Interpretation of NMR diffusion measurements in uniform- and nonuniform-field profiles

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With the use of Carr-Purcell random-walk methods, approximate expressions have been derived for the spin-echo decay envelope for spins diffusing in a restricted region in the presence of an inhomogeneous field. The sample region considered is a slab with a uniform cross section and plane boundaries. The inhomogeneous field may be either time independent or pulsed and is not required to have a uniform gradient. With consideration of different limits of the final expressions, both restricted and unrestricted diffusion can be treated. Comparison is made of our results with those found by other authors, and suggestions are given which can be used to extend the sensitivity of field-gradient NMR (nuclear magnetic resonance) diffusion measurements.

I. INTRODUCTION

The experimental determination of diffusivity covers a very wide range of technical problems and materials. The need for characterization of diffusion has led to the development of a variety of techniques including tracer, electrochemical, photobleaching, neutron scattering, and constant and pulsed field-gradient NMR methods, as well as interpretation of NMR relaxation measurements. In many ways, field-gradient NMR is a superior experimental technique. It gives a direct measure of the mean-square displacement of the diffusing particles, and the measured diffusivity is not dependent on a particular model for interpretation of the data. The atomic label placed on a diffusing nucleus in the field-gradient NMR method is simply the direction of its magnetic moment; the motions of the nuclei are unaffected by this label, and thus the process being viewed is self-diffusion. From a technical standpoint, field-gradient NMR also offers many advantages. These techniques are easy to implement, rapid to perform, and nondestructive to the sample. They can be easily adapted to high- and low-temperature environments, as well as a wide range of pressure.

The principles underlying the measurements of diffusivity using field-gradient NMR have been discussed in the earlier literature.[1–3] We will briefly outline these principles, using for illustration a Hahn pulse-echo sequence (90° pulse—T—180° pulse—T—echo, where T is a fixed time interval). The magnitude of the received signal (echo amplitude) following the pulse sequence depends critically on the relative phases of the precessing nuclear spins. The Larmor condition, $\omega=\gamma H$, specifies that the angular precession frequency of each spin is strictly proportional to the magnetic field. If an inhomogeneous magnetic field exists in a region occupied by nondiffusing nuclei, then, during the interval between the 90° and 180° pulses, the spins in regions of larger field will accumulate greater amounts of total phase. The 180° pulse sets the phases of these spins behind by precisely the amount which they were ahead immediately preceding this pulse. During the interval following the 180° pulse, the nuclei will accumulate phase in an amount equivalent to that accumulated during the first interval, and thus the ones in larger magnetic fields will "catch up," resulting in all spins having the same phase at time $2T$. This refocusing leads to the formation of a spin echo at $2T$, as was discovered by Hahn.[2] The refocusing will be complete if the magnetic field local to each spin remains constant in time. If a spin situated in an inhomogeneous field diffuses, its precession frequency will vary with time and the total accumulated phase at $2T$ will no longer be the same for all spins. Due to a spin's random motion, its phase becomes a statistical quantity. Consequently, for diffusing spins, only an incomplete refocusing of the magnetization will occur, resulting in a lower echo amplitude.

In a spatially uniform magnetic field the NMR signal would not be affected by diffusion. Normally, however, measurements are carried out in a Zeeman magnetic field which has residual imperfections. These are usually extremely small compared to any externally applied gradient, but they are large enough to cause a spin echo to form. In this case, the amplitude of the echo is largely independent of diffusion and is determined by spin interactions represented by the characteristic times T_1 and T_2. Applying an inhomogeneous magnetic field leads to reduction of this amplitude when diffusion is present. The spin-relaxation effects, T_1 and T_2, can be easily separated from diffusion effects by comparing the echo amplitudes with and without the applied inhomogeneous field.[4] The ratio of amplitudes depends only on diffusion and gives a direct measure of the diffusivity. In this paper we present general expressions for this amplitude ratio for spins diffusing under a wide variety of external conditions.

The effect of diffusion on the height of the spin echo was first calculated by Hahn[2] for an infinite sample with a time-independent uniform gradient. Hahn's ideas were extended by Carr and Purcell,[1] who introduced a discrete random-walk model to calculate the effect of diffusing nuclei on the spin-echo amplitude following different types of pulse sequences, and by Torrey,[5] who modified Bloch's differential equations[6] to account for diffusion. The differential equation and random-walk formulations give the same result for the echo attenuation when applied to unrestricted diffusion in a uniform magnetic field gradient. For the Hahn pulse sequence, the calculated amplitude is[1,5]

$$\frac{M}{M_0}=\exp(-\gamma^2G^2Dt^3/12)\ , \qquad (1)$$

where D is the diffusion coefficient, t is the amount of time elapsed between the 90° pulse and the echo peak ($t=2T$), γ is the gyromagnetic ratio of the nucleus, G is the magnitude of the field gradient, M is the echo height, and M_0 is the echo height measured at the same time with no applied gradient.

The utility of NMR methods was greatly increased with the pulsed gradient technique devised by Stejskal and Tanner.[3] Prior to this development, measurements were restricted to materials with large diffusion coefficients ($D\geq 10^{-7}$ cm^2/sec). The reason for this restriction is that the magnitude of the steady gradient that can be applied to the spins without distorting the echo is limited by the rf (radio-frequency) transmitted power (through the spectral width of the rf pulses) and the bandwidth of the detection system. With the pulsed gradient method, the gradient field is off during the rf pulses as well as at the time the echo forms. Consequently, the above limitations are removed, allowing much larger gradients to be used. In the pulse sequence used by Stejskal and Tanner, two gradient pulses of equal lengths, δ, are applied along with a Hahn rf pulse sequence. The first gradient pulse occurs between the 90° and 180° rf pulses and the second occurs between the 180° rf pulse and the echo. The length of the gradient pulses must be shorter than the time interval between the rf pulses. The echo amplitude for this sequence, assuming unrestricted diffusion, is[3]

$$\frac{M}{M_0}=\exp[-\gamma^2G^2D\delta^2(\Delta-\delta/3)]\ , \qquad (2)$$

where Δ is the time between the leading edges of the first and second gradient pulses. If the rf pulses are made very short, Δ is essentially the same as the time between them ($\Delta=T$). The pulsed gradient method has been used to measure diffusion in a wide variety of materials, including ionic conductors,[7] polymers,[8] heterogeneous catalysts,[9] liquids,[10] metals,[11] and biological tissue.[12]

In a typical measurement of diffusion, the distance moved by a nucleus may be of order one to a hundred microns. This is called the diffusion length. In some systems, such as colloids, microemulsions, or finely powdered samples, the diffusion length may be the same order of magnitude or larger than the size of the structure. In this case the assumption of unrestricted diffusion used in deriving the echo attenuation formulas given in Eqs. (1) and (2) is not valid, and these formulas will give results for the diffusivity which depend on the duration of the measurment. Several studies have discussed the effect of a restricted diffusion region on the spin-echo decay.[13–21] Starting with the modified Bloch equations, Robertson[13] has derived an expression for the spin-echo decay envelope for the case where the diffusing spins are confined to a region with plane boundaries which is finite in one direction and infinite perpendicular to this direction. The spins are situated in a time-independent magnetic field whose gradient is in the restricted direction. Wayne and Cotts[14] have studied diffusion of methane experimentally and also by numerical solution of the Bloch equations using the above sample and gradient field geometry. Stejskal[15] and Tanner and Stejskal[16] have obtained approximate echo attenuation expressions for pulsed gradients in the limit where $\Delta\gg\delta$ for various sample geometries. The technique they used was to first determine the probability distribution of the spin displacements, found by solving the diffusion equation subject to the appropriate boundary conditions. Then they computed the reduction in echo amplitude resulting from the calculated distribution of displacements. Tanner and Stejskal[16] have performed experimental tests of restricted diffusion in a variety of model systems, using their expressions for data analysis. Neuman[18] has developed a probabilistic method for calculating the echo attenuation whereby the unknown distribution of phases of the spins is approximated by a Gaussian. Using this approach, he has obtained echo amplitudes for a steady, uniform gradient in planar, spherical, and cylindrical sample geometries. Murday and Cotts[19] have extended Neuman's method to pulsed gradients and used it to calculate a spin-echo decay envelope for restricted diffusion in a spherically shaped region. The expression was then used to analyze diffusion measurements made on particles of liquid lithium. Stejskal[20] and Tanner[21] have written comprehensive reviews of the research work in field-gradient NMR measurements of restricted diffusion.

Another important aspect of NMR diffusion measurement which has not received much attention is the measurement of diffusivity using nonuniform gradient fields. Magnetic field gradients which are nonuniform may arise naturally in materials with substantial magnetic susceptibility. Formulas derived assuming a uniform gradient may not be appropriate in this case. Nonuniform gradients may also be produced by the external coils used to apply the inhomogeneous field during a measurement. To accurately measure small diffusion coefficients, the largest possible gradient is desirable. This is, in fact, a major limitation preventing the application of NMR methods to materials with low diffusivities. To produce large field gradients, efficient coil designs which provide a large gradient per unit current are necessary.[22–24] This leads to a design which sets the windings as close to the sample as is physically possible. Since coils which are designed to produce uniform-field gradients actually do so only near their centers, it is possible for much of the sample volume to be in a nonuniform gradient during a diffusion measurement. One of the motivations of this work is to allow nonuniformity of the gradient to be taken into account.

II. METHOD

In this paper we derive expressions for the spin-echo decay envelope for spins diffusing in a restricted region with plane boundaries in the presence of an inhomogeneous magnetic field that can vary in an arbitrary way along one direction. The results are applied to diffusion in an infinite region by taking appropriate limits of the final expressions. Our approach is based on the random-walk methods introduced by Carr and Purcell,[1] and incorporates the Gaussian approximation to the phase distribution used by Neuman.[18] A brief outline of the basic ideas is given here; the detailed calculations will be presented in the next section.

A Hahn pulse-echo sequence is applied to a group of nuclear spins which is placed in a magnetic field. The field is composed of a homogeneous Zeeman field and an inhomogeneous field which may be static or time dependent. The diffusion process is modeled by having the spins execute a one-dimensional random walk through the inhomogeneous field. Because of diffusive motion, the accumulated phase at the time of echo formation will be a random variable which is described by a probability distribution. A reduction in the amplitude of the spin echo will result from the lack of phase definition. The task is to find a quantitative relationship between the echo amplitude and the diffusivity of the spins for a specified form and strength of the inhomogeneous field.

We begin by reformulating the restricted diffusion problem as one of diffusion in an infinite medium. By considering spins diffusing in an infinite region in a periodic field, taking the period to be twice the length of the restricted region, it is possible to portray restricted diffusion.[14] The periodic field is expanded in a Fourier series. We describe the spin displacements by discrete random variables, with each spin accumulating phase in an amount determined by the path it takes through the inhomogeneous field. The phase of a spin at any time can be expressed in terms of its initial position and the random variables that characterize its movements. We make the approximation that the distribution of phases is Gaussian, and consequently is completely determined by its first and second moments. These can be calculated. The last remaining step is to compute the average of the cosine of the phase over this distribution at the time of echo formation. This gives the average projection of the spin moments along the direction of detection, which is proportional to the echo amplitude.

III. MODEL AND CALCULATIONS

The model system we consider consists of a group of nuclear spins confined to a region which has length R and occupies the interval along the z axis $0 \leq z \leq R$. The end surfaces of the sample at zero and R are perpendicular to the axis. Its cross-sectional shape and area play no direct role in the derivations. The normalized spin density (number of spins per unit length divided by the total number of spins) along z is denoted by $\rho(z)$. In principle it is possible to carry out the calculations, at least numerically, for any given form of $\rho(z)$. However, to obtain analytic expressions for the echo attenuation, we will later assume $\rho(z)$ to be constant when it becomes necessary to introduce a particular form. This requires the sample to have a cross section of constant area.

A large, uniform, static field and an inhomogeneous gradient field which has zero spatial average are applied to the sample, and a Hahn pulse-echo sequence is used to probe the nuclear magnetization. The magnitude of the Zeeman field, H_0, is assumed to be much greater than the magnitude of the inhomogeneous field, $H(\mathbf{r})$. Therefore, only the component of $H(\mathbf{r})$ parallel to H_0, $H_{\parallel}(\mathbf{r})$, will contribute significantly to the total magnetic field, and only the spatial variation of this component will affect the precession frequency of the spins.[5] To simplify the calculations, $H_{\parallel}(\mathbf{r})$ is constrained to vary along one direction which is taken to be z. The position-dependent labeling occurs only along this direction, so with this geometry only diffusive motion along z will be relevant. Our final results for isotropic unrestricted diffusion are more generally applicable, independent of this constraint on the direction of $H_{\parallel}$. For isotropic restricted diffusion, it will be necessary for the direction of $H_{\parallel}$ to remain fixed over at least a diffusion length. If anisotropic diffusion is considered, the direction along which $H_{\parallel}$ varies must remain constant over the entire sample region in order to unambiguously measure a particular component of the diffusion tensor.

The diffusion process is modeled by having the spins execute a one-dimensional random walk. The spins move about according to the following prescription: each remains at some position for a fixed period τ, then instantly jumps to a new position whose z coordinate differs from the z coordinate of the previous one by a fixed amount ζ. The jump may occur in the positive or negative direction with equal probabilities. This is described by setting

$$z[t=(j+1)\tau]=z(t=j\tau)+\zeta a_{j+1} , \tag{3}$$

where $z(t=j\tau)$ is the z coordinate of the spin after j jumps, ζ is the z component of the jump length, and a_j is a random variable with the probability distribution $P(a_j=1)=\frac{1}{2}$ and $P(a_j=-1)=\frac{1}{2}$. For this model the macroscopic diffusion coefficient is $D=\zeta^2/2\tau$. In our final expressions we introduce D by taking the continuum limit, $\zeta \to 0$, $\tau \to 0$, holding $D=\zeta^2/2\tau$ constant. It is irrelevant that various details of the microscopic motion, such as jump length and jump time distributions and correlations, are ignored in this description. The NMR method gives a direct measure of the mean-square displacement over macroscopic distances during a given interval of time, and the final results can be applied to all microscopic transport mechanisms.

Following Wayne and Cotts,[14] we replace the problem of diffusion of spins confined to the interval $0 \leq z \leq R$ by an equivalent problem which considers the spins diffusing along the entire z axis in a periodic inhomogeneous field. The periodic field is constructed by extending $H_{\parallel}(z)$ over the z axis so that it becomes an even function about the ends of the sample with a fundamental period $2R$, Fig. 1. Extending the inhomogeneous field in this manner is equivalent to specifying that diffusion currents across the sample boundary must vanish, i.e., the boundaries are reflecting. The total field acting on a spin is $H_0+H_{\parallel}(z)=H(z)$. A spin at the position z_0 at $t=0$ will, at time $j\tau$, be at a position

$$z(t=j\tau)=z_0+\zeta \sum_{i=1}^{j} a_i . \tag{4}$$

The spin at this time will be in a magnetic field $H(z_0+\zeta \sum_{i=1}^{j} a_i)$. During the time interval between $j\tau$ and $(j+1)\tau$, the phase accumulated by the spin is

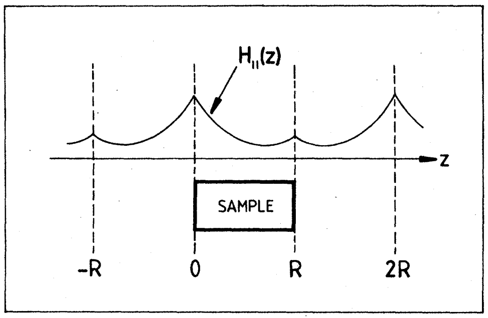

FIG. 1. Illustration of the way diffusion in a restricted region is modeled. It is assumed that the diffusion of spins in the region $0 \le z \le R$ with the inhomogeneous field $H_{||}(z)$ is equivalent to unbounded diffusion with $H_{||}$ extended over the entire z axis as shown.

$\gamma\tau H(z_0+\zeta\sum_{i=1}^{j} a_i)$. At a particular time $t=Q\tau$ ($Q\tau < T$), the total accumulated phase will be

$$\phi=\sum_{j=1}^{Q}\gamma\tau H\left[z_0+\zeta\sum_{i=1}^{j} a_i\right] . \quad (5)$$

If the spin had stayed at its initial position, the accumulated phase at $Q\tau$ would be $\phi_0=Q\gamma\tau H(z_0)$. We define the new quantity $\phi_D \equiv \phi-\phi_0$; ϕ_D is the additional phase accumulated by a spin due to its diffusion.

To calculate the diffusion related echo attenuation, an expression for ϕ_D at the time of the echo peak will be needed. This expression can be developed as follows. Let the 90° pulse occur at $t=0$. Immediately after the 90° pulse, each spin has zero accumulated phase and the magnetic moment of the sample as a whole will point along some direction in the xy plane. As time passes, the magnetic moment of the sample will precess in this plane and shrink due to dephasing of the individual moments. The 180° pulse occurs at $t=T=N\tau$ and the echo forms at $t=2N\tau$. The effect of the 180° pulse is simply to reverse the sign of ϕ for each spin at $t=N\tau$. The ϕ_0 contributions before and after the 180° pulse cancel, giving $\phi=\phi_D$ at $t=2N\tau$. If the spins were not diffusing, the accumulated phase at $2N\tau$ would be zero for every spin. With diffusion, ϕ_D at $t=2N\tau$ is given by

$$\phi_D=-\sum_{j=1}^{N}\gamma\tau H\left[z_0+\zeta\sum_{i=1}^{j} a_i\right] + \sum_{j=N+1}^{2N}\gamma\tau H\left[z_0+\zeta\sum_{i=1}^{j} a_i\right] . \quad (6)$$

$H(z)$ is a periodic function and can be represented by its Fourier expansion,

$$H(z)=\sum_k f_k e^{ikz} . \quad (7)$$

Since $H(z)$ is an even function with period $2R$, we have in the Fourier expansion the restrictions, $k=m\pi z/R$, with m an integer, and $f_k=f_{-k}$. Substituting Eq. (7) into Eq. (6), we obtain an expression for the accumulated phase

$$\phi_D=\gamma\tau\left[\sum_{j=N+1}^{2N}-\sum_{j=1}^{N}\right]\sum_k f_k \exp\left[ik\left[z_0+\zeta\sum_{n=1}^{j} a_n\right]\right] . \quad (8)$$

ϕ_D is a random variable, owing to the fact that it is a function of $\{a_i\}$ which are themselves random variables.

Since the distributions of the a_i are known, in principle it would be possible to convert the probability distribution over these to a conditional distribution over ϕ_D itself involving the starting position z_0 as a parameter. This distribution, $p(\phi_D \mid z_0)$, expresses the probability that the phase of a spin which started at z_0 will be found within $d\phi_D$ of the value ϕ_D. If $p(\phi_D \mid z_0)$ were known, the echo amplitude could be calculated in a straightforward manner. The ratio of echo heights with and without diffusion is given in terms of $p(\phi_D \mid z_0)$ by

$$\frac{M}{M_0}=\int_0^R \rho(z_0)dz_0 \int_{-\infty}^{\infty}\cos\phi_D p(\phi_D \mid z_0)d\phi_D , \quad (9)$$

where $\rho(z_0)$ is the normalized spin density at $t=0$. The integral over ϕ_D gives the average projection along the direction of detection for moments initially at z_0, and the integral over z_0 sums these projections over the entire sample to obtain the total detected magnetization. It is implicit in this equation that the macroscopic magnetic moment refocuses along the same direction with diffusion as it would if the spins were not diffusing. This will be demonstrated shortly. It is more convenient to work with a different probability distribution, $P(\phi_D)$, where $P(\phi_D)$ expresses the probability that the phase of a spin starting at an arbitrary position will be found within $d\phi_D$ of a value ϕ_D at $t=2N\tau$. $P(\phi_D)$ is found from $p(\phi_D \mid z_0)$ by averaging over initial positions of the spins:

$$P(\phi_D)=\int_0^R \rho(z_0)p(\phi_D \mid z_0)dz_0 . \quad (10)$$

Since $p(\phi_D \mid z_0)$ is not known, $P(\phi_D)$ cannot be found using Eq. (10). However, the first and second moments of $P(\phi_D)$ are

$$(\phi_D)_{\rm av}=\int_{-\infty}^{\infty}\phi_D P(\phi_D)d\phi_D \quad \text{(first moment)} \quad (11a)$$

$$=\int_{-\infty}^{\infty}\int_0^R \phi_D\rho(z_0)p(\phi_D \mid z_0)dz_0\,d\phi_D \quad (11b)$$

and

$$(\phi_D^2)_{\rm av}=\int_{-\infty}^{\infty}\phi_D^2 P(\phi_D)d\phi_D \quad \text{(second moment)} \quad (12a)$$

$$=\int_{-\infty}^{\infty}\int_0^R \phi_D^2\rho(z_0)p(\phi_D \mid z_0)dz_0 d\phi_D , \quad (12b)$$

where $(\ )_{\rm av}$ indicates the average of a quantity over the distribution $P(\phi_D)$. To calculate these moments, we return to Eq. (8) where ϕ_D is given as a function of $\{a_i\}$ and z_0, and calculate averages of ϕ_D and ϕ_D^2 over the known distributions of these variables. Once this has been done, $P(\phi_D)$ is approximated by a Gaussian distribution and the ratio of echo heights is given by

$$\frac{M}{M_0}=\int_{-\infty}^{\infty}\cos\phi_D P(\phi_D)d\phi_D . \quad (13)$$

We begin by calculating $(\phi_D)_{\rm av}$. To facilitate this calculation, the following result will be used:[25]

$$\left\langle \exp\left[ik\zeta\sum_{j=r}^{s}a_j\right]\right\rangle=[\cos(k\zeta)]^{s-r+1}\ , \tag{14}$$

where the notation $\langle\ \rangle$ indicates an average over the distributions of the a_j. From Eqs. (8) and (14), we obtain

$$\langle\phi_D\rangle=\gamma\tau\left[\sum_{j=N+1}^{2N}-\sum_{j=1}^{N}\right]\left[\sum_k f_k e^{ikz_0}[\cos(k\zeta)]^j\right]\ . \tag{15}$$

The sums over $(\cos k\zeta)^j$ are geometric, and can be evaluated, giving

$$\langle\phi_D\rangle=\gamma\tau\sum_k f_k e^{ikz_0}\frac{1}{1-\cos(k\zeta)}\times\{\cos(k\zeta)-2[\cos(k\zeta)]^{N+1}+[\cos(k\zeta)]^{2N+1}\}\ . \tag{16}$$

Here it is seen that the value of $\langle\phi_D\rangle$ at the time of echo formation for an arbitrary spin is not necessarily zero, and depends on the initial position. Next, $\langle\phi_D\rangle$ must be averaged over the initial positions of all spins. This is done as follows:

$$(\phi_D)_{\text{av}}\equiv\overline{\langle\phi_D\rangle}=\int_0^R\rho(z_0)\langle\phi_D\rangle dz_0\ , \tag{17}$$

where the overbar indicates an average over initial spin positions. To proceed further, a specific form of $\rho(z_0)$ must be inserted. Assuming constant $\rho(z_0)$ seems most reasonable, as well as simplifying the calculations. Performing the integral with $\rho(z_0)=1/R$, we obtain

$$(\phi_D)_{\text{av}}=0\ . \tag{18}$$

This is found by direct integration of Eq. (16) for all nonzero k terms and by returning to Eq. (8) to evaluate the $k=0$ term. The fact that $(\phi_D)_{\text{av}}=0$ indicates that the average of the accumulated phases for all spins in the sample at $t=2N\tau$ is zero, and the sample magnetization will refocus in the same direction as it would if there were no diffusion. $(\phi_D)_{\text{av}}$ will always be zero for an inhomogeneous field which has zero spatial average.

To calculate $(\phi_D^2)_{\text{av}}$, we first square Eq. (8), obtaining four terms of the form

$$(\gamma\tau)^2\sum_k\sum_l f_k f_l e^{i(k+l)z_0}\times\sum_m\sum_j\exp\left[i\zeta\left[k\sum_{n=1}^{j}a_n+l\sum_{p=1}^{m}a_p\right]\right]\ . \tag{19}$$

The sums over the indices m and j will run from either 1 to N or from $N+1$ to $2N$ in the different terms. $(\phi_D^2)_{\text{av}}$ can be found by first averaging over $\{a_i\}$ and then over $\rho(z_0)$ as before. However, in this case, a great deal of labor is saved by interchanging the order of these procedures. This is permissible since the averages are carried out over different variables, and are independent. We first find $\overline{\phi_D^2}$, where

$$\overline{\phi_D^2}=\int_0^R\rho(z_0)\phi_D^2\,dz_0\ . \tag{20}$$

From Eq. (20), we obtain

$$\overline{\phi_D^2}=(\gamma\tau)^2\sum_{k\neq0}f_k f_{-k}\left[\sum_{m=1}^{N}\sum_{j=1}^{N}+\sum_{m=N+1}^{2N}\sum_{j=N+1}^{2N}-\sum_{m=N+1}^{2N}\sum_{j=1}^{N}-\sum_{m=1}^{N}\sum_{j=N+1}^{2N}\right]\exp\left[ik\zeta\left[\sum_{n=1}^{j}a_n-\sum_{p=1}^{m}a_p\right]\right]\ . \tag{21}$$

The only nonzero contributions in the double sum over k and l shown in Eq. (19) are from terms where $l=-k$, with $k,l\neq0$. Next, averaging Eq. (21) over $\{a_i\}$ with the aid of Eq. (14), we obtain

$$(\phi_D^2)_{\text{av}}=2(\gamma\tau)^2\sum_{k\neq0}f_k f_{-k}\left[N+\frac{(2N-3)\cos(k\zeta)-2N\cos^2(k\zeta)+4[\cos(k\zeta)]^{N+1}-[\cos(k\zeta)]^{2N+1}}{[1-\cos(k\zeta)]^2}\right]\ . \tag{22}$$

In the Gaussian approximation, $P(\phi_D)$ is completely determined by the moments $(\phi_D)_{\text{av}}$ and $(\phi_D^2)_{\text{av}}$ given in Eqs. (18) and (22). Equation (13) can now be used to calculate the ratio of echo amplitudes. We use

$$\frac{M}{M_0}=\int_{-\infty}^{\infty}\cos\phi_D\,P(\phi_D)d\phi_D=\exp[-\tfrac{1}{2}(\phi_D^2)_{\text{av}}]\ , \tag{23}$$

where the last equality holds for a Gaussian distribution with zero mean. Equations (22) and (23) together give a general expression for the diffusion related echo attenuation in terms of the parameters which characterize the random walk of a particle. To treat the diffusion as a continuum process, we take in Eq. (22) the limits $\zeta\to0$, $\tau\to0$, $N\to\infty$, holding constant both $D=\zeta^2/2\tau$ and $t=2N\tau$. The limit $k\zeta\to0$ for all k is also taken, which has the physical interpretation that the smallest length scale for variation of the inhomogeneous field is much longer than the particle jump length. We obtain

$$\frac{M}{M_0}=\exp\left[-\gamma^2\sum_{k(\neq0)}f_k f_{-k}\left[\frac{t}{k^2D}+\frac{-3+4e^{-k^2Dt/2}-e^{-k^2Dt}}{k^4D^2}\right]\right]\ . \tag{24}$$

This is the general result for the spin-echo decay envelope for spins diffusing in a time-independent inhomogeneous field with an arbitrary profile. The magnetization is probed using a Hahn pulse sequence, with t as the time interval between the 90° pulse and the echo peak.

We will next find the decay envelope for the important case where the inhomogeneous field is pulsed. For this we consider the Stejskal-Tanner pulse sequence. The timing arrangement for the rf and gradient pulses in this sequence is as follows: a 90° rf pulse at $t=0$; a gradient field pulse starting at $t=0$, lasting until $t=M\tau$; an rf pulse applied at $t=N\tau$ $(N>M)$; a gradient pulse of equal magnitude to the first applied from $N\tau$ to $(M+N)\tau$; and finally, echo formation with the peak amplitude occuring at time $t=2N\tau$.[26] For this sequence of pulses, the phase accumulation at $t=2N\tau$ for a spin initially at z_0 is

$$\phi_D=\gamma\tau\sum_k f_k e^{ikz_0}\left[-\sum_{j=1}^{M}\exp\left[ik\zeta\sum_{n=1}^{j}a_n\right]+\sum_{j=N+1}^{N+M}\exp\left[ik\zeta\sum_{n=1}^{j}a_n\right]\right]. \quad (25)$$

Once the expression for ϕ_D is written, the same type of averages are performed as were done previously. We obtain

$$(\phi_D)_{\rm av}=0 \quad (26)$$

and

$$(\phi_D^2)_{\rm av}=2\gamma^2\tau^2\sum_{k\,(\neq 0)} f_k f_{-k}\times\left[\frac{M[1-\cos^2(k\zeta)]-2\cos(k\zeta)+2[\cos(k\zeta)]^{N+1}+2[\cos(k\zeta)]^{M+1}-[\cos(k\zeta)]^{M+N+1}-[\cos(k\zeta)]^{N-M+1}}{[1-\cos(k\zeta)]^2}\right]. \quad (27)$$

Equations (23) and (27) together give the spin-echo decay envelope for the pulsed gradient case in terms of the random-walk parameters. Again, to express the echo amplitude in terms of a macroscopic diffusion coefficient, the continuum limit is applied to Eq. (27). In this case, the proper limits are $k\zeta\to 0$, $\tau\to 0$, $N\to\infty$, $M\to\infty$ with $\zeta^2/2\tau=D$, $N\tau=\Delta$ (the time between leading edges of the gradient pulses), and $M\tau=\delta$ (the length of the gradient pulses). Taking these limits, we obtain for the echo amplitude

$$\frac{M}{M_0}=\exp\left[-\gamma^2\sum_{k\neq 0}\frac{f_k f_{-k}}{k^2 D}\left[2\delta-\frac{2-2\exp(-\Delta k^2 D)-2\exp(-\delta k^2 D)+\exp[-(\Delta-\delta)k^2 D]+\exp[-(\Delta+\delta)k^2 D]}{k^2 D}\right]\right]. \quad (28)$$

This is the general result for the echo attenuation due to diffusion in a pulsed gradient field of arbitrary profile using a Stejskal-Tanner pulse sequence. This expression is equally appropriate for the stimulated echo sequence.[27]

IV. DISCUSSION AND APPLICATION TO RESTRICTED AND UNRESTRICTED DIFFUSION

A. The uniform gradient field

The uniform gradient field is very important in applications. Quadrupole or anti-Helmholtz coils constructed around a sample provide a uniform gradient, at least near their centers. The case of restricted diffusion in a rectangular region has already been solved for a time-independent uniform gradient,[13,18] so a comparison between results is available. The field profile is

$$H_{||}(z)=\tfrac{1}{2}GR(1-2z/R)\,, \quad (29)$$

where G is the magnitude of the gradient. According to the previous discussion, the diffusion of spins in the interval $0\le z\le R$ with the gradient field given by Eq. (29) can be replaced by diffusion over the entire z axis with the gradient field given by

$$H_{||}(z)=\frac{2GR}{\pi^2}\sum_{n=-\infty}^{\infty}\frac{\exp[i(2n+1)\pi z/R]}{(2n+1)^2}\,. \quad (30)$$

An additional term representing the Zeeman field, H_0, would be added to Eqs. (29) and (30) to obtain the total magnetic field. However, it has been previously shown that a spatially uniform field does not affect $(\phi_D)_{\rm av}$ and $(\phi_D^2)_{\rm av}$. Setting $H_{||}(z)$ from Eq. (30) into the notation of Eq. (7), we find

$$k=(2n+1)\frac{\pi}{R},\quad f_k=f_{-k}=\frac{2GR}{(2n+1)^2\pi^2}\,,$$

and

$$\sum_{k\neq 0}\to\sum_{n=-\infty}^{\infty}\,. \quad (31)$$

Substituting these into Eq. (24), we arrive at

$$\frac{M}{M_0}=\exp\left[\frac{-8\gamma^2G^2R^6}{D^2\pi^6}\sum_{n=0}^{\infty}\frac{1}{(2n+1)^6}\left[\frac{Dt}{R^2}-\frac{3-4\exp[-(2n+1)^2\pi^2 Dt/2R^2]+\exp[-(2n+1)^2\pi^2 Dt/R^2]}{(2n+1)^2\pi^2}\right]\right]. \quad (32)$$

This expression is the same as that derived by Robertson[13] and Neuman.[18] In the short-time limit, $t \ll R^2/D$, the diffusion is unrestricted and Eq. (32) reduces to the well-known formula[1] for unrestricted diffusion in a time-independent uniform gradient

$$\frac{M}{M_0}=\exp\left[\frac{-\gamma^2G^2Dt^3}{12}\right], \quad t \ll \frac{R^2}{D} . \tag{33}$$

In the limit of extremely restricted diffusion, $t \gg R^2/D$, Eq. (32) becomes

$$\frac{M}{M_0}=\exp\left[-\frac{R^4\gamma^2G^2t}{120D}\right], \quad t \gg \frac{R^2}{D} . \tag{34}$$

For the uniform pulsed gradient [same form of $H_{\parallel}(z)$ as given in Eq. (29)] the echo height expression is found by substituting the parameters from Eq. (31) into the general echo attenuation formula for the pulsed gradient, Eq. (28). We obtain

$$\frac{M}{M_0}=\exp\left[\frac{-8\gamma^2G^2R^6}{\pi^6D^2}\sum_{n=0}^{\infty}\frac{1}{(2n+1)^6}\left[\frac{2\delta D}{R^2}-\frac{2-2\exp[-(2n+1)^2\pi^2D\Delta/R^2]-2\exp[-(2n+1)^2\pi^2D\delta/R^2]}{(2n+1)^2\pi^2}-\frac{\exp[-(2n+1)^2\pi^2D(\Delta-\delta)/R^2]+\exp[-(2n+1)^2\pi^2D(\Delta+\delta)/R^2]}{(2n+1)\pi^2}\right]\right] . \tag{35}$$

In the short-time limit where $\Delta,\delta \ll R^2/D$, Eq. (35) becomes

$$\frac{M}{M_0}=\exp[-\gamma^2G^2D\delta^2(\Delta-\delta/3)], \quad \Delta,\delta \ll \frac{R^2}{D} , \tag{36}$$

which agrees with the result found by Stejskal and Tanner[3] for unrestricted diffusion. The problem of restricted diffusion with pulsed gradients that we have treated here has also been discussed in a limiting case, $\delta \ll \Delta$, by Stejskal[15] and Tanner and Stejskal[16] using an approach different from ours. However, their results are not consistent with those found by taking $\delta \ll \Delta$ in Eq. (35), nor do they reduce to Eq. (36), which is generally accepted, in the short-time limit. If, on the other hand, the more restrictive limiting condition $\Delta \rightarrow \infty$ followed by $\delta \rightarrow 0$ is considered, the above authors[16] obtain

$$\lim_{\delta\rightarrow 0}\ln(\lim_{\Delta\rightarrow\infty} M/M_0)=-(\gamma\delta GR)^2/12 .$$

This is in agreement with the corresponding limit applied to Eq. (35). We believe it is likely that the echo amplitude expression given in Refs. 15 and 16 approaches the true solutions only as $\delta \rightarrow 0$ and $\Delta \rightarrow \infty$.

B. Nonuniform gradient fields

Short- and long-time limits can be found for both steady and pulsed nonuniform gradients for an arbitrary $H_{\parallel}(z)$ by taking appropriate limits of Eqs. (24) and (28). For the steady gradient field, the echo amplitude becomes

$$\frac{M}{M_0}=\exp\left[-\frac{\gamma^2Dt^3}{12}\sum_{k\neq 0}f_kf_{-k}k^2\right], \quad t \ll \frac{R^2}{D} , \tag{37}$$

in the short-time limit and

$$\frac{M}{M_0}=\exp\left[-\frac{\gamma^2t}{D}\sum_{k\neq 0}\frac{f_kf_{-k}}{k^2}\right], \quad t \gg \frac{R^2}{D} , \tag{38}$$

in the long-time limit. For the pulsed gradient in the short-time limit, the amplitude becomes

$$\frac{M}{M_0}=\exp\left[-\gamma^2\delta^2\left[\Delta-\frac{\delta}{3}\right]\sum_{k\neq 0}f_kf_{-k}k^2\right], \quad \delta,\Delta \ll \frac{R^2}{D} . \tag{39}$$

Since there are two independent time parameters in the pulsed expressions, there can be several long-time limiting conditions. Considering the case where δ, Δ, and $\Delta-\delta$ are all much greater than R^2/D, we find

$$\frac{M}{M_0}=\exp\left[-\frac{2\gamma^2\delta}{D}\sum_{k\,(\neq 0)}\frac{f_kf_{-k}}{k^2}\right], \quad \Delta,\delta,(\Delta-\delta) \gg \frac{R^2}{D} . \tag{40}$$

Both the short- and long-time limits have clear and direct physical interpretations. The nonuniform part of the field is

$$H_{\parallel}(z)=\sum_{k\,(\neq 0)}f_ke^{ikz} ;$$

then,

$$\left[\frac{dH_{\parallel}}{dz}\right]^2=-\sum_{\substack{k\,(\neq 0),\\ l\,(\neq 0)}}f_kf_lkle^{i(k+l)z} \tag{41}$$

and

$$\left[\int H_{\parallel}dz\right]^2=-\sum_{\substack{k\,(\neq 0),\\ l\,(\neq 0)}}\frac{f_kf_l}{kl}e^{i(k+l)z} , \tag{42}$$

where the integral is indefinite. The average of $(dH_{\parallel}/dz)^2$ taken over initial spin positions is

$$\overline{\left[\frac{dH_{\parallel}}{dz}\right]^2}\equiv\frac{1}{R}\int_0^R\left[\frac{dH_{\parallel}}{dz}\right]^2dz=\sum_{k\,(\neq 0)}f_kf_{-k}k^2 , \tag{43}$$

while the average of $(\int H_{\parallel}dz)^2$ is

$$\overline{\left[\int H_{\parallel}\,dz\right]^2}=\sum_{k\,(\neq 0)}\frac{f_k f_{-k}}{k^2}\,. \tag{44}$$

Replacing the Fourier component sums in Eqs. (37)—(40) by the appropriate expressions taken from Eqs. (43) and (44), it can be seen that in the short- and long-time limits the echo amplitude expressions for nonuniform gradients are very similar to those for uniform gradients. For unrestricted diffusion, G^2 is replaced by $\overline{(dH_{\parallel}/dz)^2}$ when going from uniform to nonuniform gradients, and for extremely restricted diffusion $G^2R^4/120$ is replaced by $\overline{(\int H_{\parallel}dz)^2}$.

If the diffusion is isotropic one can relax the requirement that the direction along which $H_{\parallel}$ varies (defined to be the z direction) stays constant over the entire sample region. For unrestricted diffusion, the results derived here will be more generally valid. In fact, the local z direction can be taken to follow the direction of $\nabla H_{\parallel}$. As a consequence of this, the unrestricted diffusion formulas will be valid for an inhomogeneous field which varies in an arbitrary way if $\nabla H_{\parallel}$ is substituted for $dH_{\parallel}/dz$. Furthermore, since the boundary conditions are unimportant for unrestricted diffusion, the average denoted by an overbar can be interpreted as an average over the sample volume. If the diffusion is extremely restricted, then it is likely that the sample as a whole is composed of many small entities, with diffusion allowed only within the boundaries of each one. In this case, the z direction must remain fixed over the dimensions of an entity, but can vary over larger distances. The direction z along which $H_{\parallel}$ is integrated is defined locally by the direction of the gradient, i.e., $\hat{z}=\nabla H_{\parallel}/|\nabla H_{\parallel}|$. Using results from the above discussion, the unrestricted and extremely restricted diffusion expressions for arbitrary inhomogeneous fields can be put into more compact and transparent forms. The unrestricted diffusion expressions, Eqs. (37) and (39), can be written as

$$\frac{M}{M_0}=\exp\left[-\frac{\gamma^2Dt^3}{12}\overline{(\nabla H_{\parallel})^2}\right],\quad t\ll\frac{R^2}{D}\,, \tag{45}$$

for a time-independent inhomogeneous field, and

$$\frac{M}{M_0}=\exp[-\gamma^2D\delta^2(\Delta-\delta/3)\overline{(\nabla H_{\parallel})^2}],\quad \delta,\Delta\ll\frac{R^2}{D}\,, \tag{46}$$

for a pulsed inhomogeneous field. For extremely restricted diffusion, the time-independent inhomogeneous field expression, Eq. (38), can be written as

$$\frac{M}{M_0}=\exp\left[-\frac{\gamma^2t}{D}\overline{\left[\int H_{\parallel}dz\right]^2}\right],\quad t\gg\frac{R^2}{D}\,, \tag{47}$$

and the pulsed inhomogeneous field expression, Eq. (40), can be written as

$$\frac{M}{M_0}=\exp\left[-\frac{2\gamma^2\delta}{D}\overline{\left[\int H_{\parallel}dz\right]^2}\right],\quad \Delta,\delta,(\Delta-\delta)\gg\frac{R^2}{D}\,. \tag{48}$$

In Eqs. (47) and (48), the z axis is defined to be locally along the direction $\hat{z}=\nabla H_{\parallel}/|\nabla H_{\parallel}|$.

V. VALIDITY OF THE SOLUTIONS AND APPLICATION TO EXPERIMENTS

In deriving expressions for the echo amplitudes, the assumption that $P(\phi_D)$ is Gaussian was made. We now discuss the conditions under which this is a good approximation to the actual phase distribution, and we consider the regime of validity of the results presented above.

Neuman[18] has considered the Gaussian approximation to the phase distribution for long diffusion times. He demonstrated that $P(\phi_D)$ approaches a Gaussian distribution when the time is much longer than that needed for a spin starting at an arbitrary position to diffuse throughout the entire sample region, $t\gg R^2/D$. The arguments do not depend on the type of inhomogeneous field, and apply equally well to uniform and nonuniform gradients. Thus the long-time expressions, Eqs. (47) and (48), should be valid for arbitrary inhomogeneous fields.

For $t\ll R^2/D$, the restricted diffusion problem reduces to diffusion in an infinite medium. Here, $P(\phi_D)$ has been shown to be Gaussian for a uniform gradient.[1,28] In an inhomogeneous field which does not have a uniform gradient, $P(\phi_D)$ is not Gaussian, and Eqs. (45) and (46) are only approximate. The actual form of $P(\phi_D)$ at small times can be determined by the following simple arguments, where, to be specific, we consider the time-independent inhomogeneous field. For times short enough such that the diffusion length is much smaller than the distance over which the field gradient varies, each spin can be taken to be diffusing in a locally uniform gradient. The magnitude of the gradient seen by an individual spin depends on its initial position. In this case the phase distribution for the entire system can be represented exactly as a sum of Gaussians with different variances. The three-dimensional generalization of Eq. (9) can be applied directly to this distribution to obtain for the echo amplitude

$$\frac{M}{M_0}=\frac{1}{V}\int\exp\left[-\frac{\gamma^2Dt^3}{12}(\nabla H_{\parallel})^2\right]dV\,, \tag{49}$$

where V is the volume of the sample. Equation (49) can be compared to the result based on the Gaussian distribution, Eq. (45). They are identical to first order, while the first difference term is

$$E=\frac{1}{2}\left[\frac{\gamma^2Dt^3}{12}\right]\overline{[(\nabla H_{\parallel})^2-\overline{(\nabla H_{\parallel})^2}]^2}\,. \tag{50}$$

The difference in the echo amplitudes found from Eqs. (45) and (49) will always be less than E. Therefore, they will give similar results if either the exponent is small, i.e., the echo has not been attenuated very much, or if the mean-square deviation of $(\nabla H_{\parallel})^2$ is small.

To see how well Eq. (45) performs under realistic experimental conditions, we have done a numerical calculation for the sample and coil assembly shown in Fig. 2, top. The inhomogeneous field is produced by a quadrupole coil of the type used by Assink.[29] In the arrangement shown

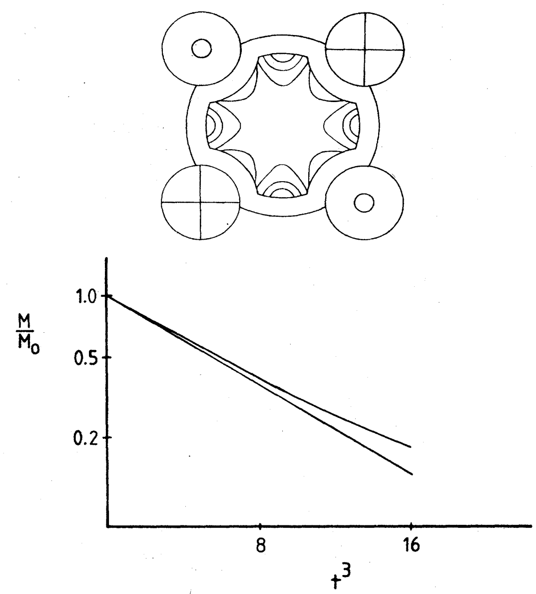

FIG. 2. (top) Model sample and quadrupole coil assembly. The sample sits in a 5-mm-diam NMR tube which has a 0.5-mm wall thickness. The wire bundles are 2 mm in diameter and are indented 0.5 mm into the sample tube. For this coil, the average gradient in the sample region is $[\overline{(\nabla H_{\parallel})^2}]^{1/2}=8.89$ g/(A cm) per turn of wire and the root-mean-square deviation of $\overline{(\nabla H_{\parallel})^2}$ is $\{[\overline{(\nabla H_{\parallel})^2-\overline{(\nabla H_{\parallel})^2}]^2}\}^{1/2}/\overline{(\nabla H_{\parallel})^2}=0.358$. The gradient field contours shown are for $\nabla H_{\parallel}=4$, 6, 8, and 10 g/(A cm) per turn of wire. (bottom) Spin-echo decay envelopes for unrestricted diffusion using the above sample and coil assembly. The upper curve is obtained by numerical evaluation of Eq. (49). The lower curve is obtained from Eq. (45). Time is measured in units of t_D, where $t_D/0.125=12/[\gamma^2 D\overline{(\nabla H_{\parallel})^2}]$. At $M/M_0=0.5$, calculated from Eq. (49), the attenuation calculated from Eq. (45) is $M/M_0=0.482$.

here, the current carrying wires are deliberately positioned very close to the sample; because of this, the gradient produced in the sample region is very strong and highly nonuniform. Numerical computation of the decay envelopes (Fig. 2, bottom) shows that as long as the echo is not attenuated to less than ~ 0.5 of its original height, Eq. (45) will be a good approximation to Eq. (49) for an inhomogeneous field of the type used during a diffusion experiment. The same considerations also apply to the pulsed-gradient case, Eq. (46).

For intermediate times, $t \approx R^2/D$, the actual phase distribution and the accuracy of the solutions are not known for any form of inhomogeneous field. However, the time-independent uniform gradient result [Eq. (32)] is identical to that obtained by other authors[13,18] using different methods.

VI. CONCLUSION

We have extended the range of external conditions for interpretation of NMR measurements of diffusion. Using Fourier expansions of the inhomogeneous magnetic field, we can present a method which allows nonuniform field gradients to be treated in an approximate way in either pulsed or steady-state modifications and for restricted or unrestricted diffusion. The results are applicable to standard spin-echo and stimulated echo diffusion measurements. The geometry we have considered is rectangular; consequently the results in the restricted diffusion case are only a rough guide if used for other boundary conditions. On the other hand, they are valid for unrestricted diffusion in samples of arbitrary shape. This is the first calculation of diffusive spin-echo attenuation for arbitrary inhomogeneous magnetic field profiles and for a pulsed gradient in a rectangular geometry. Our derivations concur with previous work in the appropriate limits with one exception; the Stejskal-Tanner calculation for restricted diffusion in a pulsed uniform gradient.

In our discussion it was necessary to make one approximation. This was that the nuclear magnetic moment phase distribution is Gaussian. The accuracy of this approximation and of the solutions under various conditions has been discussed.

Our results allow some improvement in efficiency of the NMR diffusion technique. Normally, field-gradient coils are used that optimize the uniformity of the gradient, often at the expense of its strength. This is not necessary. The most efficient design is to place the gradient coil turns as close to the sample as possible. The average squared gradient field can then be calibrated with liquids of known diffusivity using Eq. (45) or (46). If it is desirable to attenuate the echo to very low levels, Eq. (49) could be used, provided the additional condition needed for its validity is satisfied. A more complicated gradient field calibration procedure would than be necessary. We estimate that in sacrificing the uniformity condition of the applied field gradient, it should be possible to gain a factor of approximately 3 in average gradient field strength per unit current, improving the sensitivity of diffusion measurements by an order of magnitude. Of course, the additional sample heating problems created by such close proximity of the gradient coils would have to be dealt with.

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$$\left\langle \exp\left[ik\zeta\sum_{j=r}^{s} a_j\right]\right\rangle = \langle \exp(ik\zeta a_r)\rangle\langle \exp(ik\zeta a_{r+1})\rangle \times \cdots \langle \exp(ik\zeta a_s)\rangle \ ,$$

since all terms in the sum are independent. Using the probabilities $P(a_j=1)=\frac{1}{2}$ and $P(a_j=-1)=\frac{1}{2}$, the average value of each factor is found to be $\cos k\zeta$; there are $s-r+1$ factors in all.

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