Generalized Analysis of Motion Using Magnetic Field Gradients

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I. Introduction

The use of magnetic field gradients to detect the translational displacement of molecules via precessional motion of their atomic nuclear spins is almost as old as nuclear magnetic resonance (NMR) itself. In his original paper on spin echoes, Hahn (1950) pointed out that the echo amplitude would be affected by the Brownian motion in the presence of local magnetic field inhomogeneity. In their article on the use of multiple pulse trains, Carr and Purcell (1954) pointed out that diffusional attenuation could be avoided provided that the pulse spacing was made sufficiently short. These authors also developed a nice formalism for relating the echo amplitude to the discrete hops of the spins, while in a later paper, Torrey (1956) developed a continuum approach based on the magnetization diffusion equation. Later in the 1950s, Hahn suggested the measurement of flow in the presence of magnetic field gradient (Hahn, 1950) via phase shift in the spin echo.

With the suggestion by McCall, Douglass, and Anderson (1963) that the use of pulsed magnetic field gradients could lead to significant advantages in measurement strategies, a new phase in the measurement of molecular motion began. Stejskal and Tanner (1965) were responsible for initiating the methodology and theory of the pulsed gradient spin-echo (PGSE) experiment as well as for its implementation to measure diffusion in systems for which restriction to motion caused a deviation from Fickian behavior. Since then the method has been extensively developed to measure motion in restricted systems, taking advantage of a diffraction analogy based on Fourier methods. This "q-space" approach (Callaghan, 1991) to PGSE NMR is complementary to the k space of NMR imaging (Lauterbur, 1973; Mansfield and Grannell, 1973; Mansfield and Morris, 1982). With the extensive application of NMR imaging and NMR microscopy to both biological and material systems over the past decade, the combination of position and motion encoding methods in NMR has permitted the spatial localization and mapping of velocity and diffusion.

The PGSE NMR method relies on the use of two sharp gradient pulses separated by a well-defined time interval and is therefore naturally suited to time-domain analysis of motion. However, it is important to realize that this particular form of two-pulse gradient modulation is not unique. In particular, a number of other time-modulation schemes are possible in which the molecular motion is detected in a different manner. However, as we shall see, whenever modulated gradients are used to encode the spin magnetization for motion rather than position, it is appropriate to refocus any phase shift due to absolute spin position by means of a spin echo. Consequently, we refer to this more general type of experiment as modu-
lated gradient spin-echo (MGSE) NMR. A particular theme of this chapter will be the relationship of the chosen measurement technique to the type of motion analysis sought. An important aspect of the discussion will be the characterization of motion in molecular ensembles and, in particular, the effects of deviation from simple Brownian motion or simple flow. We review the measurement strategies that may be adopted along with their associated signal techniques. These strategies will include time-domain, spatial frequency-domain, and temporal frequency-domain analyses, spatial localization of motion, two-dimensional correlation and exchange analyses, and diffraction and scattering analogies. Given the recent importance of stray field and Earth’s field NMR methods, we will also consider the condition where the magnitude of the applied magnetic field gradient is comparable to the polarizing field.

II. Generalized Motion

A. The Conditional Probability Function, Self-Diffusion, and Flow

Nearly all NMR experiments are performed using large numbers of spins whose signals form a coherent superposition. It is the averaging contained in this superposition that lies at the heart of any theoretical treatment.

To begin, we assume that we can describe the general motion of a molecule $i$ in terms of some time-dependent displacement $r_i(t)$. One of the most useful ways of handling the ensemble-averaging over the $i$-spins is to introduce a density function giving the probability that a particle will have displacement between $r'$ and $r' + dr'$ at a time $t$. Usually, this probability function will depend not only on the time interval $t$, but also on the starting position. In particular we will be concerned with the self-correlation function (van Hove, 1954; Egelstaff, 1967), $P(r', t \mid r, 0)$, which gives the chance that a molecule initially at $r$ will have moved to $r'$ after a time $t$. It turns out that this is a particularly useful description for NMR since, as we shall see, this function can be determined directly using the two-pulse PGSE experiment. Interestingly, the only other experimental method able to gain direct access to this conditional probability density is incoherent inelastic neutron scattering (Bacon, 1975), a point that is discussed in more detail by Callaghan (1991).

Suppose we denote the total probability density of finding a particle at
position \( r' \) at time \( t \) by \( \phi(r', t) \). Then

\[
\phi(r', t) = \int P(r', t | r, 0) \phi(r, 0) \, dr
\]  

(1)

In general, \( \phi(r, 0) \) will be given by the time-independent particle density \( \rho(r) \). For Brownian motion, the function \( \phi(r', t) \) will obey Fick's law, where the spatial derivatives refer to the coordinate \( r' \). Consequently, we may write

\[
\frac{\partial P}{\partial t} = D \Delta P
\]  

(2)

where \( D \) is the molecular self-diffusion coefficient, \( \Delta \) is the Laplacian operator, and \( P \) obeys the initial condition

\[
P(r', 0 | r, 0) = \delta(r' - r)
\]  

(3)

For the special case of unrestricted Brownian motion, the boundary conditions lead to the solution

\[
P(r', t | r, 0) = (4\pi Dt)^{-3/2} \exp\left(-\frac{(r' - r)^2}{4Dt}\right)
\]  

(4)

The Markov nature of Brownian motion statistics is reflected in the fact that \( P \) depends only on the net displacement \( r' - r \) and not the initial position \( r \). We will refer to the vector \( r' - r \) moved over a time \( t \) as the dynamic displacement \( \mathbf{R} \).

Using the concept of the dynamic displacement, it is possible to rewrite Eq. (1) so as to define a very useful function, known as the average propagator (Karger and Heink, 1993) \( \overline{P}(\mathbf{R}, t) \). This function gives the average probability for any particle to have a dynamic displacement \( \mathbf{R} \) over a time \( t \) and is given by

\[
\overline{P}(\mathbf{R}, t) = \int P(r + \mathbf{R}, t | r, 0) \phi(r, 0) \, dr
\]  

(5)

For the case of unrestricted self-diffusion we can then write

\[
\overline{P}(\mathbf{R}, t) = (4\pi Dt)^{-3/2} \exp\left(-\frac{R^2}{4Dt}\right)
\]  

(6)

Note that for the example of simple unrestricted Brownian motion, all molecules experience an identical "average propagator," irrespective of starting position, reflecting the Markov nature of the statistics. This is just one case that will be encountered in the study of molecule translational motion using NMR methods. This case is easily extended to include simple flow with common velocity \( \mathbf{v} \). The solution is

\[
\overline{P}(\mathbf{R}, t) = (4\pi Dt)^{-3/2} \exp\left(-\frac{(\mathbf{R} - \mathbf{v}t)^2}{4Dt}\right)
\]  

(7)

Generally, we will use spin-echo NMR to study systems for which more
complex motions occur. These examples might include Brownian motion within a special set of confining boundaries, systems in which some local motion is superposed upon a longer range migration or systems in which the fluctuating or randomized flow occurs.

B. VELOCITY CORRELATION, SPECTRAL DENSITY, AND THE SELF-DIFFUSION TENSOR

A complete knowledge of the propagator $P(r', t | r, 0)$ for the ensemble of nuclear spins will, in principle, allow one to calculate the echo amplitude for any gradient modulation function. However, the propagator approach is particularly amenable to solution in the special gradient modulation case of the narrow pulse PGSE experiment. For more general modulation methods, an alternative approach, based on autocorrelation function, is helpful. The autocorrelation function of $A$ is defined as $G(t) = \langle A(t)A(0) \rangle$, where the brackets represent the molecular ensemble average (Uhlenbeck and Ford, 1963; Berne and Pecora, 1976).

For translational motion, the velocity correlation function is particularly useful and, as we will show, can be utilized to provide a relationship between the echo amplitude and the molecular dynamics in the case of general modulation wave forms. Its Fourier spectrum is simply the self-diffusion tensor ($\text{Lenk}, 1977; \text{Stepišnik}, 1981$) $D_{\alpha\beta}(\omega)$, where $\alpha$ and $\beta$ may take each of the Cartesian directions, $x, y, z$, that is,

$$
D_{\alpha\beta}(\omega) = 1/2 \int_{-\infty}^{\infty} \langle v^\alpha(t) v^\beta(0) \rangle e^{i\omega t} dt
$$

(8)

Using the even property of $G(t)$, we write the diagonal elements of this tensor as

$$
D_{zz}(\omega) = \int_{0}^{\infty} \langle v_z(t) v_z(0) \rangle e^{i\omega t} dt
$$

(9)

For simple Brownian motion the velocity autocorrelation function decays rapidly to zero over the correlation time $\tau_c$, corresponding to the average collision time. Consequently, the diffusion spectrum is relatively constant with frequencies above zero, attenuating in the vicinity of $\omega = \tau_c^{-1}$. Clearly, the lower-frequency plateau of the spectrum has amplitude $D_{zz}(0) = \langle v_z^2 \rangle \tau_c$. It should be noted that the collisional frequency for small molecules, $\tau_c^{-1}$, is exceedingly high compared with the frequency regime accessible to MGSE NMR, i.e., less than or on the order of $10^5$ Hz. However, for motion in complex fluids there may exist a number of characteristic time scales, which correspond to frequencies in the accessible regime. These might include tube disengagement times in entangled
polymers or wall collision times in simple liquids contained within porous solids. Such times relate more to the organizational structure of liquids than to local particle motion.

We will show that this diffusion spectrum may be directly probed in MGSE NMR by appropriate choice of gradient modulation wave form. For example, in the case of complex motion referred to previously, the spectrum may not be flat below $\tau_c^{-1}$, but instead contain structure that is directly related to these characteristic “organizational” frequencies. For example, where superposed slow and fast stochastic motion occurs, such structure may be apparent and the velocity correlation function will contain the essential information. By contrast, the behavior of systems for which the local motion is Brownian, but whose boundaries impose constraints over a much longer time scale than the correlation time for local stochastic motion, is very different. For these systems the velocity correlation function is zero beyond $\tau_c$ and the diffusion spectrum contains no features at low frequencies that can be related to the boundary collision. For such systems the propagator approach to describing stochastic motions provides the best means of describing the outcome of the MGSE NMR experiment.

III. Modulated Gradient Spin-Echo NMR

A. Theoretical Starting Point

In this section we derive an expression for the NMR signal amplitude for a molecular ensemble experiencing generalized magnetic fields that vary in time and space. This enables us to provide a sound theoretical starting point for different measurement techniques without the need for hidden assumptions. While the details of the theoretical analysis in this section are not essential to an understanding of the measurement and analysis methods to be described, we include a brief description of the reasoning employed so that the reader can appreciate the basis of this starting point. By deriving all our subsequent expressions for particular methods from a single equation, the inherent unity of the various techniques is emphasized. Readers wishing to skip this derivation should move directly to Eq. (41).

B. The Influence of Magnetic Fields

Consider the situation where the local magnetic field at position $r$ is the sum of a uniform field $B_0$ and a nonuniform field $B_s(r,t)$, that is,

$$B = B_0 + B_s(r,t)$$  \hfill (10)
We will be principally concerned with the situation where the molecules move a sufficiently small distance that the field experienced by a particular spin \( i \) can be expressed in terms of the zeroth and first order terms in a Taylor expansion, that is,

\[
B_i = B_{i0} + g_i(t) r_i, \tag{11}
\]

where \( r_i \) is the displacement of spin \( i \) from its local origin. Note that the zeroth order term is added to \( B_i \) to give the local value, \( B_{i0} \). \( g_i \) is necessarily a tensor since Maxwell's equations dictate that the nonuniform magnetic field cannot change in a single direction. The need to label the gradient tensor by the subscript \( i \) arises because of its local character. However, we will deal with special cases where the linear gradient is uniform across the sample and the subscript may be dropped. This definition includes some special cases of wide importance. The first concerns a uniform gradient common to all parts of the sample. In this case Eq. (11) reduces to

\[
B = B_e + g(t) r \tag{12}
\]

where \( r \) is now the displacement from the gradient origin. Most commonly we will encounter the condition in which the inhomogeneous field is weak, that is, \( |B_x(r, t)| \ll |B_e| \). Here the magnetic field components perpendicular to the static magnetic field may be neglected and we may define the remaining column of \( g(t) \) as the vector \( G(t) = \nabla B_z(r, t) \), where \( B_z \) is the component of \( B_e \) parallel to the \( z \) axis defined by \( B_e \). In this special case the total magnetic field magnitude is given by

\[
B = B_e + G(t) \cdot r \tag{13}
\]

This use of Eq. (13) has no meaning whenever the applied nonuniform magnetic field is on the order of or larger than the main magnetic field. While the small inhomogeneous field approximation will be useful in a wide class of experiments, we will find it useful to retain the more general treatment represented by Eq. (11).

In the NMR experiment the radiofrequency (rf) magnetic field

\[
B_1(t) = B_{10}(r, t) \sin \omega t \tag{14}
\]

is used to excite the magnetization from an initial thermodynamic equilibrium and to manipulate it in the due course of an experiment. The rf magnetic field may be applied as a rectangular (hard) pulse or can be modulated with the desired spectral distribution (soft rf pulse). Its spatial homogeneity is defined by the geometry of the transmitting rf coil. Generally, the amplitude of the rf pulse may be a function of time and the location of the magnetization-bearing particle, that is, \( B_{10}(r, t) \).
Our general Hamiltonian will be written in terms of spin operators $\mathcal{H}$

$$\mathcal{H} = -\hbar \omega_0 \mathcal{S} - \hbar \gamma \sum_i B_i(t) \cdot \mathcal{S} + \mathcal{H}_{\text{rf}} + \mathcal{H}_{\text{fl}}$$ (15)

with $\gamma B_x = \omega_0$ and with $\mathcal{H}_{\text{rf}}$ describing the effect of the rf pulses and $\mathcal{H}_{\text{fl}}$, including all spin interactions with the surroundings. We will find it convenient to divide $\mathcal{H}_{\text{fl}}$ into two parts. The first concerns those terms, $\mathcal{H}_{i\text{L}}$, responsible for $T_1$ and $T_2$ relaxation processes unconnected with translational motion. In the present treatment we will generally neglect these. The second term $\mathcal{H}_{\text{fl}}$ concerns those processes responsible for particle migration. In the following discussion we account for $\mathcal{H}_{\text{fl}}$ by assuming that the particle location is a time-dependent variable $r_i(t)$ and by performing the appropriate ensemble average, which we call “L-average.”

Note that the sum over $i$ represents a sum over individual spins. However, because the number of spins dealt with is usually immense ($> 10^4$), one may reasonably group the spins into separate subensembles for which the dynamical behavior may be different. For example, one might distinguish groups of spins that have differing starting points for their motion or that occupy compartments with differing diffusion coefficients. For such a grouping the averages within and between the subensembles may be separately handled. In this case we regard $i$ as a subensemble label. In either case we may separately sum over the $i$ spins before carrying out the “L-average” over the surroundings. This latter average will be important when dealing with restricted diffusion.

Following the usual practice, we use the density matrix $\rho(t)$ to describe the state of the system, where

$$\rho(t) = \mathcal{U}(t) \rho(0) \mathcal{U}^\dagger(t)$$ (16)

and the operator $\mathcal{U}(t)$ defines the evolution of the system from the initial state $\rho(0)$. Prior to the application of the first rf pulse, the initial state is determined by thermodynamic equilibrium. In this chapter we are concerned with the effect of nonuniform fields applied after preparation by a selective or nonselective rf pulse sequence. Following this preparation, we may presume (in the usual high temperature approximation) that the initial density matrix can be written very generally as

$$\rho(0) = \rho_L(0) \hbar \omega_0 \sum_i (A_i \mathcal{S}_i + B_i \mathcal{S}_i + C_i \mathcal{S}_i) = \rho_L(0) \sum_i \rho_{i\text{L}}(0)$$ (17)

Here $\rho_L$ denotes the density matrix of the spin surroundings, while $A_i$, $B_i$, and $C_i$ are the constants that denote the state of $i$th subensemble after the preparation. This decomposition of the total spin density matrix into a sum
of notional density matrices for each spin or subensemble $i$ is particularly helpful in dealing with an ensemble in which the spins have different motion subsequent to preparation. Strictly speaking, this requires that we can describe the density matrix in terms of single spin operators and, hence, that dipolar interactions are neglected.

Given the complexity of the Hamiltonian described in Eq. (15) it would appear that the time evolution operator will be exceedingly complex. However, by judicious use of the factor theorem (Evans, 1968) it is possible to express this operator as a product of simple rotation operators in spin space. The use of various spin transformations in rotating or tilted frames results in a more lucid treatment, as well as nicely accounting for the various stages of the experiment, for example, the preparation, mixing, and detecting periods. The formal relationship between the evolution operator and the Hamiltonian [Eq. (15)] is given by

$$\mathcal{U}(t) = \mathcal{T} \exp \left( -\frac{i}{\hbar} \int_0^t \mathcal{H}(t') \, dt' \right)$$  \hspace{1cm} (18)

where the operator $\mathcal{T}$ implies time ordering of the applied interaction. In the case of a spin echo, $\mathcal{U}$ takes the form of a natural time-ordered succession of evolution operators given by $\mathcal{U}_{n1}$ for the application of a nonuniform field, followed by $\mathcal{U}_n$ for the $\pi$ rf pulse, and then $\mathcal{U}_{m2}$ for the second evolution under the nonuniform magnetic field. The total evolution is therefore

$$\mathcal{U}(t) = \mathcal{U}_{m2}(t) \mathcal{U}_n \mathcal{U}_{m1}(t)$$  \hspace{1cm} (19)

This operator split neglects relaxation effects and assumes that the $\pi$ rf pulse is short enough that all other terms in the Hamiltonian may be neglected during its application. In the following discussion we will consider the details of this basic sequence, but we must bear in mind that it may be just the “joint in the chain” of a more sophisticated sequence. The effect of the nonuniform magnetic field is given by

$$\mathcal{U}_{m1,2} = \mathcal{T} \exp \left( i \int_{t_1}^{t_2} \left\{ \omega \mathcal{F} + \gamma \sum_i B_i [r_i(t'), t'] \cdot \mathcal{F} \right\} \, dt' \right)$$  \hspace{1cm} (20)

This operator can be simplified by transformation into a frame with $z$-axis along the total magnetic field at the site of the particular spin. By the use of the factoring theorem (Wilcox, 1967), the operator given in Eq. (20) breaks into the product of two parts,

$$\mathcal{U}_m(t) = \mathcal{T} \exp \left( i \int_0^t \left\{ \mathcal{F} [r_i(t'), t'] \cdot \mathcal{F} + \omega_{\text{eff}} [r_i(t), t'] \mathcal{F} \right\} \, dt' \right) \mathcal{R}(t)$$  \hspace{1cm} (21)
where
\[ \mathcal{R}(t) = \exp \left( -i \sum_i \int_0^t \dot{\phi}[r_i(t'),t'] \cdot \mathcal{J}_i dt' \right) \]  (22)

\( \mathcal{R}(t) \) is the operator that represents transformation into the new frame and corresponds to a continuous succession of infinitesimal rotations by \( |\dot{\phi}| dt \) about the local vector directed along \( \phi \). This local vector is perpendicular to the plane formed by the \( z \) axis and the direction of the total magnetic field, \( B[r_i(t),r] \). In the case of slow field variation, that is, the so-called adiabatic case,
\[ |\dot{\phi}[r_i(t),t]| \ll \omega_{\text{eff}}[r_i(t),t] \]  (23)

one can neglect the angular velocity \( |\dot{\phi}[r_i(t),t]| \) in Eq. (21) with respect to the effective precession frequency of the spins in the \( i \)th subensemble, and the only term remaining in the exponent arises from
\[ \omega_{\text{eff}}[r_i(t),t] \]
\[ = \sqrt{\left( \omega_0 + \gamma B_{x}[r_i(t),t] \right)^2 + \gamma^2 B_y^2[r_i(t),t] + \gamma^2 B_z^2[r_i(t),t]} \]  (24)

The adiabatic case invariably applies under experimental conditions. Furthermore, in nearly all experiments the nonuniform magnetic field is returned to zero at the instant in time when the rf pulse is applied and at the instant when the spin echo is formed. Consequently, the net rotation at the end of the evolution \( \mathcal{Z}_{m1} \) and \( \mathcal{Z}_{m2} \) is simply \( \mathcal{R}(t) = 1 \). (The only practical case where this return of applied fields to zero may not apply concerns the use of read gradients in imaging. In that particular case, the main field is much stronger than the inhomogeneous field, so that components parallel to \( B_0 \) only need be considered and no off-axis rotations apply.)

We are therefore able to reduce Eq. (21) into the much simpler expression
\[ \mathcal{Z}_{m1,2}(t) = \exp \left( i \sum_i \int_0^t \omega_{\text{eff}}[r_i(t'),t'] \cdot \mathcal{J}_i dt' \right) \]  (25)

with only \( z \) components of the spin operator. This operator now represents a simple rotation around the \( z \) axis.

It is worth noting that the \( \pi \) rf operator includes, in addition to rf field, the static magnetic field. By the same theorem we can split \( \mathcal{Z}_{m} \) into two operators as
\[ \mathcal{Z}_{m} = \exp(i\omega_k \mathcal{J}_z) \cdot \exp(i\pi \mathcal{J}_z) \]  (26)
This equation represents a transformation into the rotating frame in which the counterrotating oscillating terms are neglected. The $\pi$ rf operator has the effect of turning all $z$ and $y$ components of the spin operators lying on the right through 180°. It therefore results in a change of the sign of the $B_i$ and $C_i$ terms in the initial density matrix as well as acting to change the sign of the effective frequency in $\mathcal{F}_m$. All remaining spin operators contain only $z$-components and may be merged into a single operator for which time runs from the beginning to the end of the sequence.

Applying this approach to Eq. (19), the density matrix Eq. (17), during the detection period, has the form

$$\rho(t) = \rho_0(t) \sum_i \left\{ M_i \left[ \mathcal{J}_{x_i} \sin \theta_i(t) + \mathcal{J}_{y_i} \cos \theta_i(t) \right] - C_i \mathcal{F}_{x_i} \right\}$$

$$= \rho_0(t) \sum_i \rho_i(t)$$

(27)

by denoting

$$M_i = \sqrt{A_i^2 + B_i^2}$$

(28)

$$\alpha_i = \arctan \frac{A_i}{B_i}$$

(29)

$\rho_i(t)$ is the spin part of the density matrix where the spin phase appears as

$$\theta_i(t) = \int_0^t \omega_{\text{eff}}[\tau_i(t'), t'] \, dt' + \alpha_i$$

(30)

with the tilted precession frequency defined as

$$\omega_{\text{eff}}[\tau_i(t), t] = \begin{cases} -\omega_{\text{eff}}[\tau_i(t), t], & 0 < t < \tau \\ \omega_{\text{eff}}[\tau_i(t), t], & \tau < t < 2\tau \end{cases}$$

(31)

where we have assumed that the $\pi$ rf pulse acts at time $\tau$.

With a detailed understanding of this basic sequence, we are able to consider more sophisticated spin-echo sequences involving the multiple application of the gradients and $\pi$ rf pulses, sequences where the spin dephasing is created by the inhomogeneous rf field instead of a magnetic field gradient, as well as other combinations of gradient and rf pulses. In the case of multiple application of the basic PGSE sequence, the operator for each applied $\pi$ rf pulse changes the sign of all $\mathcal{J}_{x_i}$ operators on its right-hand side. Thus the sign of the precession frequency switches to the opposite sign after each $\pi$ rf pulse. The $\pi$ pulse train also changes the sign of $\mathcal{J}_{x_i}$ or $\mathcal{J}_{y_i}$ depending upon the phase of these pulses and their
number. Thus $\tau(t)$ becomes

$$
\rho(t) = \rho_{\alpha}(t) \sum_i \left\{ M_i \left[ P_x, \mathcal{F}_i \sin \theta_i(t) + P_y, \mathcal{F}_i \cos \theta_i(t) \right] - P_z, P_x, C_i, \mathcal{F}_i \right\}
$$

(32)

where $P_x$ and $P_y$ denotes the change of sign due to $\pi_x$ and $\pi_y$ pulses.

In the case of the stimulated spin echo, the $\pi$ rf pulse is replaced by two $\pi/2$ rf pulses that are separated by a “magnetization-storage” period during which migration occurs. We can write the time evolution operator for the sequence as

$$
\mathcal{U}(t) = \mathcal{U}_{m2}(t) \mathcal{U}_{\pi/2} \mathcal{U}_{rL} \mathcal{U}_{\pi/2} \mathcal{U}_{m1}(t)
$$

(33)

The intervening time between two $\pi/2$ pulses is normally sufficiently long that spin relaxation cannot be neglected and the effect of the interaction operator $\mathcal{H}_{rL}$ must be considered. By using operator factoring, we can commute the rf and $rL$ operators so as to merge both $\pi/2$ rf pulse operators into a single $\pi$ pulse. The commutation transforms $\mathcal{H}_{rL}$ into the transverse plane in such a manner as to alter the spin relaxation. Thus Eq. (32) can be used to describe the sequence of the stimulated echo by simply taking into account the spin relaxation.

We can also show that a similar procedure can be used in sequences where spin dephasing is carried out using the gradient of rf field, $\mathcal{B}_r(r,t)$, instead of using a magnetic field gradient (Canet et al., 1989). For example, the sequence of two rf gradient pulses with an intermediate $\pi$ pulse and $\pi/2$ read pulse can be described by

$$
\mathcal{U}(t) = \mathcal{U}_{\pi/2} \mathcal{U}_{\pi/2}(t) \mathcal{U}_{\pi} \mathcal{U}_{\pi/2}(t)
$$

(34)

With the appropriate manipulation this operator returns a result very similar to Eq. (27), but with the phase term given by

$$
\theta_i(t) = \int_0^t \omega_0 \left[ r_i(t'), t' \right] dt' + \alpha_i
$$

(35)

where the integration time in Eq. (35) runs from the beginning to the end of the sequence and

$$
\omega_0 \left[ r_i(t'), t' \right] = \gamma | \mathcal{E}_0(\mathbf{r}, t') |
$$

(36)

is the effective precession frequency in the rotating frame defined as in Eq. (24).

C. Spin Echo and the General Signal Response

The free precession of the spin system is observed via the voltage induced in a coil wound around the sample. The signal due to a time-
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dependent magnetization $M(t)$ is given by

$$e = -\frac{d}{dt} \left[ M(t) \cdot \frac{B_z}{i_z} \right]$$  \hspace{1cm} (37)

The coil sensitivity is characterized by means of the reciprocity theorem by the ratio $B_z/i_z$, where $B_z$ is the virtual field induced by a coil carrying virtual current $i_z$ at the location of a magnetic dipole. Clearly, the induced voltage depends upon the geometry of the coil as well as on the distribution of spins within the coil. For a coil with axis along $x$, the induced electromotive force is given by

$$e = -\hbar \gamma \frac{d}{dt} \sum_i \langle \mathcal{F}_x, S(z) \rangle$$  \hspace{1cm} (38)

with $S(r_i)$ being the $x$ component of the coil sensitivity. The angle brackets $\langle \cdots \rangle$ denote an average over the spin variables as well as over the variables associated with the migration of the particles. The microscopic nature of the magnetization- and spin-bearing molecules requires a quantum mechanical evaluation of Eq. (38). The induced voltage can be calculated, by knowing the state of the system through its density matrix $\rho(t)$, by

$$e(t) = -\hbar \gamma \frac{d}{dt} \sum_i \text{Tr} \rho(t) \mathcal{F}_x S(r_i)$$  \hspace{1cm} (39)

In order to evaluate Eq. (39) we need some detailed knowledge of the density matrix $\rho(t)$. This operator will contain information about the prior evolution in the applied magnetic field gradients as well as contain information about the relaxation processes and the NMR free precession spectrum. In order to handle this complexity it is very helpful to separate the prior evolution domain from the detection domain.

Consider the free procession signal acquired as a function of time $t'$ after the spin-echo formation at time $t$. We shall presume that the sole term acting in the Hamiltonian after the echo center is due to the Larmor precession at frequency $\omega_{oi}$ in the uniform field, where the use of the subscript $i$ allows for the range of chemical shifts in the NMR spectrum. This precession contributes an evolution operator $\exp(i \omega_{oi} t')$ to the density matrix so that we can rewrite Eq. (39) as

$$e(t + t') = -\hbar \gamma \frac{d}{dt} \sum_i \text{Tr} \rho_i(t)$$

$$\times \left\{ \text{Tr} \exp(-i \omega_{oi} t') \rho_i(t) \exp(i \omega_{oi} t') \mathcal{F}_x, S(r_i) \right\}$$  \hspace{1cm} (40)

Note that we have taken into account the form of the density matrix given
in Eq. (17) in which the trace of the spin variables $T_{r_i}$ is separated from the trace of lattice variables $T_{r_L}$. Generally, in the case of quadrature detection, we can write

$$e(t + t') = -\hbar \gamma \omega_0 \sum_i \exp(i \omega_0 t') T_{r_i} \rho_L(t) \exp(\theta(t)) M_i S(r_i)$$

$$= A_0 \sum_i \exp(i \omega_0 t') \exp(\theta(t)) M_i S(r_i)_L$$  \hspace{1cm} (41)

Equation (41) can be easily modified to allow for relaxation effects.

The importance of Eq. (41) is that it demonstrates that spin migration can be encoded in the signal phase via the magnetic field inhomogeneity and in its amplitude via the spatial variation of transmitting magnetization $M_i$ and receiving rf field sensitivity $S(r_i)$. This means that various inhomogeneities can provide information about flow or diffusion. In this chapter we mostly deal with the motions that are encoded in the spin-echo phase, but it is important to note that rf gradients also can be used for measurement of particle migration as the dephasing by rf inhomogeneity in the rotating frame and also as a correlation between the initial distribution of exited spins and the coil sensitivity to their location at the time of detection.

The approach with the truncated evolution operators requires only that the non-uniform magnetic field is returned to zero. Thus, the phase $\theta(t)$ correctly describes spin precession not only in the detection period, but also between the gradient pulses during the so-called mixing period. For example, an application of a series of basic spin-echo sequences at different times will change the spin phase at those times:

$$\theta(t_1, t_2, \ldots, t) = \int_0^{t_1} \omega_{0t} [r_i(t'), t'] dt' + \int_{t_1}^{t_2} \omega_{0t} [r_i(t'), t'] dt' + \cdots$$

$$+ \int_{t_n}^{t} \omega_{0t} [r_i(t'), t'] dt' + \alpha_i$$  \hspace{1cm} (42)

This approach can be used to study the correlations between spin locations or their velocities at different times.

D. THE NARROW GRADIENT PULSE SPIN-ECHO EXPERIMENT

We now consider the simple case of a spin echo in which two rectangular linear gradient pulses are applied as shown in Fig. 1. In this pulsed gradient spin-echo (PGSE) experiment, the time $t$ used in Eq. (41) will refer to the position of the spin-echo formation. In analyzing this experiment, we will assume the weak inhomogeneous field limit and the uniform
Fig. 1. Gradient of rf sequence for pulsed gradient spin-echo NMR using narrow gradient pulses of amplitude $g$, duration $\delta$, and separation $\Delta$.

Gradient case. We can describe the signal in terms of the normalized echo amplitude at the echo center, that is,

$$E(t) = \sum_i \langle \exp(i\theta_i(t)) \rangle_L$$

(43)

A special case arises when the two gradient pulses of duration $\delta$ separated by time $\Delta$ are very narrow. In this limit there exists a simple relationship between the nuclear spin positions and the spin phase, namely,

$$\theta_i(\Delta) = \gamma \delta G \cdot [r_i(\Delta) - r_i(0)]$$

$$= 2\pi q \cdot [r_i(\Delta) - r_i(0)]$$

(44)

Using the language of propagators, we can evaluate the $\langle \cdots \rangle_L$ average in Eq. (43) to obtain

$$E(\Delta) = \sum_i \int dr_i(\Delta) P_i(r_i(\Delta), \Delta \mid r_i(0), 0) \exp(i\theta_i(\Delta))$$

(45)

Implicit in this relation is that the starting position of spin subensemble $i$ is well defined. In this case the sum over $i$ can be translated into a sum over the starting position. We will find it convenient to rewrite the positions of a general particle at time $0$ and $\Delta$ as $r$ and $r'$. Thus the normalized echo amplitude can be rewritten

$$E(q, \Delta) = \int dr, \rho(r) \int dr' P(r', \Delta \mid r, 0) \exp(i2\pi q \cdot (r' - r))$$

(46)

Note that the more general case of a nonuniform gradient may be handled by defining a local $q$ vector, $q_i$. Clearly, $E(\Delta)$ will depend on the exper-
mentally adjustable parameters $q$ and $\Delta$, and we will find it convenient to expressly recognize this dual dimensionality by writing the echo attenuation signal as $E(q, \Delta)$.

In terms of the average propagator, Eq. (46) can also be written

$$ E(q, \Delta) = \int d\mathbf{R} \overline{F}(\mathbf{R}, \Delta) \exp(i2\pi q \cdot \mathbf{R}) $$  \hfill (47)

E. THE TREATMENT OF STOCHASTIC MOTION

It should be noted that Eq. (47) is a very special result that applies only when insignificant motion occurs during the time of application of the gradient pulses. In the following discussion we will be concerned with developing a formalism that is more generally applicable to gradient wave forms of finite duration. In doing so we will find it very helpful to separate stochastic and non-stochastic parts of the motion. In order to make the treatment as general as possible, we allow for a nonuniform gradient, but assume the weak inhomogeneous field case. The strong field case will be dealt with in Section III.

When using nuclear magnetic resonance to detect the motion of molecules undergoing Brownian motion, one cannot detect the displacements from individual molecular collisions, but rather the longer range displacements arising from innumerable such collisions. Thus we observe the cumulative effect of a large number of small perturbations of spin precession frequency. In consequence, we can assume a stochastic process in which the fluctuating deviations from the mean value of $\omega(t)$ have a Gaussian distribution.

These random collisions shift a molecule from its mean position via a stochastic displacement $\mathbf{r}_i(t)$ so that the total displacement can be written

$$ \mathbf{r}_i(t) = \mathbf{r}_{i\sigma}(t) + \mathbf{r}_{i\alpha}(t) $$  \hfill (48)

where $\mathbf{r}_{i\sigma}(t)$ corresponds to a mean displacement arising, for example, from flow. Assuming that $\mathbf{G}_i(t)$ is the gradient in magnetic field magnitude at the $i$th spin,

$$ \mathbf{G}_i(t) = \text{grad} |\mathbf{B}(\mathbf{r}_{i\sigma}, t)| $$  \hfill (49)

we can write the precession frequency as

$$ \omega_{\text{eff}}^e[\mathbf{r}_i(t), t] = \omega_{i\sigma}(t) + \gamma \mathbf{r}_{i\alpha}(t) \cdot \mathbf{G}_i(t) $$  \hfill (50)

Here $\omega_{i\sigma}(t)$ accounts for precession arising from both the static field $B_0$ and the non-stochastic motion in the presence of the gradient, $\omega_{\text{eff}}^e[\mathbf{r}_{i\sigma}(t), t]$. 

The resulting normalized spin-echo amplitude is
\[ E(t) = \sum_i \langle \exp(i[\theta_i(t) + \theta_i(t)]) \rangle_L \] (51)
where
\[ \theta_i(t) = \int_0^t \omega_i(t') \, dt' \] (52)
and
\[ \theta_i(t) = \gamma \int_0^t G_i(t')r_i(t') \, dt' \] (53)

Using the distribution function for the Gaussian process developed in the Appendix, the average over the precession frequency fluctuation in Eq. (51) can be calculated from
\[ E(t) = \sum_i \exp(i\theta_i(t)) \int f_i(\theta_i(t), t | 0, 0) \exp(i\theta_i(t)) \, d\theta_i \]
\[ = \sum_i \exp(i\theta_i(t)) \int f_i(\theta', t | \theta, 0) \exp(i(\theta' - \theta)) \, d\theta' \] (54)

Note we have once again performed the \( \langle \cdots \rangle_L \) average via the integral involving the propagator and used the notation \( \theta' - \theta = \theta_i(t) \) for the phase displacement of a general spin. As shown in the Appendix, the function describing the probability of the phase change from \( \theta \) to \( \theta' \) in time \( t \) in very general form is
\[ f_i(\theta, t | \theta', 0) = \exp\left( \frac{1}{2} A_i(t) \frac{\partial^2}{\partial \theta^2} \right) \delta(\theta - \theta') \] (55)

where \( A_i(t) \) is a frequency correlation function depending on the specific form of the gradient modulation \( G_i(t) \) and the stochastic process. Note that in the case of the narrow gradient pulse approximation, the propagator \( P(r', \Delta | r, 0) \) is common to the ensemble and any local variation in gradient is contained in the variable \( q_i \) as shown in Eq. (45). In the present instance of generalized gradient modulation, no such common distribution is possible and the phase propagator retains a local character. Hence the retention of the subscript \( i \) in Eq. (55).

As shown in the Appendix, if there exists no constraints to the possible values of phase, the distribution function \( f_i \) may be written
\[ f_i(\theta, t | \theta', 0) = \frac{1}{\sqrt{2\pi A_i(t)}} \exp\left( -\frac{(\theta - \theta')^2}{2A_i(t)} \right) \] (56)
Its substitution in Eq. (54) gives
\[ E(t) = \sum_i \exp(i\theta_{\omega}(t) - A_i(t)/2) \]
\[ = \sum_i \exp(i\theta_{\omega}(t) - \beta_i(t)) \tag{57} \]
The signal in Eq. (57) contains a phase shift term modulated by molecular flow or drift, along with the term that attenuates the signal because of random particle migration. To evaluate Eq. (57), we express the particle position in the spin phase in terms of the instantaneous velocity \( v_i(t) \) and integrate by parts to obtain
\[ \theta_{\omega}(t) = \int_0^t [F_i(t) - F_i(t')] v_i(t') \, dt' \tag{58} \]
where the phase factor
\[ F_i(t) = \gamma \int_0^t G_{\omega}(t') \, dt' \tag{59} \]
is zero at the time of spin-echo phase refocusing, \( t = 2\Delta \). Consequently,
\[ \beta_i(2\Delta) = \frac{1}{2} \int_0^{2\Delta} \int_0^{2\Delta} \mathcal{F}(t_1) \cdot \mathcal{F}(t_2) \cdot \mathcal{D}(t_1, t_2) \, dt_1 \, dt_2 \tag{60} \]
The same result follows when the average of the exponential function given in Eq. (51) is transformed using the cumulant expansion theorem and, assuming a Gaussian process, all correlations higher than second order (Stepišnik, 1981, 1985) are neglected. The particle velocity autocorrelations form a tensor
\[ \mathcal{D}(t_1, t_2) = \frac{1}{2} \begin{bmatrix} \langle v_x(t_1)v_x(t_2) \rangle & \langle v_x(t_1)v_y(t_2) \rangle & \langle v_x(t_1)v_z(t_2) \rangle \\ \langle v_y(t_1)v_x(t_2) \rangle & \langle v_y(t_1)v_y(t_2) \rangle & \langle v_y(t_1)v_z(t_2) \rangle \\ \langle v_z(t_1)v_x(t_2) \rangle & \langle v_z(t_1)v_y(t_2) \rangle & \langle v_z(t_1)v_z(t_2) \rangle \end{bmatrix} \tag{61} \]
where for convenience we drop the subscript \( L \). The damping term [Eq. (60)] can be written as
\[ \beta_i(2\Delta) = \int_0^{2\Delta} dt_1 \int_0^{2\Delta} dt_2 \mathcal{F}(t_1) \cdot \mathcal{D}(t_1, t_2) \cdot \mathcal{F}(t_2) \tag{62} \]
By inserting the Fourier transform of the velocity autocorrelation function into Eq. (62)
\[ \langle v_i(t_1)v_i(t_2) \rangle = \frac{1}{\pi} \int_0^\infty \mathcal{D}(\omega) \exp(i\omega(t_1 - t_2)) \, d\omega, \tag{63} \]
and taking the Fourier transform of the phase factor,

\[ F_i(\omega, \Delta) = \int_0^{2\Delta} F_i(t)e^{-i\omega t} \, dt \]  

(64)

we obtain the spin-echo attenuation as

\[ \beta_i(2\Delta) = \frac{1}{\pi} \int_0^\infty F_i(\omega, \Delta) : \mathcal{D}_i(\omega) \cdot F_i(-\omega, \Delta) \, d\omega \]  

(65)

In Eq. (63), \( \mathcal{D}_i(\omega) \) is the tensor representing the spectrum of autocorrelation between the velocity components as indicated in Section II.B. The product in Eq. (65) with the phase factor \( F_i \) extracts only the diagonal components of the tensor and the spin-echo attenuation. It is, in fact, the product between the spectrum of the velocity autocorrelation function and the square of the phase spectrum. Consequently, a modulated gradient NMR measurement of self-diffusion also yields information about the velocity autocorrelation. For isotropic diffusion, Eq. (65) becomes

\[ \beta_i(2\Delta) = \frac{1}{\pi} \int_0^\infty D_i(0)|F_i(\omega, \Delta)|^2 \, d\omega \]  

(66)

Suppose we consider the special case in which the molecular correlation rate \( \tau^{-1} \) is much greater than the highest-frequency component of the phase spectrum, \( F_i(\omega, \Delta) \). In that case we may write

\[ \beta_i(2\Delta) = \frac{1}{\pi} D_i(0) \int_0^\infty |F_i(\omega, \Delta)|^2 \, d\omega \]  

(67)

and, by the Parseval identity,

\[ \beta_i(2\Delta) = D_i(0) \int_0^{2\Delta} |F_i(t')|^2 \, dt' \]  

(68)

where the frequency plateau \( D_i(0) \) is identical to the local self-diffusion coefficient. Given that the diffusion coefficient and the gradient are uniform, the subscript \( i \) may be dropped and Eq. (68) is identical to Torrey's formula (Torrey, 1956).

**F. Special Cases of Interest**

We now consider two special cases in which the diffusion spectra are nontrivial and Eq. (66) may be used to evaluate the result of a modulated spin-echo experiment. The first case concerns slow molecular collision rates. As pointed out by Einstein (1956), the result

\[ \langle [x(t) - x(0)]^2 \rangle = 2Dt \]  

(69)
holds only in the limit of large $t$. More generally, one may write [Uhlenbeck and Ornstein, 1930]

$$\langle [x(t) - x(0)]^2 \rangle = 2D[t - \tau_c(1 - \exp(-t/\tau_c))]$$

(70)

where the correlation time $\tau_c = m/f$, $f$ being the coefficient of friction and $m$ the mass of the Brownian particle. The friction for small molecules in liquids results in correlation times on the order of $10^{-9}$ s or less. This is much less than the time of the shortest spin-echo sequence at around $10^{-4}$ s. However, for macromolecules, the correlation time may become large enough to be measured by the spin-echo method (Zupančič et al., 1985; Kveder et al., 1988; Fatkullin and Kimmich, 1994). Figure 2 shows that in some polymers (Grinberg et al., 1987) the self-diffusion constant measured by NMR does exhibit an unusual behavior at short times.

Using Eqs. (9) and (70) and writing $\xi = \tau_c^{-1}$, the diffusion spectrum is given by (Wang and Ornstein, 1945)

$$D(\omega) = \frac{D\xi^2}{\omega^2 + \xi^2}$$

(71)
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FIG. 3. The phase spectrum for PGSE sequence and the diffusion spectrum (dotted) for the Uhlenbeck time-dependent self-diffusion.

Suppose that we evaluate the case of a usual PGSE sequence comprising finite pulses of width δ and gradient amplitude G. The phase spectrum follows from Eqs. (59) and (64) as

$$ F(\omega, \Delta) = \gamma G \frac{(1 - e^{i\omega \delta})(1 - e^{i\omega \delta})}{\omega^2} $$

with

$$ |F(\omega, \Delta)|^2 = \left[ \gamma \delta \frac{\sin(\omega \delta/2)\sin(\omega \Delta/2)}{(\omega \Delta/2)(\omega \delta/2)} \right]^2 \tag{73} $$

Figure 3 shows both spectra. Hence it follows that

$$ \beta(2\Delta) = \frac{1}{\pi} \int_0^\infty |F(\omega, \Delta)|^2 \frac{D\xi^2}{\omega^2 + \xi^2} \, d\omega \tag{74} $$

which can be evaluated to give

$$ \beta(2\Delta) = \gamma^2 G^2 D \left\{ \delta^2 \left( \Delta - \frac{\delta}{3} \right) - \frac{2}{\xi^2} \delta + \frac{1}{\xi^3} \right. $$

$$ \times \left[ 2 + \exp(- (\Delta - \delta) \xi) + \exp(- (\Delta + \delta) \xi) $$

$$ - 2 \exp(- \Delta \xi) - 2 \exp(- \delta \xi) \right\} \tag{75} $$
Note that the spin-echo attenuation depends in a characteristic way on the NMR parameters $\Delta$ and $\delta$, as well as on the self-diffusion constant $D$ and the frictional damping $\zeta$. Equation (75) is quite general and applies to all time intervals.

Some special cases are of interest. When $\tau_\epsilon = 1/\zeta \ll \Delta$, all terms but the first can be neglected. This is a well-known classic result (Torrey, 1956). In the limit of short intervals between the gradient pulses, when $1/\zeta = \Delta$, the spin-echo damping [Eq. (75)] follows the relationship

$$\beta(2\Delta) = \frac{1}{2} \gamma^2 G^2 \Delta \delta^2$$  \hspace{1cm} (76)

When the pulses are very short, $\delta \ll \Delta$, Eq. (75) becomes

$$\beta(2\Delta) = \gamma^2 G^2 \delta^2 D \left[ \Delta - \frac{1}{\zeta}(1 - e^{-2\zeta}) \right]$$  \hspace{1cm} (77)

An inherent feature of Eq. (77) is its simple relationship [via Eq. (70)] to the mean-squared particle displacement, i.e.,

$$\beta(2\Delta) = \frac{1}{2} \gamma^2 G^2 \delta^2 \langle [x(\Delta) - x(0)]^2 \rangle$$  \hspace{1cm} (78)

This relationship holds quite generally for the narrow pulse PGSE sequence provided that the phase distribution is Gaussian. This may be seen by considering the relationship between the particle displacement and the velocity correlation:

$$\langle [r(t) - r(0)]^2 \rangle = \int_0^t dt_1 \int_0^t dt_2 \langle v(t_1) v(t_2) \rangle$$  \hspace{1cm} (79)

By transforming to the frequency domain (Stepišnik, 1993) it may be shown that the displacement in one spatial dimension is linked to spectrum of velocity correlation through

$$\langle [x(t) - x(0)]^2 \rangle = \frac{2}{\pi} \int_0^\infty D_x(\omega) \left[ \frac{\sin \left( \frac{\omega \Delta}{2} \right)}{\left( \frac{\omega}{2} \right)} \right]^2 d\omega$$  \hspace{1cm} (80)

Since it is also true that $\gamma \delta G \sin \left( \frac{\omega \Delta}{2} \right)/(\omega/2)$ is the spectrum of the PGSE sequence [Eq. (73)] with short pulses separated by $\Delta$, Eq. (78) follows directly. Note, however, that Eq. (78) gives the first term in the cumulant expansion and will only yield the correct echo attenuation if the phase distribution is Gaussian.

The next case concerns the trapping of molecules undergoing Brownian motion in the presence of some restoring force. While friction is the main parameter that determines Brownian motion in the short time limit (Wang and Ornstein, 1945; Stepišnik, 1994), when dealing with random migration of molecules in a complex environment, other long range interactions may
result in anomalous self-diffusion. This kind of deviation has been found in the modeling of Brownian movement in a periodic potential and in some specific cases of macromolecules in the random environment. The problem can be treated by using the Langevin equation along with a memory function, $K(t)$,

$$\frac{dv(t)}{dt} + \int_0^t \zeta(t - \tau) v(\tau) d\tau = f(t)$$  \hspace{1cm} (81)

where the particle velocity $v(t)$ is the dynamic variable and $f(t)$ is a stochastic driving force defined by the coupling of the particle to the surroundings. The simplest form of memory function is the exponential function

$$\zeta(t) = \frac{\zeta}{T} e^{-t/T}$$  \hspace{1cm} (82)

where $T$ is the relaxation time and is related to the degree of particle binding. With the assumption $f(t) = D\delta(t)$, Eq. (82) gives the spectrum of velocity autocorrelations as

$$D(\omega) = D\zeta^2 \left| \frac{\omega}{\omega + \frac{\zeta}{-i\omega T + 1}} \right|^2$$  \hspace{1cm} (83)

Evaluation of Eq. (66) with the spectrum Eq. (83) is shown in detail in Stepišnik (1993, 1994). For the narrow pulse and the finite pulse PGSE experiment, two relatively simple closed form expressions are obtained. Figure 2 shows the fit of evaluated mean-squared displacement to the experimental data (Grinberg et al., 1987).

G. TAILORING THE MODULATED GRADIENT

The analysis presented here has demonstrated that generalized modulated gradients can be considered as a tool for probing the spectrum of velocity correlations (Callaghan and Stepišnik, 1995a). It is also clear that the two-pulse PGSE experiment is not always the ideal vehicle for frequency-domain experiments since the spectrum of the two-pulse PGSE gradient is dominated by the zero-frequency lobe with frequency width of order $1/\Delta$. It is therefore unsuitable for extracting high-frequency information concerning $D(\omega)$. It would be useful to have a gradient modulation sequence with a frequency spectrum that contains a single peak whose frequency can be adjusted in position in order to trace out the frequency dependence of $D(\omega)$.

In Fig. 4 we show three alternative gradient modulation wave forms and their associated spectra. It is clear that the second and third of these wave
FIG. 4. Frequency-domain modulated gradient NMR rf and gradient pulse sequences, showing the (actual) gradient modulation wave form $G(t)$, the time integral of the effective gradient wave form $F(t)$, and the spectrum of $F(f)$. $|F(\omega)|^2$ directly samples the diffusion spectrum. The wave forms and spectra are for (a) double lobe/dc rectangular modulation, (b) single lobe/ac rectangular modulation, and (c) single lobe/ac sawtooth-shaped phase modulation. Note that pulse sequences (b) and (c) sample the diffusion spectrum at a single frequency.
forms, involving a repetitive Carr-Purcell-Meiboom-Gill (CPMG) train of rf pulses, produce the nearly ideal frequency sampling function. In the second of these the gradient is applied as interspersed pulses, while in the third example a steady gradient is used. This last example is easy to implement, but suffers from the disadvantage that the rf pulses will only excite the spins in a slice whose width is determined by the background gradient.

In the first example, the time integral of the effective gradient wave form has a direct current (dc) component that leads to a strong zero-frequency lobe in the associated spectrum, a dramatic change that results from positioning the gradient pulses slightly differently in the CPMG train. The zero-frequency lobe, which is also characteristic of a simple oscillating gradient experiment, hinders the sampling of the spectral density at variable frequencies.

The dominant sampling lobe of the idealized sequence is at \( \omega = 2\pi/T \) and has width of order \( 2\pi/NT \). With \( N \geq 4 \) a reasonably narrow peak can be achieved. In principle it is possible to use such a sequence to probe spectral densities in the frequency range 10 Hz–100 kHz. This becomes possible because rather than using two gradient pulses, for which the attenuation effect disappears as the gradient pulse duration \( \delta \) is shortened, the repetitive pulse train employs an increasing number of gradient pulses in any time interval \( t \), as the frequency is increased and \( T \) is reduced. Thus the frequency domain analysis extends the effective time scale of the PGSE experiments downward to the submillisecond regime.

The exact behavior of the CPMG train of \( \pi \) rf pulses interspaced by \( T/2 \) in the presence of a constant magnetic field gradient is easily described. If the first \( \pi \) pulse follows the excitation at time \( T/4 \), the phase \( F(t) \) time dependence is a sawtooth-shaped function oscillating about zero. From Eq. (64) we find its spectrum to be

\[
|F(\omega, NT)|^2 = (2\gamma|G|)^2 \frac{8 \sin^4(\omega T/8) \sin^2(N\omega T/2)}{\omega^4 \cos^2(\omega T/4)} \tag{84}
\]

Note that the number of \( \pi \) rf pulses must be a multiple of 2, \( 2N \). This spectrum has only one frequency peak at \( \omega = 2\pi/T \) with a width depending on \( N \). Figure 4 shows that even \( N = 4 \) gives a reasonably narrow peak, which can be approximated by

\[
|F(\omega, NT)|^2 = NT(\gamma T|G|)^2 \delta(\omega - 2\pi/T) \tag{85}
\]

The expected echo attenuation factors for the wave forms shown in Fig. 4b and c are, respectively, proportional to

\[
\beta(NT) = NT(\gamma |G| \delta)^2 D \left( \frac{2\pi}{T} \right) \tag{86}
\]
and

$$\beta(NT) = NT(\gamma G |T|)^2 D \left( \frac{2\pi}{T} \right)$$  \hspace{1cm} (87)$$

By varying $T$ it is possible to probe the diffusion spectrum. One convenient approach is to use the pulsed gradient version of the pulse sequence shown in Fig. 4b, employing a fixed (short) value of $\delta$ and measuring the dependence of $\beta$ on the total echo train time $NT$. In order to retain sufficient echo attenuation as $T$ is reduced, it is necessary to compensate by increasing the number of periods $N$. An example of such an application of the CPMG train with finite duration gradient pulses has been demonstrated (Callaghan and Stepišnik, 1995a) for water flowing through a column of close-packed ion-exchange beads. The spectrum of the velocity autocorrelation in this system, shown in Fig. 5, exhibits characteristic features at frequencies corresponding to the angular velocity of the fluid around the beads.

In the pulsed gradient version of the CPMG experiment, the upper limit to the sampling frequency is determined by the rate at which gradient pulses can be switched. No such upper limit applies in the case of the steady gradient version. A further advantage of the CPMG sequence with constant magnetic field gradient is its ability to avoid artifacts due to eddy
currents associated with the rapid switching of gradient pulses. However, it should be noted that shifting the peak to high frequencies by shortening $T$ can severely decrease the spin-echo attenuation. To maintain information in the signal, it is necessary to keep the product $T|G|$ constant, thus implying the availability of very large gradients. Special techniques for the generation of such gradients are discussed later in this chapter.

IV. Self-Diffusion in Restricted Geometries

For investigating the restricted motion of molecules in confined geometries, the time-domain methods are particularly helpful, and the ideal form of gradient modulation is the narrow pulse PGSE experiment. In this section we will consider the signal analysis that is possible given both the $\Delta$- and $q$-dependence of the echo attenuation. First, we consider the $\Delta$-dependence alone, illustrating the analysis with an example from polymer physics. Next we treat the problem of restricted diffusion in porous materials where both $\Delta$ and $q$ analysis will play a role. Using the propagator formalism, it is possible to use this approach to extract information not only about the motions of molecules, but also about the geometry of the boundaries and hence about the pore morphology of the surrounding medium. We will deal with cases for which an explicit formalism is available, namely, the diffusion of the fluid inside a system of confinement of molecules within an enclosing pore and interconnected pores, where molecules suffer local restrictions but are still able to migrate over large distances because of wall permeability or connectedness.

A. Time Dependence of Mean-Squared Displacement

Consider the evaluation of Eq. (47) in the low $q$ limit, that is,

$$E(q, \Delta) = 1 - i 2 \pi q \int dZ \tilde{P}(Z, \Delta) Z - \frac{1}{2} 4 \pi q^2 \int dZ \tilde{P}(Z, \Delta) Z^2$$

(88)

where $Z$ is the projection of $R$ along $q$ and $q$ is $|q|$. For Brownian motion the second term disappears and

$$E(q, \Delta) = 1 - 2 \pi^2 q^2 \langle Z^2(\Delta) \rangle_L$$

(89)

Consequently, the slope of the low $q$ echo attenuation data allows $\langle Z^2(\Delta) \rangle_L$ to be measured directly. This represents the simplest of all possible signal analysis in the case of the narrow gradient pulse PGSE experiment. In the study of hindered and restricted diffusion, such an analysis provides a useful guide to interdependence of length and time.
scales. This is illustrated in Fig. 6, where the mean-squared displacements of spins residing in very large polymer chains are plotted against the observation time $\Delta$. The scaling dependence of $\langle Z^2 \rangle$ upon $\Delta$ provides a useful test of motional constraints as predicted by theory of polymer reptation (Doi and Edwards, 1986).

B. Restricted Diffusion in a Confining Pore

We now turn our attention to the diffusion of molecules inside a completely enclosing pore. We shall see that signal analysis based on both the $q$- and $\Delta$-dependence of the echo will prove particularly illuminating. A number of exact solutions for the propagator are available by solving Fick's law using the standard eigenmode expansion (Arfken, 1970)

$$P(r',t| r, 0) = \sum_{n=0}^{\infty} \exp(-\lambda_n t) u_n(r) u_n^*(r')$$

where the $u_n(r')$ are an orthonormal set of solutions to the Helmholtz equation parameterized by the eigenvalue $\lambda_n$. Thus constructed $P$ satisfies the initial condition Eq. (3), and the eigenvalues depend on the general
boundary condition

$$D\hat{n} \cdot \nabla P + MP = 0$$

(91)

where $\hat{n}$ is the outward surface normal. For perfectly reflecting walls, $M = 0$, while for perfectly absorbing walls, $M$ is infinite and the boundary condition reduces to $P = 0$.

The special cases of plane parallel pores, cylindrical pores, and spherical pores have been solved exactly and we quote only the echo attenuation results here. The pore geometries and applied gradient directions are shown in Fig. 7. Readers seeking more information about these solutions.

**FIG. 7.** Echo attenuation $E(q, \Delta)$ for spins trapped between (a) parallel plane barriers separated by $2a$ in which the gradient is applied normal to the planes, (b) cylindrical pores of radius $a$ in which the gradient is applied across a diameter, and (c) spherical pores of radius $a$. In each case the walls are perfectly reflecting ($Ma/D = 0$) and three successive values of $\Delta$ are $0.5a^2/D$, $1.0a^2/D$, and $2.0a^2/D$. Note that the first diffraction minimum occurs near $qa = 0.5, 0.61$, and $0.73$, respectively. (d) The set of theoretical curves for $\Delta = 2.0a^2/D$, in which the wall relaxation is increased as $Ma/D = 0, 0.5, 1.0$, and $2.0$. Note that the diffraction minimum shifts to higher values of $q$ as the relaxation increases.
should consult other references (Snaar and van As, 1993; Coy and Callaghan, 1994b; Mitra and Sen, 1992; Callaghan, 1995).

1. Parallel Plane Pore

This is a one-dimensional problem in which the gradient is applied along the \(z\)-direction normal to a pair of bounding planes and these relaxing planes are separated by a distance \(2a\) and placed at \(z = a\):

\[
E(q, \Delta) = \sum_{n=0}^{\infty} \exp\left( -\frac{\xi_n^2 D \Delta}{a^2} \right) 2 \left( 1 + \frac{\sin(2 \xi_n)}{2 \xi_n} \right) \frac{\left( (2 \pi qa) \sin(2 \pi qa) \cos(\xi_n) - \xi_n \cos(2 \pi qa) \sin(\xi_n) \right)^2}{\left( (2 \pi qa)^2 - \xi_n^2 \right)^2} + \sum_{m=0}^{\infty} \exp\left( -\frac{\zeta_m^2 D \Delta}{a^2} \right) 2 \left( 1 - \frac{\sin(2 \zeta_m)}{2 \zeta_m} \right) \frac{\left( (2 \pi qa) \cos(2 \pi qa) \sin(\zeta_m) - \zeta_m \sin(2 \pi qa) \cos(\zeta_m) \right)^2}{\left( (2 \pi qa)^2 - \zeta_m^2 \right)^2}
\]

where the eigenvalues \(\xi_n\) and \(\zeta_m\) are determined by the equations

\[
\xi_n \tan(\xi_n) = \frac{Ma}{D}
\]

\[
\zeta_m \cot(\zeta_m) = -\frac{Ma}{D}
\]

2. Cylindrical Pore

This is a two-dimensional problem handled in cylindrical polar coordinates in which the longitudinal \(z\) axis is a symmetry axis for the system. The relevant coordinates are \((r, \theta, z)\) and the gradient is applied along the polar axis direction (i.e., across a diameter). The relaxing boundary is at a radial distance \(r = a\) from the cylinder center:

\[
E(q, \Delta) = \sum_{k=0}^{\infty} 4 \exp\left( -\frac{\beta_{2k} D \Delta}{a^2} \right) \frac{\beta_{2k}}{(Ma/D)^2 + \beta_{2k}^2} \times \frac{\left( (2 \pi qa) J_0(2 \pi qa) + (Ma/D) J_0(2 \pi qa) \right)^2}{\left[ (2 \pi qa)^2 - \beta_{2k}^2 \right]^2}
\]

where \(J_0\) is the Bessel function of order zero.
\[ + \sum_{n,k} 8 \exp \left[ - \frac{\beta_{nk}^2 \Delta}{a^2} \right] \frac{\beta_{nk}^2}{\left( (Ma/D)^2 + \beta_{nk}^2 \right)} \]
\[ \times \frac{\left( (2\pi qa) J_n'(2\pi qa) + (Ma/D) J_n(2\pi qa) \right)^2}{\left( (2\pi qa)^2 - \beta_{nk}^2 \right)^2} \]

where the \( J_n \) are standard (cylindrical) Bessel functions while the eigenvalues \( \beta_{nk} \) are determined by the equation
\[
\frac{\beta_{nk} J_n'(\beta_{nk})}{J_n(\beta_{nk})} = -\frac{Ma}{D} \quad (95)
\]

3. Spherical Pore

For the spherical case the gradient of magnitude \( q \) is applied along the polar axis of the spherical polar coordinate frame. The boundary is at a radial distance \( r = a \) from the sphere center:
\[
E(q, \Delta) = \sum_{n,k} 6 \exp \left( - \frac{\alpha_{nk}^2 D \Delta}{a^2} \right) \frac{(2n + 1) \alpha_{nk}^2}{\left( (Ma/D - 1/2)^2 + \alpha_{nk}^2 - (n + 1/2)^2 \right)} \]
\[ \times \frac{\left( (2\pi qa) j_n'(2\pi qa) + (Ma/D) j_n(2\pi qa) \right)^2}{\left( (2\pi qa)^2 - \alpha_{nk}^2 \right)^2} \quad (96)
\]

where the \( j_n \) are spherical Bessel functions. The eigenvalues are determined by
\[
\frac{j_n'(\alpha_{nk})}{j_n(\alpha_{nk})} = -\frac{Ma}{D} \quad (97)
\]

Examples of the echo attenuation dependence on \( q \) and \( \Delta \) are shown in Fig. 7. The characteristic minima and maxima exhibited by the curves arise quite naturally from a diffraction formalism.

C. THE DIFFUSIVE DIFFRACTION ANALOGY

We will find it convenient to consider for the moment the special case of perfectly reflecting walls. In the long time-scale limit \( \Delta \gg a^2/D \), the average propagator for fully restricted diffusion has a simple relationship to the pore geometry. This requirement on \( \Delta \), also known as the "pore equilibration" condition, implies that the time is sufficiently long that most molecules have collided with the walls. Under this condition the conditional probabilities are independent of starting position so that \( P(r', t | r, 0) \) reduces to \( \rho(r') \), the pore molecular density function.
In consequence, the averaged propagator \( \overline{P(R, t)} \) becomes an auto-correlation function of \( \rho(r') \),

\[
\overline{P(R, t)} = \int \rho(r + R) \rho(r) \, dr
\]  

(98)

and from the Wiener–Khintchine theorem, the echo attenuation function reduces to the Fourier power spectrum of \( \rho(r') \),

\[
E(q, \infty) = |S(q)|^2
\]  

(99)

\( S(q) \) is analogous to the signal \( S(k) \) measured in conventional NMR imaging (Mansfield and Morris, 1982). Note, however, that it is not the phase-sensitive spatial spectrum of the pore that is being measured, but rather its power spectrum. Hence, unlike conventional imaging the data cannot be inverse Fourier transformed in order to obtain a direct image of the pore. In fact, \( |S(q)|^2 \) is directly analogous to the diffraction pattern of the pore (Callaghan, 1991; Callaghan et al., 1990; Coy and Callaghan, 1994b; Cory and Garroway, 1990). For a rectangular barrier pore with reflecting walls, Eq. (99) gives the diffraction pattern of a single slit, namely,

\[
E(q, \infty) = |\text{sinc}(\pi qa)|^2
\]  

(100)

In a similar manner, Eq. (99) returns the diffraction patterns for the cylinder and sphere. This latter case is given by

\[
E(q, \infty) = \left| \frac{3[(2\pi qa)\cos(2\pi qa) - \sin(2\pi qa)]}{(2\pi qa)^2} \right|^2
\]  

(101)

The progression to the long time limit is clearly shown for the planar, cylindrical, and spherical geometries in Fig. 7a–c. The planar theory has been verified experimentally using samples comprising pentane trapped within a rectangular cross section microcapillary (Coy and Callaghan, 1994b).

As a consequence of this analogy, the PGSE NMR experiment for restricted diffusion in the long time limit is often termed diffusive diffraction (Callaghan, 1991). In applying the diffusive diffraction picture to interpret PGSE NMR experiments it is important to address some issues concerning the underlying approximations and assumptions. First, there is the issue of just how long \( D \) needs to be for diffraction effects to be clearly observed. Remarkably, a high degree of pore equilibration, and hence strong diffraction effects, is apparent even on intermediate time scales of order \( a^2/\Delta \), a point that is borne out by computer simulations and that is clearly demonstrated in Fig. 7, where \( \Delta = a^2/D \) and in which a diffraction minimum is clearly visible.
The second assumption concerns the use of the narrow gradient pulse approximation. Using a simple but elegant argument, Mitra and Halperin (1995) have shown that even when significant molecular motion occurs during the gradient pulse, it is still possible to employ a propagator formalism. The difference is that the propagator now refers to the displacement from the mean position of the molecules during the first pulse to the mean position of the molecules during the second pulse. It is easy to see that the impact of this is that molecules trapped within pores and starting very close to a wall at the application of the first gradient pulse will, because of wall collisions, appear to originate a little further away from the walls. A corresponding remark may be made about molecules terminating near a wall. Hence the full pore dimensions are not apparent in the finite pulse experiment and the diffraction pattern shows the effect of this reduction (Coy and Callaghan, 1994b).

An ingenious approach to the treatment of finite gradient pulse width effects has been provided by Wang et al. (1995). They demonstrate that it is possible to approximate the temporal behavior of any gradient pulse by a sum of impulses, each being in the narrow gradient pulse limit. By this means one can derive an analytical solution to the echo attenuation.

Finally, we need to consider the effect of wall relaxation. Not surprisingly, this effect is similar to the "narrowing" action of finite pulse smearing and results in a shift to higher $q$ of the diffraction minima, as shown in Fig. 7d. This can be realized by acknowledging the fact that molecules in the vicinity of the walls are more likely to suffer loss of magnetization. It is apparent that the shift effect is weak under realistic experimental conditions. However, the relaxation problem is not generally serious provided that the overall signal attenuation due to relaxation is not severe. Provided that the observation time is greater than or on the order of $a^2/D$, as would be required for diffraction effects to be observed, any relaxation effect sufficient to strongly shift the minimum would also drastically attenuate the signal amplitude at $q = 0$. For example, the apparent width reduction for the sphere is less than 10 percent provided that the zero gradient signal is not attenuated below 0.01% of its unrelaxed value. Equivalent (10% shift) relaxation amplitudes for the cylindrical and planar pores are 1 and 10%, respectively.

D. SELF-DIFFUSION IN INTERCONNECTED GEOMETRIES

We now address the case of diffusion in structures consisting of an array of confining pores with interconnecting channels that permit migration from pore to pore. The structure will be described by a superposition of $N$
local \((i)\) pores with density \(\rho_{ji}(r - r_i)\) (Callaghan, 1991, Callaghan et al., 1990, 1991, 1992) as shown schematically in Fig. 8.

For a periodic three-dimensional porous medium it is possible to apply Eqs. (90) and (91) to the study of interconnected structures using eigenmodes based on the Bloch–Floquet form (Bergman and Dunn, 1995; Dunn and Bergman, 1995). However this approach does not lend itself to the treatment of disordered media. A more general approach, but one which involves some simplifying assumptions, is the pore-hopping model of Callaghan et al. (1992). This model is as follows.

We will assume that the pore size can be characterized by a dimension \(a\) while the interpore spacing is on the order of \(b\). Furthermore, we assume a local self-diffusion coefficient \(D\) within the pore while the long range migration from pore to pore is characterized by a (generally lower) self-diffusion coefficient \(D_p\). The problem can be handled by assuming that once a molecule has migrated to pore \(j\), it quickly assumes an equal probability to be anywhere within that pore (Callaghan et al., 1992). This form of the pore equilibration requires \(a^2/D \ll b^2/D_p\). Hence the conditional probability for molecules originating in compartment \(i\) may be written

\[
P_i(r', \Delta) = \sum_{j=1}^{N} \rho(j, \Delta | i, 0) \rho(r' - r_i) \tag{102}
\]

where \(\rho(j, \Delta | i, 0)\) gives the conditional probability that a particle originat-
ing in pore i will diffuse to pore j in the time $\Delta$. This probability will be
determined by the rate of pore permeation.

It can then be shown that echo attenuation comprises the product of a
mean local pore factor and a factor $F(q, \Delta)$ that is sensitive to details of
the motion between pores, that is,

$$E(q, \Delta) = \overline{|S_0(q)|^2} F(q, \Delta)$$  \hspace{1cm} (103)

In this equation $|S_0(q)|^2$ plays the role of the form factor in diffraction
theory, while $F(q, \Delta)$ is the “reciprocal lattice” diffraction pattern. The
factor $F(q, \Delta)$ is the Fourier transform ($\mathcal{F}$) of the average propagator
parallel to the gradient direction, and may be evaluated by considering an
infinitesimal time duration $\tau$ over which molecules will have infinitesimal
but finite probability $w$ of hopping to the nearest neighbor pore shell
(Callaghan et al., 1991), but vanishingly small probability, on the order of
$w^2$, of hopping to the next neighbor shell. The finite time result then
follows by considering $M$ successive, independent, identically distributed
random hops. Clearly $C(Z, M \tau)$ will be a convolution of $M$ such probability
density functions, leading to

$$\mathcal{F}[(C(Z, \tau) \otimes C(Z, \tau) \otimes \cdots) M \text{ times}] = [\mathcal{F}(C(Z, \tau))]^M$$ \hspace{1cm} (104)

and, therefore,

$$F(q, M \tau) = [F(q, \tau)]^M$$ \hspace{1cm} (105)

For example, for a regular one-dimensional lattice it is simple to show that

$$E(q, \Delta) = |S_0(q)|^2 \left[ 1 - 2w \sin^2(\pi qb) \right]^M$$ \hspace{1cm} (106)

The parameter $w$ may be related to the permeability diffusion coefficient
$D_p$ via the low $q$ limit of Eq. (106) noting that $E(q, \Delta)$ is the ensemble
average, $\langle \exp(i2\pi qZ) \rangle$, and $S_0(q) \to 1$ as $q \to 0$. By equating the
mean-squared displacement with $D_p/2\Delta$, one obtains

$$w = \frac{2D_p \Delta}{Mb^2}$$ \hspace{1cm} (107)

Taking the limit $M \to \infty, t \to 0$, such that $Mt = \Delta$ remains fixed, the final
result is

$$E(q\Delta) = |S_0(q)|^2 \exp \left( -\frac{4D_p \Delta}{b^2} \sin^2(\pi qb) \right)$$ \hspace{1cm} (108)

Equation (108) predicts coherence peaks (reciprocal lattice positions) in
the echo attenuation when $qb$ is integer.

A more realistic porous medium structure is one that occupies three
dimensions and in which the pore lattice is without orientational order and
has a degree of variation in the interpor e spacing $b$. For such a lattice the $Z$-displacements of the successive hops are uniformly distributed between $-b$ and $b$ and the probability density function is

$$C(Z, t) = (1 - w) \delta(Z) + \frac{w}{2b} [H(Z + b) - H(Z - b)]$$ (109)

where $H$ represents the Heaviside step function. Allowing for variation in pore spacing is quite tricky here since $w$ clearly depends upon $b$. Given a standard deviation $\xi$ such that $\xi \ll b$, it is a reasonable first approximation to assume that $w$ is constant. In this case,

$$E(q, \Delta) = |S_\delta(q)|^2 \exp\left[-\left(\frac{6D_{eff}\Delta}{b^2 + 3\xi^2}\right)\right] \times \left(1 - \exp(-2\pi^2 q^2 \xi^2)\right) \left(\frac{\sin(2\pi qb)}{2\pi qb}\right)$$ (110)

Diffusive diffraction experiments in interconnected porous structures have been carried out in close-packed polymer sphere arrays (Callaghan et al., 1992; Coy and Callaghan, 1994a) as well as in emulsions (Soderman and Stilbs, 1994). An example is shown in Fig. 9.

![Graph showing echo attenuation function $E(q, \Delta)$ as a function of $q$ for a close-packed suspension of 9.870 $\mu$m polystyrene spheres surrounded by water. The times $\Delta$ are 10 ms (circles), 20 ms (solid circles), 20 ms (squares), and 40 ms (solid squares). The solid lines represent fits using Eq. (110) for which the parameters are $a = 3.0$ $\mu$m, $b = 10.7$ $\mu$m, $\xi = 0.1$ $\mu$m, and $D_{eff} = 2.4 \times 10^{-6}$ $m^2/s$. [Reproduced by permission from Coy and Callaghan, 1994.]

Fig. 9. Echo attenuation function $E(q, \Delta)$ as a function of $q$ for a close-packed suspension of 9.870 $\mu$m polystyrene spheres surrounded by water. The times $\Delta$ are 10 ms (circles), 20 ms (solid circles), 20 ms (squares), and 40 ms (solid squares). The solid lines represent fits using Eq. (110) for which the parameters are $a = 3.0$ $\mu$m, $b = 10.7$ $\mu$m, $\xi = 0.1$ $\mu$m, and $D_{eff} = 2.4 \times 10^{-6}$ $m^2/s$. [Reproduced by permission from Coy and Callaghan, 1994.]
It should be noted that the pore hopping treatment described here, while illuminating, has a number of underlying assumptions, for example, pore equilibration and equal hopping probabilities, that may not apply in all cases. An alternative theoretical approach that involves different assumptions has been developed by Mitra et al. (1992). Their model uses the device of a time-dependent diffusion coefficient to obtain a phenomenological propagator in a connected pore space of arbitrary shape. The methodology is particular helpful in dealing with very open structures for which the pore equilibration assumption breaks down.

V. PGSE and Multidimensional NMR

In the classic two-dimensional NMR experiment, the pulse train consists of the sequence "preparation-evolution-mixing-detection." We can apply this picture to the pulse trains of the PGSE NMR experiment and similarly identify opportunities for multidimensional NMR.

The signal represented by Eq. (41) corresponds to the signal induced at time $t + t'$ following a spin echo formed at time $t$. Here $t'$ is the detection period where $t$ is an evolution period. Clearly the signal amplitude is sensitive to a number of terms including the initial thermal equilibrium magnetization ($A_0$), the attenuation of phase shift factor ($\exp(i\theta(r))$) associated with motion in the presence of applied magnetic field gradients, the state of the spin system after preparation ($M_i$), and the sensitivity of the rf coil during detection. In a single acquisition of the signal following the echo, the relative contributions of these factors determining signal amplitude cannot be unraveled. However, where it is possible to modulate each of these factors independently, such an unraveling process becomes possible. This is the basis of the multidimensional analysis inherent in two- or three-dimensional spectroscopy.

As a simple example, consider two identifiable spectral domains inherent in Eq. (41). In particular there is a spectrum associated with $t'$ such that the Fourier transform of the signal with respect to $t'$ yields a single spectral "line" (or in mathematical language, a Dirac delta function in $\omega$-space) centered at frequency $\omega_0$. In other words, the modulation inherent in the oscillation $\exp(i\omega_0 t')$ permits an "unraveling" of this feature of the data by using Fourier inversion. Clearly there is, in addition, a spectral domain associated with the ensemble-averaged phase factor ($\exp(i\theta(t))$). This term is modulated, for example, by varying the evolution time $t$ prior to signal acquisition or by stepping the amplitude of the magnitude field gradients responsible for the phase shift. Provided that this domain of modulation is analyzed to yield motional parameters (for example, the molecular diffusion coefficients or velocities), then a second "spectral"
domain is accessible. By this type of two-dimensional analysis, it is possible

to separate the signal so that the remaining unresolved amplitude (i.e.,

that arising from \( A_0 \langle M' \rangle \)) is plotted in a planar representation against

the two variables \( \omega_0 \) and \( D \) (or \( \nu \)).

Other multidimensional analyses are possible. For example, by varying

the preparation such that \( M' \) is modulated, it is possible to encode the

signal for other properties of the spin system. These might include ampli-

tude or phase modulation terms due to motion prior to the evolution

represented by \( \langle \exp(i \theta(t)) \rangle \) or amplitude and phase modulation associ-

ated with positions of the spins. A description of each of these examples

will be given in the following sections. In each case we will follow the

usual convention (Ernst et al., 1987) and use the variables \( t_1, t_2, \) and \( t_3 \)

to represent the modulation or acquisition domains of the various

dimensions.

A. DIFFUSION- AND VELOCITY-ORDERED SPECTROSCOPY

The two-dimensional separation of NMR signals by Larmor frequency

\( \omega_0 \) and diffusion coefficient \( D \) or velocity \( \nu \) has been proposed and
demonstrated by Johnson and co-workers (Morris and Johnson, 1992).

Their ingenious experiment is a simple adaption of PGSE NMR in which

the high resolution NMR spectrum is obtained under the influence of a

precursor PGSE sequence in which the gradient is stepped successively to

higher values. The relevant pulse sequence is shown in Fig. 10. In order to

gain undistorted spectra at hertz resolution, it is necessary to allow the

Fig. 10. Radiofrequency and gradient pulse sequence for diffusion-ordered spectroscopy (DOSY) owing to Morris and Johnson [1992] in which a PGSE pulse pair (\( G_1 \)) represents the first \( (t_1) \) domain and the acquisition time provides the second \( (t_2) \) domain. Note the storage period \( T_e \) which allows for eddy current decay prior to data collection.
complete decay of eddy currents from the gradient pulses. This is achieved by storing magnetization along the $z$ axis for later recall once a suitable eddy current decay period has elapsed. Subsequent to Fourier transformation with respect to $t'$ (i.e., $t_z$ domain), each frequency component in the NMR spectrum is then analyzed (i.e., with respect to the $t_d$ domain) to yield the motional parameter. In the case of diffusion separation the experiment is labeled DOSY (for diffusion-ordered spectroscopy) and MOSY (for electrophoretic mobility).

Where molecules translate with velocity $v$ in the presence of a PGSE gradient pulse pair, that velocity information results in a simple phase modulation in which the exponent is proportional both to the gradient amplitude $g$ and the velocity component $v$ along the gradient axis, that is, \[ \langle \exp(i\theta_1(t)) \rangle = \exp(-i2\pi qvt). \] This modulation permits signal analysis by Fourier inversion in which transformation with respect to $q$ yields the velocity spectrum directly.

For diffusion analysis, the situation is a little more complicated. Instead of oscillatory modulation, the diffusion leads to attenuation of the form given by Stejskal and Tanner (1965). In principle, Laplace inversion should yield the spectrum of diffusion coefficients. However, the lack of orthogonality between components with different decay parameter $\lambda_n$ in the kernel $\exp(-\lambda_n t)$ results in a nonunique set of solutions. This type of signal analysis is discussed in great detail by Provencher (1982). We simply note here that a number of approaches are available, most notably the NNLS and LDP algorithms of Lawson and Hanson (1974) and the CONTIN package of Provencher (1982). An example of two-dimensional spectra involving diffusion analysis is shown in Fig. 11. This type of spectral separation proves extremely valuable in identifying different molecular components in complex mixtures.

In the characterization of multidimensional spectroscopy by Ernst et al. (1987), the different classes may be termed separation, correlation and exchange respectively. The DOSY and MOSY experiments represent a type of separation spectroscopy in which the independent chemical shift and mobility information can be independently displayed. In the next section we describe an example involving exchange spectroscopy.

B. VELOCITY EXCHANGE SPECTROSCOPY

In Eq. (41) the evolution segment of the pulse sequence clearly results in the modulation term $\langle \exp(i\theta_1(t)) \rangle$, which is sensitive to the domain of the applied gradient $g(t)$. Inherent in this equation is the understanding that the state of $M_i$ is sensitive to a preparation phase of the pulse sequence.
FIG. 11. Two-dimensional DOSY spectrum of a sample containing 1,3,5-triisopropylbenzene (TIPB) and mixed micelles in D$_2$O. SDS = sodium dodecylsulfate; HOD = partially deuterated water. [Reproduced by permission from Morris and Johnson, 1993.]

Suppose that the preparation contains a segment of pulse sequence similar to that used for the evolution due to motion under the gradient $g$, but that this segment is applied at some earlier time. We could then speak of two independent gradients $g_1$ ($t_1$ dimension) and $g_2$ ($t_2$ dimension). A simple example showing the use of narrow pulsed gradients is shown in Fig. 12. The particular sequence is called VEXSY for velocity exchange spectroscopy (Callaghan and Manz, 1994). It enables one to analyze velocity fields by taking advantage of characteristic changes over a fixed time interval $\tau_m$.

Because the sequence utilizes only the preparation and evolution periods for motion encoding, the detection phase remains for the encoding of chemical shift information. Hence it is possible to perform this spectroscopy with chemical shift selectivity. Note that the sequence shown, while useful for analysis purposes, is a little naive for many practical applications since it makes no allowance for the effects of inhomogeneous local fields, which can lead to incomplete echo refocusing when the fluid motion causes spins to move to different field regions during the delay time $\tau_m$. The best way to protect the spins from the varying background...
ANALYSIS OF MOTION USING MAGNETIC FIELDS

FIG. 12. Radiofrequency and gradient pulse sequence for velocity exchange spectroscopy (VEXSY) in which successive PGSE pulse pairs \((G_1, G_2)\), separated by a delay time \(\tau_m\), are applied. For an unambiguous correlation, \(G_1\) and \(G_2\) are required to be collinear. Note the two orthogonal Fourier domains represented (schematically) by \(t_1\) and \(t_2\). Fourier transformation with respect to the acquisition time leads to a third spectral dimension.

Field is to use a closely spaced rf pulse train to continually refocus the transverse magnetization.

The pulse sequence shown in Fig. 12 leads to a very simple form of analysis using the language of q space. Following the first 90° pulse, the transverse magnetization is phase encoded using two pairs of gradient pulses represented by encoding “wave vector” \(q_1\), and at a later time delayed by \(\tau_m\), the magnetization is encoded again by a second pair with wave vector \(q_2\). Generally we will want to use the same gradient direction for these pulse pairs; otherwise an ambiguity arises. For example, the encoding from the two pairs of pulses could lead to the same result for a constant oblique velocity and a velocity that changed in direction. Consequently we need only consider motion in the fixed direction parallel to the gradients. The exponents arising from the separate preparation and evolution modulations are simply \(\exp(i2\pi q_1 Z_1)\) and \(\exp(i2\pi q_2 Z_2)\), where \(Z_1\) and \(Z_2\) are the distances moved by a spin over the well-defined time interval \(\Delta\), which are themselves separated by a further time delay \(\tau_m\)—the equivalent of the “mixing” time in our experiment.

The PGSE gradient pulse pairs are stepped so as to phase-encode the spins for molecular translational motion. Because both pairs of \(q\)-pulses are applied in the same direction, a spin isochromat corresponding to a set
of molecules traveling at constant velocity will have identical \( Z_1 \) and \( Z_2 \) displacements, thus contributing to points on the diagonal in \((Z_1, Z_2)\) space. On the other hand, a migration of spins from one region of the displacement spectrum to another over the time \( \tau_m \) will lead to cross-peaks. Suppose that the probability of migrating in this fashion is given by \( P(Z_2, \tau_m \mid Z_1, \Delta) \). Then the transverse magnetization at the formation of the second echo is given by

\[
E(q_1, q_2, \tau_m) = \iint \bar{P}(Z_1, \Delta) P(Z_2, \tau_m \mid Z_1, \Delta) \\
\times \exp[i2\pi(q_1 Z_1 + q_2 Z_2)] dZ_1 dZ_2
\]  

(111)

Inverse Fourier transformation with respect to \((q_1, q_2)\) returns the two-dimensional Fourier spectrum

\[
S(Z_1, Z_2) = \bar{P}(Z_1, \Delta) P(Z_2, \tau_m \mid Z_1, \Delta)
\]  

(112)

Several special cases of Eq.(112) are of interest:

1. **Stationary Velocity Distribution**
   Here \( P(Z_2, \tau_m \mid Z_1, \Delta) \) is the Dirac delta function \( \delta(Z_1 - Z_2) \) and the two-dimensional spectrum is identically

\[
S(Z_1, Z_2) = \bar{P}(Z_1, \Delta) \delta(Z_1 - Z_2)
\]  

(113)

This corresponds to a purely diagonal spectrum with distribution \( \langle P(Z_1, \Delta) \rangle \) along each orthogonal axis.

2. **Unrestricted Brownian Motion**
   Here \( Z_1 \) and \( Z_2 \) are entirely uncorrelated and both \( \bar{P}(Z_1, \Delta) \) and \( P(Z_2, \tau_m \mid Z_1, \Delta) \) are independent Gaussians. Thus

\[
S(Z_1, Z_2) = (4\pi D\Delta)^{-1} \exp[-(Z_1^2 + Z_2^2)/4D\Delta]
\]  

(114)

3. **Rotational Flow in a Narrow Annulus**
   Consider the case where a circular annulus of fluid is undergoing circular motion at radius \( r \) with angular speed \( \omega \). The two-dimensional VEXSY spectrum has the character of a Lissajous figure:

\[
S_\omega(Z_1, Z_2) = (2\pi \omega R)^{-1} [1 - Z_1^2/(\Delta^2(\omega^2 r^2))]^{-1/2}
\times \left[ (1/2) \delta(Z_2 \Delta^{-1} - (Z_1 \Delta^{-1} \cos(\omega \tau_m)) \right.
\left.+ (\omega^2 r^2 - Z_1^2 \Delta^{-2})^{1/2} \sin(\omega \tau_m)) \right]
\]
\[+(1/2) \delta \left[ Z_2 \Delta^{-1} - \left(Z_1 \Delta^{-1} \cos(\omega \tau_m)\right) - \left(\omega^2 r^2 - Z_2^2 \Delta^{-2}\right)^{1/2} \sin(\omega \tau_m)\right]\] 

(115)

An example of such a spectrum is shown in Fig. 13. It was obtained using a Couette cell comprising a 10-mm-o.d. (8.9-mm-i.d.) NMR tube with a concentric 5-mm NMR tube connected to an external shaft driven by a variable speed motor. The space between the cylinders was filled with water containing a small amount (0.5%) of high molar mass polyethylene oxide, which had the effect of increasing the viscosity and thus ensuring laminar flow.

Note that the VEXSY experiment allows a third \( t_z \) spectral dimension and may therefore be performed with chemical shift selectivity.

C. VELOCITY AND DIFFUSION IMAGING

It is easy to image a wide variety of multidimensional spectroscopies arising from the signal scheme represented by Eq. (41). We will consider one more such scheme, in this case a three-dimensional separation in which one dimension is the spectrum of translational motion while the other two represent the domain of nuclear spin positions. The position domain is associated with conventional NMR imaging in which position encoding occurs via a reciprocal space \((k\text{-space})\) in which both phase modulation and frequency modulation may be employed. It is beyond the scope of this chapter to review this subject; many other references provide descriptions in greater detail (Xia and Callaghan, 1991; Moran, 1982; Bryant et al., 1984; Redpath et al. 1984; Altobelli et al., 1986; Callaghan et al., 1988; Caprihan and Fukushima, 1990; and Callaghan and Xia, 1991).

Figure 14 shows a pulse sequence in which the PGSE method is amalgamated with NMR imaging so that the signal acquired is effectively modulated both in \(k\) and \(q\) space.

Clearly slice selection and phase encoding form part of the preparation segment of the sequence, evolution occurs under the influence of the PGSE pulse pair, and detection occurs in the presence of the read gradient. Given excitation of a single slice, the number of dimensions is reduced to two in \(k\) space and one in \(q\) space. We may combine all these influences to write

\[S(k, q) = \int \rho(r) E(q, \Delta) \exp(i2\pi k \cdot r) \, dr \tag{116}\]

\[= \int \rho(r) \int \bar{F}(Z, \Delta) \exp[i2\pi qZ] \, dZ \exp(i2\pi k \cdot r) \, dr \tag{117}\]
FIG. 13. Succession of two-dimensional VEXSY images for cylindrical Couette flow where $r_w$ corresponds to (a) 0.15, (b) 0.50, (c) 1.00, and (d) 2.00 rotation cycles for the central rotating cylinder. The theoretical image is shown on the left with the corresponding experimental data on the right. The full width of the image corresponds to 33 cm s$^{-1}$. [Reproduced by permission from Callaghan and Manz, 1993.]
ANALYSIS OF MOTION USING MAGNETIC FIELDS

FIG. 14. Radiofrequency and gradient pulse sequence for velocity and diffusion imaging in which the molecular motion is measured in the domain of two spatial dimensions \((x, y)\) of a slice selected normal to the \(z\) axis. Note that the PGSE pulse pair \((g)\) provides the third dimension—that of motion—while the phase encode \((G_x)\) and read gradients \((G_y)\) provide the first and second spatial dimensions.

where implicitly \(\overline{P}(Z, \Delta)\) is the average propagator at each pixel \(r\) of the image. Double inverse Fourier transformation of \(S(k, q)\) with respect to both \(k\) and \(q\) returns \(\rho(r)\overline{P}(Z, \Delta)\). By normalizing this function with the image density \(\rho(r)\) acquired under zero PGSE gradient, one reconstructs \(\overline{P}(Z, \Delta)\) for each pixel of the image.

Generally, it is conventional to apply the \(q\) gradient in a single direction in any given experiment, stepping its value from zero to some maximum number \(n\) of order 10-20 steps. In that sense the method is similar in practice to multislice imaging. For each step (or “\(q\) slice”) a complex image is reconstructed. This set of images may be processed in the remaining third dimension by zero-filling from \(n\) to \(N\) (so as to improve digital resolution), following which the modulated image signal in each pixel is Fourier transformed along the \(q\) direction to return \(P(Z, \Delta)\) for that pixel.

When one has obtained the local propagator for each pixel, the details of the local motion can be easily calculated. For example, the width of \(P(Z, \Delta)\) is determined by the root mean square Brownian motion \((2D\Delta)^{1/2}\), while the displacement of \(P(Z, \Delta)\) along the \(z\)-axis is determined by the
flow displacement $\nu \Delta t$, where $\nu$ is the local molecular velocity. Using this approach, simple algorithms may be implemented so that maps of $D(r)$ and $\nu(r)$ may be constructed. While flow imaging has been widely used in medicine for many years, this type of multidimensional velocity and diffusing imaging has been used to study fluid transport in plants and is proving of increasing importance in materials science investigations, in particular for studying the molecular basis of complex rheological properties in non-Newtonian fluids.

A simple example of velocity imaging is shown in Fig. 15. The figure

![Graphs showing velocity profiles across a diametral slice obtained in the rotating Couette cell for (a) water and (b) a solution of 5% polyethylene oxide in water, at rotation speed ranging from 0.60 to 10 rad s$^{-1}$. Note that the left- and right-hand sides of the annulus yield similar profiles but with oppositely signed velocities. [Reproduced by permission from Rofe et al., 1994.]](image)
shows a velocity map obtained from a Couette shear cell in which the signal arises from protons in pure water and a polyethylene oxide solution placed in the annular region between an inner rotating cylinder and an outer stationary wall. Other studies involving capillary and Couette geometry include investigations of other random coil polymer solutions, solutions of rigid rod polymers, and solutions of surfactants. Combined with other spectral parameters related to relaxation time of molecular order, this method has the potential to provide a vital link between molecular and mechanical properties of soft, complex materials.

VI. Self-Diffusion with a Strong Inhomogeneous Magnetic Field

One of the fundamental limits faced by the pulsed gradient spin-echo method concerns of the lower limit to spatial resolution. This limit depends both on the maximum available magnetic field gradient and the degree to which the gradient pulse amplitudes can be accurately matched. Having achieved this coil strength, the experimenter is then faced with the need to match the gradient pulse areas in each pulse pair by a degree sufficient to avoid random phase fluctuations that would lead to echo amplitude degradation during the process of signal averaging. To measure a 100-nm displacement in a 5-mm sample requires obtaining a matching better than $2 \times 10^{-3}$.

One solution to these difficulties, suggested and demonstrated by Kimmich and co-workers (Kimmich et al., 1991; Kimmich and Fisher, 1994), is to utilize the very large steady gradients available in the fringe field of a superconducting magnet and to simulate the effect of pulsing by means of the stimulated echo sequence. Because the steady gradient produces phase evolution only for magnetization placed in the transverse plane, it effectively encodes only during the intervals of phase evolution between the first pair of 90° pulses and subsequent to the third 90° pulse when the magnetization is recalled from storage along the z axis. This method has enabled spin-echo diffusion measurements with gradient strengths in excess of 50 T m$^{-1}$.

With very slow molecular migrations ($\leq 10^{-14}$ m$^2$ s$^{-1}$) when one needs to apply extremely strong magnetic field gradients, it is possible that the weak inhomogeneous field condition will break down. Another situation in which the inhomogeneous field can be strong concerns the measurement of diffusion using Earth's field NMR (Stepániík et al., 1994). Here the necessary spin dephasing is brought about by a nonuniform magnetic field that is comparable to or larger than the weak, homogeneous Earth's field. In both these examples the inhomogeneous component of the field is of the same order of magnitude as the homogeneous one and a different
treatment is called for. In this section we show how the signal should be analyzed under the influence of such a strong inhomogeneous field.

Large inhomogeneous fields imply deviations from a simple linear relationship between the intensity of the magnetic field and one space coordinate (the direction of the field gradient in the conventional magnetic field gradient representation). This leads to a nonuniform spin-echo attenuation. In the strong inhomogeneous magnetic field, all components are relevant. By taking into account Maxwell's equations for the magnetic field inside the gradient coils, \( \nabla \times \mathbf{B} = 0 \), the gradient of the magnetic field magnitude in Eq. 49 may be transformed into

\[
\mathbf{G} = \nabla |\mathbf{B}| = \frac{(\mathbf{B} \cdot \nabla)\mathbf{B}}{|\mathbf{B}|} \quad (118)
\]

The right-hand side of the expression is simply the derivative of the magnetic field along the magnetic field vector. The vector \( \mathbf{G} \) points in the direction of the magnetic field variation along its line, \( \mathbf{B} \cdot \nabla \mathbf{B} \), and only migration along this direction affects the spin-echo attenuation. Thus, the former role of the gradient of only one component of the weak inhomogeneous magnetic field is now assumed by the variation of the magnetic field along its line. We call this "the line gradient of the magnetic field" (Stepišnik, 1995). In the following discussion let us consider the effect of isotropic and anisotropic self-diffusion on the spin-echo attenuation in the inhomogeneous magnetic field created by different coils.

**A. Quadrupolar Coils**

Near the center of the coils the total magnetic field of quadrupolar gradient coils and of the main field \( B_0 \), which is perpendicular to the coil axis, can be approximated by

\[
\mathbf{B} = (-Gz, 0, -Gx + B_0) \quad (119)
\]

\( G \) is the first derivative of the nonuniform magnetic field at the cylinder axis. The gradient of the field magnitude is

\[
\nabla |\mathbf{B}| = G \frac{(-Gx + B_0, 0, -Gz)}{|\mathbf{B}|} \quad (120)
\]

with absolute value

\[
|\nabla |\mathbf{B}||^2 = G^2 \quad (121)
\]

The absolute value of the line gradient is constant and the resulting spin-echo attenuation is uniform in the sample. In the article by Stepišnik
(1995) the distribution of the square of the line gradient for the real quadrupolar coil is shown. It turns out that the approximation in Eq. (119) is correct in a very broad region around the coil axis. For generality we consider the case of anisotropic diffusion. With the main axes of the diffusion tensor oriented along the coordinate axes, one has

$$\mathcal{D}(t_1 - t_2) = \begin{bmatrix} D_1 & 0 & 0 \\ 0 & D_2 & 0 \\ 0 & 0 & D_3 \end{bmatrix} \delta(t_1 - t_2)$$ (122)

and the spin-echo signal follows from Eq. (62) as

$$E(\Delta) = \int \int \exp\left(-\gamma^2 G^2 f(\Delta) \frac{D_1 (-B_o + Gx)^2 + D_3 G^2 z^2}{(-B_o + Gx)^2 + G^2 z^2} \right) dx dy dz$$

(123)

with $f(\Delta) = \delta^2(\Delta - \delta/2)$. Clearly the anisotropic migration of particles causes a nonuniform distribution of the spin-echo attenuation that depends both on the sample dimensions and on the degree of anisotropy. This nonuniform attenuation [Eq. (123)] results in a spin-echo intensity that does not follow the usual dependence on the gradient amplitude and duration. The approximate evaluation of Eq. (123) yields

$$E(\Delta) = E_o \exp\left(-\gamma^2 G^2 D_1 f(\Delta)\right)$$

$$\times \left[1 + \frac{\gamma^2 G^2 (D_1 - D_2)}{3} f(\Delta) \left(\frac{G^2 I_x^2}{B_o^2} + \frac{G^3 I_z^2 I_x}{B_o^3} + \cdots \right) \right]$$ (124)

This equation holds when $Gl_x$ and $Gl_z \ll B_o$, where $l_x$ and $l_z$ denote the sample dimensions.

**B. Maxwell Pair Coils**

In the center of a Maxwell pair the radial component of the magnetic field is half the longitudinal component. With the main field $B_o$ pointing parallel to the coil axis, the total magnetic field is

$$\mathbf{B} = (-Gx/2, -Gy/2, Gz + B_o)$$ (125)

and the gradient of the field magnitude is

$$\text{grad} |\mathbf{B}| = G \left[ \frac{Gx/4, Gy/4, [Gz + B_o]}{|\mathbf{B}|} \right]$$ (126)

The square of the line gradient is not constant. In consequence, the spin-echo attenuation depends upon the spin location in the sample.
FIG. 16. The spin-echo signal as a function of the magnetic field gradient for isotropic self-diffusion in a Maxwell pair coil system. Note the deviation from ideality as the polarizing field, $B_0$, decreases.

even for an isotropic self-diffusion. Figure 16 shows the result of the exact numerical calculation using Eq. (126) for a sample consisting of a cylinder of length $a$ and radius $a$. It illustrates the deviations in echo attenuation expected when $Ga > B_0$.

With the condition $B_s(r, t) \ll B_0$, the solution of Eq. (68) for isotropic diffusion given

$$E(\Delta) = E_0 \exp(-\gamma^2 DG^2 f(\Delta)) \left[ 1 - \gamma^2 DG^2 f(\Delta) \frac{G^2(l_x^2 + l_y^2)}{B_0^2} + \cdots \right]$$

(127)

where once again $l_x$ and $l_y$ denote the transverse sample dimensions.

C. SIMPLE COILS AS A MODEL OF THE FRINGE FIELD OF A MAGNET

The use of the fringe field of superconducting magnets for the measurement of very slow diffusion processes is now well established [Kimmich and Fisher, 1994]. In considering the violation of the small inhomogeneous field approximation, we note that the fringe field may not be as well defined as that produced by quadrupolar coils or Maxwell pair coils. In order to provide a simple model, we will consider the magnetic field distribution created by a simple coil of radius $r_o$. 
FIG. 17. The planar distribution of the spin-echo attenuation $\log|E|$ (in arbitrary units) for isotropic diffusion in the near field of a coil at the fixed value of $\gamma^2 G^2 f(\Delta) D_0$.

The spatial distribution of the spin-echo damping has been obtained by numerical evaluation of $|G|^2$ [Eq. (118)], for the magnetic field around the coil axis (Fig. 17). It has a maximum at $z = 0.5r$ with a broad homogeneous front.

The approximate calculation of Eq. (68) for a sample of radius $r$ and thickness $z$ located at $z_0$ on the coil axis gives the spin-echo intensity

$$E(\Delta) = E_0 \exp(-\gamma^2 G^2(z_0) f(\Delta))$$

$$\times \left[ 1 - \gamma^2 G^2(z_0) f(\Delta) \left( \frac{3}{32} \frac{(8r_0^2 - 23z_0^2)r^2}{r_0^2 + z_0^2} + \frac{4z_0^2 - r_0^2}{r_0^2 + z_0^2} \frac{z}{z_0} \right) + \cdots \right]$$

(128)

if $r \ll r_0$ and $z \ll z_0$. With $N$ windings and current $I$, the gradient

$$G(z_0) = \frac{\mu_0 N r^2 z_0}{2(r_0^2 + z_0^2)^{3/2}}$$

(129)
has a maximum at \( z = r_0/2 \). This position provides the most suitable site for the placement of a small sample or for a slice selected from a larger specimen in order to avoid a nonuniform distribution of attenuation. In general, the appropriate location for a sample in the fringe field of a magnet is at the point where \( g = |\text{grad}\|B\|^2 \) has a maximum. Away from this point one must exercise caution with regard to the sample dimension in order to avoid large attenuation inhomogeneity. The width of a slice \( z \) should be less than \( g/(dg/dz) \) with \( dg/dz \) being the derivative perpendicular to a slice.

D. SPATIALLY DISTRIBUTED PULSED GRADIENT SPIN-ECHO NMR USING SINGLE-WIRE PROXIMITY

The primary disadvantage of the fringe field method is its inherent low signal sensitivity. Because the rf pulses are applied in the presence of the gradient, they act as soft, slice-selective pulses, exciting a layer of spins only micrometers in thickness. Consequently, the method relies on long periods of signal averaging. Furthermore, the experimental constraints are demanding, with a need to use high voltage rf pulses, to avoid apparatus vibration and to fix the sample in the magnetic reference frame rather than in the frame of the rf coil.

Most methods for producing large pulsed magnetic field gradients rely on the use of a specialized wire array that surrounds the rf coil and produces a linear magnetic field gradient over the sample. The problems associated with this configuration may be simply stated as follows. When large numbers of turns are used in order to generate large gradients, the resulting inductance tends to limit the rate at which the current may be switched, while significant stray magnetic fields result in persistent eddy currents in the surrounding magnet structure. While the stray field problems may be limited to a degree by active shielding, the practical limitations of the conventional coil lead to an upper gradient limit on the order of \( 20 \text{T m}^{-1} \).

An alternative method of generating very large amplitude gradient pulses, indeed larger than can be achieved in the stray field method, was suggested by use (Callaghan and Stepišnik, 1995b). This method has high intrinsic signal sensitivity and dynamic range and permits rapid switching. The technique utilizes micro-imaging to spatially resolve the sample, thus gaining access to the divergence in gradient strength that occurs in the vicinity of a current-carrying wire. Rather than surrounding the sample with an external gradient coil, the current-carrying wire is inserted into the sample itself. For a long straight wire carrying current \( I \) and oriented transverse to the polarizing field \( B_o \), as shown in Fig. 18a, this gradient in
Fig. 18. (a) Distribution of gradient vectors superposed on equigradient contours. The contours are circles concentric with the wire shown schematically in black. (b)–(d) NMR images (field of view 3 mm) of the solution of polyethylene oxide in water obtained using the PGSE sequence with \(\Delta = 20\) ms. In (b) \((I = 0 \text{ A})\), the white superposed circles show the inner glass capillary wall and the wire position. Note the crescent of the water diffusion boundary which expands from (b) to (c) \((I = 1.2 \text{ A}, \delta = 2 \text{ ms})\), while from (c) to (d) \((I = 7.7 \text{ A}, \delta = 10.0 \text{ ms})\) the polymer boundary develops and expands. [Reproduced by permission from Callaghan and Stepišnik, 1995a.]

The \(x\)-\(y\) plane is given by

\[
g(x, y) = \frac{\mu_0 I}{2\pi(x^2 + y^2)^{3/2}(a^2 - 2xy + x^2 + y^2)^{1/2}} \times [(x^2 - y^2 - ax)i + (2xy - ay)j] \tag{130}\]

where \(a = \mu_0 I/2\pi B_0\) and \(i\) and \(j\) are unit vectors in the normal plane, where \(j\) refers to the direction of the polarizing field \(B_0\).

Figure 18a also shows the radiating pattern of local gradient vectors along with the equigradient contours. These contours are centered on the
wire and exhibit an inverse square relation

\[ g(x, y) = |g(x, y)| = \frac{\mu_e I}{2\pi(x^2 + y^2)} \]  

(131)

Because of the quadratic dependence on \( g \), the echo attenuation for an isotropically diffusing fluid in the vicinity of the wire depends exponentially on the fourth power of the distance \( r \) from the wire center. This results in an enormous dynamic range across the image plane transverse to the wire so that it is possible to measure molecular diffusion coefficients that differ by many orders of magnitude without the need to greatly vary the amplitude or duration of the current pulses.

Figure 18a–d shows a succession of spin-echo amplitude images of a solution of 5\% 1.0 \times 10^3\text{Da} polyethylene oxide in water in a glass capillary tube of 1.6-mm i.d. taken at successively increased values of the product \( I\delta \), where \( I \) is the amplitude of the current pulse. At zero current in the wire the image exhibits a uniform amplitude and the dark region on the left-hand edge shows quite clearly the outline of the circular wire cross section along with the meniscus of the epoxy resin used to secure the wire to the inner wall of the glass capillary. At the smallest value of \( I\delta \) \((I = 0.4 \, \text{A}, \delta = 10 \, \text{ms}) \) the attenuation boundary for the water molecules is clearly apparent at a distance of about 1 mm from the wire center. As \( I\delta \) is increased, this boundary, as expected, moves further from the wire. On each side of the water boundary the plateau regions are clearly delineated: the water and polymer protons contribute on the far side, whereas on the near side, the water signal has vanished, leaving a constant polymer proton plateau. In the early images, the local magnetic field gradient is sufficient to dephase the polymer proton spin echo only in the few pixels very close to the wire. As \( I\delta \) is increased further, this inner polymer attenuation boundary recedes from the wire and moves clearly out into the capillary space.

As predicted, the attenuation boundaries for both the water and the polymer closely approximate circles centered on the wire, clearly indicating that the diffusion is indeed isotropic. These circles can also be used to accurately locate the wire.

The spatially distributed PGSE experiment provides a nice means of demonstrating diffusion anisotropy. The intensity of the image pixel depends on the local gradient \( g \) and the self-diffusion tensor as

\[ E(x, y, \Delta) = \exp(-\gamma^2 g(x, y)D(x, y)g(x, y)\eta(\Delta)) \]  

(132)
Fig. 19. Images of the lamellar phase of aerosol OT/water in which the lamellae are presumed to be concentric cylinders aligned parallel to the glass surface, thus enabling free azimuthal diffusion and hindered radial diffusion. (a) $I = 0$ A and (b) $I = 5.6$ A. In both cases $\delta = 1$ ms and $\Delta = 3.6$ ms. [From Callaghan and Stepišnik, 1995a.]

Figure 19 shows the shape of the boundary image in the case of a fluid where the diffusion is clearly anisotropic. This system is the lamellar phase of the lyotropic liquid crystal, aerosol OT (bis(2-ethylhexyl) sodium sulfosuccinate; 50/50 w/w with water) in which water diffusion parallel to the lamellar bilayers is known to be more than an order of magnitude faster than diffusion in the normal direction. Around the walls of the glass capillary the bilayers assume a preferential orientation parallel to the interface. In consequence, the system organizes itself with concentric bilayers in which azimuthal diffusion is free, while radial diffusion is strongly hindered. The resulting attenuation boundary is the "butterfly wing" shape apparent in the image.

The potential applications of spatially distributed pulsed gradient spin-echo NMR using single-wire proximity are numerous. It has particular utility in the frequency-domain applications referred to earlier. At high frequency, high gradients are required since any shortening of pulse duration values requires a corresponding increase in gradient amplitude if the same sensitivity to molecular displacement is to be preserved. This increase is provided by the quadratic rise in gradient amplitude in the vicinity of the wire. Furthermore, the very small inductances of the gradient "coil" make rapid pulse switching entirely feasible, thus providing access to the submillisecond regime.
VII. Migration in an Inhomogeneous rf Field

In the general echo attenuation expression, Eq. (41), which also can be written as

\[ e(t) = -\hbar \gamma w_o \sum_i \exp(i\theta_i(t))M_i S[r_i(t)] \]

the NMR signal depends on a correlation between the distribution of the initial spin excitation \( M_i = M[r_i(0)] \) and the distribution of spins in the field of the coil sensitivity \( S(r_i) \) at the time of detection. This correspondence affects the signal in almost any flow experiment, since any finite length coil suffers a degree of rf inhomogeneity. One technique of flow measurement by time-of-flight involves two coils and relies on a determination of the time of travel distance between the tagging coil associated with \( M[r_i(0)] \) and the detector coil associated with \( S[r_i(t)] \). Another method (the inflow–outflow technique) uses a single coil and relies on effects arising from outflow of excited spins and inflow of fresh spins [Hemminga, 1984; van As and Schaaftsma, 1985]. In liquids there is seldom significant outflow of spins from the coils, but in gases, where the diffusion rate is about \( 10^{-3} \) to \( 10^{-1} \) m\(^2\) s\(^{-1}\), self-diffusion can strongly affect the NMR signal. This has been demonstrated in an experiment performed with the spins of \(^3\)He gas oriented by optical pumping (Barbé et al., 1974). The unusual resonance curve exhibits strong broadening along with a superposed narrow line when the rf field is inhomogeneous.

In the absence of magnetic field gradients and neglecting spin relaxation, the amplitude of the NMR signal depends on a correlation of spin location over the interval of measurement as

\[ e(t) = \sum_i \langle M_i S[r_i(t)] \rangle \]

Expressing the spatial distributions \( S[r_i(t)] \) and \( M[r_i(0)] \) in terms of the Fourier integral over the reciprocal space dimension \( q \) conjugate to \( r \) results in

\[ e(t) = \frac{1}{4\pi^2} \sum_i \int M(q') \int S(q') \exp(i[q'\cdot r_i(0) + qr_i(t)]) dq' dq \]

Allowing that, during the experiment, a particle shifts from its mean location with velocity \( v_\eta(t') \), then

\[ r_i(t) = r_i(0) + \int_0^t v_\eta(t') dt' \]

(136)
and Eq. (135) becomes
\[ e(t) = \frac{1}{4\pi^2} \sum_i \int M(q') \int S(q) \left\{ \exp \left( i \int_0^t q \cdot v_i(t') \, dt' \right) \right\}_L \times \exp\left(i(q' + q)\cdot r_i(0)\right) \, dq' \, dq \]
(137)

When the changes in the particle velocity are due to random collisions with Gaussian character, \( v_i(t) = v_i(t) \), we can use the known procedure to evaluate the average. Equation (137) becomes
\[ e(t) = \frac{1}{4\pi^2} \sum_i \int M(q') \int S(q) \exp(-q \cdot \mathcal{D}_i \cdot q) \times \exp\left(i(q' + q)\cdot r_i(0)\right) \, dq' \, dq \]
(138)

where \( \mathcal{D}_i \) is the self-diffusion tensor for the \( i \)th particle. Clearly the damping effect of diffusion is greater for the components with the highest values of \( q \). For the cases involving a nonuniform distribution of flow velocity or where the diffusion varies across the sample, we must rely on the general result represented by Eqs. (137) and (138). For the special case where the sample and the velocity field are uniform over the whole region of the receiver, Eq. (137) becomes
\[ e(t) = \frac{\hbar}{2\pi} \gamma \omega_o \int M(-q) S(q) \exp(-i v \cdot q t) \, dq \]
(139)

and for uniform diffusion, Eq. (138) becomes
\[ e(t) = \frac{\hbar}{2\pi} \gamma \omega_o \int M(-q) S(q) \exp(-q \cdot \mathcal{D} \cdot q t) \, dq \]
(140)

Figure 20 shows how flow changes the signal when a thin slice of excited spins is moving through the detecting coil. The frequency of the weak modulation is determined by the product of the first moment of \( S(q) \) and the flow velocity.

The initial spin distribution shaped as a Gaussian function is used when considering the diffusion case as given by Eq. (140). As shown in Fig. 21, the spin outflow is responsible for the initial fast decay of the signal and results in spectral line broadening. The slow decay belongs to spins left in the coil and gives the narrow spectral line at the magnetization measurement in \(^3\)He (Barbé et al., 1974). The width of the broad line is proportional to the product of the self-diffusion constant and the second moment of \( S(q) \).
FIG. 20. NMR signal as a function of time when a thin slice of excited spins is moving through the detecting field of the coil.

FIG. 21. NMR signal as a function of time when the spin outflow from the coil is caused by a fast particle self-diffusion.

VIII. Conclusions

The number of NMR groups specializing in PGSE NMR methods has, until recently, been relatively small. This situation is partly because of a perception that the method is solely applicable to the measurement of self-diffusion coefficients, but also because of the difficulty in developing a reliable apparatus. Since the advent of gradient pulse switching capabilities
in standard NMR spectrometers, the situation has changed considerably. The magnetic field gradient equipment and rf pulse selectivity necessary for PGSE NMR and motional imaging applications is similar in most respects to that required for gradient-accelerated two-dimensional NMR spectroscopy, for three-dimensional NMR, for microimaging, for solvent signal suppression methods, and for chemical-selective excitation methods. New methods for generating large magnetic field gradients have extended downward the distance over which the motion of spins may be detected.

We have shown here that the generalized MGSE NMR approach allows one to design probes of the spin motion appropriate to the problem under investigation. We have also shown that it is necessary to give consideration to the range of dimensionality that is accessible. These dimensionalities include spatial and spatial frequency domains as well as time and temporal frequency domains. These perspectives are particularly powerful because they draw upon well-established methodologies such as diffraction analysis, spectral density analysis, and the various correlation and exchange schemes of multidimensional NMR.

The methods outlined here help demonstrate some of the measurement possibilities that result from such a generalized gradient modulation viewpoint. They also provide a menu from which suitable experiments can be selected and implemented.

Appendix

A. Randomly Modulated Oscillator—Distribution Function Approach

In stochastic theory there are two ideal cases that are very basic: Gaussian and Poisson. Gaussian modulation corresponds to many weak perturbations involving similar small disturbances and allows application of the central limit theorem. On the other hand, in Possion modulation the oscillator may occasionally suffer strong perturbation, but is mostly free. Some physical processes are intermediate and it is difficult to treat them rigorously. Brownian motion is supposed to comprise a large number of random jumps. It results in a great number of small perturbations of the spin-echo signal

\[ s(t) = s_o \exp(\imath \omega_c t + \imath \theta(t)) \] (141)

where the stochastic variation of phase is related to the precession fre-
frequency fluctuations through

\[ \theta(t) = \int_0^t \omega(t') \, dt' \quad (142) \]

where \( \langle \omega \rangle = 0 \). The relationship between the phase and the frequency indicates that the probability distribution function of the spin phase \( f(\theta, t) \) obeys the equation

\[ \frac{\partial f(\theta, t)}{\partial t} = -\omega(t) \frac{\partial}{\partial \theta} f(\theta, t) \quad (143) \]

This relationship gives the changes of \( f(\theta, t) \) in terms of a function of random variables \( \omega(t) \). A formal solution of Eq. (143) with the initial condition

\[ f(\theta, 0) = \delta(\theta - \theta') \quad (144) \]

for a given sample of \( \omega(t) \) is

\[ f(\theta, t) = \exp \left( -\int_0^t \omega(t') \, dt' \frac{\partial}{\partial \theta} \right) \delta(\theta - \theta') \quad (145) \]

where \( \partial / \partial \theta \) is considered as a parameter. The expectation of this function for the probability distribution of the random process \( \omega(t) \) over the ensemble of \( \omega(t) \) is

\[ f(\theta, t \mid \theta', 0) = \langle f(\theta, t) \rangle = \left( \exp \left( -\int_0^t \omega(t') \, dt' \frac{\partial}{\partial \theta} \right) \right) \delta(\theta - \theta') \quad (146) \]

which gives the probability of being at \( \theta \) at time \( t \) if starting at \( \theta' \) at \( t = 0 \). We assume the random process of \( \omega(t) \) to be Gaussian and write the average of Eq. (146) to second order of a cumulant expansion:

\[ f(\theta, t \mid \theta', 0) = \exp \left( \frac{1}{2} A(t) \frac{\partial^2}{\partial \theta^2} \right) \delta(\theta - \theta') \quad (147) \]

with

\[ A(t) = \int_0^t \int_0^t \langle \omega(t_1) \omega(t_2) \rangle \, dt_1 \, dt_2 \quad (148) \]

If there is no restriction to the possible values of the phase angle and if we use the Fourier transform representation of \( \delta(\theta - \theta') \), we find

\[ f(\theta, t \mid \theta', 0) = \frac{1}{\sqrt{2 \pi A(t)}} \exp \left( -\frac{(\theta - \theta')^2}{2A(t)} \right) \quad (149) \]

For times larger than the correlation time \( \tau_c \) of the random fluctuations,
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The equation for the function $f$ obeys the diffusion equation:

$$\frac{\partial f}{\partial t} = \Delta^2 \tau_c \frac{\partial^2 f}{\partial \theta^2} \quad (150)$$

In the foregoing relationships, by replacing $\theta$ with the particle coordinate and $\omega$ with its velocity, we obtain the standard equations of Brownian motion. In the long time limit, $A(t) \sim 2Dt$ with $D = \int_0^t \langle v(0)v(t) \rangle \, dt$ and Eq. (150) becomes the well-known Fick–Einstein diffusion equation. Obviously, the Gaussian process and its long time limit are inherent in this equation.

REFERENCES


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