describing the evolution of the magnetisation with diffusion and flow present, after an initial $\pi/2$ pulse is

$$M^+(\boldsymbol{r}, t) = M_0 \exp(-t/T_2) \exp(-i\gamma \boldsymbol{G}.\boldsymbol{r}t) \exp\left(-i\gamma \boldsymbol{G}.\boldsymbol{v} \int_0^t t \, dt\right)$$
$$\times \exp(-\gamma^2 |\boldsymbol{G}|^2 D 2\tau^3/3)$$

At $t = 2\tau$

$$M^+(\boldsymbol{r}, 2\tau) = M_0 \exp(-2\tau/T_2) \exp(-i\gamma \boldsymbol{G}.\boldsymbol{v}\tau^2) \exp(-\gamma^2 |\boldsymbol{G}|^2 D 2\tau^3/3) \tag{9}$$

2.1. Imaging

Let us incorporate the simple diffusion experiment into the spin-warp imaging method. We will assume for simplicity that the diffusion gradient is switched on immediately following the phase-encoding gradient. The effect of the spin-warp gradient is to modify the initial magnetisation from M_0 to $M_0 \exp(-i\gamma \int_{-t_{sw}}^{0} G_x(t) \, dt)$ where t_{sw} is the time the phase encoding gradient G_x is applied in the x direction. The magnitude of the frequency encoding gradient is small compared to that of the diffusion gradient and its net effect is to slightly change the direction of the diffusion measurement. To avoid this problem, this gradient could be switched on at the centre of the echo.

3. Discussions and results

Case (1) describes the T_2 imaging method which is well established. Case (2) demonstrates that the mapping of the translational diffusion coefficient is possible. We obtain an image without the diffusion gradient ($M(0)$) and one with the gradient present ($M(G)$), then on division of the two images

$$\frac{M(G)}{M(0)} = \exp(-\gamma^2 |\boldsymbol{G}|^2 D 2\tau^3/3)$$

In case (3) the effect of flow is to introduce a velocity dependent phase encoding. Thus, by repeating the experiment for a number of different $\boldsymbol{G}$ values it is possible, by means of a simple Fourier transform, to determine the velocity $\boldsymbol{v}$ in a manner analogous to the spin-warp or Fourier imaging technique. In practice to obtain all three components of $\boldsymbol{v}$, three separate experiments should be carried out. Case (4) presents no real problems. The diffusion coefficient can be obtained from the magnitude of the magnetisation, and knowing this the velocity of flow can be found as in case (3).

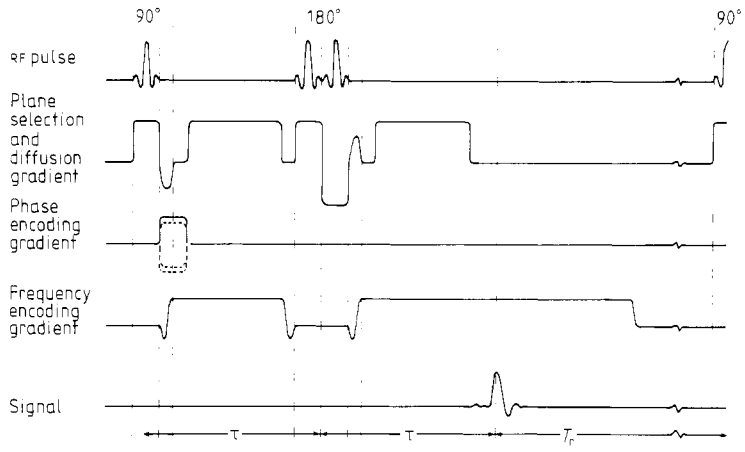


Figure 1. The pulse sequence for diffusion imaging using the spin-warp method.

We have demonstrated diffusion imaging using a gradient in the z direction. The imaging system used is based upon a 7 in (17.8 cm) room temperature bore, superconducting magnet operating at 0.4 T. The sequence is that shown in figure 1. Selection is performed by the $\pi/2$ and π pulses and a plane width of 4 mm is defined; resolution within the plane is 1 mm × 1 mm. A hen's egg was chosen as a suitable phantom since the white and yolk have significantly different spin-spin relaxation rates and diffusion coefficients. The strength of the diffusion gradient was 0.2 mT cm^{-1} and was measured using a sample of known diffusion coefficient, distilled water. Four images were taken, three without a diffusion gradient and with $\tau = 16$, 21 and 27 ms, and one with the diffusion gradient and $\tau = 27$ ms. The repetition time T_r was 5s in all cases. The T_2 relaxation rates and diffusion coefficients were calculated from these images and are presented in table 1. The images obtained are shown in figure 2. It should be noted that in practice equation (5) was modified to that for the pulsed field gradient technique (Stejskal and Tanner 1965) to allow for G_z not being on for the whole pulse interval. The two treatments, in the limit are identical.

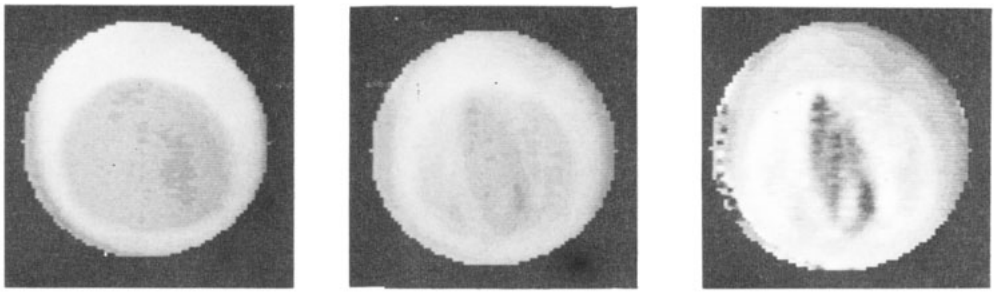
Table 1. Comparison of the diffusion coefficients and T_2 values of the yolk and white of a hen's egg obtained by the NMR imaging technique with those published in the literature from bulk measurements.

	T_2 (ms)	$D \times 10^5$ (cm^2 s^{-1})
Yolk: image	27	0.6
bulk†	19–27	0.37–0.6
White: image	395	1.4
bulk†	440	1.66–1.71

† From James and Gillen (1966).

4. Conclusion

We have clearly demonstrated the feasibility of mapping the diffusion coefficient using a modified spin-warp pulse sequence. Table 1 shows good agreement in all cases between the values obtained by imaging and those obtained by more traditional



(*a*) (*b*) (*c*)

Figure 2. NMR cross sectional images of a hen's egg from (*a*) the spin-echo sequence, (*b*) the spin-echo plus diffusion sequence and (*c*) the division of images (*a*) and (*b*) thus leaving a pure 'diffusion weighted' image. The feature in the centre of the yolk appears to be a property of these eggs but as yet no complete explanation has been found for it.

methods. Significantly, the diffusion image shows an inversion of contrast between the white and the yolk. Thus this additional parameter could be of use in aiding contrast between tissues, in looking at cell size through restricted diffusion and perhaps most importantly in monitoring blood perfusion through tissues. Perfusion rates are only an order of magnitude greater than the diffusion rates and well within the range of the measurement technique. However, the technique must be used with care on living subjects as the sequence is sensitive to all types of movement.

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References

Hayward R J, Packer K J and Tomlinson D J 1972 *Mol. Phys.* **23** 1083–102
James T L and Gillen K T 1966 *Mol. Phys.* **11** 515
Packer K J 1969 *Mol. Phys.* **17** 355–68
Slichter C P 1978 *Principles of Magnetic Resonance* (New York: Springer-Verlag) pp377–82
Stejskal E O 1965 *J. Chem. Phys.* **43** 3597–602
Stejskal E O and Tanner J E 1965 *J. Chem. Phys.* **42** 288–92