Restricted Internal Segmental Rotational Diffusion Model with Segment-Segment Interactions. Application to $^{13}$C NMR

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The restricted rotational-diffusion model developed by Wittebort and Szabo (J. Chem. Phys. 69, 1722 (1978)) and London and Avitabile (J. Am. Chem. Soc. 100, 7159 (1978)) is extended to include in a mean field sense, dynamic interactions between the diffusing motional unit, and an environment that may have Fourier components on the same time scale as the reorienting unit. Furthermore in contrast to previous work, an exact closed form, analytical expression for the spectral density is derived. Illustrative calculations are presented for the spin–lattice relaxation time, $T_1$, spin–spin relaxation time, $T_2$, and nuclear Overhauser enhancement factor for a $^{13}$C nucleus relaxing by a dipolar mechanism with the directly bonded proton; a comparison of $T_1$, $T_2$, and NOE of the weak and strong coupling limits of the segment-segment dynamic interaction model is also made. It is proposed that NMR relaxation experiments be performed over a range of external field strengths $H_0$ to differentiate between a restricted rotational model with and without dynamic interactions.

INTRODUCTION

Over the past few years various motional models have been proposed to interpret NMR relaxation measurements of quantities such as spin–lattice relaxation times, $T_1$, and nuclear Overhauser enhancement factors. These motional models include jump models between lattice sites (1–9), continuous (isotropic or anisotropic) rotational diffusion models (10–14), and more recently a restricted rotational diffusion model for angular motion within a sector (5, 9, 15–17). We focus here on the restricted rotational diffusion model because of its possible widespread applicability. It has been proposed to account for the $^{13}$C NMR relaxation measurements of protein side chains in solution (5, 15–17) and as a possible mechanism of spin–lattice relaxation in solids (9). The present treatment differs from previous work on the restricted rotational diffusion model in two respects. Rather than expressing the spectral density, $J(\omega)$, as a sum over an infinite series of rational polynomials we derive a closed form analytic expression for $J(\omega)$. Furthermore, based on our previous work on orientational-diffusion models of polymer local, main-chain motion (18–20), we extend the restricted rotational-diffusion model to include motional segment–segment dynamic interactions in a mean-field approximation via the inclusion of a complex damping constant in the diffusion equation for the probability density. Representative calculations are performed for the $^{13}$C spin–lattice and spin–spin relaxation times and for the NOE factor for systems with and without appreciable segment–segment interactions.
Let us begin with an examination of the conditions under which a restricted rotational-diffusion model is and is not appropriate. The restricted rotational-diffusion model should be applicable to those situations where the effective rotational potential possesses a broad potential energy minimum with "walls" (i.e., very high potential barriers) that effectively restrict the motion to lie within an angular sector of extent, $\phi_0$. The "walls" may conceivably arise either from the intrinsic vacuum phase rotational potential of the reorienting unit, i.e., an intramolecular effect, or perhaps (and more likely) from geometric constraints due to the packing of the neighbors about the motional segment, i.e., an intermolecular effect, or possibly a combination of both effects. The interacting motional segments may in reality be different pieces of the same or different chains in the case of polymers or proteins or may be different small (asymmetric) molecules in a low molecular weight amorphous solid. If the "wall" remains fixed and rigid on the NMR time scale, we have the restricted orientational-diffusion model developed previously (5, 15-17). However, as shown in previous work (20), in addition to the low-frequency component schematically represented in the model by the rigid wall, the motional segments can in principle interact with each other, conceivably causing loss or gain in orientational correlation, e.g., by segment-segment collisions. We can account for these effects by the inclusion of a complex damping constant in the diffusion equation describing the temporal and spatial evolution of the probability density. By varying the magnitude of the imaginary part of the damping constant, one can qualitatively examine the relative importance of such segment-segment interactions.

If the effective rotational potential permits only relatively small angular excursions, then the rotational potential is quite steep and the orientational motion within the potential well is oscillatory rather than diffusional in nature. In this case a torsional oscillator model that is either underdamped or overdamped depending on the situation is a more realistic description of the physics. The papers of Shore and Zwanzig (21), Barkley and Zimm (22), Allison and Schurr (23) and Carpenter and Skolnick (24) contain a more detailed discussion of the torsional oscillator model. Thus, while the $\phi_0 \to 0$ limit of the restricted rotational-diffusion model is well defined mathematically, it does not adequately describe the physical situation (16).

In the other extreme, the $\phi_0 \to 2\pi$ limit of the restricted rotational-diffusion model is also unphysical (16), since it requires a single $\delta$-function thick reflecting wall in the molecule (a most unlikely situation). In this case, a continuous rotational-diffusion model is clearly to be preferred. Hence, the restricted angular sector model is appropriate only when the allowed sector $\phi_0$ lies between the limit of small and very large ($2\pi$) values of $\phi_0$.

It should be pointed out that the restricted rotational-diffusion model described below is applicable both to dilute solutions and amorphous solids and is valid given that orientational coupling between multiple internal rotations can be ignored. If not, the methodology described by Wittebort and Szabo could be employed to extend the present work (5).

In the following section entitled General Theory, we derive a series expression for the autocorrelation function and an exact closed-form solution for the spectral density of the restricted rotational-diffusion model with complex damping (the details of the latter derivation are relegated to the Appendix). These quantities are in turn related
to properties measured in a typical $^{13}$C NMR experiment, namely $T_1$, $T_2$, and the NOE. Then in the section entitled Numerical Results we calculate $T_1$, $T_2$ and NOE for the restricted diffusion model with and without intersegment interactions. We point out several characteristic signatures indicating when the inclusion of the imaginary part of the damping constant representing segment–segment interactions is necessary. The Summary section summarizes the conclusions of the present work and points out possible directions of future research.

COMPLEX DAMPED RESTRICTED ROTATIONAL-DIFFUSION MODEL: GENERAL THEORY

Let the axis of rotation lie along the $\hat{z}$ axis and suppose for definiteness that the C–H vector lies at $(\theta, \phi)$ in spherical coordinates. Hence the C–H vector makes an angle $\theta$ with respect to the axis of rotation and is a priori constrained to lie between

$$0 \leq \phi \leq 2\pi.$$  \[1\]

We shall assume that the dominant mechanism for the $^{13}$C nuclei is dipolar relaxation with the directly bonded proton (25, 26). (Actually, for the development of the model we need not limit ourselves to the assumption of $^{13}$C–$^1$H relaxation mechanism, but need merely require that the dominant relaxation mechanism probe the motion of some vector that undergoes restricted rotational diffusion.) By analogy to the previously developed damped orientational-diffusion model of polymer local, main-chain motion the conditional probability $p[\phi(t), \phi(0)]$ that the system is at an angle $\phi(t)$ at time $t$ given that it started out at $\phi(0)$ at time zero obeys the equation

$$\frac{\partial p}{\partial t} = D \frac{\partial^2 p}{\partial \phi^2} - (\beta + i\gamma)p$$  \[2\]

where $D$ is the rotational diffusion constant characterizing motion about the molecule fixed $\hat{z}$ axis and $\beta$ is the real part of the damping constant and can arise from various sources. If the overall molecular motion is isotropic and diffusional in character

$$\beta = 6D_0$$  \[3\]

where $D_0$ is the isotropic diffusion constant (16). By analogy to the polymer case, $\beta$ is more generally a frictional damping term reflecting the interaction of the reorienting segment with the high-frequency modes of the solvent if the system is in solution, or with adjacent motional units if the system is a solid. Finally $\gamma$ accounts for the exchange of orientational correlation between neighboring motional segments. The complex damped-diffusion equation may be derived by a multiple scattering treatment in the mean-field approximation of the segment–segment interactions using an optical potential to account for the sources and sinks of orientational correlation. For a more detailed description of the derivation we refer to previous work (20).

Equation [2] is to be solved subject to the boundary condition

$$\left( \frac{\partial p}{\partial \phi} \right)_{\phi=0, \phi_0} = 0.$$  \[3a\]
That is, reflecting walls are located at $\phi = 0$ and $\phi = \phi_0$. Equation [3a] specifies that there is no flux through the walls. We must also solve Eq. [2] subject to the initial condition

$$\rho[\phi(t), \phi(0)]_{t=0} = \delta[\phi(t) - \phi(0)] \tag{3b}$$

The general solution to Eq. [2] can be written as

$$\rho[\phi(t), \phi(0)] = \phi_0^{-1} \sum_{n=0}^{\infty} (2 - \delta_{n0}) e^{-\lambda_n t} \cos \left[ n\pi \phi(0)/\phi_0 \right] \cos \left[ n\pi \phi(t)/\phi_0 \right], \tag{4a}$$

with $\delta_{n0}$ the Kronecker delta, and

$$\lambda_n = \frac{Dn^2\pi^2}{\phi_0^2} + \beta + i\gamma. \tag{4b}$$

In the following we shall require ensemble averages of the form

$$\langle C(t) \rangle_{\text{int}} = \int_0^{\phi_0} d[\phi(t)] \int_0^{\phi_0} d[\phi(0)] C(t) \rho[\phi(t), \phi(0)]/\phi_0 \tag{5a}$$

with

$$C(t) = \cos k[\phi(t) - \phi(0)] \tag{5b}$$

and $k$ an integer. Note that $1/\phi_0$ is the a priori probability of finding the system at time zero with $\phi(0)$.

Substituting Eq. [4a] into Eq. [5a] and evaluating the integrals we find

$$\langle C(t) \rangle_{\text{int}} = 4k^2 e^{-\lambda t} \sin^2 \left( k\phi_0/2 \right) + \frac{4k^2}{\phi_0} \sum_{n=1}^{\infty} A_{kn} e^{-\lambda_n t} \tag{6a}$$

where

$$A_{kn} = \frac{\left[ 1 - (-1)^n \cos k\phi_0 \right]}{(k^2 - n^2\pi^2/\phi_0^2)} \tag{6b}$$

if $k \neq n\pi/\phi_0$. If $k = n\pi/\phi_0$ applying L'Hospital's rule to Eq. [6b] we have

$$A_{kn} = \frac{\phi_0^2}{8k^2}. \tag{6c}$$

It may be readily verified that Eqs. [6a]–[6c] (with $\gamma = 0$) are equivalent to Eq. [12] of London and Avitabile if one assumes that the axes of rotation, $z$, are randomly oriented (16); that is, that a powder average may be taken (see below). The present form of Eqs. [6a]–[6c] is more suitable for further analysis.

Actually what will be required for the calculation of $T_1$, $T_2$, and NOE is not the autocorrelation function itself, but the cosine transform of the $C(t)$ given by

$$j_k(\omega) = \text{Re} \int_0^{\phi_0} dt e^{-i\omega t} \langle \cos \{k[\phi(t) - \phi(0)]\} \rangle_{\text{int}}. \tag{7a}$$

Substituting Eq. [6a] into Eq. [7a] and performing the integration gives

$$j_k(\omega) = \frac{4\beta \sin^2 \left( k\phi_0/2 \right) + 4k^2}{k^2\phi_0^2[\beta^2 + (\omega - \gamma)^2]} \sum_{n=1}^{\infty} A_{kn} \left( \beta + Dn^2\pi^2/\phi_0^2 \right)^2 + (\omega - \gamma)^2. \tag{7b}$$
It is readily apparent that the only consequence of introducing segment–segment
dynamic interactions is to introduce a shift factor $\gamma$ into the frequency dependence
of $j_k(\omega)$. Setting $\gamma = 0$ in Eq. [7b], we recover the previously derived infinite series
expression for restricted rotational diffusion with real damping.

The series expression of $j_k(\omega)$ can be summed (see Appendix for the details of the
method) yielding as an exact analytic expression

$$j_k(\omega) = \frac{\Phi_0}{D\pi^4} \left[ -2\pi \gamma^2 (R_1 - R_2 \cos \pi \gamma) + \frac{\pi^2 (\gamma^2 + \beta')}{(\gamma^2 + \beta')^2 + c^2} \right]$$

with

$$\gamma = k\phi_0/\pi$$  \hspace{1cm} \[9a\]
$$\beta' = \beta(\phi_0/D\pi^2)$$ \hspace{1cm} \[9b\]
$$c = \omega' - \gamma'$$ \hspace{1cm} \[9c\]

where

$$\omega' = \omega(\phi_0^2/D\pi^2)$$ \hspace{1cm} \[9d\]
$$\gamma' = \gamma(\phi_0^2/D\pi^2).$$ \hspace{1cm} \[9e\]

The functions $R_1$ and $R_2$ are defined in the Appendix by Eqs. [A-13] and [A-22],
respectively. This completes the derivation of $j_k(\omega)$.

By way of illustration in Fig. 1 we have plotted $j_2(\omega)$ for $D = 10^{10}$ rad/sec, $\beta = 6 \times 10^6$ rad/sec, $\gamma = 0$, and $\phi_0 = 120^\circ$, typical values of these parameters (16), see
below. In the limit of small $\omega$, $j_k(\omega)$ has a broad plateau region, while in the limit of
large $\omega$, $j_k(\omega) \propto \omega^{-2}$. Finally, we note that introduction of a complex damping merely
shifts the effective frequency from $\omega$ to $\omega - \gamma$.

![Graph of $j_2(\omega)$ vs $\omega$](image)

**Fig. 1.** $j_2(\omega)$ vs $\omega$ with $D = 10^{10}$ rad/sec, $\beta = 6 \times 10^6$ rad/sec, $\gamma = 0.0$, and $\phi_0 = 120^\circ$. 
Assuming a dipolar relaxation mechanism of the $^{13}$C nuclei with the directly bonded
$^1$H, $T_1$, $T_2$, and $\eta$ are related to the temporal Fourier cosine transform of the second-rank
spherical harmonic angular correlation function of the C–H bond vector defined
with respect to the laboratory fixed frame and are given explicitly by (14, 26)

\[
\frac{1}{T_1} = 4\pi N h^2 \gamma_C^2 \gamma_H^2 \frac{1}{10 r^6} \left[ J_0(\omega_H - \omega_C) + 3 J_1(\omega_C) + 6 J_2(\omega_C + \omega_H) \right] \tag{10}
\]

\[
\frac{1}{T_2} = \frac{4\pi N h^2 \gamma_C^2 \gamma_H^2}{20 r^6} \left[ 4 J_0(0) + J_0(\omega_H - \omega_C) + 3 J_1(\omega_C) + 6 J_1(\omega_H) + 6 J_2(\omega_C + \omega_H) \right] \tag{11}
\]

and the NOE is

\[
\text{NOE} = 1 + \eta = 1 + \frac{\gamma_H}{\gamma_C} \left[ \frac{6 J_2(\omega_C + \omega_H) - J_0(\omega_H - \omega_C)}{J_0(\omega_H - \omega_C) + 3 J_1(\omega_C) + 6 J_2(\omega_C + \omega_H)} \right]. \tag{12}
\]

In the above, $N$ is the number of protons directly bonded to the carbon nucleus, $\gamma_C$, $\gamma_H$ and $\omega_C$, $\omega_H$ are the gyromagnetic ratios and Larmor frequencies of the $^{13}$C and
$^1$H nuclei, respectively, and $r_{CH}$ is the C–H bond distance, taken to be 1.09 Å in the
calculations presented in the Numerical Results section.

The spectral densities, $J_m(\omega)$, in Eqs. [10]-[12] are in general given by

\[
J_m = \Re \int_0^\infty dt e^{i \omega t} \left\langle Y_m^2[\theta_L(t), \phi_L(t)] Y_m^2[\theta_L(0), \phi_L(0)] \right\rangle \tag{13}
\]

in which the spherical harmonic autocorrelation function defined with respect to the
laboratory fixed frame is (28)

\[
\left\langle Y_m^2[\theta_L(t), \phi_L(t)] Y_m^2[\theta_L(0), \phi_L(0)] \right\rangle = \int \int_{\text{unit sphere}} dS(t) dS(0) Y_m^2[\theta_L(t), \phi_L(t)] Y_m^2[\theta_L(0), \phi_L(0)] g[\theta_L(t), \phi_L(t); \theta_L(0), \phi_L(0)]. \tag{14}
\]

where $g[\theta(t), \phi(t); \theta(0), \phi(0)]$ is the conditional probability that the C–H bond vector
has spherical polar coordinates $[\theta(t), \phi(t)]$ at time $t$ given they were at $[\theta(0), \phi(0)]$ at
time zero; $dS(t) = d\theta(t) d\phi(t) \sin^2 \theta(t)$.

Expressing the spherical harmonics in terms of the local spherical polar coordinates
$(\theta, \phi)$ defined with respect to molecular fixed $\hat{z}$ axis defined previously, we have

\[
Y_m^{2,2}[\theta_L, \phi_L] = \sum_{m'} Y_m^{2,2}[\theta, \phi] D_{m'm}[\Omega] \tag{15}
\]

where $\Omega$ are the Euler angles corresponding to the rotational transformation from
the molecule fixed-coordinate system to the space fixed system, and $D_{m'm}[\Omega]$ are the
Wigner rotation matrices (28). We then substitute Eq. [15] into Eq. [14] and assume
we can decompose the average indicated in Eq. [13] into two parts

\[
\left\langle \cdots \right\rangle = \left\langle \cdots \right\rangle_{\text{int}} \left\langle \cdots \right\rangle_{\text{powder}} \tag{16a}
\]
where the averaging process represented \( \langle \rangle_{\text{in}} \) has been given in Eq. [5a] and \( \langle \rangle_{\text{powder}} \) is defined by

\[
\langle q \rangle_{\text{powder}} = \frac{1}{8\pi^2} \int d\Omega q.
\]

That is, the powder average is an unweighted average over all orientations of the Euler angles specifying the location of the motional unit with respect to the laboratory fixed frame. Of course, as is always the case in taking a powder average we are suppressing orientational information. If the experimentalist has such information (as is possible in a solid) by taking the powder average over all orientations of the solid he will arrive at the identical quantity defined in Eq. [16b]. Finally we arrive at

\[
\langle Y_m^2[\theta_L(t), \phi_L(t)]Y_m^2[\theta_L(0), \phi_L(0)] \rangle = \frac{1}{5} \sum_{m=-2}^{+2} \langle Y_m^2[\theta(t), \phi(t)]Y_m^2[\theta(0), \phi(0)] \rangle. \tag{17a}
\]

Let \( u(t) \) represent the orientation of the C–H bond vector at time \( t \) [zero]. Using the well-known addition theorem for spherical harmonics we have

\[
\langle Y_m^2[\theta(t), \phi(t)]Y_m^2[\theta(0), \phi(0)] \rangle = \frac{1}{4\pi} \langle P_2[u(t) \cdot u(0)] \rangle \tag{17b}
\]

where \( P_2 \) is the second Legendre polynomial (29). Thus for any model in which Eq. [16a] is valid all the \( J_m(\omega) \) defined in Eq. [13] are independent of \( m \).

Expressing \( u(t) \) and \( u(0) \) in spherical polar coordinates, it can be readily shown for the restricted rotational diffusion model that

\[
\langle P_2[u(t) \cdot u(0)] \rangle = A \exp[-(\beta + i\gamma)t] + B \langle \cos [\phi(t) - \phi(0)] \rangle + C \langle \cos 2[\phi(t) - \phi(0)] \rangle \tag{18a}.
\]

Here

\[
A = \frac{1}{2} \left[ 3 \cos^4(\theta) + \frac{3}{2} \sin^4(\theta) - 1 \right], \tag{18b}
\]

\[
B = \frac{3}{4} \sin^2(2\theta), \tag{18c}
\]

\[
C = \frac{3}{4} \sin^4(\theta), \tag{18d}
\]

and \( \langle \cos k[\phi(t) - \phi(0)] \rangle, k = 1, 2, \) are given by Eq. [6a].

Upon taking the Fourier cosine transform of Eq. [18a] we find that

\[
4\pi J_m(\omega) = \frac{A\beta}{\beta^2 + (\omega - \gamma)^2} + B j_1(\omega) + C j_2(\omega) \tag{19}
\]

where \( j_k(\omega) \) is given by Eq. [7b].

**Limiting Behavior**

In the motional narrowing limit where \( \beta \to \infty \) we would expect \( J_m(\omega) \) to be independent of \( \phi_0 \) beyond a certain minimum value of \( \phi_0 \), say \( \phi_{\text{min}} \). Basically, once
the allowed angular sector exceeds $\phi_{\min}$ the orientational correlation dies out due to the damping before the reorienting vector ever sees the wall. Thus in the limit of large damping constant, $T_1$, $T_2$, and NOE are insensitive probes of the allowed angular sector. Furthermore if $\gamma \ll \beta$ with $\beta$ large we remain in the motional narrowing large $\beta$ limit. However, if $\gamma$ is on the order of $\beta$, even though $T_1$, $T_2$, and NOE are essentially independent of $\phi_0$, they will depend on the value of $\gamma$.

Now let us consider the limit where $D \to \infty$; it follows most readily from the series representation of $j_k(\omega)$, Eq. [7b], that

$$
\lim_{D \to \infty} j_k(\omega) = \frac{4\beta \sin^2 (k\phi_0)}{k^2 \phi_0^2 [\beta^2 + (\omega - \gamma)^2]}. \tag{20}
$$

In the large $D$ limit, $j_k(\omega)$ and therefore $J_m(\omega)$ probe the full allowed angular range and are therefore in principle sensitive functions of $\phi_0$. We should also point out that it is also possible to show that Eq. [8] reduces to Eq. [20] in the limit that $D \to \infty$.

Clearly if $\omega \gg \gamma$, $T_1$, $T_2$, and $\eta$ will not be significantly altered by a nonzero $\gamma$; i.e., we are in the weak coupling limit. However, when $\omega$ is of the same order of magnitude as $\gamma$, since the effective frequency is $\omega - \gamma$, significant changes in $T_1$, $T_2$, and $\eta$ are expected. When $\omega$ is about equal to $\gamma$, this is equivalent to shifting $j_k(\omega - \gamma)$ to the low frequency plateau regime (see, for example, Fig. 1) of the equivalent system where segment-segment dynamic interactions are unimportant. While this has no effect on any of the motional narrowing limits discussed above provided $\gamma < D$ or $\beta$, it has significant consequences in the slow orientation regime. We take up illustrative examples below.

Suppose that the external magnetic field is adjusted such that $\omega = (\omega_C + \omega_H, \omega_C, \omega_H, \text{or } \omega_H - \omega_C) = \gamma$, then the spectral density is several orders of magnitude larger in the vicinity of $\omega = \gamma$ than at other frequencies. In this limit, when $J(\omega = \gamma)$ completely dominates the relaxation parameters we find from Eqs. [10] and [11] that, if $\gamma = \omega_C, \omega_H \pm \omega_C$

$$
T_2 = 2T_1. \tag{21a}
$$

Suppose that $\omega = \omega_H$

$$
\frac{1}{T_2} = \frac{4\pi N_H^2 \gamma^2 \gamma_C^2}{20\nu^6} [4J_0(0) + 6J_1(\omega_H)]. \tag{21b}
$$

Furthermore, for $\gamma = \omega_H - \omega_C$,

$$
\eta = -\frac{\gamma_H}{\gamma_C}, \tag{22a}
$$

for $\gamma = \omega_C$

$$
\eta = 0, \tag{22b}
$$

and for $\gamma = \omega_H + \omega_C$

$$
\eta = \frac{\gamma_H}{\gamma_C}. \tag{22c}
$$

It should be pointed out that values of the NOE normally encountered lie between one and three (25). The model with dynamic coupling affords the possibility of values of $-3 \leq \text{NOE} \leq 5$. While we know of no such values of the NOE encountered for the case of a segmental diffusion model as applied to protein side chain motion (17),
this by no means a priori precludes the possibility of the measurement of an anomalous \( \eta \) of the type indicated in Eqs. [22a]–[22c] in either the whole sample or a fraction thereof in the future. Thus, if a negative NOE is observed for a fraction of the sample it should not be suppressed. The restricted internal segmental diffusion model with chain–chain coupling provides a rational basis for the interpretation of such a negative value of the NOE.

In the region where the Larmor frequencies \( \omega_c \) and \( \omega_H \) are on the order of \( \gamma \), but \( J_{\mu} (\omega = \gamma) \) does not completely dominate \( T_1^{-1} \), we would expect \( T_2 \) values to be larger than \( T_1 \) and the NOE to undergo appreciable variation over a fairly small frequency range. Thus, provided one is in the slow reorientation (\( \gamma \) and \( \beta < D \)) limit it should be possible to differentiate between systems possessing weak coupling (\( \gamma \sim 0 \)) and fairly strong coupling \( \gamma = \mathcal{O}(\omega_c) \). Observe that in the limit \( \gamma \gg \omega_H \) we would expect very long \( T_1 \) and \( T_2 \) values and an \( \eta \) typical of that encountered in the slow reorientation limit in the absence of chain–chain coupling. Hence there exist characteristic signatures indicating when dynamic coupling is important in the restricted rotational-diffusion model of segmental reorientation.

NUMERICAL RESULTS

General Considerations

In this section, we shall flesh out and substantiate by illustrative calculations the qualitative picture developed above. Calculations will be presented for the \( ^{13}C \) \( T_1 \), \( T_2 \), and NOE relaxation parameters as a function of \( \phi_0 \), the maximum allowed angular excursion, \( \gamma \), the motional segment–segment interaction parameter, and \( \beta \), the real part of the damping coefficient. In particular comparison of results for the nonzero \( \gamma \) with the \( \gamma \sim 0 \) limit derived previously by Wittebort and Szabo (5) and London and Avitabile (16) will be made.

To verify the validity of the closed-form analytical expression for the spectral density, we performed a whole series of calculations comparing the closed form solution, Eq. [8], with the infinite series solution, Eq. [7b]. In both the underdamped and overdamped limit, virtually identical (to at least seven significant figures) agreement between the analytic and series expression was obtained for values of \( 5^\circ \leq \phi_0 < 360^\circ \), over a range of \( 0 \leq \beta \leq 6 \times 10^{10} \), and \( 0 \leq \gamma < 10^{11} \), \( 10^6 \leq D \leq 10^{10} \), and \( \omega \leq 10^{10} \) rad/sec.

As pointed out by London and Avitabile (16), the most pronounced nonmonotonic behavior in \( j_k (\omega) \) occurs for \( \theta = 90^\circ \), i.e., for C–H bond vectors located at right angles to the axis of rotation. Thus in the calculations presented below we restrict ourselves to \( \theta = 90^\circ \); moreover we shall take the C–H bond length to be 1.09 Å and set \( \omega_c \) equal to 25.2 MHz.

Motional Narrowing Limit

We begin with a discussion of the large damping (\( \beta > D \)) motional narrowing limit. We have calculated \( NT_1, \ NT_2, \) and NOE vs \( \phi_0 \) in the large \( \beta \) limit; \( \beta \) was set equal to \( 10^{10} \) rad/sec, \( D \) was chosen to be \( 10^6 \) rad/sec, and \( \gamma \) was set equal to 0 and \( 10^{10} \) rad/sec. We found that in the large damping limit all three relaxation parameters
are essentially independent of $\phi_0$. Thus as indicated previously in the large damping limit $T_1$, $T_2$, and NOE cannot provide any information whatsoever on the angular amplitude of the motion. Moreover, $NT_1$ and $NT_2$ are essentially equal, with values 0.4844 vs 0.4840, respectively, when $\gamma = 0$ and values 0.9112 and 0.9198, respectively when $\gamma = 10^{10}$ rad/sec (in the motional narrowing limit both parameters essentially all probe $J(0)$). However, while the NOE is essentially independent of $\gamma$ (going from 2.9821 when $\gamma = 0$, to 3.044 when $\gamma = 10^{10}$ rad/sec), $NT_1$ and $NT_2$ have increased with increasing $\gamma$ by about a factor of 2.

**Approach to Slow Reorientation Limit**

We now turn to the other limit where $D$ is either the same magnitude as $\beta$ or several orders of magnitude larger. To facilitate comparison with London and Avitabile we have set $D = 10^{10}$ rad/sec and calculated $NT_1$, $NT_2$, and NOE using the analytic expression for the spectral density for $\beta = 6 \times 10^6$, $6 \times 10^7$, $6 \times 10^8$, $6 \times 10^9$, and $6 \times 10^{10}$ rad/sec. For $\gamma = 0$, we reproduce the curves given previously by London and Avitabile (16). In Figs. 2A–C we have plotted $NT_1$, $NT_2$, and NOE vs $\phi_0$ for $D = 10^{10}$ rad/sec, $\beta = 6 \times 10^{10}$ rad/sec, and $\gamma = 0$ (solid curves) and $\gamma = 10^{11}$ rad/sec (dashed curve), respectively. Observe that as would be expected the changes in the $NT_1$ and $NT_2$ vs $\phi_0$ curves are most appreciable for small values of $\phi_0$. For $\beta$ on the order of $D$ the diffusing C–H vector can see the walls before the orientational correlation dies off. However, as is characteristic of the motional narrowing regime,
NT₁ and NT₂ are identical when γ = 0, and lie very close to each other when γ = 10^{11} rad/sec. Observe that increasing γ has increased the magnitude of both NT₁ and NT₂. Finally, we point out that the NOE remains essentially unchanged on increasing γ from 0 to 10^{11} rad/sec.

Effect of γ in Slow Reorientation Limit

Let us now examine the small damping limit (slow overall reorientation superimposed on internal rotational diffusion). In Figs. 3–5, respectively, we have plotted NT₁, NT₂, and NOE versus φ₀ for D = 10^{10} rad/sec, β = 10^6 rad/sec, and γ = 0, 1.29 × 10^8 rad/sec; 4.71 × 10^8 rad/sec, (γ = ω_H - ω_C); 7.87 × 10^8 rad/sec, (γ = ω_H + ω_C); and 10^{10} rad/sec in curves A–E, respectively. As might be expected in the β/D < 1 limit, the NT₁ and NT₂ relaxation parameters depend on φ₀. In the limit that γ is appreciably smaller than ω_C, NT₁ is larger than NT₂, as is typically encountered in the “slow” reorientation limit. However, as γ becomes the same order of magnitude as the 13C and ¹H Larmor frequencies, NT₁ becomes less than NT₂, with NT₁ decreasing in magnitude and NT₂ increasing in magnitude relative to the γ = 0 limit. In the limit that γ becomes appreciably greater than the 13C and ¹H Larmor frequencies, (e.g., γ = 10^{10} rad/sec) both NT₁ and NT₂ become appreciably larger than the γ = 0 limit.

![Graph showing NT₁ in seconds vs φ₀ for various γ values](image-url)
ROTATIONAL DIFFUSION WITH SEGMENT INTERACTIONS

![Graph](image)

**Fig. 4.** $N_T$ in seconds vs $\phi_0$ for $D = 10^{10}$ rad/sec, $\beta = 10^6$ rad/sec, and $\gamma = 0$, $\gamma = 1.29 \times 10^8$ rad/sec; $4.71 \times 10^8$ rad/sec ($\gamma = \omega_H - \omega_C$); $7.87 \times 10^8$ rad/sec ($\gamma = \omega_H + \omega_C$); and $10^{10}$ rad/sec in curves A-E (identified in the figure), respectively.

In the $\gamma = 0$ limit, the NOE curve A of Fig. 5 changes by a factor of 2 over the range of $5^\circ \leq \phi_0 \leq 360^\circ$. Once $\gamma$ is increased to be of the same order of magnitude as $\omega_C$ the NOE becomes a less sensitive function of $\phi_0$ and basically just depends to a great extent on the spectral density of that frequency ($\omega_C$, $\omega_C \pm \omega_H$) closest to $\gamma$. On increasing $\gamma$ such that $\gamma > \omega_C + \omega_H$ the NOE again depends somewhat on $\phi_0$ until the plateau value (see Fig. 6) is reached.

It should be pointed out that the mere ability of a given motional model to fit $T_1$, $T_2$, or NOE relaxation data by no means guarantees the validity of the basic motional model. For simplicity let us assume that the segmental motion is in fact restricted rotational diffusion. If $N_T$, $N_{T_2}$, and NOE are measured at a fixed external field $H_0$, since the character of the spectral density is similar for the model with or without interactions, it may be possible to fit these quantities with both a zero and nonzero $\gamma$. The question thus arises how can one tell if segment–segment interactions are important and if so, can they merely be subsumed in effective values of $\phi_0$, $D$, and $\beta$? To address this question we first note that if $\gamma$ is very much less than $\omega_C$, the NOE is bounded above by a number less than 3.25 for every numerical calculation we have done and the NOE is bounded below by unity; whereas if $\gamma$ is on the order of $\omega_C$, $-3 \leq \text{NOE} \leq 5$. Thus the measurement of a relatively large positive NOE or a negative NOE is characteristic only of the strongly interacting system.

To further illustrate the behavior of the NOE we have plotted NOE vs $\gamma$ in Fig. 6 for a fixed $\phi_0 = 120^\circ$, a value typical of the range of allowed angular amplitude.
for which a restricted diffusion model makes sense. We have assumed \( \omega_C = 1.58 \times 10^8 \text{ rad/sec} \) and \( \omega_H = 6.29 \times 10^8 \text{ rad/sec} \); \( D = 10^{10} \text{ rad/sec} \), and \( \beta = 6 \times 10^6 \text{ rad/sec} \). Calculations of the NOE vs \( \gamma \) at other values of \( \phi_0 \) show a similar behavior. Note the prominent negative minimum at \( \omega_H - \omega_C = \gamma \) \( (4.71 \times 10^8 \text{ rad/sec}) \) and maximum at \( \omega_H + \omega_C = \gamma \). For values of \( \gamma \) appreciably above or below this range of \( \gamma \), the NOE values span the same range as those calculated in the \( \gamma = 0 \) limit. Basically as mentioned previously \( \gamma \) behaves like a chemical-shift parameter in the sense that it shifts the effective frequency of the spectral density from \( \omega \) to \( \omega - \gamma \). Thus to correctly differentiate between the two models one must measure \( N \), \( N_T \), and the NOE as a function of the external magnetic field \( H_0 \). It may then be possible to determine whether or not \( \gamma = 0 \). It is apparent from Fig. 6 that the existence of the negative NOE minimum is an unambiguous indication that segment–segment interactions are important.

**SUMMARY OF RESULTS**

In this paper we have extended the restricted rotational-diffusion model to include in a mean-field sense dynamic interactions between the diffusing motional unit and an environment undergoing motion that has Fourier components on the same time scale as the reorienting unit. It should be pointed out that the restricted rotational sector model is quite general. The derived model should be applicable to both the
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FIG. 6. NOE vs $\gamma$ with $\phi_0 = 120^\circ$, $\omega_C = 1.58 \times 10^8$ rad/sec, $\omega_H = 6.29 \times 10^8$ rad/sec, $D = 10^9$ rad/sec, and $\beta = 6 \times 10^6$ rad/sec.

liquid phase, e.g., to describe protein side-chain motion in solution, and to amorphous solids in the approximation that coupling between multiple internal rotations is ignored. That is, we assume independent units are undergoing rotational motion about a fixed axis, an axis that is itself on the average randomly oriented with respect to the laboratory. In contrast to previous work, we have derived an exact closed-form analytical expression for the spectral density valid over the entire range of parameters for all values of $\gamma$. Illustrative calculations have been performed and a comparison of the weak and strong coupling limits of the segment-segment interaction model has been made. It is proposed that NMR relaxation experiments be performed at a variety of magnetic field strengths to differentiate between the restricted rotational-diffusion model with and without dynamic interactions. It will be interesting to see under what conditions, if any, such dynamic segment-segment interactions are important.

If the allowed range of angular excursion is sufficiently large that the restricted diffusion model makes physical sense, yet permits the existence of multiple, broad potential minima, it should be possible to extend the present model to include the hopping between different angular sectors via the inclusion of source and sink terms in the rotational diffusion equation, i.e., a "two-site," restricted rotational potential minima model. While the calculations are likely to be somewhat messier than those of the present model, the derivation is in principle straightforward. This will be the focus of future work.
APPENDIX

Derivation of the Exact Analytic Expression for the Spectral Density

In this appendix we outline the derivation of Eq. [8]. Let us begin by rewriting the infinite sum in terms of the reduced variables defined in Eqs. [9a]–[9e]. Thus,

\[ S_0 = \frac{4k^2\phi_0^4}{\pi^2D} \sum_{n=1}^{\infty} \frac{[1 - (-1)^n \cos (\pi y)](n^2 + \beta')}{(n^2 - y^2)^2[(n^2 + \beta')^2 + c^2]} \quad \text{(A-1)} \]

It is readily apparent from Eq. [A-1] that in the limit \( \phi_0 \to 0, y, \beta', \) and \( c \to 0 \) and we have a simple series in \( n^{-6} \), the sum of which can be readily found in existing texts.

\[ \lim_{\phi_0 \to 0} S_0 = \frac{4k^2\phi_0^4}{\pi^2D} \frac{[2\pi^3 - 1]}{6!} B_3 \quad \text{(A-2)} \]

with \( B_3 \) the third Bernoulli number.

More generally, for arbitrary values of \( y, \beta', \) and \( c \) we need to examine the two constituent series of \( S_0 \), namely

\[ S_1 = \sum_{n=1}^{\infty} f(n) \quad \text{(A-3)} \]

and

\[ S_2 = \sum_{n=1}^{\infty} (-1)^n f(n) \quad \text{(A-4)} \]

where

\[ f(n) = (n^2 + \beta')\{(n^2 - y^2)^2[(n^2 + \beta')^2 + c^2]^{-1} \quad \text{(A-5)} \]

We employ a contour-integral method, originally due to Barnes (30), which states that for functions \( f \) such that \( \lim_{|z| \to \infty} |zf(z)| = 0 \),

\[ \sum_{n=-\infty}^{\infty} f(n) = - \sum_{\text{poles of } f(z)} \text{Res } [\pi \cot (\pi z)f(z)] \quad \text{(A-6)} \]

and

\[ \sum_{n=-\infty}^{\infty} (-1)^nf(n) = - \sum_{\text{poles of } f(z)} \text{Res } [\pi \csc (\pi z)f(z)] \quad \text{(A-7)} \]

We can use Eqs. [A-6] and [A-7] to evaluate \( S_1 \) and \( S_2 \), respectively, since \( f(n) \) is an even function of \( n \). It is apparent from Eq. [A-5] that \( f(z) \) has two double poles at \( z = \pm y \) and four simple poles at \( z = \pm \alpha, \pm \alpha^* \), where

\[ \alpha = (-\beta' - ic)^{1/2} \quad \text{(A-8)} \]

or

\[ \alpha = a + ib \quad \text{(A-9)} \]

Taking the real and imaginary parts of \( \alpha \) gives

\[ a = \left[ \frac{(\beta'^2 + c^2)^{1/2} - \beta'^{1/2}}{2} \right]^{1/2} \quad \text{(A-10a)} \]
and

\[ b = \left[ \frac{(\beta^2 + c^2)^{1/2} + \beta}{2} \right]^{1/2}. \]  
(A-10b)

The explicit evaluation of Eqs. [A-6] and [A-7] is thus straightforward but quite tedious. After a significant amount of algebra and rearrangement that involves among other things taking the imaginary part of a fifth-degree complex polynomial, it is possible to cast Eqs. [A-3] and [A-4] in the form

\[ S_1 = -\frac{\pi}{2} (R_1 + Q_1) - \beta/2y^4(\beta^2 + c^2) \]  
(A-11)

and

\[ S_2 = -\frac{\pi}{2} (R_2 + Q_2) - \beta/2y^4(\beta^2 + c^2). \]  
(A-12)

In the above equations

\[ R_1 = \mathcal{S}_1/p \]  
(A-13)

where

\[ p = 2ab(a^2 + b^2)((a^2 + b^2)^2 - 2y^2(a^2 - b^2) + y^4) \]  
(A-14)

and

\[ \mathcal{S}_1 = \mathcal{P}_1 \sin (2\pi a) - \mathcal{P}_2 \sinh (2\pi b) \]  
(A-15)

for which

\[ \mathcal{P}_1 = -\beta[4a^4b - 8a^2b^3 + b(a^2 - b)^2 - 2y^2(3a^2b - b^3) + by^4] \]

\[ + (a^2 + b^2)(b^3 - 3a^2b) + 2y^2b(a^2 + b^2)^2 + y^4(a^2 + b^2) \]  
(A-16)

and

\[ \mathcal{P}_2 = \beta[4ab^4 - 8a^3b^2 + a(a^2 - b^2)^2 - 2y^2(a^3 - 3ab^2) + ay^4] \]

\[ + (a^2 + b^2)(a^3 - 3ab^2) - 2ay^2(a^2 + b^2)^2 + ay^4(a^2 + b^2). \]  
(A-17)

Furthermore

\[ Q_1 = [-\pi(y^2 + \beta') \csc^2 (\pi y) + q_2 \cot (\pi y)/q_3]/q_1. \]  
(A-18)

Here,

\[ q_1 = 2y^2[(y^2 + \beta')^2 + c^2], \]  
(A-19)

and

\[ q_2 = -(3y^2 + \beta')y^2 + \beta')^2 + c^2(y^2 - \beta'), \]  
(A-20)

and

\[ q_3 = y[(y^2 + \beta')^2 + c^2]. \]  
(A-21)

In a similar fashion, \( R_2 \) given in Eq. [A-12] is defined by

\[ R_2 = \mathcal{S}_2/p \]  
(A-22)

where

\[ \mathcal{S}_2 = \frac{\mathcal{P}_1 \sin (\pi a) \cosh (\pi b) - \mathcal{P}_2 \cos (\pi a) \sinh (\pi b)}{\sin^2 (\pi a) \cosh^2 (\pi b) + \cos^2 (\pi a) \sinh^2 (\pi b)}. \]  
(A-23)

\( \mathcal{P}_1 \) and \( \mathcal{P}_2 \) are defined in Eq. [A-16] and [A-17], respectively. Furthermore \( Q_2 \) appearing in Eq. [A-12] is explicitly given by

\[ Q_2 = \csc (\pi y)[-\pi(y^2 + \beta') \cot (\pi y) + q_2/q_3]/q_1 \]  
(A-24)

with \( q_1 \), \( q_2 \), and \( q_3 \) defined in Eqs. [A-19]–[A-21], respectively.
Combining the two terms $S_1$ and $S_2$ in the expression for $S_0$ (Eq. [A-1]), we find that the terms containing $q_1/q_3$ in $Q_1$ and $Q_2$ precisely cancel and using the trigonometric identity
\[
csc^2 x - \cot^2 x = 1
\]
gives
\[
S_0 = \frac{4 \phi^2 y^2}{D \pi^4} \left\{ -\frac{\pi}{2} [R_1 - R_2 \cos (\pi y)] + \frac{\pi^2 (y^2 + \beta')}{4y^3[(y^2 + \beta'^2) + c]} - \frac{\beta'[1 - \cos (\pi y)]}{3y^4(\beta'^2 + c)} \right\}.
\]  
[A-25]

Substituting Eq. [A-25] into Eq. [7b] and combining like terms gives $j_k(\omega)$ defined in Eq. [8], an analytical expression valid for all values of $y$, $\beta'$, and $c$.

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