

● *Invited Lecture***GENERALISED CALCULATION OF NMR IMAGING EDGE EFFECTS ARISING FROM RESTRICTED DIFFUSION IN POROUS MEDIA**

PAUL T. CALLAGHAN AND SARAH L. CODD

Department of Physics, Massey University, Palmerston North, New Zealand

The theoretical problem of how to describe apparent image spin density under conditions of restricted diffusion, given any general gradient sequence, is intrinsically complex. Here we demonstrate a simple approach to calculating the signal and the corresponding density in nuclear magnetic resonance (NMR) imaging experiments by means of an impulse-propagator method based on matrix multiplication. The multiplication scheme bears a natural and straightforward relationship to the k-space sampling, while the matrices themselves are calculated from the eigenmodes of the pore diffusion equation. Good agreement is found between theoretical predictions and the results of micro-imaging experiments on water trapped in rectangular pores whose walls are spaced by 100 μm along the read direction. © 1998 Elsevier Science Inc.

Keywords: Restricted diffusion; Edge enhancement; Pulsed gradient spin echo.

INTRODUCTION

It is well known that molecular self-diffusive motion can lead to image “blurring” in magnetic resonance imaging (MRI) experiments performed at microscopic resolution. Indeed such an effect may fundamentally limit the resolution achievable in nuclear magnetic resonance (NMR) microscopy.¹ For fluid imbibed in porous media however, self-diffusion and its inhibition at pore boundaries can provide dramatic and potentially useful image contrast, an effect first suggested in 1991 by W.B. Hyslop and P.C. Lauterbur² and subsequently theoretically examined by B. Pütz et al.³ The idea proposed by Hyslop and Lauterbur and by Pütz et al. was based on motional averaging and consequent distortion of the NMR spectrum associated with the frequency-encoding magnetic-field gradient. This averaging depends both on the precise details of the molecular displacement distribution and on the time dependence of the gradient waveform. In the formulation given in Refs. 2 and 3, the frequency-encoding gradient amplitude is constant (as in projection reconstruction), while the molecular displacement distribution is inhomogeneous due to impeded diffusion in the vicinity of pore boundaries.

In fact, the edge effects associated with spectral dis-

tortion are weak in comparison with those which can arise from a quite different source inherent in NMR microscopy. Callaghan et al. showed⁴ that very strong edge effects could be observed when the image was acquired using a spin echo, for example, as in a standard spin-warp encoding sequence. They showed that this effect was caused by diffusive attenuation rather than diffusive line-shape distortion and further argued that for spin-echo sequences, such attenuation effects would always overwhelm line-shape distortion effects irrespective of the diffusion coefficient of the molecular species being imaged.

Quantitative estimation of these effects is essential if edge enhancement phenomena are to be effectively utilised in studies of pore morphology in porous media via NMR microscopy. Unfortunately the calculation of image contrast and distortion effects arising from these phenomena is not at all simple, and until now no general analytic expressions were available which would work for generalised gradient waveforms or pore geometries. In the present article, we present a powerful mathematical tool which is ideally suited to rapid calculation and may be very simply adapted to any chosen gradient sequence.

Address correspondence to Dr. Paul T. Callaghan, Department of Physics, Massey University, Private Bag 11222, Palmer-

ston North, New Zealand. E-mail: p.callaghan@massey.ac.nz

THEORY

Motional Averaging and Diffusive Attenuation

For the purpose of this article, we will focus on a simple didactic example, the case of a rectangular pore in which diffusing fluid molecules are contained between parallel compartment walls of separation a . In the presence of a read (frequency-encoding) gradient of amplitude G applied in a direction normal to the walls, the Larmor spectrum for stationary molecules would be rectangular with spectral width $\omega = \gamma Ga$, γ being the nuclear gyromagnetic ratio. By contrast, the translational motion associated with self-diffusion causes molecules to sample a variety of local Larmor frequencies, thus motionally narrowing the spectrum, the relevant exchange time, τ , being $a^2/2D$, on the order of the time taken to traverse the compartment. For $\omega\tau \gg 1$ the spectrum is undistorted and should yield the expected rectangular image; whereas when $\omega\tau \ll 1$, the spectrum will reduce to a narrow line yielding an image of the compartment in which all the spins appear to reside at the compartment centre. In the intermediate exchange region, $\omega\tau \sim 1$, restricted diffusion near the compartment walls causes a gentle “peaking of the spectrum” as reflections at the walls pushes the mean molecular positions slightly towards the centre of the diffusion interval.

The calculations of Pütz et al. showed that even such very slow exchange conditions as $\omega\tau \approx 10^4$ can lead to noticeable edge enhancement effects, according to this model. However, such effects are intrinsically difficult to observe because the spatial resolution in NMR microscopy is limited by intrinsic signal-to-noise ratios^{2,4} to a voxel limit of around $(10 \mu\text{m})^3$, or where voxels are extended in one dimension, to a pixel limit of around $(5 \mu\text{m})^2$. Given that the effect, if it is to be resolved, must be observed over several pixels, this implies net motion on the scale of hundreds of microns, thus requiring long acquisition times and unrealistically small sampling bandwidths. The analysis contained in Ref. 4 suggests that such effects are at the margins of attainability in practical NMR microscopy.

However, in most applications of NMR imaging involving liquids, spin or gradient echoes are employed (see, for example, the spin-warp imaging sequence in Fig. 1), and this leads inevitably to signal attenuation due to self-diffusion. This attenuation is sensitive to the local molecular self-diffusion coefficient and consequently leads to significantly reduced signal attenuation near restrictive boundaries. For acquisition of N $\mathbf{k}$ -space points along the read axis with dwell time T (corresponding to an acquisition bandwidth $1/T$) the Stejskal–Tanner equation⁵ predicts a read gradient-echo attenuation factor for the case of unrestricted diffusion of:

$$E(\mathbf{k} = 0) = \exp(-\gamma^2 G^2 D (NT/2)^2 (\Delta - NT/6)), \quad (1)$$

where Δ is the separation of the leading edges of the read gradient pulses and T is the acquisition dwell time. Note that the echo attenuation given by Eq. (1) refers to the amplitude of the signal at the centre of $\mathbf{k}$ -space, in other words, to the peak of the time domain echo signal.

For compression of Δ to the minimum possible duration, $NT/2$, this yields:

$$\begin{aligned} E(\mathbf{k} = 0) &= \exp(-\gamma^2 G^2 D (NT/2)^2 (NT/3)) \\ &= \exp\left(-\frac{1}{3} \pi^2 NTD/\Delta x^2\right) \end{aligned} \quad (2a)$$

or

$$E(\mathbf{k} = 0) = \exp\left(-\frac{1}{3} \pi^2 N^3 TD/\text{FOV}^2\right), \quad (2b)$$

where the field of view (FOV) is $N\Delta x$ and Δx is the pixel dimension. Diffusive contrast effects will be significant when the exponent in Eq. (2) exceeds unity, giving the inequality $D \geq 3\gamma G \text{FOV}^3/2\pi^3 N^3$ or $D \geq 3\gamma Ga^3/2\pi^3 N_a^3$, where N_a is the number of pixels spanning the dimension of the pore. By comparison, spectral distortion enhancement at an exchange parameter $\omega\tau \approx 10^4$ requires $D \geq \gamma Ga^3/2 \times 10^4$. Clearly diffusive relaxation will dominate, provided $N \geq 10$.

The discussion so far serves to indicate the regime under which diffusive effects will be important. It relies on a simple analysis of the echo amplitude at the centre of $\mathbf{k}$ -space, based on a comparison of the signals from “restricted” and “unrestricted” spins. The problem with such an analysis is that, while it provides simple physical insight, it fails to provide an exact, complete, and quantitative description of the dynamics of restricted diffusion; it fails to take into account the effect of surface relaxation of the spins; and it fails to deal with the important question of how the echo signal is affected over all values of $\mathbf{k}$ and not just at the centre of the echo. This latter point is crucial if we are to describe imaging phenomena.

Recently one of us⁶ demonstrated a new computational method based on the multiple propagator approach of Caprihan et al.⁷ This method was developed so as to calculate the height of the echo (E) at the centre of $\mathbf{k}$ -space, the relevant signal in the pulsed-gradient spin-echo q -space diffraction experiment. The method depends on the representation of the gradient waveform by a succession of sharp gradient impulses, and it leads to $E(q)$ being expressed as a product of matrix operators

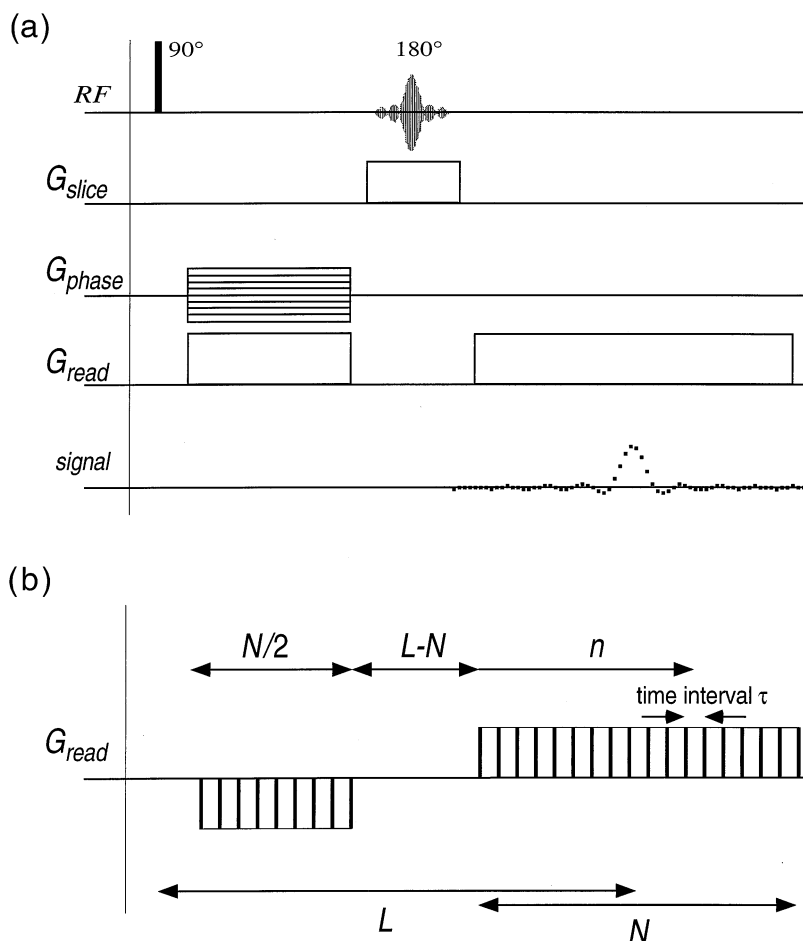


Fig. 1. (a) The spin-warp sequence used to obtain the experimental images. (b) This schematic illustrates the formation of the matrix products used to calculate the expected one-dimensional image profiles.

corresponding quite naturally to the successive sandwich of phase evolution and Brownian migration events. This technique is easily adapted to the more general problem of encoding in $\mathbf{k}$ -space. Rather than being used to evaluate the signal amplitude at $\mathbf{k} = 0$ alone, the matrix method readily yields the signal at all points in $\mathbf{k}$ -space.

The Matrix/Impulse Propagator Technique

Details of this method may be found in Ref. 6, and we summarise only the key features here. The key to the treatment lies in the ability to describe the propagator for molecular displacements in terms of the standard eigenmode expansion⁸:

$$P_s(\mathbf{r}|\mathbf{r}', t) = \sum_{n=0}^{\infty} \exp(-\lambda_n t) u_n(\mathbf{r}) u_n^*(\mathbf{r}'). \quad (3)$$

In fact, these eigenmodes are well known for plane parallel, cylindrical, and spherical pores, including the

case of pore surface relaxation effects.⁸ In the impulse-propagator description, the gradient waveform is represented by a sequence of sharp impulses, such that molecular translational motion is subdivided into a sequence of discrete time intervals, with all spin phase evolution taking place at well-defined times at the boundaries of those intervals. The succession of impulses is required to yield the same time integral function, $\mathbf{F}(t)$, as the actual gradient waveform.

Suppose that we break the waveform into N time intervals τ , each bounded by impulses $\mathbf{k}_n$, $\mathbf{k}_{n+1}$, etc. The NMR signal at any point in time corresponding to the n^{th} interval is given by:

$$E = S(\mathbf{k}_1) RA(\mathbf{k}_2) RA(\mathbf{k}_3) \dots RA(\mathbf{k}_n) RS^*(-\mathbf{k}_{n+1}), \quad (4)$$

where the row vectors S and matrices A and R are defined by:

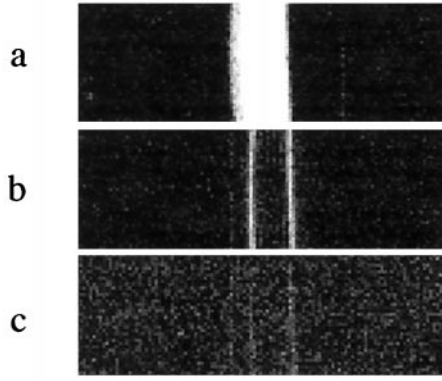


Fig. 2. The liquids are all contained in rectangular glass capillaries, 100 μm wide (Camlab, Cambridge, UK). The bandwidth is 40 kHz, the horizontal FOV is 2 mm, and the pixel dimension is $(8 \mu\text{m})^2$. The slight distortion is due to diamagnetic susceptibility effects which arise from the rectangular geometry of the glass capillary and the alignment of its walls normal to the polarizing field. (a) In a phantom of glycerol ($D = 2.2 \times 10^{-12} \text{ m}^2 \text{ s}^{-1}$) very little diffusive attenuation occurs but chemical shift effects act to blur the image. (b) Water, $D = 2.3 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$, $\Delta = 9.2 \text{ ms}$, temp = 25°C. (c) Water, $D = 2.3 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$, $\Delta = 56.8 \text{ ms}$, temp = 25°C.

$$S_{\mathbf{k}}(\mathbf{k}) = V^{-1/2} \int d\mathbf{r} u_{\mathbf{k}}(\mathbf{r}) \exp(i2\pi\mathbf{k}\cdot\mathbf{r}) \quad (5)$$

$$R_{\mathbf{k}\mathbf{k}} = \exp(-\lambda_{\mathbf{k}}\tau) \quad (6)$$

$$A_{\mathbf{k}\mathbf{k}'}(\mathbf{k}) = \int d\mathbf{r} u_{\mathbf{k}}^*(\mathbf{r}) u_{\mathbf{k}'}(\mathbf{r}) \exp(i2\pi\mathbf{k}\cdot\mathbf{r}). \quad (7)$$

If the waveform amplitude $\mathbf{G}(n\tau)$ is expressed in units of dimension $\mathbf{G}_{\text{step}}$, then at time $n\tau$ the impulse will be $\mathbf{k}_n = m_n \mathbf{k}$, where $\mathbf{k} = (2\pi)^{-1} \gamma \delta \mathbf{G}_{\text{step}}$ and m_n is some positive or negative integer, depending on the local magnitude and sign of $\mathbf{G}(n\tau)$. Noting that $A(n\mathbf{k}) = A(\mathbf{k})^n$, it is clear that:

$$\begin{aligned} E(\mathbf{k}_n) \\ = S(\mathbf{k}) R[A(\mathbf{k})]^{m_2} \dots R[A(\mathbf{k})]^{m_n} \dots R[A(\mathbf{k})]^{m_n} R S^\dagger(-\mathbf{k}). \end{aligned} \quad (8)$$

Thus, any waveform may be handled, provided that we calculate just three matrices, $R(\tau)$, $S(\mathbf{k})$, and $A(\mathbf{k})$, where $\mathbf{k}$ is the smallest impulse used to digitise the waveform.

Fig. 1a shows a standard spin-warp imaging sequence in which the image is acquired in two dimensions of $\mathbf{k}$ -space using both frequency and phase encoding. We shall be particularly concerned with the evolution of the

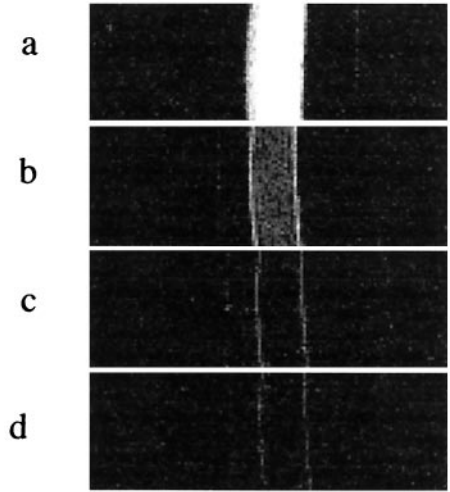


Fig. 3. The liquids are all contained in rectangular glass capillaries, 100 μm wide. The bandwidth is 40 kHz, the horizontal FOV is 2 mm, and the pixel dimension is $(8 \mu\text{m})^2$. (a) In a phantom of glycerol ($D = 2.2 \times 10^{-12} \text{ m}^2 \text{ s}^{-1}$) very little diffusive attenuation occurs. (b) Water, $D = 1.45 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$, $\Delta = 9.2 \text{ ms}$, temp = 8°C. (c) Water, $D = 1.45 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$, $\Delta = 15.4 \text{ ms}$, temp = 8°C. (d) Water, $D = 1.45 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$, $\Delta = 21.6 \text{ ms}$, temp = 8°C.

spin system under the effect of the read gradient when the parent molecules undergo restricted diffusion in a pore space. Eq. (8) provides a means of handling both the read and phase gradient evolution, but for the purpose of illustrating its application, we will restrict our discussion to the effect of read gradient effects only, using as our example the case of a rectangular pore in which the read gradient direction is normal to the pore boundary.

A particularly convenient way to handle the computation of the signal under a read gradient is to set the successive evolution intervals equal to the acquisition dwell time, T , and Fig. 1b shows the relevant impulse train. In this example the impulses are all equal in magnitude, and $m_n = 1$. Thus, if N acquisition points are used, then the spin warp sequence of Fig. 1 yields the signal:

$$E(k_n) = S(k) [RA(k)]^{N/2} R^{L-N/2} [RA^\dagger(k)]^n R S^\dagger(k), \quad (9)$$

where $L = \Delta/T$, k is the impulse time integral $(2\pi)^{-1} \gamma \delta \mathbf{G}_{\text{step}}$, and n ranges from 1 to N .

Reconstruction of the spin-density image, $\rho(\mathbf{r})$, proceeds by taking the Fourier transform of the echo signal in $\mathbf{k}$ -space via:

$$\rho(r) = \int E(\mathbf{k}) \exp(i2\pi\mathbf{k}\cdot\mathbf{r}) d\mathbf{k}, \quad (10)$$

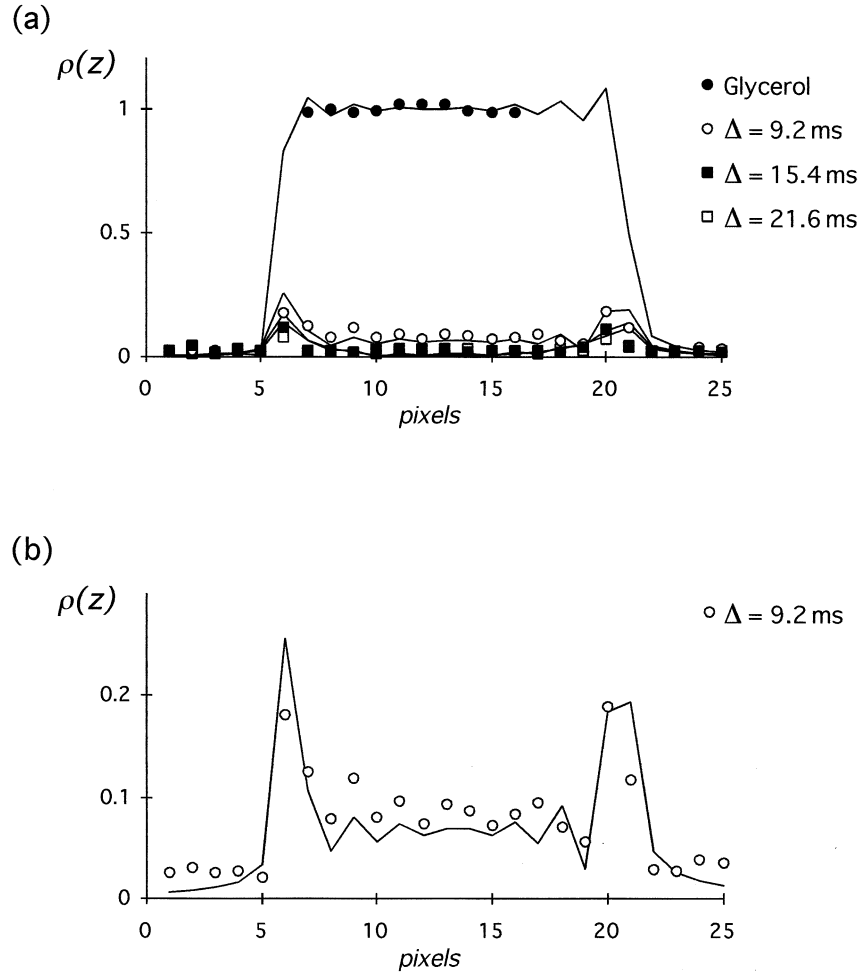


Fig. 4. Data from the profiles across the images in Fig. 3b–d are compared with the calculated profiles. The agreement is very good. It should be noted that there are no fitted parameters.

where $\mathbf{k}$ is the integral value, $(2\pi)^{-1}\gamma \int_0^t \mathbf{G}(t') dt'$. For the pulse sequence shown in Fig. 1, the read gradient component of $\mathbf{k}$ -space at time $t = n\tau$ is simply $n\mathbf{k}$, so the one-dimensional projection image results by calculating the discrete Fourier transform:

$$\rho(z_m) = N^{-1} \sum_0^N E(n\mathbf{k}) \exp(i2\pi n\mathbf{m}/N), \quad (11)$$

where the spatial dimension is given by $z_m = m/kN$.

Expressions for the S , A , and R matrices in the case of the rectangular pore can be found in Ref. 6. Finally, despite our use of the rectangular pore geometry as a model system, we have found exact solutions for the S , A , and R matrices in the case of spherical pores, so the results demonstrated here may be easily generalised to this more relevant case.

RESULTS

Fig. 2a shows an image obtained using the spin warp sequence of Fig. 1a for a phantom of glycerol ($D = 2.2 \times 10^{-12} \text{ m}^2 \text{ s}^{-1}$) contained in a rectangular glass capillary tube of interior wall spacing $100 \mu\text{m}$. We have chosen to use glycerol for a reference because the very low diffusion coefficient means that no diffusive effects are present in the image. However, the existence of chemical shift difference does lead to some blurring, as apparent in Fig. 2a. The read gradient is applied normally to the walls of the capillary. For this image, obtained at a bandwidth of 40 kHz, the value of N is 256, the horizontal FOV is 2 mm, the pixel dimension is $(8 \mu\text{m})^2$, and very little diffusive attenuation occurs in the read gradient. Precise alignment of the sample with respect to the gradient direction enabled us to use a slice thickness of 1 mm.

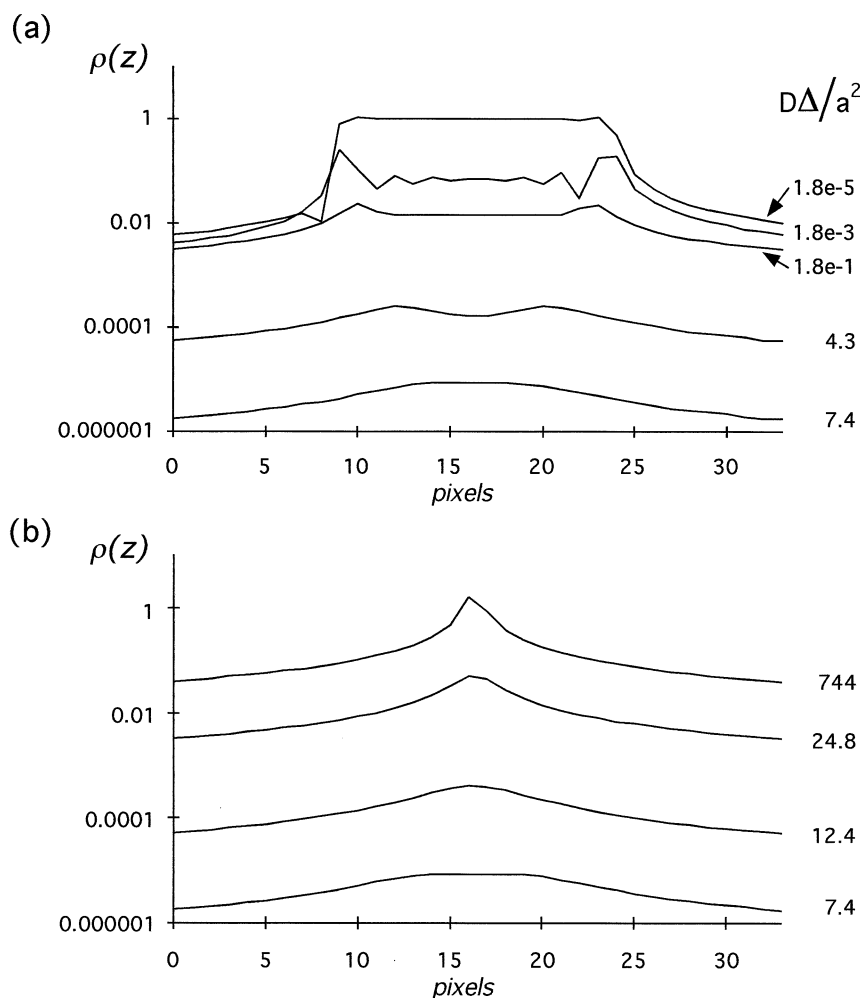


Fig. 5. (a) As the evolution time, Δ , increases, the image profile suffers diffusive attenuation and edge enhancement. Eventually the high-intensity peaks at the pore boundaries broaden and shift slightly, demonstrating the onset of spectral distortion. (b) As the evolution time is lengthened even further, motional narrowing occurs, and the image becomes a central line that increases in intensity again.

By contrast, Fig. 2b and c show images obtained under identical conditions but where the capillary is filled with water whose diffusion coefficient is $2.3 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$ at the sample temperature of 25°C. According to Eq. (1) the freely diffusing water will suffer an attenuation factor of $e^{-2.3}$ and e^{-11} , respectively, in the two images. Near the walls, where diffusion is restricted, the effect of local reduction in D causes dramatic edge enhancement effects as the attenuation exponent reduces.

The experimental examples shown in Fig. 2b and c corresponds to the case where diffusive attenuation for unrestricted spins is severe. We have also investigated the regime where such attenuation is weak. Eq. (2) illustrates that the exponent responsible for this attenuation varies as $N^3 TD/\text{FOV}^2$ so that much weaker attenuation can be found by reducing N , increasing the bandwidth,

T^{-1} , or increasing the field of view. We have chosen the remaining alternative of reducing the diffusion coefficient, D , by reducing the temperature of the water to 8°C. Fig. 3a shows the glycerol reference again, while Figs. 3b–d show the water image at 8°C for successively increasing values of Δ from 9.2 ms to 21.6 ms.

Profiles across the images of Fig. 3a–d are shown in Fig. 4a, while Fig. 4b shows an expanded profile for the case $\Delta = 9.2$ ms. We now calculate the expected image profile using Eq. (9). (Note that the data have been properly normalised to take account of the differing proton signal amplitudes for glycerol and water.) A key factor in such calculations is the choice of matrix dimensionality and the need to retain as complete a basis set as necessary for the required precision. This will be determined by the need to ensure sufficient decay of the

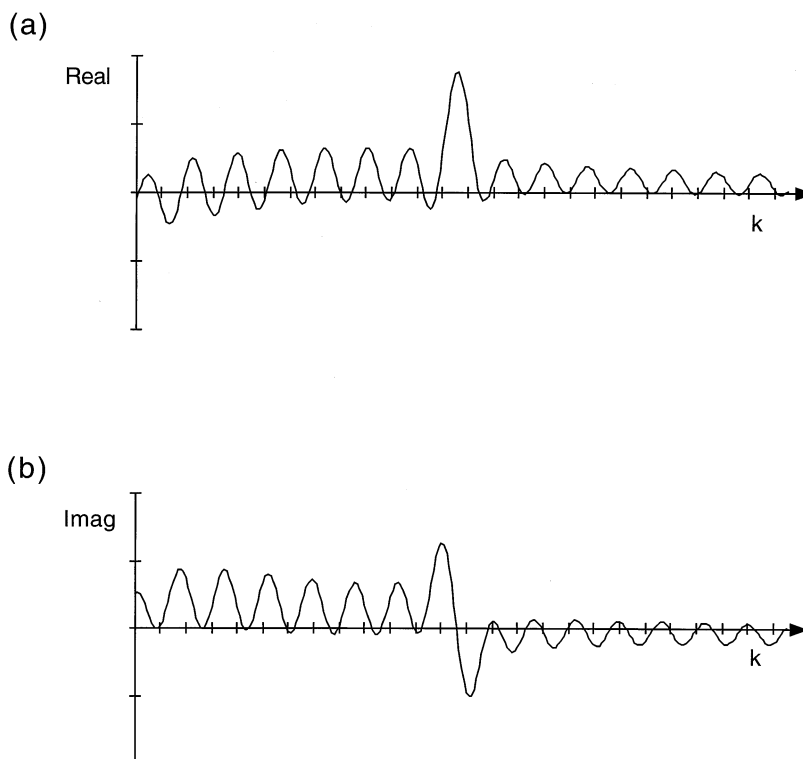


Fig. 6. Time domain echo signal, $E(k)$, real and imaginary, corresponding to the profile $\rho(z)$ for $D\Delta/a^2 = 1.8 \times 10^{-3}$ in Fig. 5.

diagonal elements of the matrix R_{kk} with increasing k , a requirement directly related to the choice of digitisation size, N , for the rectangular pore, $R_{kk} = \exp(-k^2 D\Delta / Na^2)$. We have found that for $N \leq 256$, 30×30 matrices are sufficient. A , R , and S , and the resulting signal amplitude $E(\mathbf{k}_n)$, are all calculated in Matlab on a Power Macintosh 7200, the entire 256 acquisition and subsequent FFT taking 10 s.

The results of our calculations for the experimental conditions depicted in Fig. 3 are shown in Fig. 4. The agreement is very good. We note that at the longer evolution time, the effects of spectral distortion are just beginning to be apparent with a broadening and slight shift of the high-intensity peak at the pore boundary. However, the onset of this effect coincides with a severe loss of signal-to-noise under the experimental conditions which are able to be achieved in practical NMR microscopy. There are no such limitations in the calculated profile, and we are able to demonstrate this trend to motional narrowing clearly in Fig. 5. A succession of profiles are shown for increasing values of $D\Delta/a^2$, ranging from $D\Delta/a^2 \ll 1$ to $D\Delta/a^2 \gg 1$. In the latter case, motional narrowing leads to a collapse of the profile into a single peak with an amplitude similar to the undistorted profile obtained when $D\Delta/a^2 \ll 1$. The ability of the impulse-propagator formalism to handle such a wide

range of motional conditions provides graphic evidence of its utility.

Finally we demonstrate the direct relationship between the calculation method and the way in which data is collected in the NMR imaging experiment by showing, in Fig. 6, one of the raw $\mathbf{k}$ -space (time domain) signals, $E(\mathbf{k})$, corresponding to a $\rho(z)$ profile from Fig. 5. We note that the method outlined here can be adapted to any pulse sequence whatsoever and, in particular, that it may be used to predict the effect of phase gradients and read gradients as well as handling full three-dimensional encoding.

CONCLUSIONS

The matrix multiplication scheme demonstrated in Ref. 6 was originally developed to deal with the pulsed-gradient spin-echo NMR experiments in which the echo amplitude is the parameter of interest. Such experiments include diffusive diffraction and frequency domain modulated-gradient spin-echo NMR. In this present paper we have shown that this calculation scheme may be very easily adapted to the case of imaging where the entire echo signal is sampled in $\mathbf{k}$ -space. Indeed the succession of impulses and evolution periods inherent in the theory nicely mimics the actual process of evolution and sam-

pling inherent in data acquisition under a read gradient. Furthermore, the theoretical signal is generated quite naturally in the time domain, a point which is illustrated in Fig. 6, where we show both the calculated time domain signal $E(k)$ and its Fourier transform, the image profile. The calculation scheme is fast, requiring only a few seconds on a Power PC platform. Finally we note that the method may be easily extended to other pore geometries (for example, spherical), with or without wall relaxation effects, by calculating the S , A , and R matrices using the corresponding spherical pore eigenfunctions.⁸ Complete details of the spherical pore case will be given in a forthcoming publication.

Acknowledgments—The authors are grateful to the New Zealand Foundation for Research, Science and Technology for financial support. Sarah L. Codd acknowledges the support of a Royal Society of New Zealand, Science and Technology Postdoctoral Fellowship.

REFERENCES

1. Callaghan, P.T. *Principles of NMR Microscopy*. Oxford: Oxford University Press; 1991.
2. Hyslop, W.B.; Lauterbur, P.C. Effects on restricted diffusion on microscopic NMR imaging. *J. Magn. Reson.* 94: 501–510; 1991.
3. Pütz, B.; Barsky, D.; Schulten, K. Edge enhancement by diffusion in microscopic MRI. *J. Magn. Reson.* 97:27–53; 1992.
4. Callaghan, P.T.; Coy, A.; Forde, L.C.; Rofo, C.J. Diffusive relaxation and edge enhancement in NMR microscopy. *J. Magn. Reson.* A110:347–350; 1993.
5. Stejskal, E.O.; Tanner, J.E. Spin diffusion measurements: Spin-echoes in the presence of a time-dependent field gradient. *J. Chem. Phys.* 42:288–292; 1965.
6. Callaghan, P.T. A simple matrix formalism for spin echo analysis of restricted diffusion under generalised gradient waveforms. *J. Magn. Reson.* 129:74–84; 1997.
7. Caprihan, A.; Wang, L.Z.; Fukushima, E. A multiple-narrow-pulse approximation for restricted diffusion in a time-varying field gradient. *J. Magn. Reson.* A118:94–102; 1996.
8. Callaghan, P.T. Pulsed Gradient Spin Echo NMR for planar, cylindrical and spherical pores under conditions of wall relaxation. *J. Magn. Reson.* A113:53–59; 1995.