Principles of Nuclear Magnetic Resonance Microscopy

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6.2 Introduction to translational dynamics

6.2.1 *The conditional probability function and self-diffusion*

In NMR a signal is never detected from one spin alone but instead via a coherent superposition of signals from a very large number of spins. Because of this we need to adopt an 'ensemble-averaged' view in order to depict the overall behaviour. This section describes approaches for dealing with translational motions in molecular ensembles.

In general, the motion of a molecule i can be characterized by some time-dependent displacement $r_i(t)$. This function will often vary in a random way from molecule to molecule so that one is forced to adopt the language of statistics. There are a variety of mathematical tools which can be helpful in this approach. For example, we can speak of the probability that a particle will have displacement r' at a time t. Usually, this probability function will depend not only on the time interval t but also on the starting position r. One such function is well known in scattering theory and sometimes called the Van Hove correlation function,[5] $P(r|r', t)$. $P(r|r', t)$ gives the likelihood of finding *any* scattering centre 'positioned' at (r', t) if there was a scattering centre at $(r, 0)$. The Van Hove function determines the nature of the inelastic scattering which will occur when X-rays, light, or neutrons are incident on an ensemble of moving scatterers.[6] The problem with the Van Hove function is that it correlates the positions of $r_i'(t)$ and $r_j(0)$ for $i \neq j$ as well as for $i = j$ and is therefore sensitive to relative motions.

There is another conditional probability which describes the correlations when $i = j$ only. This is the *self*-correlation function,[7] $P_s(r|r', t)$ which gives the chance that a molecule initially at r will have moved to r' after a time t. Obviously the facility to measure P_s would be very helpful since descriptions of self-motion are so much simpler. At the microscopic level only two techniques have the inherent labelling required to measure self-correlations. These are pulsed gradient spin echo (PGSE) NMR[8-11] and polarized neutron scattering[12-14] in which the polarized and depolarized scattering cross-sections separately reveal $P(r|r', t)$ and $P_s(r|r', t)$. In the case of neutron diffraction the depolarization of the neutrons is associated with spin flips in the scattering nuclei, an effect which makes it intrinsically possible to locate the scattering centre. The associated 'collapse of the wavefunction' necessarily removes interference effects, a point which is delightfully described in the book by Feynman, Leighton, and Sands,[15] so removing all dynamical effects due to relative motion. An obvious analogy is possible in the case of nuclear magnetic resonance where the observed photon can be clearly identified with a specific nucleus via the characteristic Larmor frequency. Any sensitivity to motion in NMR necessarily reveals the self-motion rather than relative motion of the nuclei.

It is important to note that the total probability, $\Psi(r', t)$ of finding a particle at position r' at time t is given by

$$\Psi(r', t) = \int \Psi(r, 0) P_s(r|r', t) dr \tag{6.1}$$

where $\Psi(r, 0)$ is, of course, just the particle density, $\rho(r)$.

A nice application of the function Ψ can be found in the example of self-diffusion. The classical description of diffusion is via Fick's law[16] where the particle flux (per unit area per unit time) is set proportional to the particle concentration gradient. For self-diffusion, there is no net concentration gradient. None the less, the Fick's law description is possible using $\Psi(r', t)$ in place of the concentration, since, like a concentration function, $\Psi(r', t)$ describes the likelihood of finding a particle in a certain place at a certain time. The difference in approach arises from the fact that, whereas concentration refers to the density of any particle of a particular type, $\Psi(r', t)$ is a sort of ensemble-averaged probability concentration for a *single* particle. It is therefore appropriate in considering self-diffusion. Because the spatial derivatives in Fick's equations refer to the coordinate r', inspection of eqn (6.1) shows that they can be written in terms of P_s with the initial condition,

$$P_s(r|r', 0) = \delta(r' - r). \tag{6.2}$$

Thus

$$J = -D\nabla' P_s \tag{6.3}$$

where J is the 'conditional probability flux'. Because the total conditional probability is conserved, the continuity theorem applies and

$$\nabla' \cdot J = -\partial P_s / \partial t. \tag{6.4}$$

Combining eqns (6.3) and (6.4) we obtain the differential equation sometimes known as Fick's second law,

$$\partial P_s / \partial t = D\nabla'^2 P_s \tag{6.5}$$

where D is the molecular self-diffusion coefficient.

We will first obtain the solution to eqn (6.5) for the special boundary condition which applies for unrestricted self-diffusion. This is simply $P_s \to 0$ as $r' \to \infty$ and, combined with the initial condition of eqn (6.2), yields,

$$P_s(r|r', t) = (4\pi Dt)^{-3/2} \exp\{-(r' - r)^2/4Dt\}. \tag{6.6}$$

The fact that P_s depends only on the net displacement, $r' - r$, and not the initial position, r, reflects the Markov nature of Brownian motion

statistics.[17] In a fundamental sense it is this net displacement which is measured in PGSE NMR. For the purpose of this book we will refer to the vector $r' - r$ moved over a time t as the dynamic displacement R. This is illustrated in Fig. 6.1.

It is important to distinguish this dynamic displacement from the static quantity r measured in k-space imaging. In neutron scattering the momentum transfer determines the dynamic displacement scale giving an upper limit of around 100 Å. The relevant time-scale of neutron scattering is determined by the energy resolution, the best result being achieved by the neutron spin echo method[18,19] for which the time-scales are a few microseconds or less. By contrast, PGSE NMR is limited, in practice, to dynamic displacements of between 100 Å and 100 μm and over time-scales of a few milliseconds to a few seconds. The two methods are therefore complementary. The dimensional scale of PGSE NMR corresponds to the 'organizational' domain. It includes structural features of macromolecular solutions, mesophase structure of liquid crystals, emulsions, porous solids, and highly disperse biological tissue.

Developing this concept of the dynamic displacement it is possible to use eqn (6.1) to define a new and very useful function, sometimes called the 'average propagator',[20] $\overline{P}_s(R, t)$. This function gives the average probability for any particle to have a dynamic displacement R over a time t and is given by

$$\overline{P}_s(R, t) = \int P_s(r|r + R, t)\rho(r)\, dr. \tag{6.7}$$

In cases such as the free self-diffusion example just considered, where $P_s(r|r + R, t)$ is independent of starting position, the average propagator is common to all molecules in the ensemble so that the bar above may be dropped. We could then write

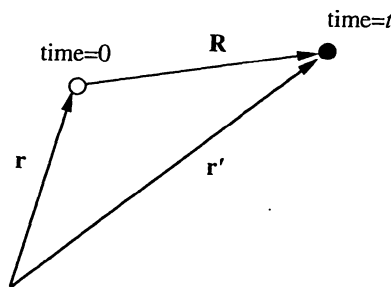$$P_s(R, t) = (4\pi Dt)^{-\frac{3}{2}} \exp(-R^2/4Dt). \tag{6.8}$$

For completeness we now make a simple extension to eqn (6.8) which applies when the diffusion is superposed on flow of velocity v. In this case a term $\nabla' \cdot v P_s$ must be added to the right-hand side of eqn (6.5) to give[10,21]

$$\partial P_s/\partial t = \nabla' \cdot v P_s + D\nabla'^2 P_s. \tag{6.9}$$

If v is constant then the solution is

$$P_s(R, t) = (4\pi Dt)^{-\frac{3}{2}} \exp\{-(R - vt)^2/4Dt\}. \tag{6.10}$$

Note that P_s is a normalized Gaussian function of dynamic displacement R, with width increasing as time advances. Sometimes it is helpful to write $P_s(R, t)$ in Cartesian component form as

$$P_s(R, t) = (4\pi Dt)^{-\frac{3}{2}} \exp\{-(X - v_x t)^2/4Dt\} \exp\{-(Y - v_y t)^2/4Dt\}$$
$$\times \exp\{-(Z - v_z t)^2/4Dt\} \tag{6.11}$$

and where we are concerned only with motions along one dimension (e.g. the z-axis) we can integrate over the remaining two dimensions to obtain

$$P_s(Z, t) = (4\pi Dt)^{-\frac{1}{2}} \exp\{-(Z - v_z t)^2/4Dt\}. \tag{6.12}$$

The behaviour of $P_s(Z, t)$ as a function of time is illustrated in Fig. 6.2 in the cases where the velocity is finite. It is a useful exercise in calculating ensemble-averaged properties to evaluate the mean square dynamic displacement for $v_z = 0$. Using a bar to represent an ensemble average,
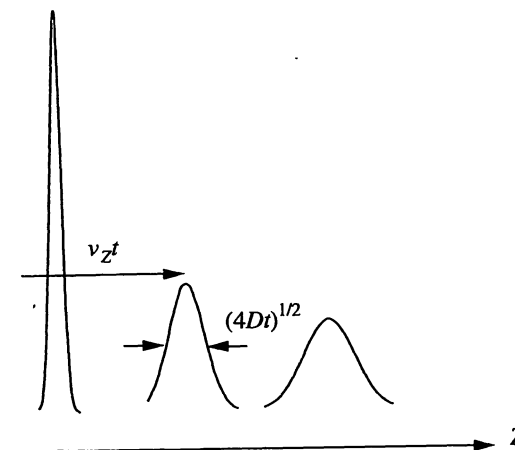

Fig. 6.1 Displacement of particle from r to r^1 over time t.

Fig. 6.2 Behaviour of the conditional probability function, P_S, for an ensemble of particles undergoing Brownian motion and flow. The successive Gaussians correspond to successively increasing time.

$$\overline{Z^2} = \int_{-\infty}^{\infty} Z^2 P_s(Z, t) \, dZ$$

$$= 2Dt. \tag{6.13}$$

Once again it must be emphasized that the Markov statistics of self-diffusion are a special case and care must be exercised in using the propagator function $P_s(\mathbf{R}, t)$. Later we shall deal with specific examples of $P_s(\mathbf{r}|\mathbf{r}', t)$ for more complicated motion where no common propagator exists for all particles in the system. In such cases the averaging process appropriate to the NMR experiment must be carefully adopted.

6.2.2 Velocity correlation, spectral density, and the self-diffusion tensor

$P_s(\mathbf{r}|\mathbf{r}', t)$ helps us calculate averages across the ensemble of spins. Sometimes a problem naturally lends itself to a description in terms of this function but in other situations the connection is not so obvious. One alternative approach in dealing with behaviour which fluctuates with time is to define families of autocorrelation functions. Suppose we have some molecular quantity A which is a function of time. The autocorrelation function of A is[22,23]

$$G(t) = \int_0^{\infty} A(t')A(t' + t) \, dt'.^{\dagger} \tag{6.14}$$

Now suppose that we are dealing with a *stationary ensemble*. This means that the origin of time does not matter, only the interval over which we measure. In effect this means that the NMR experiment can begin whenever we like and that the result will always be the same. This will be a very good assumption, except in those special cases dealt with in Chapter 8 where slow or periodic fluctuations occur. In a stationary ensemble the average over time implied by eqn (6.14) could equally be an average over the particles in the ensemble since one particle is representative of all particles over a long enough time interval. Incorporating these ideas we will rewrite $G(t)$ as

$$G(t) = \overline{A(0)A(t)}. \tag{6.15}$$

If we happen to know the function A in terms of position coordinates rather than time coordinates, then we can calculate $G(t)$ with the help of P_s since

$$\overline{A(0)A(t)} = \iint \rho(\mathbf{r})P_s(\mathbf{r}|\mathbf{r}', t)A(\mathbf{r}')A(\mathbf{r}) \, d\mathbf{r}' \, d\mathbf{r}. \tag{6.16}$$

In effect $G(t)$ measures the rate at which $A(t)$ 'loses memory' of its pre-

†Strictly speaking eqn (6.14) should read $A(t')A^*(t' + t)$ but we shall mostly be concerned with observable, and hence real, functions.

vious values. The time-scale for this loss of memory is called the correlation time, τ_c, and is defined by[22,23]

$$\tau_c = \frac{\int_0^{\infty} \overline{A(0)A(t)} \, dt}{\overline{A(0)^2}}. \tag{6.17}$$

In some experiments it is the spectrum, or Fourier transform, of $G(t)$ which is important. For example, where A corresponds to the dipolar interaction between spins which fluctuates as a molecule rotates, the spin relaxation times are sensitive to the spectrum of $G(t)$, and, in particular, to its value at certain characteristic frequencies. Notice that for rotational motion the treatment is similar to that shown in eqn (6.16) except for the use of angular displacement variables instead of translational displacement variables. In relaxation theory the spectrum of the dipolar Hamiltonian correlation function is known as the spectral density function[24] $J(\omega)$. In translational motion theory the spectrum of the velocity correlation function is known as the self-diffusion tensor,[25,26] $D_{\alpha\beta}(\omega)$, where α and β may take each of the Cartesian directions, x, y, z. Hence

$$D_{\alpha\beta}(\omega) = \tfrac{1}{2} \int_{-\infty}^{\infty} \overline{v_\alpha(0)v_\beta(t)} \exp(i\omega t) \, dt. \tag{6.18}$$

Generally we shall not be concerned with correlations between differing components of $\mathbf{v}(t)$ except where we deliberately apply magnetic field gradients which fluctuate in direction. We shall therefore focus on the diagonal elements of D and, using the even property of $G(t)$, we write

$$D_{zz}(\omega) = \int_0^{\infty} \overline{v_z(0)v_z(t)} \exp(i\omega t) \, dt. \tag{6.19}$$

Eqn (6.19) tells us that the zero-frequency component of D is simply the time integral of the velocity correlation function, i.e.,

$$D_{zz}(0) = \int_0^{\infty} \overline{v_z(0)v_z(t)} \, dt. \tag{6.20}$$

By definition, therefore, $D_{zz}(0)$ is $\overline{v_z^2}\,\tau_c$.

6.2.3 The relationship between $\overline{v_z(0)v_z(t)}$ and P_s

In order to find the relationship between $\overline{v_z(0)v_z(t)}$ and P_s we employ eqn (6.16). The correlation $\overline{z(t_1)z(t_2)}$ can be obtained from

$$\overline{\{z(t_1) - z(t_2)\}^2} = \overline{z^2(t_1)} + \overline{z^2(t_2)} - 2\overline{z(t_1)z(t_2)}$$